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Evaluation itérative des potentialités multiples de la chromatographie liquide couplée à la spectrométrie de masse à haute résolution pour la recherche à large spectre de multirésidus dans les aliments : un outil au service de l'exposome et de la sécurité alimentaire de demain

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par

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« The battles of life are not won by the strongest or the fastest, but by those who never give up »

Hassan II, former King of Morocco from 1961-1999

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Résumé en Français de la thèse

1. Introduction générale

L'Anses est un établissement public créé en 2010, sous la tutelle de différents ministères (Santé, Agriculture, Environnement, Travail et Consommation). Elle regroupe plusieurs laboratoires et directions scientifiques travaillant dans les domaines de la sécurité sanitaire des aliments, de la santé animale, de la santé végétale et de la santé publique. L'Anses délivre et retire également les autorisations de mise sur le marché des médicaments vétérinaires, des produits phytopharmaceutiques, des matières fertilisantes et des biocides en France. Pour cela, elle évalue leur efficacité et les risques qu'ils représentent pour la santé humaine et les écosystèmes.

Ses activités d'appui scientifique et technique fournissent une aide à la décision aux autorités sanitaires, et concernent principalement la référence, le diagnostic, l'épidémiosurveillance, ainsi que la recherche et le développement de méthodes. Le laboratoire de sécurité alimentaire dans lequel je travaille est organisé en plusieurs unités. L'une d'entre elles, l'Unité Pesticides et Biotoxines Marines (UPBM), se concentre sur le contrôle des résidus de pesticides dans les échantillons alimentaires.

En France et dans le monde entier, les résidus de pesticides sont utilisés massivement dans l'agriculture moderne pour augmenter la productivité agricole en réduisant les pertes de récoltes dues aux ravageurs et aux maladies (Md Meftaul et al., 2020 ; Sharma et al., 2019). Les résidus de pesticides jouent un rôle très important dans notre société, contribuant largement à la disponibilité d'une grande variété de fruits, de légumes et de céréales tout au long de l'année. Cependant, ils suscitent également de vives inquiétudes, en particulier chez les agriculteurs, leurs familles et les consommateurs, car ces composés ne sont pas sans risque pour la santé humaine. (Carvalho, 2017 ; Mostafalou et Abdollahi, 2017).

Dans l'Union européenne (UE), l'Autorité européenne de sécurité des aliments (EFSA) est l'instance qui réglemente l'utilisation et la commercialisation des pesticides. L'EFSA fixe des limites maximales de résidus (LMR) en tant que limites supérieures de résidus de pesticides légalement autorisées dans ou sur les denrées alimentaires ou les aliments pour animaux. Ces limites réglementaires sont établies en tenant compte au préalable des bonnes pratiques agricoles et sont également basées sur l'exposition la plus faible nécessaire pour protéger les consommateurs vulnérables (EFSA, 2023). Les différents États membres de l'UE doivent donc contrôler la présence de résidus de pesticides dans les produits alimentaires afin de s'assurer du respect des seuils réglementaires fixés par l'EFSA. En France, des plans de surveillance et de contrôle (PSC) sont mis en œuvre pour évaluer le niveau d'exposition des consommateurs aux résidus de pesticides, ainsi que pour vérifier le respect des LMR et des bonnes pratiques agricoles.

Actuellement, la chromatographie liquide ou gazeuse couplée à la spectrométrie de masse en tandem (LC/GC-MS/MS) fonctionnant en mode MRM (multiple reaction monitoring) est reconnue comme l'outil de référence pour l'analyse des résidus de pesticides dans les denrées alimentaires (Villaverde et al., 2016 ; Alder et al., 2006). Ces techniques sont très spécifiques et sensibles, mais manquent d'exhaustivité car elles se limitent à une liste préétablie de substances à rechercher a priori, et pour lesquelles les standards analytiques sont disponibles en laboratoire. Tout contaminant ne figurant pas sur la liste initiale ne peut être analysé, alors qu'il

est potentiellement présent dans les aliments et présente un risque pour les consommateurs. L'actualité récente nous alerte sur le fait qu'aucun système n'est parfait, le cas récent de la contamination inattendue d'œufs par le fipronil en étant un parfait exemple (Eskola et al., 2020 ; Authority (EFSA) et al., 2018).

Récemment, les méthodes de chromatographie liquide ou gazeuse couplées à la spectrométrie de masse à haute résolution (LC/GC-HRMS) sont apparues comme des techniques prometteuses pour améliorer le système de sécurité alimentaire. Ces techniques apparaissent comme des technologies de pointe qui permettent de pallier le manque d'exhaustivité des analyses conventionnelles (Weng et al., 2020). En effet, le HRMS élargit considérablement le champ d'analyse, avec la possibilité de réaliser des analyses ciblées à grande échelle sans limites, ainsi que des analyses dites suspectes et non ciblées pour étudier les produits chimiques pour lesquels les normes analytiques ne sont pas disponibles en laboratoire (Dubocq et al., 2021 ; Phillips et al., 2018). Ainsi, le HRMS s'avère être une technologie de rupture, permettant d'aller bien au-delà d'une simple liste de composés priorisés. D'un point de vue toxicologique, et compte tenu de la grande diversité des substances chimiques présentes dans les denrées alimentaires, la réglementation des substances individuelles et l'analyse séparée des molécules par famille apparaissent insuffisantes. En fait, de par leur alimentation variée, les consommateurs sont exposés à des mélanges chimiques plutôt qu'à des substances individuelles, ce qui peut entraîner des effets combinés et des "effets cocktail" ayant un impact sur la santé humaine, et dont les effets ne sont pas toujours bien connus. Cela implique un changement dans le système actuel de sécurité alimentaire, et des outils et méthodes analytiques exhaustifs sont donc nécessaires pour fournir un état plus global et réaliste de l'exposition dynamique et fluctuante des consommateurs à des mélanges chimiques nocifs.

Cependant, malgré ses avantages, la HRMS n'est toujours pas considérée comme un outil de référence pour l'analyse officielle et le contrôle des échantillons alimentaires. En effet, il reste des défis à relever, notamment en ce qui concerne la sensibilité instrumentale et les workflows de retraitement dédiés aux approches suspectes et non ciblées, qui peuvent être complexes à appréhender.

2. Objectif du projet de thèse

Le projet AlimOmic, financé par l'ANR JCJC (**ANR-19-CE21-0002**), vise à combler les "lacunes" mentionnées ci-dessus, tout en contribuant à une meilleure caractérisation de l'exposition des consommateurs aux produits chimiques, ainsi qu'à diffuser la LC-HRMS dans les laboratoires de contrôle afin d'améliorer la sécurité alimentaire en France et à l'étranger. A cette fin, il propose de développer et de valider des méthodes LC-HRMS pour l'analyse ciblée, suspecte et non ciblée d'une large gamme de contaminants (>600 molécules) dans différentes matrices alimentaires. Ce travail de recherche permettra d'évaluer les performances de ces dispositifs et approches, afin de pouvoir proposer les méthodes dans un cadre officiel de surveillance de routine. Le projet AlimOMIC intègre plusieurs thèses et projets de recherche, dont ceux de Thierno Diallo (Amphibie) et de moi-même. Durant les trois années de notre thèse, Thierno et moi avons pu travailler en étroite collaboration sur l'ensemble de nos projets. En effet, le projet AlimOMIC nécessite le développement de méthodes sur une variété de matrices alimentaires, dont les aliments pour bébés, les produits sucrés et les produits de la pêche, qui sont fréquemment consommés. A ce titre, Thierno Diallo était responsable du développement des produits de la pêche, et moi des autres matrices alimentaires étudiées. Cela nous a permis

de travailler en binôme, ce qui nous a été bénéfique tant sur le plan scientifique que psychologique et social, tout en multipliant le nombre d'articles pour chacun d'entre nous.

Les travaux présentés ci-dessous, ont donc été menés en collaboration avec Thierno, mais également sur la base d'une progression itérative et continue. En effet, chaque travail mené permet de répondre aux lacunes du précédent, et apporte certaines nouveautés et points d'amélioration non négligeables.

3. Principaux résultats

3.1. (Makni et al., 2022)

Nous avons réalisé avec Thierno Diallo, un premier développement de méthode pour l'analyse multirésidus de 204 résidus de pesticides dans l'alimentation infantile. Les produits alimentaires pour bébés sont soumis à une réglementation plus stricte de la part de la Commission européenne, avec des LMR fixées à 0,01 $mg.kg^{-1}$ pour tous les résidus de pesticides (Commission européenne, 2006). Certaines substances chimiques, comme les pesticides, peuvent être associées à des risques toxicologiques pour l'homme (Ntzani et al., 2013). De plus, ces risques sont exacerbés chez les nourrissons et les jeunes enfants, en raison de leur faible poids corporel et de l'immaturité de leur système immunitaire (Nougadère et al., 2020). La caractérisation de leur exposition aux résidus de pesticides est un enjeu majeur de santé publique. Cependant, les données sur l'exposition des nourrissons et des jeunes enfants à un large spectre de contaminants chimiques sont assez limitées. En raison de l'importance et de la diversité compositionnelle et matricielle de ces produits alimentaires infantiles, nous avons voulu proposer une méthode optimisée qui pourrait être correctement adaptée à l'analyse multirésidus de différents types d'aliments pour bébés. Ce travail a pu faire l'objet d'une publication scientifique, accessible en ligne via le DOI suivant : https://doi.org/10.1016/j.foodchem.2022.133573.

Dans cette étude, une préparation d'échantillon basé sur le protocole QuEChERS, ainsi qu'une analyse UHPLC-Q-TOF MS (ESI+) a permis le dépistage de 204 pesticides dans les aliments pour bébés. La procédure d'extraction a été optimisée sur la base des méthodes QuEChERS, afin de mettre en place un protocole de préparation des échantillons pouvant être adapté à divers aliments pour bébés. Différents sels d'extraction et méthodes de purification ont été évalués dans le cadre de l'optimisation de la préparation d'échantillons. Au final, l'acétate de sodium a été sélectionné comme sel d'extraction des contaminants, ainsi qu'une purification des extraits à base de $MgSO_4$ / PSA. Par la suite, nous avons évalué différents seuils sur les critères utilisés pour la détection (analyse de l'ion précurseur = molécule entière ionisée) en HRMS, afin de trouver le juste équilibre entre minimiser les faux négatifs ainsi que les faux positifs obtenus. Les critères du guide SANTE de la commission européenne (t_R ± 0,1 min, mesure précise de la masse ± 5 ppm) ont montré le meilleur équilibre entre les faux négatifs avec 16 % et 5 % à 0,01 mg.kg-1 et 0,1 mg.kg-1, respectivement, et les faux positifs avec un taux acceptable de 5 %. En ce qui concerne l'identification (analyse de l'ion précurseur + les ions de fragmentation), nous avons évalué l'impact d'une liste d'inclusion sur les taux obtenus, ainsi que différents algorithmes de comparaison de spectres MS/MS. L'intégration d'une liste d'inclusion (pour prioriser la fragmentation des composés d'intérêts) et la comparaison spectrale à l'aide de l'algorithme FIT et d'un score de similarité >70%, ont été sélectionnés pour la méthode et ont démontré de bonnes performances avec des taux de faux négatifs de 37% et 15%, à 0,01 $mg.kg^{-1}$ et 0,1 $mg.kg^{-1}$, respectivement.

La méthode a ensuite été validée sur la base du guide SANTE de la commission européenne pour les méthodes de dépistage HRMS : 95 % et 73 % des pesticides présentaient une SDL et une LOI ≤ 0,1 mg.kg^{-1}, respectivement. La méthode proposée a permis d'identifier sans équivoque le pesticide difénoconazole et un plastifiant, le TCEP, dans certains des aliments pour bébé étudiés.

3.2. (Diallo et al., 2022)

Ce deuxième projet impliquait le développement d'une méthode d'analyse multirésidus de pesticides dans des échantillons de bivalves. Ces matrices présentent un intérêt écologique et économique majeur. Les bivalves sont des espèces sentinelles de la qualité de l'environnement. De plus, des taux de mortalité de moules anormalement élevés ont été observés dans les Pertuis-Charentais (France), or cette zone d'intérêt représente 22% de la production française de bivalves. La mortalité des moules représente donc un enjeu économique majeur. Ce travail a été principalement mené par mon collègue Thierno Diallo, doctorant au laboratoire de sécurité alimentaire de l'Anses, dont le sujet est de mieux comprendre l'impact des contaminants chimiques sur la surmortalité des moules dans la zone des Pertuis-Charentais (France). L'objectif principal de cette étude était d'optimiser une méthode d'extraction efficace pour l'analyse des résidus de pesticides dans les bivalves, et de l'appliquer à des échantillons de terrain pour tenter de mettre en lumière une éventuelle contamination chimique impliquée dans la mortalité des moules.

Le développement et la validation d'une méthode QuEChERS-LC-HRMS en mode IDA permettant le criblage de 204 pesticides dans les bivalves ont été réalisés conformément aux directives du guide SANTE/12682/2019 de la commission européenne. La liste des composés cibles intégrait des pesticides de différentes familles ayant des propriétés physicochimiques très distinctes. L'utilisation des plans d'expérience factoriels fractionnés pour l'optimisation des paramètres de la méthode QuEChERS, a considérablement simplifié le processus d'optimisation de méthode. Nous avons évalué l'impact des différents modes d'acquisition en HRMS, IDA et DIA (SWATH®), sur un QTOF 5600 d'AB Sciex. En effet, le premier mode (IDA) permet d'obtenir des spectres de fragmentation d'une très haute qualité, mais tous les composés d'intérêts en sont pas fragmentés, entachant leur identification. A contrario, le second mode (DIA – SWATH) permet la fragmentation de tous les composés analysés, mais fournit des spectres de fragmentation bien plus complexes et difficiles à interpréter. Nous avons ainsi comparé ces modes d'acquisition sur la base des taux de détection et d'identification obtenus et avons démontré la meilleure efficacité du mode IDA avec liste d'inclusion (IDA-PIL). La majeure partie des composés ciblés ont été détectés aux trois niveaux de concentration (0,01, 0,05 et 0,1 mg.kg^{-1}) avec des taux de faux positifs très faibles (2,5%). L'identification sans équivoque était problématique à la concentration la plus faible (0,01 mg.kg^{-1}) en raison de la plus faible abondance des ions produits, mais elle était possible pour la plupart des analytes au niveau de concentration le plus élevé (0,1 mg.kg^{-1}).

La méthode a ensuite été validée sur la base du guide SANTE de la commission européenne pour les méthodes de dépistage HRMS : La SDL et la LOI étaient égales ou inférieures à 0,1 mg.kg^{-1} pour 87 % et 67 % des pesticides, respectivement. L'applicabilité de cette approche pour le dépistage des pesticides a finalement été démontrée par l'analyse de plusieurs échantillons de moules et d'huîtres collectés dans le sud-ouest de la France. Le diuron et le

fenpropimorph ont été les seuls analytes identifiés dans les échantillons étudiés à l'aide de l'analyse ciblée. La méthode a également démontré sa polyvalence pour identifier d'autres contaminants organiques (pesticides ou autres composés) que ceux inclus dans la validation de la méthode par criblage de suspects. Cela a permis d'identifier le métabolite du diuron 1-(3,4-dichlorophényl)-3-méthylurée et d'autres contaminants tels que les retardateurs de flamme et les plastifiants.

Bien que les modes d'acquisition aient été optimisés, le mode IDA retenu à l'issue de ces travaux reste limitant au regard du taux de non-fragmentation qui reste élevé, ainsi que de la faible sensibilité obtenue sur les ions de fragmentation. Ceci affecte directement l'identification des composés d'intérêt dans les matrices alimentaires, puisque si un analyte n'est pas fragmenté, il ne peut être identifié sans équivoque. De plus, même si l'analyte est fragmenté, si les niveaux de sensibilité obtenus pour les ions de fragmentation sont trop faibles, cela peut rendre difficile la comparaison des spectres MS/MS. Ces limitations ont donc été prises en compte afin d'améliorer les performances globales de la méthode. Les méthodes développées visent également à être utilisées pour des analyses suspectes et non ciblées, afin de cribler d'autres produits chimiques pour lesquels les normes analytiques ne sont pas disponibles dans le laboratoire. Dans ce cas, il est impossible de générer des listes d'inclusion pour la fragmentation par ordre de priorité.

En complément de ce travail, le mode d'acquisition IDA a été par la suite, optimisé pour surmonter les limitations mentionnées ci-dessus. Les résultats de cette optimisation supplémentaire n'ont pas été publiés dans un article.

3.3. (Makni et al., 2023a)

Cette troisième étude a porté sur le développement d'une méthode d'analyse à très large spectre de 694 contaminants et substances chimiques dans les produits sucrés, en utilisant la spectrométrie de masse à temps de vol. Les produits sucrés tels que le miel, les confitures, les gelées et les sirops sont très populaires et, par conséquent, largement consommés par les adultes et les enfants. Toutefois, hormis le miel, qui est largement étudié, il existe peu de données publiées sur la contamination d'autres produits riches en sucre tels que les confitures et les gelées, qui sont des produits intermédiaires non réglementés. Il existe donc un réel besoin de pouvoir fournir des données qui soutiendront la caractérisation du risque associé à l'exposition aux contaminants chimiques dans ce type de produits alimentaires très populaires et consommés. Cela permettrait également d'alerter sur la nécessité de réglementer certains produits intermédiaires de consommation (confitures, gelées, sirops, etc.). Pour atteindre ces objectifs, l'étude avait pour but d'optimiser une méthode de préparation d'échantillons adaptée à l'analyse multirésidus de plusieurs centaines de contaminants dans des produits appartenant au groupe des matrices à très haute teneur en sucre et à faible teneur en eau. Par ailleurs, nous souhaitions également faire évoluer nos méthodes de criblage vers celles offrant la possibilité de semi-quantifier des composés d'intérêt ciblés, plus simplement qu'avec les méthodes de quantification conventionnelles, afin d'aller plus loin dans la caractérisation du risque associé à l'exposition aux produits chimiques.

L'étude réalisée présente une méthode unique pour le dépistage multirésidus des contaminants dans différents produits sucrés populaires. La préparation d’échantillons a été optimisée en

suivant une approche par plan d'expérience factoriel fractionné. La mise en œuvre d'une méthode générique QuEChERS (sels d'extraction d'acétate de sodium et purification des extraits avec $MgSO_4$ / PSA), suivie d'une étape de concentration des extraits finaux s'est avérée très efficace pour couvrir une large gamme de contaminants avec une sensibilité élevée. L'utilisation de l'UHPLC-Q/ToF comme système analytique a permis l'analyse simultanée et automatisée de 694 contaminants, incluant principalement des résidus de pesticides, mais également des produits de transformation, certains médicaments ainsi que des contaminants environnementaux/industriels.

La méthode a été validée conformément aux directives SANTE/11312/2021. Les limites de détection et d'identification ont été établies comme étant inférieures ou égales à 0,05 mg.kg-1 pour 89 % et 74 % des contaminants, respectivement. La méthode de dépistage validée a été appliquée à 50 produits sucrés concentrés. Dans l'ensemble, 46 % des échantillons se sont révélés positifs aux résidus de pesticides. La plupart des échantillons positifs (78 %) contenaient des mélanges de résidus de pesticides. Trois stratégies pratiques permettant de gagner du temps et de l'argent et adaptées à l'analyse à haut débit ont été proposées pour la semi-quantification ciblée des contaminants précédemment identifiés dans les échantillons.

L'utilisation d'instruments HRMS offre la possibilité d'élargir considérablement le champ d'analyse, ce qui est nécessaire compte tenu de l'objectif d'amélioration de la caractérisation des risques associés à la présence de mélanges de produits chimiques dans les aliments, dans un contexte basé sur l'exposition alimentaire. En effet, la présence de mélanges de résidus de pesticides et de PT a été identifiée dans le miel et les fruits transformés, ce qui confirme la nécessité de surveiller ces produits pour garantir la protection et la sécurité des consommateurs. En outre, de nouvelles stratégies de semi-quantification ont été proposées, basées sur la configuration de courbes d'étalonnage procédurales de tout un groupe de produits sucrés (méthode a), d'une famille (méthode b) ou d'un échantillon spécifique (méthode c). Elles sont configurées une seule fois et réutilisables par la suite pour fournir une estimation des résultats quantitatifs des contaminants dans les échantillons.

La méthode a été validée conformément au guide SANTE/11312/2021 de la commission européenne. Les SDL et LOI (paramètres de validation en LC-HRMS) ont été établies comme étant inférieures ou égales à 0,05 $mg.kg^{-1}$ pour 89 % et 74 % des contaminants, respectivement. La méthode de dépistage validée a été appliquée à 50 produits sucrés achetés en commerce. Dans l'ensemble, 46 % des échantillons se sont révélés positifs aux résidus de pesticides. La plupart des échantillons positifs (78 %) contenaient des mélanges de résidus de pesticides, plutôt que des substances présentes individuellement. Trois stratégies pratiques permettant de gagner du temps et de l'argent et adaptées à l'analyse à haut débit ont été proposées pour la semi-quantification ciblée des contaminants précédemment identifiés dans les échantillons. Aucun contaminant retrouvé n'avait de concentration estimée dépassant les limites réglementaires dans les miels, sachant que les produits intermédiaires (confitures, gelées, etc) ne sont à ce jour, toujours pas réglementés.

3.4. (Diallo et al., 2023)

Cette quatrième étude s'inscrit dans le cadre d'un projet entrepris par mon collègue Thierno Diallo, qui travaille pour mieux comprendre l'impact des polluants chimiques sur la surmortalité des moules dans la région des Pertuis-Charentais en France. L'objectif de cette étude était donc de développer une nouvelle méthode de préparation des échantillons, couvrant

un spectre plus large de contaminants que les méthodes QuEChERS conventionnelles, pour l'analyse à large spectre de 850 contaminants dans les produits de la mer (poissons, crustacés, bivalves, etc). Cette méthode sera ensuite utilisée par Thierno, pour caractériser l'exposition à d'éventuels contaminants qui pourraient être impliqués dans la surmortalité des moules dans la région des Pertuis-Charentais (France). Cette méthode est également destinée à être utilisée pour caractériser l'exposition des consommateurs aux substances chimiques présentes dans une variété de produits de la mer largement consommés par la population, d'où leur inclusion dans l'étude en plus des espèces bivalves.

Ce travail a permis de mettre en avant une nouvelle méthode de préparation d'échantillons, appelée QuEChUP, qui consiste en une extraction séquentielle QuEChERS avec de l'acétonitrile et QuPPE avec un mélange acetonitrile:methanol (80:20 v:v), ainsi que d'une purification des extraits combinés avec de l'EMR-lipid. L'utilisation d'un plan d'expérience factoriel fractionné pour l'optimisation des paramètres QuEChERS et QuPPe a considérablement simplifié le processus de développement de la méthode. Après avoir obtenu une méthode optimale pour chaque classe de contaminants, leur performance a été évaluée pour tous les contaminants. La procédure QuEChUP a fourni les meilleurs taux de détection des contaminants ciblés. De plus, cette nouvelle méthode d'extraction est très appropriée dans un contexte d'exposome pour extraire les contaminants les plus divers. La méthode originale QuEChUP-LC-HRMS pour le dépistage de 850 contaminants organiques dans les fruits de mer a ensuite été validée conformément aux directives du guide SANTE/11312/2021 de la commission européenne. La liste des composés cibles comprenait des pesticides, des médicaments vétérinaires et des produits chimiques industriels de différentes familles ayant des propriétés physicochimiques très distinctes. La plupart des composés de la liste cible ont été détectés (ion précurseur) et identifiés (ion précurseur + ions fils) aux trois niveaux de concentration (0,001, 0,01 (LMR) et 0,1 $mg.kg^{-1}$) d'étude. La SDL et la LOI étaient égales ou inférieures à 0,01 $mg.kg^{-1}$ pour 92 % et 78 % des contaminants ciblés, respectivement, ce qui est considérablement meilleur que les performances obtenues dans le cadre du premier travail sur les produits de la pêche (Diallo et al., 2022).

L'applicabilité de cette méthode pour le criblage de contaminants multi-classes a été démontrée par l'analyse de plusieurs échantillons de bivalves, de poissons et de crustacés. Tous les échantillons analysés par criblage ciblé se sont révélés positifs à des mélanges de contaminants. En effet, 59 % de ces contaminants étaient des pesticides, 26 % des médicaments vétérinaires et 15 % des produits chimiques industriels. Le diuron (herbicide) et le diclofénac (AINS) ont été les contaminants identifiés avec les concentrations moyennes estimées les plus élevées, en particulier dans les échantillons de moules avec 0,076 et 0,068 $mg.kg^{-1}$. Le védaprofène (AINS) a également été trouvé à des concentrations bien supérieures à la LMR par défaut dans des échantillons de poissons et de crustacés, et deux antibiotiques tels que la clarithromycine et la dapsone ont été trouvés à des concentrations légèrement supérieures à la LMR dans des échantillons de bivalves. Le reste des contaminants a été trouvé à des concentrations égales ou inférieures à la LMR par défaut. Ces concentrations ont été estimées à l'aide de différentes stratégies de semi-quantification, déjà présentées dans l'une de nos précédentes études (Makni et al., 2023a).

La méthode a également démontré sa polyvalence pour identifier d'autres contaminants organiques que ceux inclus dans la validation de la méthode par approche « suspect-screening » automatisée via le logiciel open access MSDial. Cela a permis d'identifier d'autres mélanges

de contaminants, principalement des produits pharmaceutiques, ainsi que des drogues illicites et des produits de soin personnel.

Dans cette étude, les résultats combinés de l'analyse ciblée et suspecte permettent une meilleure estimation de l'ensemble des contaminants susceptibles d'être présents dans les échantillons analysés, et ceci pourrait représenter un avantage considérable en routine pour étendre le champ de surveillance et mieux caractériser le risque auquel le consommateur est exposé (différents contaminants, mélanges chimiques, effets cocktails, etc).

3.5. (Makni et al., 2023b)

Cette cinquième et dernière étude n'est pas un développement analytique, mais donne un aperçu de la polyvalence de la HRMS et de sa capacité à effectuer différents types d'analyse sur des échantillons alimentaires. L'objectif était de rassembler et de résumer en une seule étude les principaux avantages offerts par la HRMS, et la manière dont cet outil pourrait être utilisé efficacement pour améliorer les systèmes officiels de sécurité et d'authenticité des aliments. Le miel a été sélectionné car il s'agit d'un produit sucré très populaire et consommé, à fort potentiel économique, soumis à de nombreuses contaminations ainsi qu'à des pratiques frauduleuses et trompeuses. Il était donc intéressant pour nous d'utiliser le miel pour démontrer la robustesse de la HRMS pour le criblage de contaminants à large spectre, mais aussi pour mettre en évidence des marqueurs de différenciation de miel (floraux, géographiques). Pour mener à bien ce travail, nous avons réutilisé la méthode QuEChERS précédemment développée et publiée dans le cadre de l'étude sur les produits sucrés (Makni et al., 2023a).

Les échantillons ont été analysés à l'aide du système LC-ESI-Q-ToF-MS/MS dont nous disposons au laboratoire, et qui a été utilisé dans le cadre de l'ensemble de nos études. Pour les objectifs de ce travail, une seule séquence analytique en ESI^+ et en ESI^- a été utilisée avec des procédures d'assurance et de contrôle de la qualité appropriées, conformes aux exigences des normes de qualité pour les études métabolomiques et non-ciblées. À l'aide de cette méthode, nous avons effectué avec succès (a) l'analyse ciblée à grande échelle de 52 échantillons de miel afin de dépister 694 contaminants divers pour lesquels les étalons de référence étaient disponibles au laboratoire; (b) L'analyse « suspect-screening » à large spectre à l'aide d'un logiciel MSDial en libre accès pour effectuer des recherches supplémentaires de contaminants pour lesquels les étalons de référence ne sont pas disponibles au laboratoire ; (c) De l'analyse non-ciblée et multivariée, pour une recherche approfondie des signaux qui pourraient être des marqueurs d'origine florale et géographique des échantillons de miel étudiés.

Tout d'abord, l'analyse ciblée de 52 échantillons de miel a permis d'identifier sans équivoque 23 produits chimiques, dont des néonicotinoïdes, des fongicides à base de triazole et des synergistes. Ensuite, l'analyse « suspect-screening » à l'aide du logiciel MSDial a permis d'annoter 30 produits L'analyse « suspect-screening » a également permis de mettre en évidence des marqueurs de miel de châtaignier (désoxyvasicinone, 2-quinolone, acide indoleacrylique et acide kynurénique) et des miel d'agrumes (caféine, 2-oxindole et indole-3-carbinol). Enfin, une analyse non ciblée a permis de séparer les miels en fonction de leur type (urban ou rural), de leurs origines florales (châtaigner, agrumes, lavande) et géographiques (France, Espagne, Italie).

4. Conclusion générale et perspectives de la thèse

4.1. Conclusion

Face à l'ampleur de l'augmentation des pathologies chroniques et multifactorielles, dont certaines sont associées à l'exposition alimentaire aux produits chimiques, un changement d'approche s'impose dans le système actuel de sécurité alimentaire, qui ne prend pas suffisamment en compte les éventuels effets combinés et « cocktail » des mélanges chimiques. L'objectif des travaux menés au cours de cette thèse était de mettre en évidence l'efficacité de la HRMS pour améliorer le système actuel de sécurité alimentaire, et de mieux caractériser l'exposome chimique alimentaire des français. Pour ce faire, il était impératif de développer des outils et des méthodes capables d'analyser plusieurs centaines, voire plus d'un millier de produits chimiques en une seule analyse, et ce, dans une diversité de matrices alimentaires.

Dans ce contexte, divers développements analytiques et optimisations de méthodes ont été réalisés, pour l'analyse à large spectre et multirésidus de contaminants dans une variété de produits alimentaires. En effet, nous avons réussi à développer des méthodes pour l'analyse de 204 résidus de pesticides dans les aliments pour bébés (Makni et al., 2022) et chez les bivalves (Diallo et al., 2022), ainsi que pour l'analyse de 694 et 850 contaminants dans les produits sucrés (Makni et al., 2023a) et les produits de la pêche (Diallo et al., 2023), respectivement. Un effort important a été fait pour optimiser la préparation des échantillons, qui est l'étape clé d'une analyse pour couvrir le plus large spectre possible de contaminants. Pour ces optimisations, nous avons utilisé des plans d'expérience factoriels fractionnaires de type Taguchi, qui permettent d'évaluer simultanément plusieurs paramètres qui influencent les performances de la méthode, tout en réduisant le nombre d'expériences nécessaires. Ce travail nous a également permis de proposer une nouvelle méthode de préparation d'échantillons, QuEChUP, qui est une méthode séquentielle consistant en une extraction initiale de QuEChERS, suivie d'une extraction QuPPE, et d'une purification commune des deux extraits combinés. Cette nouvelle méthode est prometteuse, car dans la littérature, les méthodes d'extraction QuEChERS sont les plus couramment utilisées pour l'analyse multirésidus dans les matrices alimentaires. Cependant, l'extraction de composés polaires tels que certains médicaments vétérinaires nécessitent généralement des méthodes complémentaires. La nouvelle méthode QuEChUP permet d'analyser des produits chimiques polaires tels que certains résidus de médicaments, mais couvre également des composés ayant une plage de polarité plus dynamique, tels que les résidus de pesticides ou certains contaminants industriels, extraits classiquement avec un protocole QuEChERS. Il s'agit d'une avancée significative dans le domaine de l'analyse multirésidus des contaminants dans les denrées alimentaires, car cette méthode étend la couverture chimique et couvre donc un spectre plus large de contaminants. Les méthodes d'extraction multirésidus développées et proposées à l'issue de ce projet de thèse s'inscrivent dans la logique des analyses étendues en LC-HRMS, pour mieux caractériser l'exposition des consommateurs et améliorer le système de sécurité alimentaire.

En plus de la préparation des échantillons, d'autres aspects de l'analyse en LC-HRMS ont été évalués au cours de cette thèse, tels que les critères et les algorithmes utilisés pour la détection et l'identification, ainsi que les modes d'acquisition de données MS/MS. De nombreuses optimisations ont été réalisées, notamment sur les modes d'acquisition qui représentent un enjeu important en LC-HRMS. Le mode IDA a été préféré au mode SWATH-MS, car il fournissait des spectres MS/MS de bien meilleure qualité, facilitant l'identification des composés, surtout

à bas niveau. Cependant, une optimisation plus poussée du mode IDA a été nécessaire pour améliorer les performances globales de la méthode et réduire la possibilité de non-fragmentation de certains analytes d'intérêt. Cela nous a permis d'améliorer significativement les performances de la méthode obtenue entre les deux premiers travaux de développement analytique (Diallo et al., 2022 ; Makni et al., 2022), et les deux suivantes (Diallo et al., 2023; Makni et al., 2023a).

Aussi, l'une des principales forces et originalités des travaux menés a été de proposer des méthodologies pour la semi-quantification ciblée de plusieurs centaines de contaminants dans les matrices alimentaires. Ces méthodes de semi-quantification ont été publiées avec succès, qui sont faciles à mettre en œuvre, peu coûteuses et compatibles avec l'analyse de contaminants multirésidus et d'échantillons à haut débit. D'autres études sont toutefois nécessaires pour vérifier leur exactitude et leur fiabilité dans le temps. Néanmoins, ces méthodes de semi-quantification pourraient être très utiles pour l'analyse à haut débit d'échantillons en LC-HRMS, car elles fourniraient des données quantitatives pour un spectre plus large de contaminants que ceux qui sont priorisés et analysés en routine par spectrométrie de masse en tandem. S'il est mis en œuvre, cela conduirait à une meilleure caractérisation du risque associé à l'exposition alimentaire à des substances chimiques.

De plus, les travaux menés auront permis de mettre en place des approches robustes et automatisées de type « suspect-screening », pour une recherche étendue de produits chimiques émergents et peu étudiés, sans que les étalons analytiques ne soient disponibles en laboratoire. Ces approches, exclusives à la LC-HRMS, représentent un véritable atout pour améliorer le périmètre de surveillance et mieux caractériser l'exposition alimentaire des consommateurs.

Enfin, des analyses non ciblées et multivariées ont été mises en œuvre, afin de caractériser les échantillons de miel en fonction de leur type, de leurs origines florales et géographiques. Cela pourrait s'avérer très utile dans le contexte de l'authenticité et de la traçabilité des aliments, mais aussi pour la sécurité alimentaire dans le cas où les marqueurs responsables de la séparation des échantillons alimentaires sont des contaminants ou des produits chimiques préoccupants.

Dans l'ensemble, cette recherche a contribué au sein de l'agence à mettre en évidence la LC-HRMS comme un outil de choix pour améliorer la salubrité des aliments et mieux caractériser les contaminants et les mélanges chimiques auxquels les consommateurs sont exposés. Ce système pourrait être bien intégré dans les laboratoires de routine en complément de la LC-MS/MS, en tant que système d'alerte précoce. En effet, la LC-HRMS pourrait être utilisé pour élargir les listes de contaminants et de produits chimiques recherchés, au-delà de ceux qui sont prioritaires ou qui présentent un intérêt pour le laboratoire. Cela pourrait aider à alerter sur d'éventuelles émergences telles que l'occurrence controversée et presque omniprésente de certains PFAS dans l'environnement et la chaîne alimentaire. Elle pourrait également permettre d'alerter sur les abus, permettant d'éviter des scandales sanitaires comme en 2017, lorsque des œufs belges ont été contaminés par du Fipronil, une substance interdite.

4.2. Perspectives

Au vu des travaux réalisés, il serait nécessaire d'inclure d'autres familles de contaminants et de denrées alimentaires dans les futurs développements analytiques. En effet, pour des raisons de coût et de praticité, les résidus de pesticides et de médicaments vétérinaires ont été les principales familles de substances chimiques utilisées pour le développement et la validation des méthodes au cours de cette thèse. Cependant, en gardant à l'esprit que nous souhaitons utiliser ces méthodes pour mieux caractériser l'état réel de l'exposition des consommateurs, sans se limiter exclusivement aux pesticides et aux médicaments, il est crucial d'évaluer les méthodes sur d'autres types de produits chimiques fréquemment trouvés dans les denrées alimentaires. En ce sens, cet aspect fait défaut dans les travaux menés et représente donc une limitation majeure

En outre, des développements analytiques utilisant des systèmes GC-HRMS devraient être menés. En effet, la complémentarité entre les analyses LC et GC est essentielle pour couvrir les contaminants polaires à moyennement polaires, ainsi que les substances non polaires. Malheureusement, cette complémentarité est un élément manquant dans les travaux de cette thèse, car le laboratoire de sécurité alimentaire de l'Anses Maisons-Alfort n'est pas encore équipé d'un système GC-HRMS. Ceci représente une limitation importante à la recherche et au développement de méthodes qui peuvent être effectuées en interne, car une partie de la couverture chimique analytique n'est pas prise en compte.

Toujours d'un point de vue instrumental, les méthodes développées en HRMS n'ont pas été comparées à celles disponibles en LC-MS/MS au sein du laboratoire. Il serait important de démontrer que les sensibilités obtenues avec les deux types d'instruments ne sont pas très éloignées, outre le fait que les systèmes HRMS permettent d'augmenter considérablement le champ de surveillance, comme cela a été souligné au cours de cette thèse. Ceci serait un argument supplémentaire convaincant en faveur de l'intégration de la HRMS dans les plans de surveillance et plans de contrôle, en complément de la spectrométrie de masse en tandem.

Toutes les méthodes déjà développées, ainsi que celles qui le seront prochainement (développement dans les fruits, légumes et viandes), seront utilisées pour l'analyse d'échantillons massifs dans le cadre des études de l’alimentation totales (EAT) réalisées par l'Anses. Ces études officielles sont précieuses pour évaluer l'exposition des consommateurs, avec un échantillonnage à grande échelle représentatif des habitudes alimentaires françaises. L'analyse par HRMS de ces échantillons, en complément des analyses LC/GC-MS/MS, permettrait de détecter de nouveaux contaminants émergents qui ne sont pas ciblés dans cette nouvelle EAT. En collaboration avec le DER de l'Anses, ces données pourraient être utilisées pour alerter sur les mélanges de substances chimiques auxquels les consommateurs français sont exposés, afin d'améliorer l'investigation et la surveillance de leurs effets sur la santé humaine.

4.3. Quid de l’intégration de la LC-HRMS en routine ?

Bien que la LC-HRMS soit un outil de premier ordre pour améliorer le système actuel de sécurité alimentaire, son acquisition implique une des coûts plus élevés par rapport à la spectrométrie de masse en tandem. Cela représente une limitation considérable, car tous les laboratoires, ou même certains pays en développement, ne disposent pas des budgets nécessaires pour s’équiper avec de tels instruments.

Une autre limite actuelle à l'intégration de la LC-HRMS en routine, est le manque de protocoles d'analyse standardisés. En effet, lorsque des méthodes sont développées et validées dans des laboratoires de référence tels que le laboratoire de sécurité alimentaire de l'Anses, elles sont officiellement partagées avec le réseau des laboratoires de contrôle alimentaire de routine. Cela nécessite toutefois une évaluation préalable des performances réalisées par les laboratoires du réseau lors de leur participation à un essai d'aptitude inter laboratoire. Néanmoins, un manque de normalisation des méthodes HRMS pourrait rendre difficile la comparaison des résultats, ainsi que l'application des méthodes à d'autres instruments à haute résolution. Il apparaît crucial que les protocoles et les critères d'identification utilisés en HRMS soient standardisés, afin que les opérateurs puissent s'appuyer sur un consensus commun permettant de fournir des résultats fiables et comparables.

Une dernière limite serait la plus grande complexité du traitement des données en LC-HRMS, en particulier pour les analyses suspectes et non ciblées. Cela nécessite des compétences supplémentaires par rapport au traitement conventionnel des données ciblées. Un transfert de compétences considérable est nécessaire pour adapter les opérateurs et les analystes de routine à ces analyses complexes. Ces approches nécessitent également une normalisation des outils et des critères à utiliser, car les analyses suspectes et non ciblées impliquent que les normes analytiques ne sont pas disponibles dans le laboratoire

Contents

GENERAL INTRODUCTION 27

CHAPTER 1. State of the art on consumer exposure to chemical substances and their analysis in food products 31

1.1. The concept of exposome 32
1.2. The food chemical exposome 33
1.3. Exposure to pesticide residues 35
1.3.1. General informations 35
1.3.2. The risk of exposure to pesticide residues 37
1.3.3. Regulation 40
1.3.4. Monitoring and control plans of pesticide residues in foodstuffs 40
1.4. Exposure to veterinary drug residues 41
1.4.1. General informations 41
1.4.2. Risks of exposure to veterinary drug residues through food 42
1.4.3. Regulation 43
1.4.4. Monitoring and control plans for veterinary drug residues in animal origin foodstuffs 43
1.5. Exposure to mixtures of chemical substances: cocktail effects 44
1.6. Risk assessment of exposure to chemical mixtures 45
1.7. The current limits in regulation of chemical mixtures 46
1.8. What are the challenges to address for improving food safety? 47
1.9. Sample preparation for analysis of contaminants in food 48
1.9.1. Liquid-liquid extraction (LLE) 48
1.9.2. Solid phase extraction (SPE) 49
1.9.3. Solid phase microextraction (SPME) 51
1.9.4. Accelerated solvent extraction (ASE) 52
1.9.5. Quick Easy Cheap Effective Rugged and Safe (QuEChERS) 53
1.9.6. Quick Polar Pesticide Extraction (QuPPE) 56
1.9.7. The “Mega-methods” 58
1.10. The analytical instruments used for the multiresidue analysis of contaminants in food 62
1.10.1. Chromatographic separation techniques 62
1.10.2. Detection using tandem mass spectrometry 64
1.10.3. Advantages and drawbacks of LC/GC-MS/MS 67
1.10.4. High-resolution mass spectrometry (HRMS) 68
1.10.5. Advantages of HRMS over MS/MS 71
1.11. Aim of the thesis 73

CHAPTER 2. Development of analytical methods for the multiresidue and large-scale screening of contaminants in food samples 74

2.1. Development of a multiresidue method for the analysis of pesticides in baby foods 75

2.1.1. Context and aim of the study 75

2.1.2. Key points of the study 75

2.1.3. **ARTICLE 1** (**Makni et al., 2022**) 75

2.1.4. Summary & main results 94

2.1.5. Limitations and prospects for improvements 94

2.2. Development of a multiresidue method for the analysis of pesticides in bivalves 95

2.2.1. Context and aim of the study 95

2.2.2. Key points of the study 95

2.2.3. **ARTICLE 2** (**Diallo et al., 2022**) 96

2.2.4. Summary & main results 115

2.2.5. Limitations and prospects for improvements 115

2.3. Optimization of IDA mode 116

2.3.1. Context of optimization 116

2.3.2. Materials & Method 116

2.3.3. Results of the optimization of IDA mode 118

2.3.4. Conclusion 120

2.4. Development of a method for the multiresidue analysis and semi-quantification of 694 contaminants in sugary products 121

2.4.1. Context and aim of the study 121

2.4.2. Key points of the study 121

2.4.3. **ARTICLE 3** (**Makni et al., 2023a**) 122

2.4.4. Summary and main results 142

2.4.5. Limitations and prospects for improvements 142

2.5. Development of a method for the multiresidue analysis and semi-quantification of 850 contaminants in seafood 143

2.5.1. Contexte and aim of the study 143

2.5.2. Key points of the study 143

2.5.3. **ARTICLE 4** (**Diallo et al., 2023**) 144

2.5.4. Summary & main results 163

2.5.5. Limitations and prospects for improvements 163

CHAPTER 3. The versatility of HRMS: targeted, suspected and non-targeted analyses 164

3.1. A proof-of-concept study on honey 165

3.1.1. Context and aim of the study 165

3.1.2. Key points of the study 165

3.1.3. **ARTICLE 5** (**Makni et al., 2023b**) 166

3.1.4. Summary and main results 184

3.1.5. Limitations and prospects for improvements 184

GENERAL CONCLUSION AND OUTLOOK 185

1. Conclusion 186
2. Limitations and outlook 189

a. Limitations and outlook of our works 189

b. Current limitations to integrate HRMS in routine 189

ANNEXES (Electronic Supplementary Materials) 191

CHAPTER 2: Development of analytical methods for the multiresidue and large-scale screening of contaminants in food samples 191

ARTICLE 1 (**Makni et al., 2022**): "Improving the monitoring of multi-class pesticides in baby foods using QuEChERS-UHPLC-Q-TOF with automated identification based on MS/MS similarity algorithms" 191

ARTICLE 2 (**Diallo et al., 2022**): "Development and validation according to the SANTE guidelines of a QuEChERS-UHPLC-QTOF-MS method for the screening of 204 pesticides in bivalves" 226

ARTICLE 3 (**Makni et al., 2023a**): "Optimisation and implementation of QuEChERS-based sample preparation for identification and semi-quantification of 694 targeted contaminants in honey, jam, jelly, and syrup by UHPLC-Q/ToF high-resolution mass spectrometry" 242

ARTICLE 4 (**Diallo et al., 2023**): "Wide-scope screening of multi-class contaminants in seafood using a novel sample preparation (QuEChUP) procedure coupled with UHPLC-Q-TOF-MS: Application for semi-quantitation of real seafood samples" 298

CHAPTER 3: The versatility of HRMS: targeted, suspected and non-targeted analyses 359

ARTICLE 5 (**Makni et al., 2023b**): "A proof-of-concept study on the versatility of liquid chromatography coupled to high-resolution mass spectrometry to screen for various contaminants and highlight markers of floral and geographical origin for different honeys" 359

REFERENCES 393

CHAPTER 1: State of the art on consumer exposure to chemical substances and their analysis in food products 393

CHAPTER 2: Development of analytical methods for the multiresidue and large-scale screening of contaminants in food samples 403

ARTICLE 1 (**Makni et al., 2022**): "Improving the monitoring of multi-class pesticides in baby foods using QuEChERS-UHPLC-Q-TOF with automated identification based on MS/MS similarity algorithms" 403

ARTICLE 2 (**Diallo et al., 2022**): "Development and validation according to the SANTE guidelines of a QuEChERS-UHPLC-QTOF-MS method for the screening of 204 pesticides in bivalves" 406

ARTICLE 3 (**Makni et al., 2023a**): "Optimisation and implementation of QuEChERS-based sample preparation for identification and semi-quantification of 694 targeted contaminants in honey, jam, jelly, and syrup by UHPLC-Q/ToF high-resolution mass spectrometry" 409

ARTICLE 4 (**Diallo et al., 2023**): "Wide-scope screening of multi-class contaminants in seafood using a novel sample preparation (QuEChUP) procedure coupled with UHPLC-Q-TOF-MS: Application for semi-quantitation of real seafood samples" 412

CHAPITRE 3: The versatility of HRMS: targeted, suspected and non-targeted analyses 415

ARTICLE 5 (**Makni et al., 2023b**) 415

List of abbreviations

(24MoBT) 2-(4-morpholinyl)benzothiazole
(2HBzN) 2-hydroxybenzonitrile
(AA) acetic acid
(ACN) acetonitrile
(ANMV) National Agency for Veterinary Medicines
(ANR) French National Research Agency
(APCI) atmospheric-pressure chemical ionization
(ASE) accelerated solvent extraction
(C18) octadecylsilane
(CAG) cumulative assessment group
(CARs) carbamates
(CDS) calibration device system
(CE) collision energy
(CID) collision-induced fragmentation
(CLD) chlordecone
(CUR) curtain gas
(CVMP) Committee for Medicinal Products for Veterinary Use
(DBP) di-n-butyl phthalate
(DBS) dibutyl sebacate
(DDT) dichlorodiphenyltrichloroethane
(DEA) diethylaminopropyl
(DEET) N,N-diethyl-*m*-toluamide
(DEP) diethyl phthalate
(DER) Risk Assessment Department
(DGAL) Directorate General for Food
(DGCCRF) General Directorate for Competition, Consumer Affairs and Fraud Control
(DIA) data-independent acquisition
(DMA) 2,4-dimethylaniline
(DMF) N-(2,4-dimethylphenyl)formamide
(DoE) Design of Experiment
(DP) declustering potential
(d-SPE) dispersive-SPE
(EFSA) European Food Safety Authority
(EHDPP) 2-ethylhexyl diphenyl phosphate
(EI) electronic impact
(EIC) extracted ion chromatograms
(EMA) European Medicines Agency
(ESI) electrospray ionization
(EU) European Union
(EURL) European Union reference laboratories
(FA) Formic acid
(FIT) “Fit” MS/MS algorithm
(FoA) frequency of appearance
(F-SWATH) fixed-sequential window acquisition of all theoretical fragment ion spectra
(GC) gas chromatography

(GCB) graphitized carbon black
(GS1) nebulising gas
(GS2) heater gas
(HBM4EU) Human Biomonitoring for European Union
(HCDB) homemade compound database
(HRMS) High-resolution mass spectrometry
(IDA) information-dependent acquisition
(ISVF) ion spray voltage floating
(LC) liquid chromatography
(LC/GC-MS/MS) liquid or gas chromatography coupled to tandem mass spectrometry
(LLE) liquid-liquid extraction
(LOD) limit of detection
(LOI) limit of identification
(LOQ) limit of quantification
(LSAL) ANSES Food Safety Laboratory
(*m/z*) mass-to-charge ratio
(MCPs) monitoring and control plans
($MgSO_4$) magnesium sulfate
(MoNA) Mass Bank of North America
(MRL) maximum residue level
(MRM) multiple reaction monitoring
(MRPL) minimum required performance limit
(NaCl) sodium chloride
(NaOAc) sodium acetate
(NSAIDs) non-steroidal anti-inflammatory drugs
(NTA) non-targeted analysis
(OCs) organochlorine
(OPs) organophosphate pesticides
(PARC) Partnership for the Assessment of Risks in Chemicals
(PCA) Principal component analysis
(PCA-Da) Principal component discriminant analysis
(PCBs) polychlorinated biphenyls
(PDMS-DVB) polydimethylsiloxane–divinylbenzene
(PE) phthalate esters
(PFCs) perfluorinated compounds
(PIL) precursor-inclusion list
(PLE) pressurized liquid extraction
(PPR) Panel on Plant Protection Products
(PSA) primary and secondary amines
(PUR) “Purity” MS/MS algorithm
(PYR) pyrethroids
(QA) quality assurance
(QC) quality control
(QqQ-MS) triple-quadrupole mass spectrometry
(Q-ToF) quadrupole time-of-flight
(QuEChERS) Quick Easy Cheap Effective Rugged and Safe
(QuEChERSER) Quick Easy Cheap Effective Rugged, Safe, Efficient and Robust

(QuPPE) Quick Polar Pesticide Extraction
(r^2) coefficient of determination
(rcf) relative centrifugal force
(RFIT) “Reverse Fit” MS/MS algorithm
(RP-LC) reversed-phase liquid chromatography
(S/N) signal-to-noise ratio
(SDL) screening detection limit
(SPC) single-point calibration
(SPE) solid-phase exctraction
(SPME) solid-phase microextraction
(SSA) suspect-screening analysis
(SWATH) sequential window acquisition of all theoretical fragment ion spectra
(TCEP) tris(2-chloroethyl) phosphate
(TDS) Total Diet Studies
(TEM) source temperature
(TIC) total ion chromatogram
(TOA) Taguchi Orthogonal Array
(ToF) time-of-flight
(TP) transformation product
(t_R) chromatographic retention time
(TRIA) triazine herbicides
(TriAZ) triazole
(UHPLC) ultra-high performance liquid chromatography
(UPBM) Pesticides and Marine Biotoxins Unit
(US EPA) US Environmental Protection Agency
(VD) veterinary drug
(V-SWATH) variable-sequential window acquisition of all theoretical fragment ion spectra

Publications and communications

Publications

Makni, Y., Diallo, T., Guérin, T., Parinet, J., 2022. Improving the monitoring of multi-class pesticides in baby foods using QuEChERS-UHPLC-Q-TOF with automated identification based on MS/MS similarity algorithms. Food Chem. 395, 133573. https://doi.org/10.1016/j.foodchem.2022.133573

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List of figures

General introduction

Fig.1. Construction of the "AlimOMIC" project 29

Chapitre 1. State of the art on consumer exposure to chemical substances and their analysis in food products

Fig.1. The concept of exposome 32
Fig.2. The food exposome concept 34
Fig.3. World population growth from 1960 to the present, with estimates for the coming decades. 35
Fig.4. The quantities of pesticides used worldwide since the 1990s 36
Fig.5. The amounts of pesticides imported and exported since the 1990s in different regions of the world, and the associated costs. 37
Fig.6. The impact of pesticides on cellular activity. 38
Fig.7. Approaches used to assess the hazard of chemical mixtures, as well as the main combined effects 46
Fig.8. Principle of liquid-liquid extraction technique 48
Fig.9. Principle of solid phase extraction technique 49
Fig.10. Overview of a schematic diagram of an ASE system 52
Fig.11. Evolving interest of researches related to QuEChERS since 2003 based on a litterature search on ScienceDirect according to the following keywords: "QuEChERS", "QuEChERS, pesticides" and "QuEChERS, contaminants". 54
Fig.12. Diagram of a QuEChERS-based protocol 55
Fig.13. QuPPE method 57
Fig.14. Schematic diagram of a LC system. (1) binary pump for aqueous and organic mobile phases, (2) autosampler, (3) stationary phase 64
Fig.15. Principle of electrospray ionization (ESI) in mass spectrometry 65
Fig.16. Trajectory of ions following an oscillatory pattern within the quadrupole analyzer. 66
Fig.17. Configuration of a triple-quadrupole mass spectrometer. 67
Fig.18. Diagram of the three common geometries of orthogonal time-of-flight analyzer 69
Fig.19. Diagram of an Orbitrap analyzer. 70
Fig.20. Diagram of a conventional Q-ToF mass spectrometer with V-ion trajectory. 71
Fig.21. Evolving interest of researches related to analysis of contaminants in food using HRMS with the following key words: "HRMS, contaminants, food". 73

Chapitre 2. Development of analytical methods for the multiresidue and large-scale screening of contaminants in food samples

Fig.1. Cycle of iterative and continuous improvement – part 1 96
Fig.2. Cycle of iterative and continuous improvement – part 2 115
Fig.3. Cycle of iterative and continuous improvement – part 3. 122
Fig.4. Cycle of iterative and continuous improvement – part 4. 144
Fig.5. Cycle of iterative and continuous improvement – final part 166

Figures in the following article « *Improving the monitoring of multi-class pesticides in baby foods using QuEChERS-UHPLC-Q-TOF with automated identification based on MS/MS similarity algorithms* »

Fig.1. Comparison of different QuEChERS-based procedures for sample preparation optimisation... 82
Fig.2. Impact of different extraction and purification procedures on the false negative rates (%) obtained for (a) baby food 1; (b) baby food 2; (c) baby food 3; and (d) baby food 4. The error bars correspond to the standard deviation for the response measured (Mean ± SD, n=3)..... 84
Fig.3. Unexpected identification of difenoconazole in non-spiked baby food 5, with corresponding (a) extracted ion chromatogram; (b) isotopic pattern; and (c) experimental and reference fragmentation spectra comparison using FIT algorithm..... 89
Fig.4. Identification of tris(2-chloroethyl) phosphate in non-spiked baby food 1, with corresponding (a) extracted ion chromatogram; (b) isotopic pattern; (c) experimental and reference fragmentation spectra comparison using FIT algorithm. 92

Figures in the following articles « *Development and validation according to the SANTE guidelines of a QuEChERS-UHPLC-QTOF-MS method for the screening of 204 pesticides in bivalves* »

Fig.1. Evaluation and comparison of IDA, IDA-PIL, F-SWATH and V-SWATH methods with 20, 30, 40 and 50 windows for pesticide detection (a) identification rates using Purity > 70% as search algorithm (b), identification rates using Purity > 50% as search algorithm (c), identification rates using Fit > 70% as search algorithm (d), and identification rates using Fit > 50% as search algorithm (e) at 0.01 µg.mL^{-1} in ACN of the target 204 pesticides. 107
Fig.2. Zoxamide MS spectrum with isotopic profile pattern (a), MS/MS spectrum acquired in SWATH® (b) and IDA-PIL mode (c) in spiked sample at 0.01 µg.mL^{-1}. 109
Fig.3. Percentage of pesticides presenting SDL (a) and LOI (b) at 0.01, 0.05, 0.1 and > 0.1 mg.kg^{-1} under optimised conditions. Detection (c) and identification rates (d) across different bivalve samples spiked at 0.01, 0.05 and 0.1 mg.kg^{-1}. 111

Figures of chapter II.3 « *Optimization of IDA mode* »

Fig.1. Variation in detection, identification and non-fragmentation rates for 204 pesticides using different IDA topN methods and adjusted and unadjusted accumulation times. 119
Fig.2. Identification rates obtained in high-resolution, high-sensitivity fragmentation ion mode. 120
Fig.3. Comparison of the identification of a fungicide, fuberidazole, with a high-resolution mode (a) and a high-sensitivity mode (b).. 120

Figures in the following articles « *Optimisation and implementation of QuEChERS-based sample preparation for identification and semi-quantification of 694 targeted contaminants in honey, jam, jelly, and syrup by UHPLC-Q/ToF high-resolution mass spectrometry* »

Fig.1. Final sample preparation workflow for determining contaminants in concentrated sugary products. 133
Fig.2. Analytical performances of the optimised method with **(a)** detection rates and **(b)** identification rates obtained in 20 concentrated sugary products at 0.001, 0.01 and 0.05 mg.kg^{-1}. 134
Fig.3. Unequivocal identification of **(a)** azoxystrobin in multi-flower honey; **(b)** fluopyram in cherry jam and **(c)** pyrimethanil in current/raspberry jelly. **(i)** Extracted ion chromatogram; **(ii)** Isotopic pattern and mass error of the precursor ion; **(iii)** Experimental fragmentation spectrum (in blue) matched against the library spectrum made by injecting standard in solvent (in red). 139

Figures in the following articles « *Wide-scope screening of multi-class contaminants in seafood using a novel sample preparation (QuEChUP) procedure coupled with UHPLC-Q-TOF-MS: Application for semi-quantitation of real seafood samples* »

Fig.1. Effects of extraction solvent (a), dispersive solid phase extraction (dSPE) sorbent (b) and dilution (c) on the detection rates of pesticides and veterinary drugs, with the significance of the ANOVA test *p*-value < 0.05 (*) and *p*-value < 0.01 (**). The error bars correspond to the standard deviation (SD) for the response measured (Mean ± SD, n = 3)..... 154
Fig.2. Protocol of the four different sample preparation methods (QuEChERS, QuPPe, QuEChERS + QuPPe and QuEChUP, see text for method definitions) for the simultaneous analysis of 364 organic contaminants..... 155
Fig.3. Comparison of the QuEChERS, QuPPe, QuEChERS + QuPPe and QuEChUP sample preparation methods for detection of pesticides and veterinary drugs. The error bars correspond to the standard deviation (SD) (Mean ± SD, n = 3). 156
Fig.4. Percentage of pesticides presenting screening detection limits (SDLs) (a) and limits of identification (LOIs) (b) at 0.001, 0.01, 0.1 and > 0.1 $mg.kg^{-1}$ under optimised conditions. Detection (c) and identification rates (d) across different seafood samples spiked at 0.001, 0.01 and 0.1 $mg.kg^{-1}$.. 158
Fig.5. Positive finding of diuron (a) and diclofenac (b) in a mussel sample, with corresponding extracted ion chromatogram (i); isotopic pattern (ii); experimental and reference MS/MS spectra comparison using the Fit algorithm (iii). 159

Chapitre 3. The versatility of HRMS: targeted, suspected and non-targeted analyses

Figures in the following article « *A proof-of-concept study on the versatility of liquid chromatography coupled to high-resolution mass spectrometry to screen for various contaminants and highlight markers of floral and geographical origin for different honeys* »

Graphical abstract..... 167
Fig.1. Data processing workflow used in this study..... 174
Fig.2. Heatmaps of endogenous compounds to identify markers of floral origin as a function of the hierarchical clustering of the samples. The scale of high to low relative abundance is shown in red and blue, respectively. Heatmaps generated in (a) ESI^+ and (b) ESI^-. 178
Fig.3. Tentative identification in ESI^+ of potential floral origin markers: (a) deoxyvasicinone in the chestnut honey group; (b) 2-quinolone in the chestnut honey group; (c) caffeine in the citrus honey group and (d) 2-oxindole in the citrus honey group. From left to right: the expression profile of the compounds in the honey groups and QC-pooled samples; the extracted ion chromatograms of the compound in the samples; experimental fragmentation spectrum (in blue) matched against an available external fragmentation spectrum acquired in other analytical conditions (in red). 179
Fig.4**.** Principal component analysis (PCA) of the dataset of 52 honey samples with the quality control (QC)-pooled samples to assess data quality. (a) PCA generated in ESI^+ (b) PCA generated in ESI^-. (i) PCA score plots of honey samples (ii) PCA loading plots of honey samples. 180
Fig.5. Separation of the groups of honey samples to identify potential markers of floral origin using principal component discriminant analysis (PC-Da): (a) dimension 1 (D1) and D2 in ESI^+; (b) D1 and D3 in ESI^+; (c) D1 and D2 in ESI^-; (d) D1 and D3 in ESI^-. 181
Fig.6. Separation of chestnut honey samples according to their geographical origin using principal component discriminant analysis (PC-Da): (a) PC-Da generated in ESI^+ (b) PC-Da generated in ESI^-. (i) PC-Da score plots of chestnut honey samples; (ii) PC-Da loading plots of chestnut honey samples. 183

General conclusion and outlook

Fig.1. Summary of the work conducted and articles published within the framework of the AlimOMIC project and thesis. 188

Listes of Tables

Chapitre 1. State of the art on consumer exposure to chemical substances and their analysis in food products

Table 1. Studies reporting the use of SPE for separation, preconcentration of contaminants, or purification of food matrices, for multi-residue analysis of contaminants. 50
Table 2. Overview of some studies that reported the use of ASE technique for extraction of various organic contaminants from foodstuffs. 53
Table 3**.** Overview of some QuEChERS-reporting studies for multiresidue analysis of contaminants in food samples. 56
Table 4. Summary of main advantages and drawbacks for each sample preparation technique. 59

Chapitre 2. Development of analytical methods for the multiresidue and large-scale screening of contaminants in food samples

Tables in the following article « *Improving the monitoring of multi-class pesticides in baby foods using QuEChERS-UHPLC-Q-TOF with automated identification based on MS/MS similarity algorithms* »

Table 1**.** Impact of different thresholds on the t_r and accurate mass measurement criteria regarding the false negatives (%), in a set of 10 baby food samples in triplicate, at 0.01 and 0.1 mg.kg^{1} 86
Table 2**.** Impact of a PIL and different algorithm-score combinations on the false negatives (%), in a set of 10 baby food samples in triplicate, at 0.01 and 0.1 mg.kg^{-1} 87

Tables in the following article « *Development and validation according to the SANTE guidelines of a QuEChERS-UHPLC-QTOF-MS method for the screening of 204 pesticides in bivalves* »

Table 1**.** Control factor and levels in the QuEChERS extraction and clean-up. 100
Table 2**.** Pesticide detection rates of L9 TOA (3^4) for the optimisation of QuEChERS extraction and clean-up. 104
Table 3**.** Pesticide S/N of L9 TOA (3^4) for the optimisation of QuEChERS extraction and clean-up. 105

Table du chapitre II.3 « *Optimisation approfondie du mode d'acquisition IDA pour limiter les taux de non fragmentation et améliorer les taux d'identification* »

Table 1**.** Paramètres d'évaluation du mode IDA. 117

Tables in the following article « *Optimisation and implementation of QuEChERS-based sample preparation for identification and semi-quantification of 694 targeted contaminants in honey, jam, jelly, and syrup by UHPLC-Q/ToF high-resolution mass spectrometry* »

Table 1**.** Factors and levels used for the optimisation of sample preparation. 128
Table 2**.** Contaminants identified in the 50 sweet products. 136
Table 3**.** Frequency of appearance (%) of contaminants identified in 50 sweet products. 138

Tables in the following article « *Wide-scope screening of multi-class contaminants in seafood using a novel sample preparation (QuEChUP) procedure coupled with UHPLC-Q-TOF-MS: Application for semi-quantitation of real seafood samples* »

Table 1**.** Control factors and levels in the sample preparation process. 149

Start

General introduction

Anses is a public body created in 2010, under the supervision of various ministries (Health, Agriculture, Environment, Labour, and Consumer Affairs). It groups together several laboratories and scientific directions working in the fields of food safety, animal health, plant health and public health. Anses also issues and withdraws marketing authorizations for veterinary medicines, plant protection products, fertilizers and biocides in France. To do so, it assesses their efficacy and the risks they represent for human health and ecosystems.

Its scientific and technical support activities provide decision-making assistance to the health authorities, and mainly concern reference, diagnosis, epidemiosurveillance, as well as research and the development of methods. The food safety laboratory in which I work is organized into several units. One of them, the Pesticides and Marine Biotoxins Unit (UPBM), focuses on monitoring pesticide residues in food samples.

In France and throughout the world, pesticide residues are used on a massive scale in modern agriculture to increase agricultural productivity by reducing crop losses due to pests and diseases (Md Meftaul et al., 2020; Sharma et al., 2019). Pesticide residues play a very important role in our society, making a major contribution to the availability of a wide variety of fruit, vegetables and cereals throughout the year. However, they also give rise to serious concerns, particularly among farmers, their families and consumers, as these compounds are not without risk for human health (Carvalho, 2017 ; Mostafalou and Abdollahi, 2017).

In European Union (EU), the European Food Safety Authority (EFSA) is the instance that regulates the use and marketing of pesticides. The EFSA set maximum residue levels (MRLs) as upper limits of pesticide residues legally approved in or on food or feed. These regulatory limits are established with prior regards to the Good Agricultural Practice, and are also based on lowest exposure necessary to protect vulnerable consumers (EFSA, 2023). As so, the different EU Member States have to monitor the presence of pesticide residues in food products to ensure compliance with the regulatory thresholds set by EFSA. In France, monitoring and control plans (MCPs) are implemented to assess the level of consumer exposure to pesticide residues, as well as to check compliance with MRLs and good agricultural practice.

At present, liquid or gas chromatography coupled to tandem mass spectrometry (LC/GC-MS/MS) operating in multiple reaction monitoring (MRM) mode is recognized as the reference tool for analyzing pesticide residues in foodstuffs (Villaverde et al., 2016; Alder et al., 2006). These techniques are highly specific and sensitive, but lack completeness because they are limited to a pre-established list of substances to be researched a priori, and for which the analytical standards are available in the laboratory. Any contaminant not included in the initial list cannot be analysed, even though it is potentially present in food and poses a risk to consumers. Recent news warns us that no system is perfect, the recent case of the unexpected fipronil contamination of eggs being a perfect example (Eskola et al., 2020; Authority (EFSA) et al., 2018).

Recently, liquid or gas chromatography methods coupled with high-resolution mass spectrometry (LC/GC-HRMS) have emerged as promising techniques for improving the food safety system. These techniques appear to be cutting-edge technologies that overcome the lack of comprehensiveness of conventional analyses (Weng et al., 2020). Indeed, HRMS considerably extends the field of analysis, with the possibility of carrying out large-scale targeted analyses without limitations, as well as so-called suspect and non-targeted analyses to investigate chemicals for which analytical standards are not available in the laboratory (Dubocq et al., 2021; Phillips et al., 2018). Thus, HRMS is proving to be a breakthrough technology, making it possible to go far beyond only a prioritized list of compounds. From a toxicological point of view, and given the wide diversity of chemicals occurring in foodstuffs, regulation of

individual substance and segregated analysis of molecules by family appears insufficient. In fact, through their varied diet, consumers are exposed to chemical mixtures rather than individual substances, which may result in combined and "cocktail effects", impacting human health, and whose effects are not always well known. This implies a change in the current food safety system, and exhaustive analytical tools and methods are thus needed to provide a more global and realistic state of the dynamic and fluctuating exposure of consumers to harmful chemical mixtures.
However, despite its advantages, HRMS is not currently considered a reference tool for official analysis and monitoring of food samples. Indeed, there are still some challenges to be addressed, especially regarding instrumental sensitivity and workflows dedicated to suspect and non-targeted approaches, which may be complex.

The AlimOmic project, funded by the ANR JCJC (ANR-19-CE21-0002), aims to fill the above-mentioned "gaps", while contributing to a better characterization of the exposure of consumers to chemicals, as well as to disseminate LC-HRMS to control laboratories in order to improve food safety in France and abroad. To this end, it proposes to develop and validate LC-HRMS methods for targeted, suspect and non-targeted analysis of a wide range of contaminants (>600 molecules) in various food matrices. This research work will enable us to evaluate the performance of these devices and approaches, to be able to offer the methods within an official framework for routine monitoring. The AlimOMIC project integrates various theses and research projects, including those of Thierno Diallo (Amphibie) and myself. During the three years of our thesis, Thierno and I were able to work closely together on all our projects. Indeed, the AlimOMIC project requires the development of methods on a variety of food matrices, including baby food, sweet products and fish products, which are frequently consumed. As such, Thierno Diallo was responsible for the development of fishery products, and I for the other food matrices under study. This enabled us to work in pairs, which benefited us scientifically as well as psychologically and socially, while multiplying the number of papers for both of us. This thesis context is summarized in **Fig.1**. below.

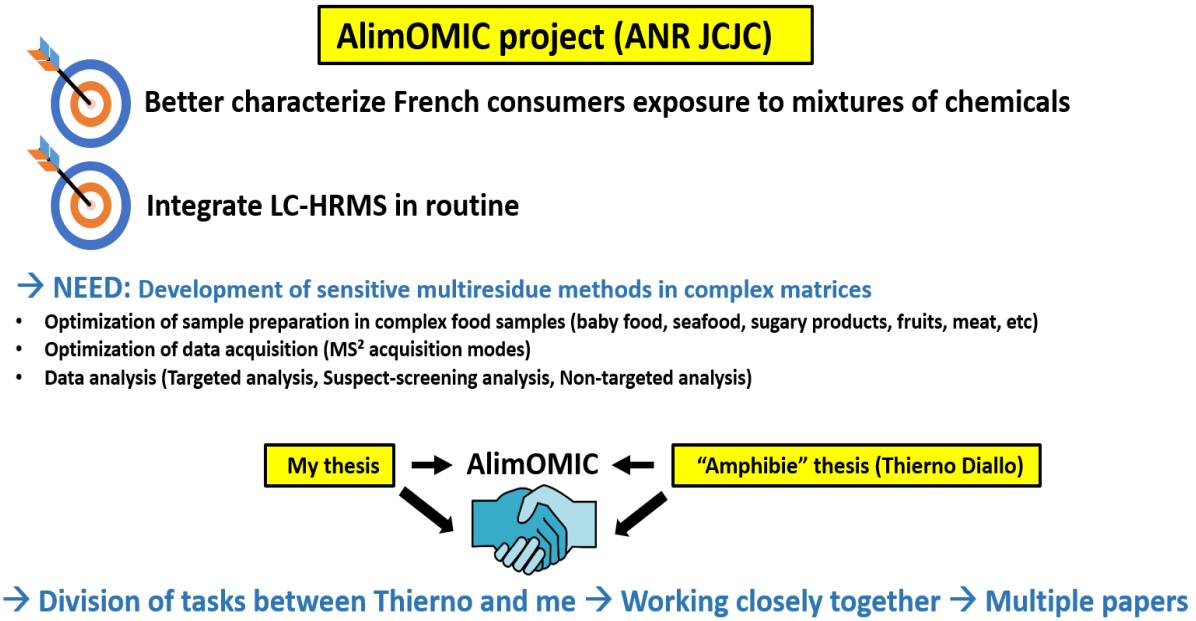

Fig.1. Construction of the "AlimOMIC" project

The work carried out during the three years of this thesis is presented in this manuscript in the form of three chapters:

Chapter I of my thesis is devoted to a review of the literature, with the aim of taking stock of the state of the art in terms of consumer exposure to chemical contaminants, the associated risks and current regulations, as well as taking a closer look at the methods and techniques for analyzing these contaminants in food samples.

Chapter II of my thesis is devoted to the development and validation of LC-HRMS screening methods for the multi-residue analysis of organic contaminants, in a variety of food matrices. Indeed, a large number of pesticide residues are used and found in foodstuffs, along with other types of contaminants such as veterinary drugs, pharmaceuticals, certain industrial contaminants and so on. All the different contaminants found in food products have different structural and physico-chemical properties. The identification of these compounds in food matrices therefore requires the development of robust methods, capable of being exhaustive and generic to cover the widest possible range of chemicals. The aim was to highlight the ability of HRMS to carry out targeted broad-spectrum analyses (>500 contaminants in a single analysis), as well as suspect-screening approaches to considerably extend the scope of monitoring. We also wanted to demonstrate that the LC-HRMS methods developed were sufficiently sensitive to analyze regulated contaminants well below their MRLs. The ultimate objective would be to highlight the potential of LC-HRMS as a tool that could be integrated into an official control system.

Chapter III of my thesis is devoted to a "proof-of-concept" study carried out on honey samples, with the aim of highlighting the versatility of HRMS. Indeed, we also wanted to emphasize the fact that HRMS can be adapted to different applications in the field of food sample analysis, with a broad-spectrum contaminant screening capability, but also to perform sample categorization thanks to non-targeted and chemometric analyses in particular. With this study, the idea was to bring together the advantages offered by HRMS, as well as its usefulness in an official control system for food safety, but also for food authenticity and fraud detection.

Finally, the manuscript ends with a conclusion, the limitations and perspectives arising from this research work

CHAPTER

State of the art on consumer exposure to chemical substances and their analysis in food products

1

Preamble

This first chapter provides an overview of the state of the art regarding the exposure of individuals to chemicals of concern, as well as the various methodologies and tools used for analysis and control in foodstuffs. This chapter covers the concepts of exposome and food chemical exposome, and the importance of understanding what humans may be exposed to, particularly through their diet, and how this may influence their overall physiological state and health. Thus, food safety is an aspect widely discussed both with regard to the families of substances that can be found in foodstuffs, as well as regulations and the limits and challenges to be addressed to better protect the consumer. This chapter also summarizes sample preparation methods used for the extraction of contaminants in complex matrices, as well as analytical tools for the official monitoring and control of foodstuffs. Finally, this chapter outlines the main strategies applied to the analysis of contaminants in food samples using HRMS, and its advantages over tandem mass spectrometry to improve food safety and provide more exhaustive exposure data of consumers to cocktail of chemicals.

1.1. The concept of exposome

In 2005, Dr. Christopher Wild, then epidemiologist and Director of the International Agency for Research on Cancer, introduced the exposome concept in an article published in the journal *Cancer Epidemiology, Biomarkers & Prevention*. (Wild, 2005). The exposome can be defined as the set of environmental sources and exposure factors to which an individual is exposed throughout his life, and which cause chronic and multifactorial pathologies. (Wild, 2005). This concept was initially proposed as a complement to the human genome, which is insufficient on its own to explain the ethology of a number of chronic pathologies. Dr. Christopher Wild's initiative drew attention to the need to consider "non-genetic" sources of exposure in epidemiological studies, to better understand the origins of certain physiological disorders and diseases, and thus be able to undertake prevention.

Various definitions of the exposome have been proposed since the one introduced by C. Wild in 2005, but all incorporate the complementarity of three factors to be measured in assessing the exposome: (1) firstly, the internal environment, which incorporates endogenous factors such as gut microbiota, oxidative stress, aging processes, etc.; (2) the specific external environment, which incorporates exposure to radiation, pathogens, chemicals and environmental contaminants, as well as lifestyle factors such as physical activity, diet, tobacco and alcohol consumption, etc.; and (3) a more general external environment which includes the socio-economic influences of the individual, mental and psychological stress, as well as the environment (urban, rural, climatic conditions, etc.). (Karlsson, 2023; Vineis et al., 2020; Siroux et al., 2016; Miller and Jones, 2014; Wild, 2012). All these factors interact with each other in complex ways, and the resulting biological response influences the physiological state and health of an individual. Figure 1 summarizes the concept of exposome.

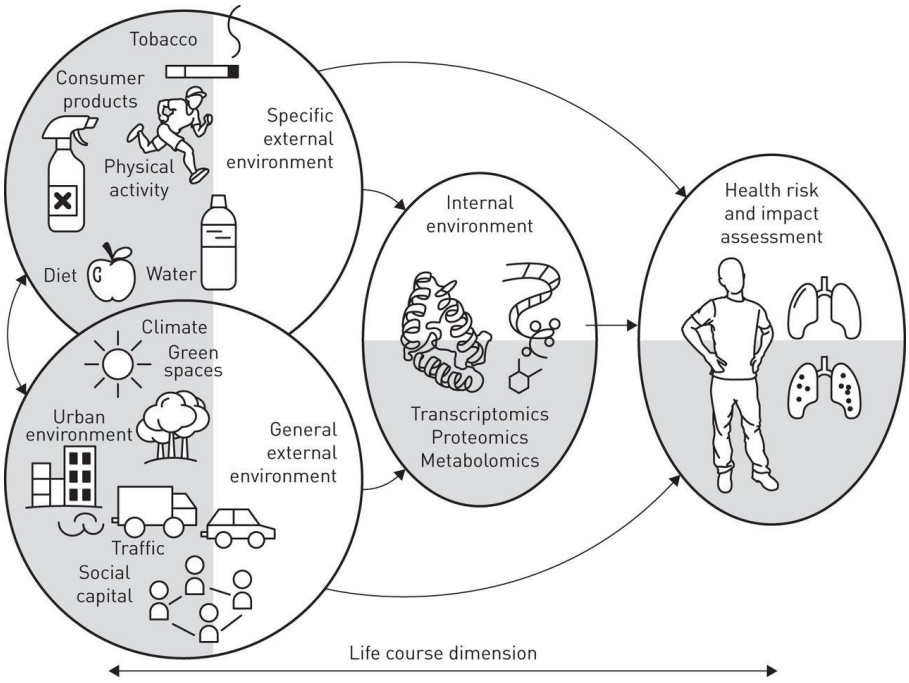

Fig.1. The concept of exposome (from Siroux et al., 2016)

Moreover, since its introduction in 2005, various research projects and initiatives around the exposome have emerged (Siroux et al., 2016). For example, the European HELIX approach (https://www.projecthelix.eu/fr) was developed to explore new methodological tools to characterize a growing child "early" exposome, as well as its mother's exposure to different environmental factors, and to relate these exposures to the associated risks to the child health, growth and development. Other projects, such as the "Health and Environment-wide Associations based on Large population Surveys (HEALS, http://www.heals-eu.eu/index.php/project/)" project funded by the European Commission, are gathering and organizing a whole range of data, bioinformatics procedures and biological response modeling tools to support exposome studies. There is also an American project, HERCULES (https://emoryhercules.com/about/), which provides the web infrastructure and expertise needed to develop and improve new technologies to better understand the exposome.

The interest around the exposome is because understanding the complex processes of interactions between different "non-genetic" factors could help scientists to better understand the origins of certain pathologies and physiological disorders, and thus propose appropriate prevention strategies. (Karlsson, 2023; Wild, 2012). Indeed, numerous studies have already reported the association of certain lifestyle and environmental factors, and exposure to pollutants and chemicals, with certain pathologies and physiological disorders. For example, an exposure to certain dietary contaminants may be associated with an imbalance of the intestinal microbiota, inflammation of the liver, and certain pollutants may increase the risk of the development of certain liver pathologies such as NAFD, NASH, cirrhosis and cancer. (Barouki et al., 2023). Lifestyle factors such as alcohol consumption are also known to considerably increase the risk of developing cirrhosis and liver cancer (Barouki et al., 2023). It has also been reported that the external exposome, including exposure to various chemicals, may be associated with disruptions of the epithelial barrier, participating in the pathogenesis and increasing prevalence of certain allergic conditions such as asthma, atopic dermatitis, allergic rhinitis, chronic rhinosinusitis, and certain food allergies (Celebi Sozener et al., 2022). These examples underline the importance of the exposome concept in achieving a better understanding of the complex mechanisms of interaction between environmental exposure sources and the onset of certain diseases, with a view to proposing prevention strategies and improving public health.

Among the routes of human exposure to chemicals, regular diet is one of the most important, and is attracting particular interest. Therefore, the following state-of-the-art will focus on the exposure of individuals to various hazardous chemicals through diet, as well as the associated risk on human health.

1.2. The food chemical exposome

An important part of the human exposome concerns the dietary exposome, i.e. the total dietary exposures of an individual throughout his or her life. (Tralau et al., 2021). Figure 2 below illustrates the concept of the dietary exposome. It is well known that the diet and dietary habits of each individual can influence beneficial or deleterious biological responses, limiting or promoting the incidence of certain multifactorial chronic diseases such as cardiovascular disease, a number of cancers, as well as obesity and diabetes. (Scalbert et al., 2019). Various dietary guidelines recommend varying the foods we eat and adopting a balanced diet, as this contributes to the proper functioning and health of the body. (Scalbert et al., 2019). Because of

its diversity, food is a complex mixture of beneficial natural substances including macronutrients, vitamins, micronutrients (polyphenols, flavonoids, carotenoids, etc.), and trace elements. (Scalbert et al., 2019). However, it is also a major source of exposure to potentially hazardous chemical substances. More than 350,000 chemical substances are listed and approved for production and use in various applications worldwide (Wang et al., 2020). Specific inventories exist for certain types of products such as agrochemicals, pharmaceuticals and cosmetics. (Wang et al., 2020). Throughout their lifecycle, some of these chemical substances may be released and dispersed into various environmental compartments, contributing to the exposure of biodiversity and humans. In food products, chemical substances may be added intentionally, as in the case of food additives and preservatives. They may also be used in the food production process and then unintentionally end up in foodstuffs, such as pesticide and veterinary drug residues, and packaging materials. (Eskola et al., 2020). Other chemical compounds (e.g. environmental contaminants, natural toxins) which are not used in the food manufacturing process and which are not supposed to be found in our foodstuffs, are dispersed in the environment and can ultimately contaminate food products.

Some chemical substances draw particular attention because of their occurrence in food products and the risks they entail for human health. This is particularly true of pesticide residues (Valcke et al., 2017), which are at the forefront of consumer concerns and contribute to their distrust of the agri-food industry. In addition to pesticide residues, food can also be a source of exposure to veterinary drug residues. (Baynes et al., 2016), perfluorinated compounds (PFCs) (Vorst et al., 2021), phthalate esters (Authority (EFSA) et al., 2020), bisphenols (Catenza et al., 2021), polychlorinated biphenyls (PCBs), certain natural toxins (Hamad et al., 2023; Otero and Silva, 2022), heavy metals (Rai et al., 2019) as well as other contaminants that are raising new concern. Thus, the chronic and continuous exposure of individuals to these harmful substances is an important part of the food chemical exposome, and represents a major challenge in terms of food safety and public health.

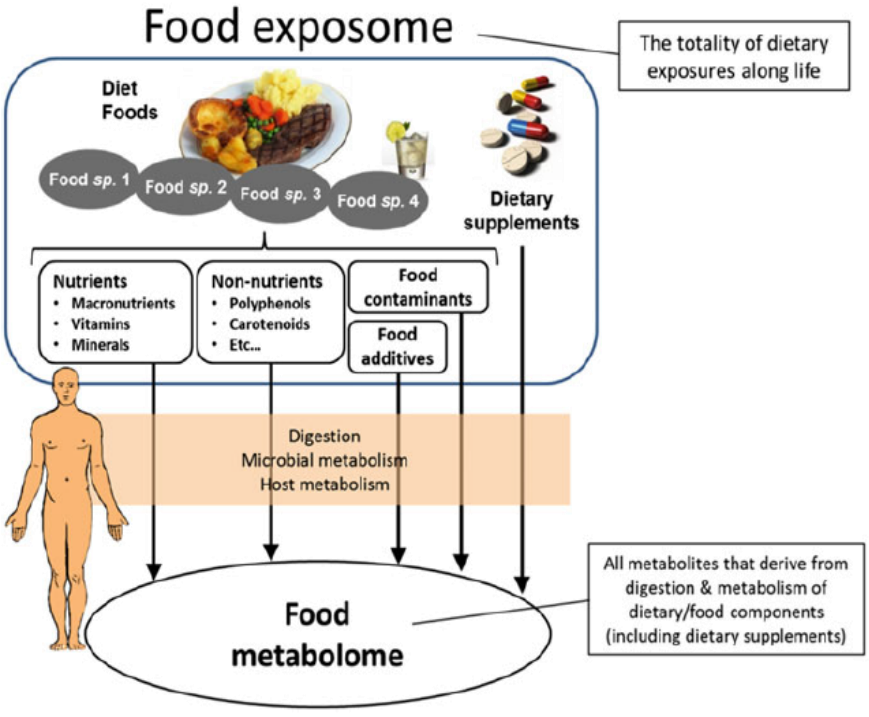

Fig.2. The food exposome concept (from Scalbert et al., 2019).

The following sections will present some of these substances of concern, in particular pesticide and veterinary drug residues, which are the main chemical compounds integrated and analyzed during this thesis work.

1.3. Exposure to pesticide residues

1.3.1. General informations

Pesticide residues are among the chemicals most commonly found in food, drawing a growing attention and concern from consumers. These are bioactive chemical compounds of low molecular weight (<1000 Da), massively used and spread in present-day agriculture to combat insect pests, weeds and other parasites responsible for the destruction of crops and food stocks. (Md Meftaul et al., 2020; Sharma et al., 2019). Pesticide residues can be distinguished according to the organism they target (insecticides, herbicides, fungicides, molluscicides, nematicide, rodenticide, etc.), or their chemical structure (organochlorine, organophosphate, carbamate and pyrethroids) (Narenderan et al., 2020).

Every year, it is estimated that pests are responsible for the loss of an average of 35% of potential crop yield before harvest. (Popp et al., 2013). These losses and the resulting consequences would be far greater if the use of pesticides were prohibited. Indeed, without the intensive use of pesticides, it is estimated that there would be an average loss of nearly 78% in fruit production, 54% in vegetable production and 32% in cereal production (Tudi et al., 2021). In addition, the significant reduction in food production would lead to a considerable rise in food prices. (Popp et al., 2013). The explosion in global population growth contrasts with the declining availability of agricultural land. In the 1960s, the world population was 3 billion, compared with around 7 billion in 2010. It is estimated that the world population will be over 8 billion in 2030, and over 9 billion in 2050. (Popp et al., 2013). Figure 3 below illustrates the explosion in world population over the last few decades, and the estimates for the coming decades.

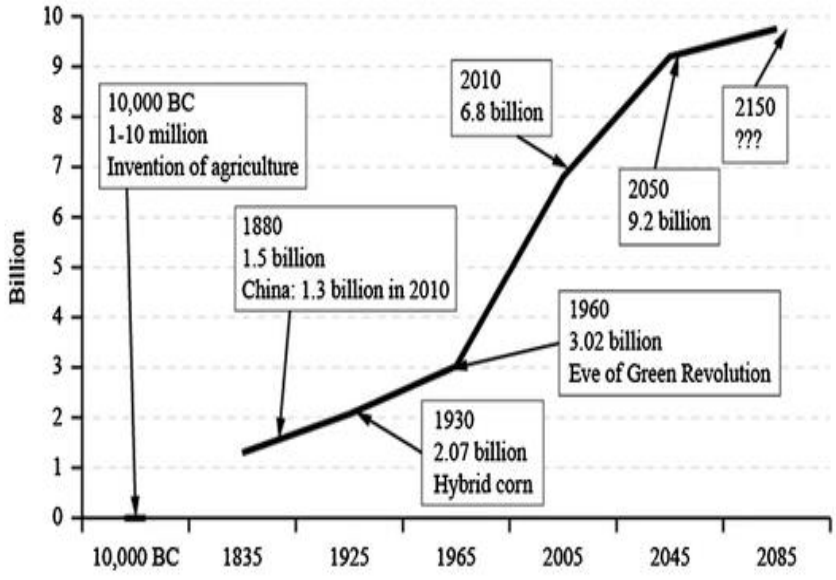

Fig.3. World population growth from 1960 to the present, with estimates for the coming decades (from Popp et al., 2013).

The massive consumption of pesticides has therefore rapidly become an indispensable tool for meeting ever-increasing food requirements. Indeed, as **Figure 4** below shows, total pesticide consumption worldwide has risen sharply since the 1990s, with around 1.8 million tons (Mt) used, compared with 3.54 Mt in 2021 (FAO, 2023).

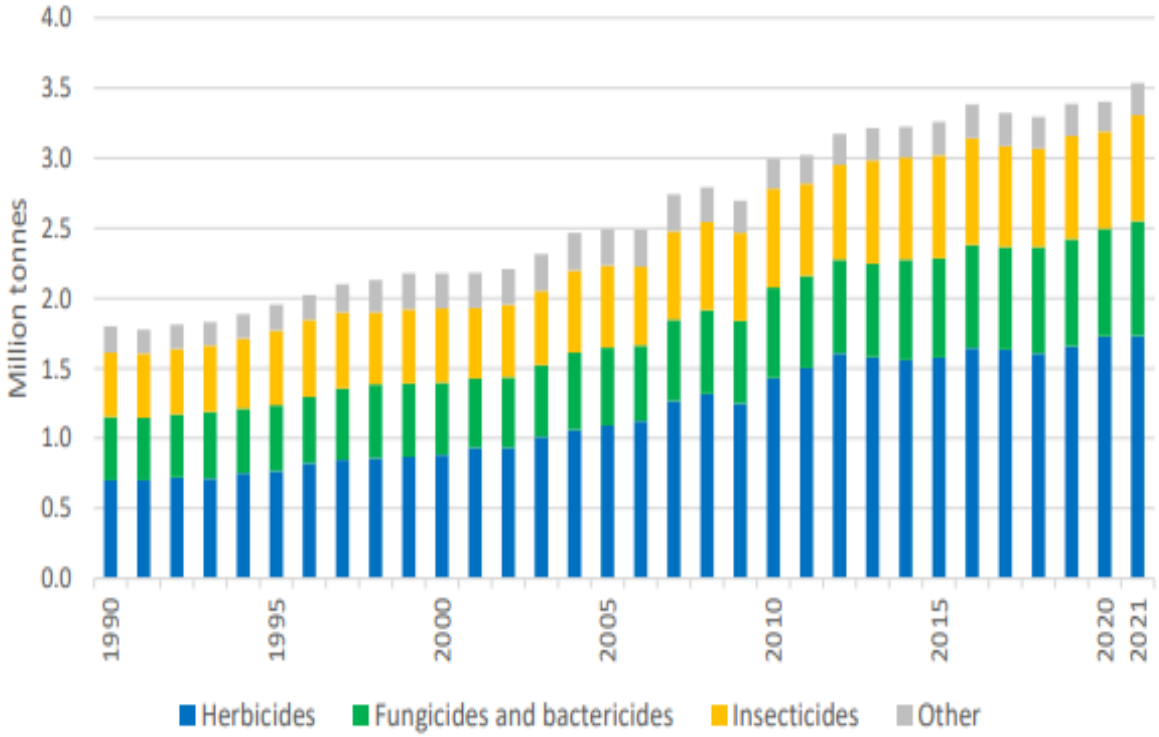

Fig.4**.** The quantities of pesticides used worldwide since the 1990s (from FAO, 2023).

The costs associated with their widespread use have also skyrocketed. Figure 5 below summarizes the amounts of pesticides imported and exported since the 90s on the five continents, and the associated costs. In 1990, for example, the quantities of pesticides exported by America, Europe and Asia were 0.29 Mt (corresponding to a market value of $1.41 billion), 0.74 Mt (corresponding to a market value of $5.2 billion) and 0.14 Mt (corresponding to a market value of $0.65 billion) respectively (Fig.5) (FAO, 2023). By 2021, the quantities of pesticides exported by America, Europe and Asia had exploded to 0.989 Mt (worth $7 billion), 2.31 Mt (worth $18 billion) and 3.66 Mt (worth $17 billion), respectively (Fig.5) (FAO, 2023). These figures reflect the heavy weight of the pesticide market (several billion dollars), and the ever-growing need to increase productivity and food availability, in a context where the world population is exploding while the availability of agricultural land is decreasing.

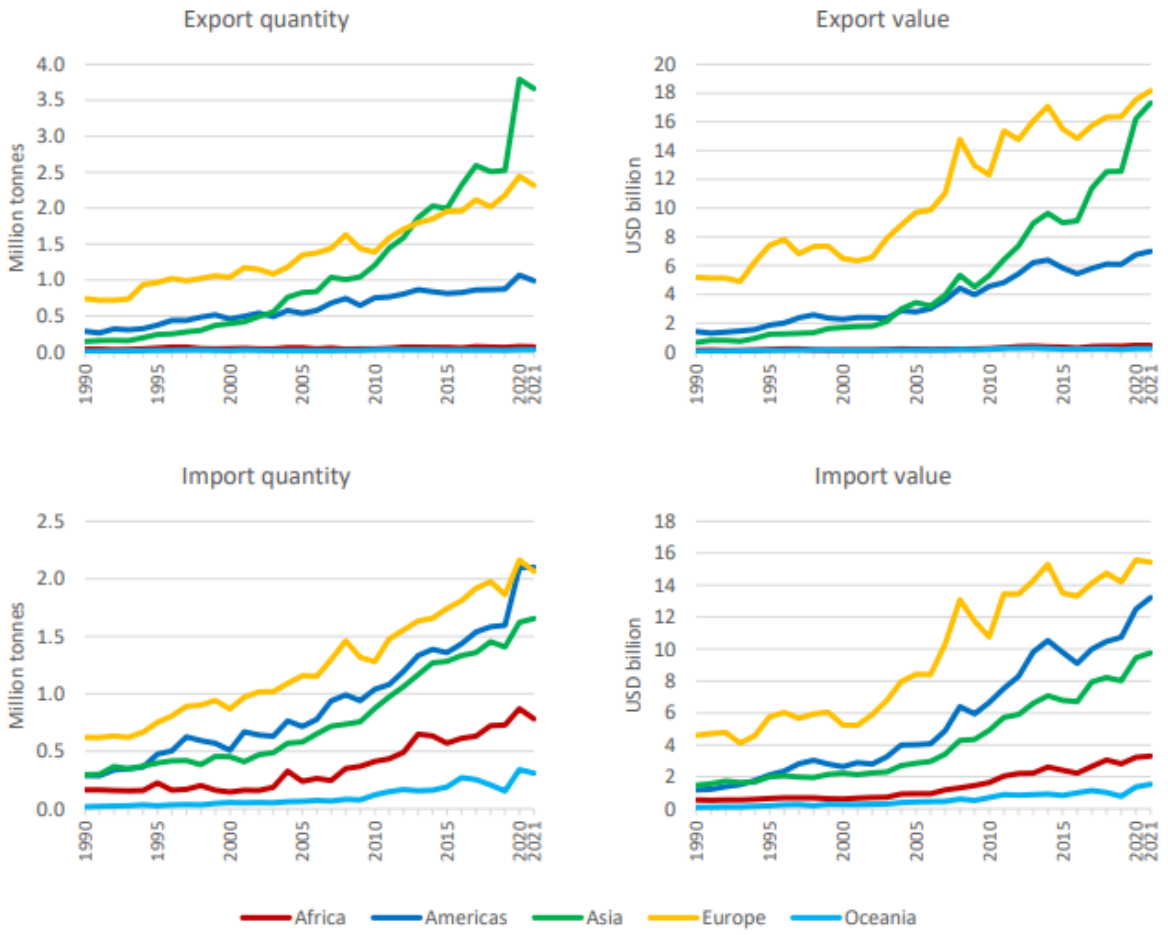

Fig.5. The amounts of pesticides imported and exported since the 1990s in different regions of the world, and the associated costs (from FAO, 2023).

In France, the Ecophyto plan was established and lunched in 2008 to reduce dependence on plan protection products by 50% over 2018, in order to limit their impact on both human health and ecosystems (French government, 2023; Ecophyto, 2016). In 2015, in response to unsatisfactory results, a 2nd version of the plan was established to meet the initial objective of reducing use of plan protection products by 50%, but this time over 2025 (French government, 2023; Ecophyto, 2016). Although the results of the Ecophyto plan have not lived up to expectations, they are far from zero. In 2021, national sales for pesticides not suitable in organic farming amounted to 43,013 t, and were 19% below the 2012-2017 average (French government, 2022). Meanwhile, between 2020-2021, a 13% increase in the use of alternative solutions suitable with organic farming, such as bio-pesticides, was observed (French government, 2022). However, to date, France remains one of Europe biggest consumer and seller of pesticides.

1.3.2. The risk of exposure to pesticide residues

So far, we have documented the value of the massive use of pesticides in society as an indispensable tool for increasing food productivity by controlling pests. Despite this, pesticides represent a major public health issue, due to their toxic potential on the cells of non-target organisms as well as in humans. Indeed, it is known that certain pesticide residues are capable of exerting specific effects at cell level, and of altering certain pathways regulating metabolism, growth, differentiation and cell survival. (Rizzati et al., 2016). Some pesticides are also known

to cause damages to DNA, or to induce mitochondrial respiratory chain dysfunction, leading to metabolic imbalance or cell apoptosis (Rizzati et al., 2016). Individually, pesticides reduce the antioxidant capacity of cells and promote oxidative stress, through the formation of reactive oxygen species and free radicals. This oxidative stress can lead to deleterious cascading reactions, deregulating cellular metabolic activities and apoptotic signaling pathways, or damaging DNA, which can promote the development of certain cancers (Rizzati et al., 2016). Figure 6 below summarizes the cellular and molecular targets of pesticides, and their effects on cellular activity.

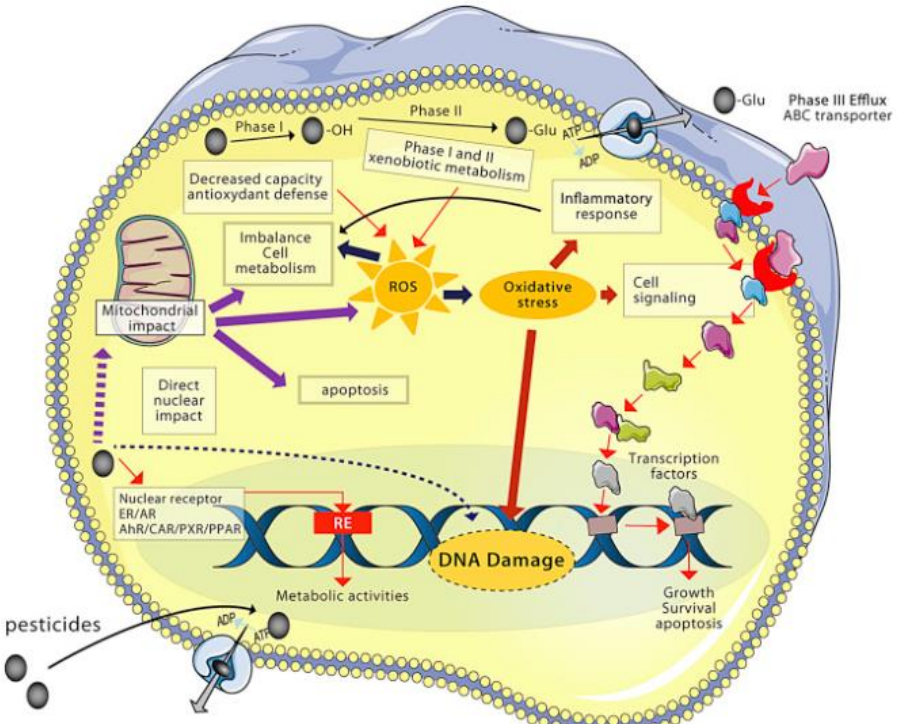

Fig.6. The impact of pesticides on cellular activity (from Rizzati et al., 2016).

Depending on the dose and time of exposure to pesticides, the toxicity induced in the body can be acute or chronic. For example, there have been several cases of pesticide poisoning among farmers and families of rural workers, due to high-dose exposure or inappropriate use. (Carvalho, 2017). In the event of acute pesticide poisoning, symptoms may include skin rashes, dizziness, nausea, abdominal pain, tremors, confusion, paresthesia, eye irritation, altered heart rhythm, and in the most severe cases, convulsions, coma and respiratory failure. (Osaili et al., 2023; Saillenfait et al., 2015; Jokanović, 2009). It is estimated that over 350,000 people die every year from unintentional pesticide poisoning. (Carvalho, 2017). It is also suspected that low-dose and extended exposure of rural workers and their families to pesticides may be linked to certain cancers, neurodegenerative and reproductive disorders (Inserm, 2021; Nougadère et al., 2014).

Humans are mainly exposed to pesticide residues chronically, through food. (Nougadère et al., 2014). Indeed, pesticides applied to crops can be transferred to different environmental compartments, outside their area of application. They can accumulate in soils and edible plant parts, and can also be transported by run-off water to watersheds and coastal lagoons, compromising terrestrial and aquatic food resources. (Carvalho, 2017). As a result, pesticide

residues can contaminate foodstuffs and accumulate in humans, exposing consumers to health risks.

Certain pesticides, such as organochlorine insecticides, which were massively used during the last century, were gradually prohibited worldwide after the 1960s (Narenderan et al., 2020). Indeed, due to their lipophilic nature, certain organochlorine (OCs) insecticides such as dichlorodiphenyltrichloroethane (DDT), dieldrin or lindane persist in soils and the environment over a long period, and repeated and continuous exposure of humans through contaminated foodstuffs may be associated with certain non-negligible health risks. For example, DDT was massively used from the 1940s onwards to control certain insects that carry malaria, and then banned in 1972 in the United States, and more gradually in other countries, due to concerns about its impact on human health and biodiversity. (Richardson et al., 2019; Eskenazi et al., 2009). Some studies suggest that exposure to DDT may promote the development of certain cancers, such as liver and pancreatic cancer (Eskenazi et al., 2009), as well as certain neurophysiological disorders such as cognitive dysfunction (Richardson et al., 2019). From the 1950s onwards, dieldrin was widely used to control insect pests such as termites, grasshoppers, locusts and textile parasites. (Kanthasamy et al., 2005). In 1987, the US Environmental Protection Agency (US EPA) banned the use of dieldrin in almost all its applications, due to its ability to bio-accumulate in humans and its carcinogenic, genotoxic and neurotoxic potential. (Richardson et al., 2019; Kanthasamy et al., 2005). As for lindane, it was massively used from the 50s onwards as an organochlorine insecticide, but also in lotions and 1% shampoos to combat certain vector-borne diseases such as gall and pediculosis (Nolan et al., 2012). Chronic human exposure to lindane is associated with serious systemic effects, including prevalent neurotoxicity, but also possible liver dysfunction and cardiac disorders (Nolan et al., 2012). Another well-known example is the massive use of the organochlorine insecticide chlordecone (CLD) in the French West Indies between 1973 and 1993, to combat the banana weevil, a pest of banana plants (Dallaire et al., 2012). Due to its physico-chemical properties, CLD has impregnated a large part of the West Indian ecosystem, accumulating in soils and along the trophic chain over time (Dallaire et al., 2012). Local populations were exposed to chlordecone mainly through the consumption of contaminated foodstuffs. This insecticide has been associated with an increased risk of prostate cancer, as well as some developmental disorders in children (Dallaire et al., 2012; Multigner et al., 2010).

Historically, organochlorine pesticides have been progressively replaced by organophosphate pesticides (OPs) and carbamates (CARs), because they have low environmental persistence, accumulate less in human tissues, and can act against a wide range of insect pests. More recent synthetic insecticides, the pyrethroids (PYR), are widely used as replacements for certain OCs and OPs, due to their action on a broad spectrum of parasitic insects and much lower toxicity on mammalian species, including humans (Gajendiran and Abraham, 2018; Saillenfait et al., 2015). Although considered less toxic than OCs, chronic exposure to OPs, CARs and PYRs is not without risk to human health either.

Overall, the literature reports various reviews and epidemiological studies associating chronic exposure to various pesticide residues (fungicides, herbicides, insecticides, etc.) with risks of cancer development (Mostafalou and Abdollahi, 2017; Alavanja et al., 2013), diabete (Mostafalou and Abdollahi, 2017), neurological disorders (Aloizou et al., 2020; Richardson et al., 2019; Mostafalou and Abdollahi, 2017), and reproductive and foetal development disorders (Sabarwal et al., 2018; Mostafalou and Abdollahi, 2017; Gilden et al., 2010).

Their use and the presence of residues in food products need to be strictly regulated, to protect users and consumers alike.

1.3.3. Regulation

In the EU, the marketing and use of pesticides are strictly regulated by European Commission Regulation (EC) No. 1107/2009 (Regulation (EC) No 1107/2009). No active substance in a plant protection product can be used without the approval of the European Commission (EC), whose health and environmental risk assessment is carried out by the EFSA. Following this assessment, EFSA establishes MRL for each individual substance, the regulatory threshold concentration of a residue above which the marketing of a foodstuff is prohibited. These regulatory limits are established with prior regards to the GAP for crop protection, and are based on lowest exposure necessary to protect vulnerable consumers (EFSA, 2023). Before an MRL is set, EFSA conduct assessment regarding the behavior of the residue and possible risks for human health through food. If risk assessment does not highlight any unacceptable risks to consumers, MRLs are set and harmonized among the EU member states (EFSA, 2023). European Commission Regulation No. 396/2005 covers all MRLs for pesticides, veterinary medicines and other bioactive substances (Nougadère et al., 2020; Regulation (EC) No 396/2005). Their monitoring in foodstuffs is therefore highly controlled, with particular emphasis on those intended for babies, which are sensitive matrices subject to stricter regulations and monitoring. Indeed, MRL are set and standardized at 0.01 $mg.kg^{-1}$ for all pesticide residues in baby foods (Nougadère et al., 2020).

The use of pesticides in the agricultural production system, and the presence of residues in foodstuffs, are therefore subject to strict regulations within the European jurisdiction. They represent a major public health issue, requiring the implementation of programs to monitor and control them in foodstuffs, in order to protect consumer health.

1.3.4. Monitoring and control plans of pesticide residues in foodstuffs

In the EU, the different Member States have to monitor the presence of pesticide residues in food products to ensure compliance with the regulatory thresholds set by EFSA. Regulation (EC) No.396/2005 sets out the rules for coordinating a multi-annual monitoring program across the various EU Member States (article 29). (Regulation (EC) No 396/2005). Under this program, the European Commission draws up a common list of food products and pesticide residues for analysis by the individual Member States. Food products are sampled at random, so as to assess the overall exposure of European consumers to pesticide residues (EFSA, 2023). In France, MCPs are organized by the Directorate General for Food (DGAL) and General Directorate for Competition, Consumer Affairs and Fraud Control (DGCCRF). The DGAL manages these programs at the primary production level, while the DGCCRF focuses on the downstream end of the food chain, right up to the consumer.

- Monitoring plans aim to provide a complete picture of the status of marketed products, in order to assess the level of exposure of consumers to pesticide residues. To obtain a representative, reliable and objective picture of the occurrence of residues, samples are collected randomly. To avoid bias in the results, targeted sampling is excluded (French government, 2013).

- The control plans consist in targeting sampling on foodstuffs from operators for whom previous results have revealed non-compliance, or for whom there are strong suspicions. The aim of these programs is to check compliance with MRLs and, in this respect,

compliance with good agricultural practices (particularly pre-harvest intervals), as well as the absence of the use of prohibited substances. In all cases, MRL exceedances are subject to a follow-up that takes into account the danger presented by the residue, and the level of foreseeable exposure to the foodstuff concerned (French government, 2013).

- Data from food monitoring programs is often inappropriate, as it is not representative of the entire French dietary habits, and therefore of consumers overall level of exposure (Hulin et al., 2014). As so, Anses carries out Total Diet Studies (TDS) to assess the presence of chemical substances of interest in foods as consumed by the French consumers. A list of food products is drawn up, based on the most consumed foodstuffs in terms of quantity/percentage of consumers, as well as food products thought to be the main sources of exposure to chemicals of interest (Hulin et al., 2014). These official studies are invaluable for assessing overall consumer exposure, with large-scale sampling representative of French dietary habits.

The Risk Assessment Department (DER) of Anses is responsible for assessing the exposure of French consumers to pesticide residues. Each year, Anses publishes an opinion based on the analytical data generated by the MCPs, to guide risk managers, make recommendations for future monitoring, and control programs (Nougadère et al., 2014).

The data generated by the European and national monitoring and control programs are published in an annual report by EFSA, providing information on food product compliance levels within the EU, as well as consumer exposure to pesticide residues. (EFSA, 2023). These data also enable EFSA to formulate recommendations for future monitoring programs, with the aim of best protecting the European consumer.

1.4. Exposure to veterinary drug residues

1.4.1. General informations

The production of livestock for human consumption depends on the use of veterinary medicines to prevent and control infection and disease, and to meet the ever-increasing demand for animal protein for human consumption. (Van Boeckel et al., 2015). It is estimated that global consumption of antimicrobial agents for veterinary use will increase by 11.5%, with 93,309 t used in 2017 and 104,079 t in 2030. Asia is the biggest consumer of antimicrobial agents, with 57,167 t in 2017, and an estimated 63,062 t in 2030. By contrast, Africa is the continent with the lowest consumption of antimicrobial agents, with 4606 t in 2017 (Tiseo et al., 2020). In 2017, China was the largest consumer of veterinary antimicrobial agents (45% of global use), and is expected to remain the largest consumer in 2030 (43%). The top 10 consumers in 2017 were China (45%), Brazil (7.9%), USA (7.0%), Thailand (4.2%), India (2.2%), Iran (1.9%), Spain (1.9%), Russia (1.8%), Mexico (1.7%) and Argentina (1.5%). For the period 2030, it is estimated that these countries will use around 72% of all veterinary antimicrobial agents consumed worldwide (Tiseo et al., 2020).

In France, the "Ecoantibio" plan was set up to reduce the use of antibiotics for veterinary use. In 2020, the volume of antibiotic sales amounted to 415 t, corresponding to a 54.8% reduction compared with 2011, the reference year for the first "Ecoantibio" plan (Anses-ANMV, 2021). The second "Ecoantibio" plan initiated in 2017, aims to consolidate achievements and maintain the momentum for the prudent and responsible use of antibiotics in veterinary medicine, in order to limit as far as possible the development of antibiotic resistance (Anses-ANMV, 2021).

Different types of drugs are authorized in different jurisdictions for veterinary indications in farm animals intended for human consumption. These include antimicrobial agents, which are the most widely used veterinary drugs and comprise a variety of drug classes (penicillin, tetracyclines, aminoglycosides, sulfonamides, nitroimidazoles, etc.). (Baynes et al., 2016). Other drugs include non-steroidal anti-inflammatory drugs (NSAIDs), used to combat chronic inflammatory pain, beta-agonists, antiparasiticides, growth hormones, etc. (Baynes et al., 2016). They can be used for (1) therapy, i.e. the treatment of animals presenting clinical symptoms; (2) metaphylaxis, i.e. the use of curative and preventive drugs on a herd of animals exposed to the same infectious risk. In other words, metaphylaxis aims to prevent the development of disease or infection in infected animals that are not yet showing clinical symptoms; (3) prophylaxis, i.e. the treatment of healthy animals to prevent disease and infection. (Aarestrup, 2005). Controversially, they can also be added continuously to farm animal feed to stimulate growth, but this practice is now prohibited by many jurisdictions as it promotes antibiotic resistance. Jurisdictions distinguish between the therapeutic use of drugs for animal health and welfare, and their use as growth promoters to improve feed efficiency. (Baynes et al., 2016).

1.4.2. Risks of exposure to veterinary drug residues through food

Misuse and abuse of veterinary drugs in food-producing animals, such as failure to observe withdrawal times after treatment, can leave residues in edible animal tissues, but also in milk and eggs (Baynes et al., 2016). These residues may correspond to the pharmacologically active substance of the drug, or they may be found in foodstuffs in the form of conjugated metabolites (Baynes et al., 2016). However, exposure to veterinary drug residues through food is not without risk to human health. Several studies link exposure to drug residues in animal-derived foodstuffs to the risk of developing antibiotic resistance (Baynes et al., 2016; Aarestrup, 2005). Indeed, the intensive use of antimicrobial agents in the modern food animal production system has favored selection pressures on bacteria, which have evolved to acquire resistance genes to these drugs (Aarestrup, 2005). This selection for resistance to antimicrobial agents in animals intended for human consumption could pose a risk to health, as the development of resistant bacteria in humans could make it difficult to treat certain infections (Baynes et al., 2016; Aarestrup, 2005). To reduce this risk, many jurisdictions no longer approve the use of antimicrobial agents as growth promoters in farm animals. Thus, a distinction is made between uses for therapeutic purposes for animal welfare and health, and growth promotion to improve feed productivity in food animals (Baynes et al., 2016).

In addition to antibiotic resistance, there are also possible links between exposure to veterinary drugs and the development of allergic reactions. For example, consumer exposure to penicillin contained in animal-derived foodstuffs favors the development of minor (rash) or severe (anaphylaxis) allergic reactions (Baynes et al., 2016). Other classes of drugs, such as sulfonamides, there is little data correlating potential risks associated with the consumption of

animal-derived foodstuffs containing traces. However, sulfonamide toxicity in humans is known and adverse reactions are common, such as skin rashes, severe toxidermia, blood dyscrasias, hemolytic anemia, etc (Baynes et al., 2016).

Although data on the risks of consuming animal-derived foodstuffs containing traces of drug residues are not always available, those on the risks of using certain classes of drugs in humans, such as sulfonamides, are. They alert us to the possible risk of exposure to these residues through food, and to the need to regulate their use and presence in foodstuffs from food-producing animals.

1.4.3. Regulation

In Europe, the Committee for Medicinal Products for Veterinary Use (CVMP) of the European Medicines Agency (EMA) is responsible for establishing MRLs for veterinary medicinal products used in food-producing animals. European Regulation n°470/2009 establishes Community procedures for setting MRLs for residues of pharmacologically active substances in animal-derived foodstuffs (Regulation (EC) No 470/2009). Table 1 (Annex) of European Commission Regulation n°37/2010 on pharmacologically active substances and their classification with regard to MRLs in animal-derived foodstuffs, classifies authorized pharmacologically active substances, with their respective MRLs (or non-applicable MRLs) (Regulation (EU) No 37/2010). Table 2 of the annex to this regulation classifies pharmacologically active substances banned from use (Regulation (EU) No 37/2010).

The European Union has also introduced the principle of a minimum required performance limit (MRPL), which corresponds to the minimum concentration at which a residue must be found and confirmed in animal-derived foodstuffs after analysis (Delatour et al., 2018). This was put in place to better protect consumers from pharmacologically active substances that have been banned from use in the EU but are present in imported foodstuffs, such as chloramphenicol, nitrofurans and medroxyprogesterone acetate (Delatour et al., 2018). In addition, the EU has also prohibited the use of pharmacologically active substances for growth promotion in food-producing animal species, to limit the development and spread of antibiotic resistance in humans (Baynes et al., 2016).

The use of veterinary drugs in the production of farmed animals intended for consumption, and the presence of residues in animal-derived foodstuffs, are therefore subject to strict regulations. This reflects the risks they pose to human health, as well as the need for effective programs to monitor and control veterinary drug residues in these products, in order to protect the consumer.

1.4.4. Monitoring and control plans for veterinary drug residues in animal origin foodstuffs

In the EU, individual member states must monitor the presence of veterinary drug residues in food-producing animals and in animal-derived foodstuffs. Regulations (EU) 2022/1644 and (EU) 2022/1646 cover the legislation for the implementation of randomized monitoring plans and risk-based control plans (Regulation (EU) No 2022/1644; Regulation (EU) No 2022/1646). In France, the DGAL organizes the implementation and management of these MCPs, and the Anses, under cover of the National Agency for Veterinary Medicines (ANMV), is responsible for assessing and managing the risk of consumer exposure to veterinary drug residues. The data

generated by the national monitoring and control plans are published in an annual report by EFSA, to provide information on animal-derived foodstuffs compliance levels within the EU, as well as the degree of consumer exposure to veterinary drug residues. These data also enable EFSA to formulate recommendations for future monitoring programs, with the aim of better protecting the consumer.

1.5. Exposure to mixtures of chemical substances: cocktail effects

The wide range of chemicals found in food products implies that the consumer is continually exposed to combinations of different substances that can interact with each other, even at low doses, and induce joint effects that can affect the overall level of toxicity (Hernández et al., 2017; Rizzati et al., 2016). Chronic and continuous exposure to mixtures of chemical substances, such as pesticide residues, is a more realistic consumer exposure scenario, involving different interactions and combination of effects (Hernández et al., 2017). These combinations of effects are also known as "cocktail effects", and can result in additive effects or synergistic or antagonistic interactions.

Chemicals with a similar molecular mechanism of action can lead to a "dose addition" effect, with a risk of cumulative toxicity (Bopp et al., 2018; Hernández et al., 2017; Rizzati et al., 2016). These effects can be modeled and predicted from the sum of the concentration of the different substances in the mixture and sharing the same mechanism of action. Models based on "dose addition" effects are the most frequently used, and provide reliable estimates for risk assessment (Hernández et al., 2017). Conversely, when the toxicological effects of substances in a mixture are the consequence of different molecular mechanisms of action, the term "independent action" is used (Bopp et al., 2018; Hernández et al., 2017). This combined response model is calculated from the biological responses of each substance using the probability theory of independent random events (Hernández et al., 2017; Kortenkamp, 2007). Finally, the different substances in a mixture can interact with each other through synergism or antagonism (Bopp et al., 2018). Synergism occurs when the toxic effects of a mixture are greater than the responses of non-interacting models, and potentiation occurs when a non-toxic compound exacerbates the toxicity of a co-exposed toxic compound (Hernández et al., 2017; Rizzati et al., 2016; Kortenkamp, 2007). In contrast, antagonism occurs when the effects of a mixture result in less toxicity than expected (Hernández et al., 2017; Rizzati et al., 2016; Kortenkamp, 2007). Synergistic combined effects pose real concerns for food safety and public health. They are less predictable, and induced toxicological responses can occur at concentrations below the regulatory thresholds set for each individual substance.

Recently, an overview of reviews published by Eales et al. (2022) highlighted that exposure to different phthalates (plastic-related chemicals) and metabolites may result in potential additive or synergistic “cocktail effects”, inducing toxicological effects at levels below the "safe doses" set by regulatory authorities.

In 2017, Hernández et al (2017) published a review reporting examples of combined toxicological effects between different pesticide residues. For example, a synergy is possible between triazine herbicides (TRIA) and OPs pesticides, with an induction of CYP450 monooxygenase enzymes by TRIA herbicides, which promotes the metabolization of

organophosphorothioate pesticides to their far more toxic -oxon form, significantly increasing their toxicity (Hernández et al., 2017). Other examples of synergistic interactions concern the toxicity of PYR insecticides, which is enhanced by the presence of fungicides from the triazole family (TriAZ), as these inhibit CYP450 proteins required for the metabolism of lipophilic xenobiotics such as PYRs (Hernández et al., 2017). The study conducted by Rizzati et al. (2016) highlights synergistic interactions between the OC insecticide endosulfan and the CAR insecticide carbofuran, as well as between two TRiAZ fungicides (tebuconazole/etaconazole) and a dicaboximide fungicide (vinclozolin), in human breast tumor cells at low doses. The synergistic effect of a mixture of malathion (OP) / cypermethrin (PYR), bitertanol & propiconazole (TriAZ) / terbuthylazine (TRIA), was significantly observed and at low concentrations (Rizzati et al., 2016). Although these various results remain to be confirmed on other human and animal cell lines, they suggest the potential non-negligible impact that chemical mixtures can have on human health.

1.6. Risk assessment of exposure to chemical mixtures

Two approaches can be used to assess the potential hazard of a mixture of chemical substances. The first is the "top-down" approach, involving an assessment of the entire mixture. However, the substances primarily involved in toxic responses, as well as possible interactions, cannot be characterized (Hernández et al., 2017). In contrast, the "bottom-up" approach assesses the toxicity of each individual substance in the mixture. Mathematical and predictive models are then used to predict the combination effect of the mixture (Hernández et al., 2017). Figure 7 below, summarizes these two approaches, as well as the main combined effects of mixtures of chemical substances. Various cumulative risk assessment methods have been developed in different jurisdictions (Rotter et al., 2018).

In Europe, EFSA is developing a cumulative risk assessment methodology for pesticide residues, and designates each individual substance to a cumulative assessment group (CAG) based on its toxicological profile. If individually assessed substances induce a common toxicological effect on a target organ, they are assigned to the same CAG (Caldas, 2023). Recommendations are available for grouping individual substances into CAGs, for cumulative human risk assessment. EFSA has also published "proof of concept" reports on the allocation of pesticide residues within GACs for their effects on the thyroid and nervous system in particular (Authority (EFSA) et al., 2019a, 2019b). EFSA then recommends using the "dose addition" model to assess the cumulative risks of the substances in the mixture ("bottom-up" approach, Fig.7). Indeed, EFSA Panel on Plant Protection Products and their Residues (PPR) states that while the toxic interaction of residues in food cannot be excluded, there is no evidence that this can occur at exposure levels in food to the extent that it affects human health (Authority (EFSA), 2008a).

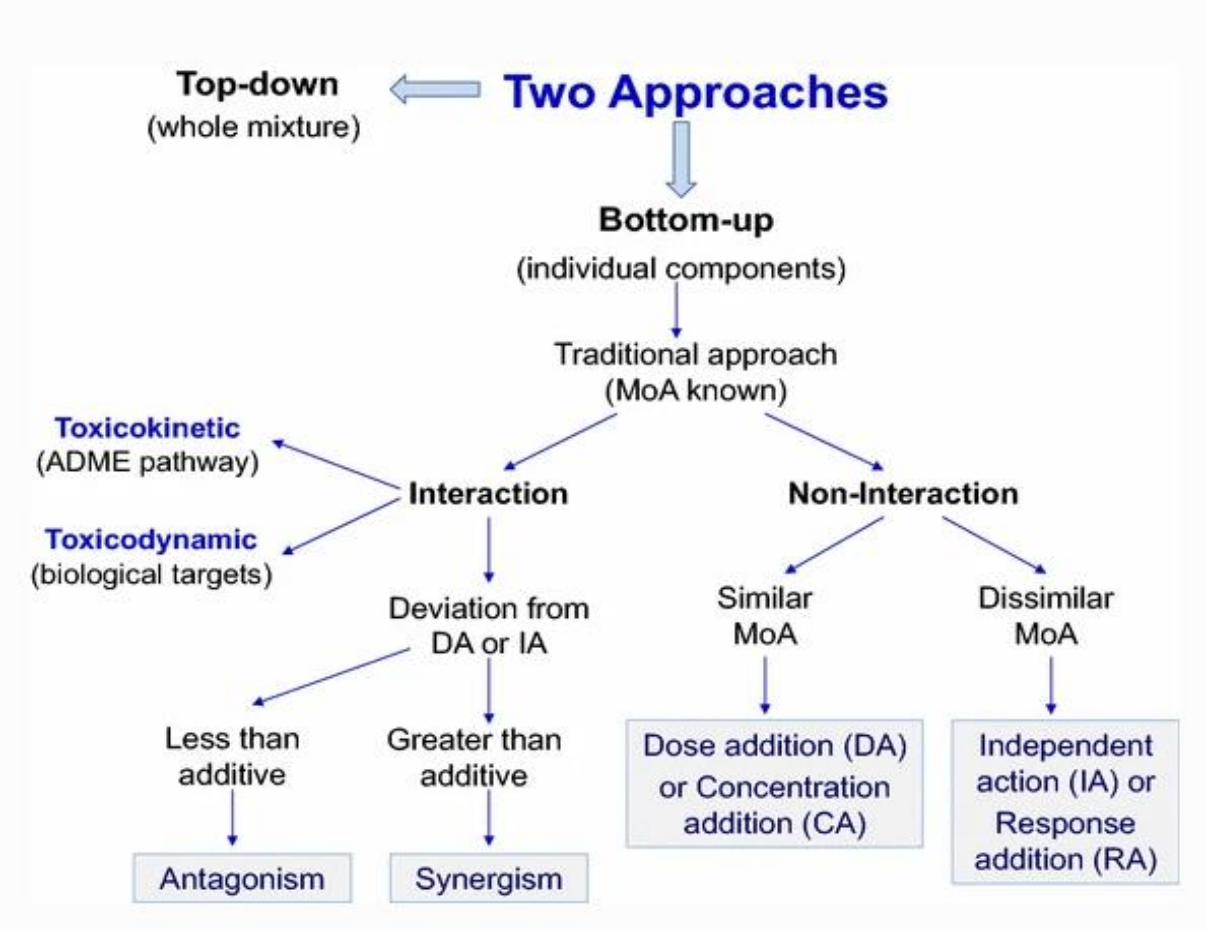

Fig.7. Approaches used to assess the hazard of chemical mixtures, as well as the main combined effects (from Hernández et al., 2017).

1.7. The current limits in regulation of chemical mixtures

The European Commission recommends that the cumulative effects of mixtures of pesticide residues be taken into account when assessing dietary risks, and where appropriate methodologies for cumulative risk assessment exist (Caldas, 2023). However, some concerns have been expressed regarding current regulations, as the MRLs covered by European Commission Regulation 396/2005 only depend on the risk assessment for each individual substance (Regulation (EC) No 396/2005).

In the USA, regulations do not take cumulative risk assessment into account when setting MRLs in foodstuffs, although they do serve to provide recommendations to guide risk management measures to protect the consumer (Caldas, 2023).Aspects relating to the risks of combined effects are very complex to address, as it should be kept in mind that there is a considerable number of chemical substances to which humans are exposed through food, as well as virtually unlimited combinations of mixtures. Moreover, not all the toxicological profiles and molecular mechanisms of action of the chemical compounds found in foodstuffs are known, in addition to the possible interactions and synergies between substances that cannot be excluded.

All these parameters further complicate and limit the current cumulative risk assessment and regulation of chemical mixtures. In the field of water, for example, cumulative risk is taken

into account in regulations, as a quality limit of 0.5 µg.L^{-1} was fixed as the sum of all individual pesticide residues quantified in drinking water, in compliance with appendix 1 of the decree of January 11, 2007 of the public health code (French government, 2007).

In the food field, the difficulty would be to define limits for which there would be no cumulative effects for mixtures prevalent in products and of concern to human health. Tackling all the scientific and legal issues surrounding chemical mixtures in foodstuffs is a long and complex normative process, but the methodologies implemented to address them, as well as the scientific thinking around these aspects, are becoming increasingly developed.

1.8. What are the challenges to address for improving food safety?

As discussed so far, foodstuffs can be a source of exposure to multiple chemical substances, which can individually or in combination present a risk to the consumer. The European Union regulates the presence of contaminants such as pesticide or veterinary drug residues in foodstuffs, and sets MRLs for each individual substance. Priority lists are then drawn up for the official monitoring and control of residues in food products. However, there are two main drawbacks with the current system:

The first issue is that contaminants of concern that do not feature on the prioritized lists of molecules are not monitored, even though they are likely to be found in foodstuffs. This could be the result of accidental contamination, or misuse and illegal use of certain products. For example, some food products, such as pork and wild mushrooms, were accidentally contaminated with dioxins and nicotine respectively (Eskola et al., 2020; Authority (EFSA), 2009; Authority (EFSA), 2008b). In 2013, beef was substituted for horsemeat in some food products from various EU countries, and an illegal veterinary drug, phenylbutazone, was identified (Eskola et al., 2020; Authority (EFSA) and Agency (EMA), 2013). More recently, in 2017, a Europe-wide food safety scandal broke out, in which the illegal use of a veterinary drug, fipronil, led to the contamination of eggs from Belgium, which were then distributed to other EU member states (Eskola et al., 2020; Authority (EFSA) et al., 2018). These examples, although uncommon, remind us that no system is perfect, but that it is nonetheless necessary to open a common reflection to identify its shortcomings and make improvements, in order to better protect the consumer.

The second problem, discussed in the previous section, is that MRLs are only set following risk assessments for each individual substance. However, a substantial number of substances can be found in food products, with the possibility of them combining and interacting with each other, causing toxic effects at levels below the MRLs. Current regulations do not reflect a realistic risk of consumer exposure.

In the light of these issues, it becomes imperative for laboratories to dispose of methodologies and tools that can improve the characterization of the food chemical exposome of the French consumer. In other words, the development of multi-residue methods for contaminants in food products is essential to monitor residues that would otherwise not be prioritized officially for analysis, and to highlight as far as possible the prevailing mixtures of chemical substances to which consumers are exposed. Such methods, and the data generated,

can be used not only for more realistic risk assessment, but also for a better understanding of what surrounds individuals, and what characterizes their external exposome.

The remainder of this state of the art will focus on the methodologies and analytical tools used for the analysis of contaminants in foodstuffs, with an overview of what is officially used in routine laboratories, the advantages and limitations, and the tools that could considerably improve the food safety system.

1.9. Sample preparation for analysis of contaminants in food

Improvements in sample preparation techniques over the last two decades have led to the development of the concept of multi-residue analysis of contaminants in complex matrices. This section compares and contrasts sample preparation methods used for the analysis of organic contaminants. It describes several sample preparation techniques including: (1) liquid-liquid extraction (LLE); (2) solid-phase exctraction (SPE); (3) solid-phase microextraction (SPME); (4) accelerated solvent extraction (ASE); (5) Quick Easy Cheap Effective Rugged and Safe (QuEChERS); (6) Quick Polar Pesticide Extraction (QuPPE); (7) and so-called "mega-methods". The advantages and limitations of each method presented are discussed in this section.

1.9.1. Liquid-liquid extraction (LLE)

LLE is one of the best-known and well-established method for the extraction of organic contaminants such as pesticides. It is reliable and compatible with most instrumentations including LC/GC-MS/MS and -HRMS. LLE principle relies on the difference in affinity of a solute towards two immiscible or partially miscible solvents, which is determined by the equilibrium distribution coefficient (Wahab et al., 2022). LLE often uses hexane, acetonitrile, ethyl acetate, chloroform and 1,2-dichlorometane as organic solvents for the extraction of pesticide residues (Wahab et al., 2022). The principle of LLE technique is summarize in Figure 8.

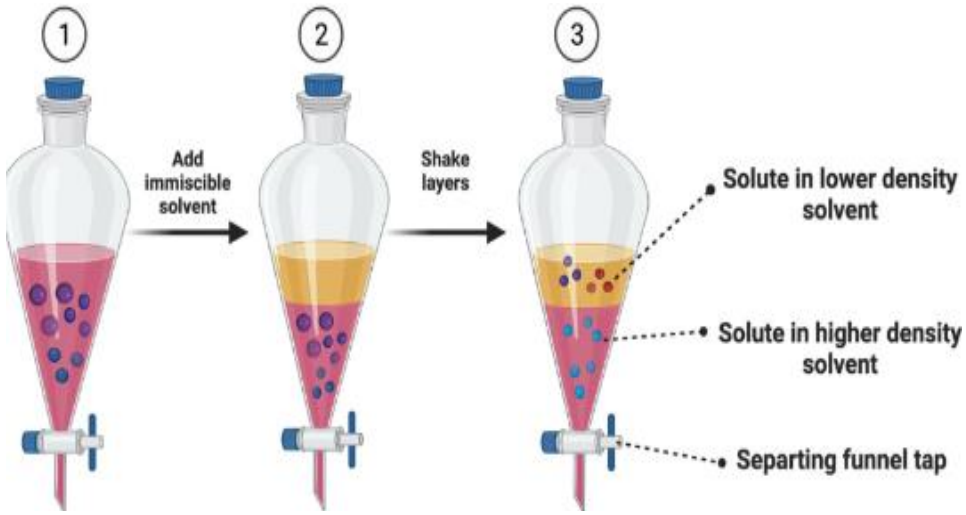

Fig.8. Principle of liquid-liquid extraction technique (from Wahab et al., 2022).

In litterature, some studies reported the use of LLE for the extraction of pesticide residues from food samples. For example, Sannino et al. (2004) used LLE with acetate-cyclohexane (50:50 v/v) as organic solvents for the extraction of 24 pesticide residues in apple and tomato purees and concentrated lemon juice. Bedendo et al. (2012) used hollow fiber microporous membrane LLE technique for the extraction of 18 pesticide residues from different classes in orange juices. More recently, Shin et al. (2022) used LLE technique in comparison with a QuEChERS-based protocol (which will be discussed later), for the extraction of 275 multiclass pesticide residues in spinach, rice, and mandarins.

LLE technique is easy-to-follow and suitable for multiclass analysis of pesticides, and displays low-cost per analysis and for material requirements (Qin et al., 2023; Song et al., 2022). However, LLE also consumes toxic organic solvents, it is time-consuming and less effective for polar analytes (Mandal et al., 2023; Song et al., 2022; Wahab et al., 2022). Moreover, since it is producing emulsion during extraction process, some of analytes of interest could be loss in evaporation.

1.9.2. Solid phase extraction (SPE)

SPE is an extraction technique developed in the 70s, and has since become one of the most widely used procedures for the separation and concentration of residues of interest, as well as the purification of food samples (Chen et al., 2010). This technique relies on the selective affinity of compounds contained in a liquid (the mobile phase) for an adjacent porous solid phase (stationary phase), through which the sample is percolated (Mandal et al., 2023; Wahab et al., 2022; Lucci et al., 2012). The adsorbent materials of the stationary phase are preconditioned and activated with water or organic solvent (Mandal et al., 2023; Wahab et al., 2022; Lucci et al., 2012). The analytes of interest are adsorbed onto the solid phase, while certain impurities are removed with the mobile phase. A selective cleaning step removes matrix impurities retained on the stationary phase. An elution step using an appropriate organic solvent is then required to desorb the analyte from the stationary phase (Mandal et al., 2023; Wahab et al., 2022; Lucci et al., 2012). The organic solvent used in SPE depends on the physico-chemical properties of the analyte (ionic or non-ionic). Figure 9 below illustrates the principle of SPE.

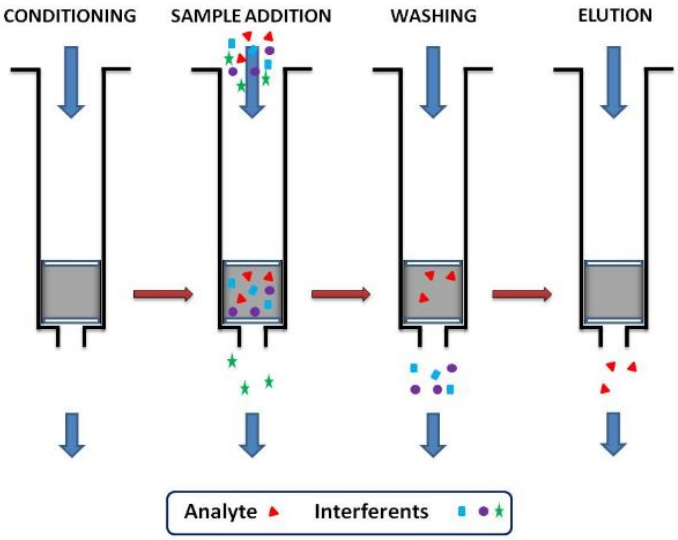

Fig.9. Principle of solid phase extraction technique (from Lucci et al., 2012).

The adsorbents used can be polar (normal phase), non-polar (reverse phase), or used for ionic or immunoaffinity retention (Lucci et al., 2012). The selection of the SPE cartridge depends on the properties of the analytes of interest to be analyzed, as well as the matrix impurities to be removed. Various materials can be used for separation, analyte preconcentration and purification of food extracts, such as Florisil, octadecyl (C18), graphitized carbon black (GCB) and Envi-carb cartridges. Weak anion exchange sorbents such as primary and secondary amine (PSA), aminopropyl (NH2) or diethylaminopropyl (DEA)-modified silica, can be used in combination with strong anion exchange sorbents (SAX, QMA) to purify food extracts (Mandal et al., 2023). Table 1 below gives an overview of some studies that have reported the use of SPE during sample preparation, for the multi-residue determination of contaminants in various food matrices.

Table 1. Studies reporting the use of SPE for separation, preconcentration of contaminants, or purification of food matrices, for multi-residue analysis of contaminants.

Sample preparation	Sorbent(s) used during SPE	Matrix	Class of organic contaminant	Recovery (%)	LOQs ($\mu g.kg^{-1}$)	Reference
SPE	Graphitized Carbon Bulk (Envi-carb™)	wheat grains, peaches, lettuce aubergine, cabbage, cauliflower, guava, okra, onion, potato, apple, banana, grape, mango, orange and pomegranate	25 multiclass pesticide residues	73-117	0.5-10	(Balinova et al., 2007)
SPE	GCB/PSA		60 multiclass pesticide residues	74-111	0.8-11.8	(Sivaperumal et al., 2015)
SPE	PS-DVB or PS-DVB + Diethylaminopropyl (DEA) modified silica	fresh fruits and vegetables	90 multiclass pesticide reisdues	61-121 (in apples, green beans, oranges)	10 or 20 (in apples, green beans, oranges)	(Štajnbaher and Zupančič-Kralj, 2003)
SPE	SBA-15-C18	meat	23 veterinary drugs (β-blockers, β-agonists and non-steroidal anti-inflammatory drugs)	28-98	0.02-62.50	(Casado et al., 2016)
QuEChERS and SPE	Carbon/NH_2	fruits and vegetables	439 multiclass pesticide residues	70-120 (in apple, tomato, grappe, spinach)	/	(Li et al., 2018)
SPE	C_{18} and GCB/PSA	green tea leaves	400 multiclass pesticide residues	55-130	2--10	(Ly et al., 2020)
SPE	SAX/PSA, Florisil, C_{18}	grape, orange, tomato, carrot, green mustard	9 organochlorine and pyrethroids pesticides	74-108* **(SAX/PSA)**, 83-119* **(Florisil)**, 50-180 **(C18)**	10-50 (in orange samples)	(Sharif et al., 2006)

*recoveries for captafol were not included as >> 120%

The SPE technique offers certain advantages over traditional liquid-liquid extractions: it requires a lower solvent volume, is faster, automatable and provides clean extracts with high recoveries for analytes of interest, as well as good repeatability (Song et al., 2022; Lucci et al., 2012). However, it displays also certain drawbacks: SPE can be tedious and difficult to master. Indeed, application of SPE requires in-depth optimization as various parameters could impact the efficiency of procedure such as the amount of sorbent used, the volume and type of organic solvent, pH of the sample and time required for desorption (Song et al., 2022). Moreover, SPE generally requires a high sample volume (Moinfar et al., 2022), and the selection of suitable adsorption materials for multiresidue analysis of contaminants with different physico-chemical properties can be problematic (Mandal et al., 2023; Wahab et al., 2022). Finally, as mentionned by Song et al. (2022), adsorbents materials are prone to clogging, and the SPE setups commercially available would considerably increase the cost in case of high-throughput analysis of samples, which is a non-negligible aspect for laboratories.

1.9.3. Solid phase microextraction (SPME)

SPME is a simple, fast and solvent-free extraction method that was first introduced by Arthur and Pawliszyn in 1990 (Arthur and Pawliszyn, 1990). Its principle relies on the partitioning of analytes between a fixed fiber coated with a liquid or solid extraction phase (or both), and the sample matrix (Narenderan et al., 2020). The analytes are then absorbed or adsorbed depending on whether the extraction phase is liquid or solid, respectively. The fiber is then removed, and desorption of the analytes usually takes place with its introduction into a gas (thermal desorption) or liquid (solvent desorption) chromatographic system (Arthur and Pawliszyn, 1990).

Since its introduction, several SPME fibers were marketed and used for extraction of organic contaminants and chemicals. In litterature, Cortés-Aguado et al. (2008) used a polydimethylsiloxane–divinylbenzene (PDMS-DVB) SPME fiber coupled with GC-MS and GC-MS/MS for the determination of 54 pesticide residues in orange, pineapple and peach juices. First, a 10-min required SPME extraction-screening method was carried out for the detection of residues above a predetermined concentration with GC-MS operating in full-scan mode (Cortés-Aguado et al., 2008). Then, the non-negative juice samples were re-analyzed using a 55-min required SPME extraction-quantitative method coupled with GC-MS/MS detection, to confirm and quantify residues. The method provided recoveries ranged between 73-96%, and limits of detection (LODs) between 0.4-19.6 $\mu g.L^{-1}$ (Cortés-Aguado et al., 2008). All the procedure only required 1 mL of juice, and was easy-to-use, semi-automated, and provided high sensitivity and selectivity. Abdulra'uf and Tan. (2015) reported the use of PDMS fiber-type for SPME extraction of 14 pesticide residues in apple, tomato, cuncumber and cabbage. SPME extraction was coupled to GC-MS detection. Recoveries were between 73-118% and LOQs between 1.15-27.76 $\mu g.kg^{-1}$ (Abdulra'uf and Tan, 2015).

Although SPME technique is easy-to-follow, fast and solvent-free, the main drawbacks are the quality and fragility of the fibers, and instability of the coatings (Song et al., 2022; Narenderan et al., 2020). Furthermore, application of SPME is mainly limited for non-polar and volatile organic compounds, and the cost per analysis is high (Song et al., 2022). With regards to these limitations, application of SPME in routine for high-throughput analysis of samples and to extend the analytical scope appears to be limited.

1.9.4. Accelerated solvent extraction (ASE)

ASE, also known as pressurized liquid extraction (PLE), is an automated solid-liquid extraction method, which relies on the extraction of compounds from a solid or semi-solid matrix using conventional solvent under high temperature (50-200°C) and high pressure (500-3000 psi) (Barp et al., 2023; Qin et al., 2023). The increased temperature leads to a decrease of the viscosity of the solvent, allowing better interactions with matrix and making it easier diffusion of analytes. This enables increasing extraction efficiency while reducing time required for extraction (Barp et al., 2023; Qin et al., 2023). The increased pressure allows keeping solvent at liquid state, below its boiling point. Figure 10 below describes the set-up required and the different steps during ASE.

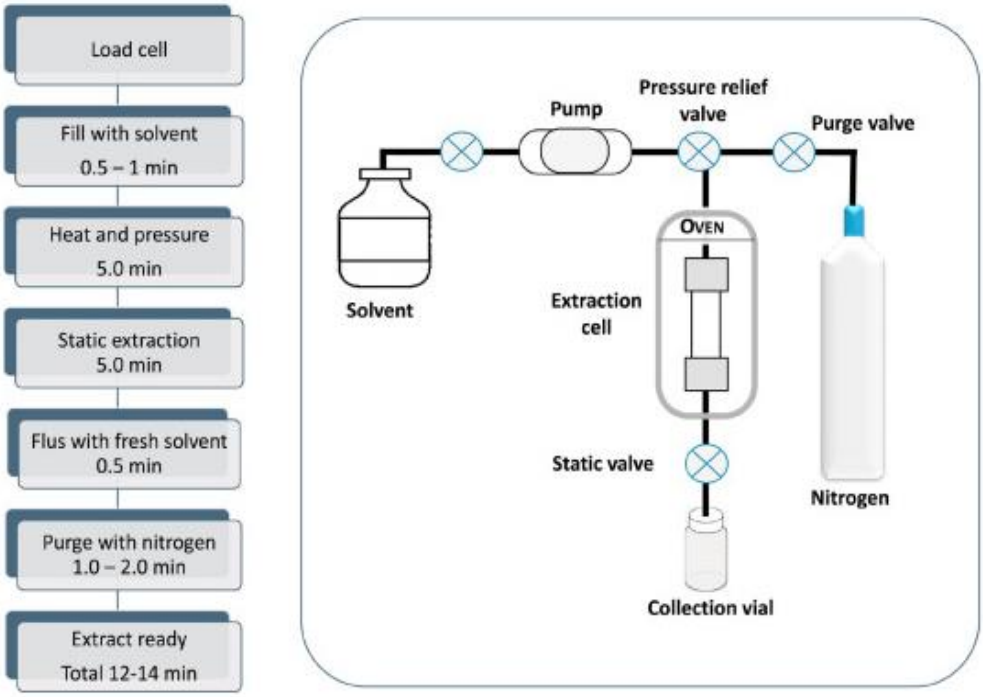

Fig.10. Overview of a schematic diagram of an ASE system (from Andreu and Picó, 2019).

In comparison with other extraction methods, ASE displays many advantages. Indeed, this technique results in equal or higher extraction efficiency while reducing time of extraction and solvent consumption required, and the automation of ASE allows simplifying analytical process and increase reproducibility (Barp et al., 2023; Qin et al., 2023). Furthermore, ASE has shown to be suitable for extraction of various organic contaminants from food samples. However, ASE could result in co-extraction in high proportion of impurities from the sample. Thus, this extraction technique is oftenly employed in simultaneously with various purification materials to reduce co-extractive matrix compounds (Huerta et al., 2013). Table 2 below displays relevant publications that reported the use of ASE for the extraction of multiclass chemicals in various foodstuffs.

Table 2. Overview of some studies that reported the use of ASE technique for extraction of various organic contaminants from foodstuffs.

Matrix	Class of organic contaminant	Extraction solvent	Additional sample treatment	Recovery (%)	LOQs (µg.kg^{-1})	Reference
fish	18 polychlorinated biphenyls (PCBs)	acetone/*n*-hexane (1:1, v/v)	SPE (Extrelut-NT3 and Silica cartridges)	87-105	1.3-3.8	(Ottonello et al., 2014)
clam and crab	7 dioxins, 10 furans, 12 PCBs	**PCBs**: dichlorometane/hexane (1:1, v/v) **dioxins and furans**: toluene	concentration	70-120	/	(Subedi et al., 2014)
fish (liver and tissues)	20 pharmaceuticals and metabolites	methanol	gel permeation chromatography (GPC)	28-126	0.04-3.28	(Huerta et al., 2013)
fatty foods	12 pharmaceuticals (steroid hormones and antibiotics)	*n*-hexane/methanol/acetonitrile (2:1:1, v/v/v)	concentration + filtration (0.22 µm nylon membrane filters)	82.2-115	0.4-25.0	(Wang et al., 2019)
tuber crops	150 multiclass pesticide residues	ethyl acetate	water partitionning + concentration	70-120	0.1-10	(Khan et al., 2018)

As displayed in Table 2, ASE technique is appropriate for the extraction of various organic contaminants, such as pesticide residues, pharmaceuticals, dioxins, PCBs, and metabolites among others, in complex food matrices. However, despite all the advantages, major drawbacks of ASE consist in requirements of additional sample treatment after extraction, which may be tedious, as well as the high instrumentation cost of the commercially available systems, explaining why ASE is not as widespread in laboratories (Parrilla Vázquez et al., 2019).

1.9.5. Quick Easy Cheap Effective Rugged and Safe (QuEChERS)

The QuEChERS technique was first introduced in 2003 by Anastassiades et al. (2003) originally for the analysis of multiclass pesticide residues in food samples with high moisture content. This method rapidly became a well-established in laboratories, and nowadays, QuEChERS stands out as the most widely used technique for the monitoring of contaminants in various foodstuffs. A fast litterature search in ScienceDirect database (Elsevier) was performed using the following keywords: “QuEChERS”, “QuEChERS, pesticides” and “QuEChERS, contaminants” to highlight the increasing interest in QuEChERS over years. Since 2003, 5439 articles were published using “QuEChERS” as keyword, and 3819 and 2640 when using “QuEChERS, pesticides” and “QuEChERS, contaminants”, respectively. Particularly, as shown in Figure 11 below, the use of QuEChERS method has considerably increased since 2010, and the number of articles published per year is constantly rising. This can be explained by the fact that the method can address the main limitations of the other extraction techniques described previously. Indeed, QuEChERS requires less time and solvent consumption for sample extraction, it is easy-to-follow and inexpensive, and suitable for the

high-throughput determination of hundreds of contaminants with high recoveries in various food samples (Musarurwa et al., 2019).

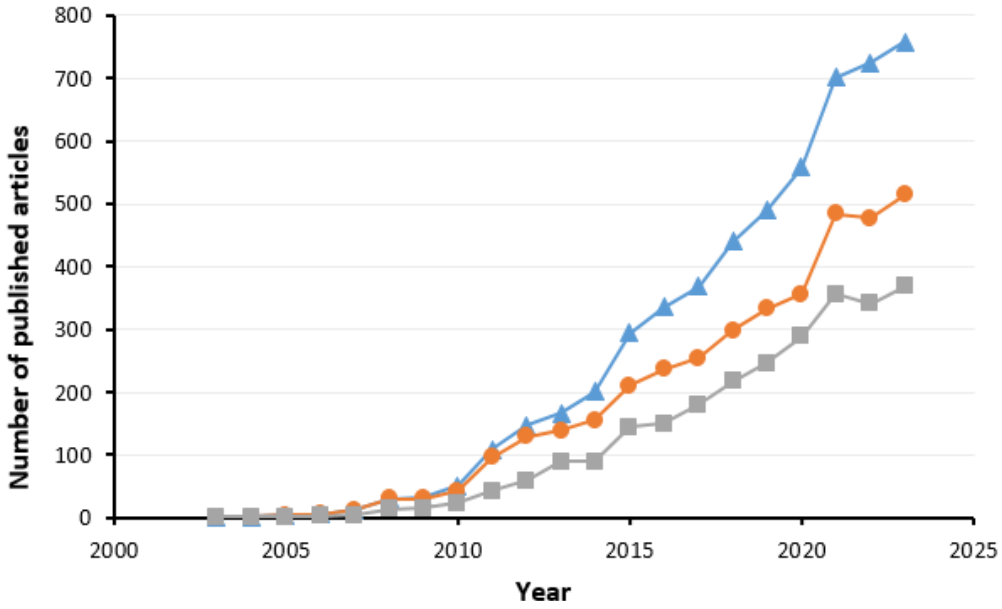

Fig.11. Evolving interest of researches related to QuEChERS since 2003 based on a litterature search on ScienceDirect according to the following keywords: "QuEChERS", "QuEChERS, pesticides" and "QuEChERS, contaminants".

The QuEChERS method involves a liquid-liquid extraction step using acetonitrile as extraction solvent and salting out for partitionning, followed by a cleanup of the extracts using dispersive-SPE (d-SPE) (Musarurwa et al., 2019; Santana-Mayor et al., 2019). Acetonitrile is used as extraction solvent for its polarity and miscibility with water, making easy to penetrate the aqueous fraction of the sample, allowing extract a wide range of contaminants with different physio-chemical properties. The addition of salts reagents enables the partitionning of organic and water phases, facilitating the extraction (Musarurwa et al., 2019).

a. Original method

There are three widespread-used standard QuEChERS protocols for the analysis of contaminants in food matrices, including the original method proposed by Anastassiades et al. (2003), as well as two declined and buffered-versions of QuEChERS. Original method used anhydrous magnesium sulfate ($MgSO_4$) and sodium chloride (NaCl) as extraction salts to remove water from samples and induce partitionning, forcing analytes to migrate towards the organic supernatant (Musarurwa et al., 2019; Santana-Mayor et al., 2019). A following cleanup of the extract using d-SPE with a combination of $MgSO_4$/PSA for removal of fatty acids, some sugars and pigments, while $MgSO_4$ removes the remain containing of water (Alcântara et al., 2019; Musarurwa et al., 2019).

b. Buffered versions of QuEChERS

Lehotay et al. (2007) proposed a version of QuEChERS using acetate buffer to stabilize pH-sensitive and acidic-sensitive compounds, called AOAC 2007.01 method. The method implies the use of acetonitrile (1% acetic acid), as well as $MgSO_4$ and sodium acetate (NaOAc) as

extraction salts. The following d-SPE to clean the extracts is performing using a combination of $MgSO_4$/PSA. The European commission proposed a citrate-buffered version of QuEChERS (EN

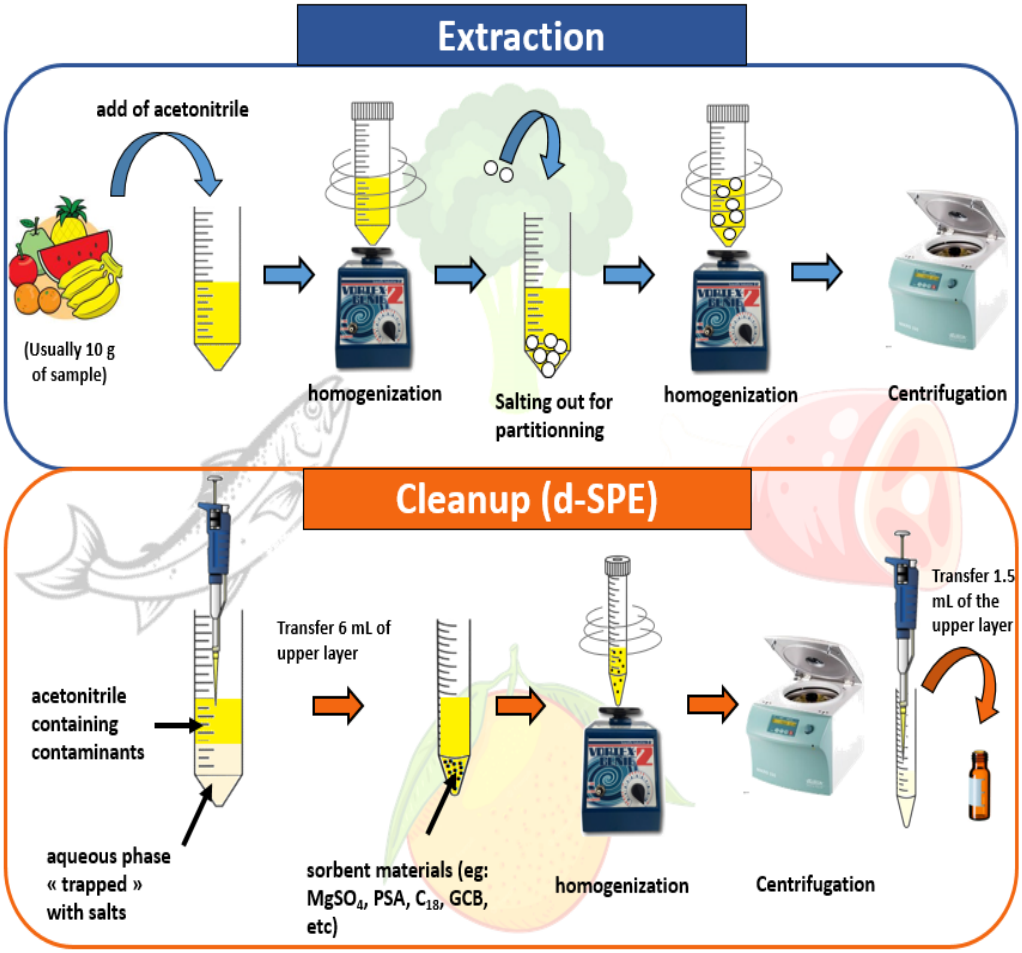

Fig.12. Diagram of a QuEChERS-based protocol.

15662) using $MgSO_4$, NaCl, sodium citrate and sodium citrate sesquihydrate for liquid-liquid partitionning under optimal pH conditions for acidic-sensitive compounds or those sensitive to pH variations (Anastassiades et al., 2007a). A d-SPE is then carried-out using a combination of $MgSO_4$/PSA /C_{18}, with C_{18} being used in addition to remove additional lipid contents from fatty foods. Figure 12 below overview the main steps of a QuEChERS protocol.

Although these three protocols are well-established, QuEChERS can be easily optimized and adapted depending on the matrix to be treated. In litterature, several papers report the use of QuEChERS-based method for the analysis of several hundred contaminants. For example, Pérez-Ortega et al. (2017) reported the use of acetate-buffered version of QuEChERS (AOAC 2007.01) and d-SPE ($MgSO_4$/PSA) for the analysis of 630 multiclass contaminants (including pesticides, veterinary drugs, mycotoxins, food-packaging chemicals, perfluorinated compounds and sweeteners) in tomato, orange and baby food samples. More recently, Wang et al. (2019) successfully used acetate-buffered version of QuEChERS following by d-SPE with $MgSO_4$/PSA/C_{18} or MgSO4/PSA+ChloroFiltr, for the determination of 845 multiclass pesticide residues in fruits and vegetables. Table 3 below overviews some studies reporting QuEChERS for the large-scale determination of contaminants in food, including our own works.

Table 3. Overview of some QuEChERS-reporting studies for multiresidue analysis of contaminants in food samples.

Matrix	Class of organic contaminant	type of QuEChERS	dispersive-SPE	Reference
apple, banana, grape, orange, strawberry, carrot, potato, tomato, broccoli, lettuce	845 multiclass pesticide residues	acetate-buffered version	$MgSO_4$/PSA/C_{18} or MgSO4/PSA+ChloroFilt r (lettuce)	(J. Wang et al., 2019)
tomato, orange, baby food	630 multiclass contaminants (pesticide and veterinary drug residues, mycotoxins, food-packaging contaminants, perfluorinated compounds, sweeteners)	acetate-buffered version	$MgSO_4$/PSA	(Pérez-Ortega et al., 2017)
honey, jam, jelly, syrup	694 multiclass contaminants (pesticide residues, transformation products, industrial contaminants)	acetate-buffered version	$MgSO_4$/PSA	(Makni et al., 2023)
honey	346 multiclass pesticide residues	acetate-buffered version	$MgSO_4$/PSA/C_{18}-E	(Oymen et al., 2022)
blackcurrent	180 multiclass pesticide residues	citrate-buffered version	$MgSO_4$/PSA/C_{18}/GCB	(Walorczyk, 2014)
milk	195 multiclass pesticide residues	citrate-buffered version	MgSO4/C_{18}	(Wu et al., 2022)
bivalve	204 multiclass pesticide residues	orginal method	$MgSO_4$/PSA/C_{18}	(Diallo et al., 2022)
peppers	12 brominated flame retardants	citrate-buffered version	$MgSO_4$/PSA/C_{18}/carbon	(Fernandes et al., 2020)
prcessed foods	16 per- and poly-fluoroalkyl substances (PFAs)	orginal method	$MgSO_4$/PSA/GCB	(Genualdi et al., 2022)

Overall, the use of QuEChERS is a first choice method in laboratories mainly due to its simplicity of processing, low cost, and capability of extracting a wide-scope of contaminants with high recoveries. This technique also suits very well in research field to broaden the analytical scope for in-depth monitoring of the samples regarding other chemicals non-prioritized. Although all these advantages, the use of acetonitrile as extraction solvent may not be appropriate for extraction of very polar compounds such specific residues (glyphosate, glufosinate, AMPA, etc) or some classes of pharmaceuticals / veterinary drugs (Lehotay, 2022). As so, complementary methods may be needed to achieve their extraction in food samples, such as the QuPPE method or so-called “mega-methods” which will be presented and discussed below.

1.9.6. Quick Polar Pesticide Extraction (QuPPE)

QuPPE method was first introduced by EU reference laboratories (EURL) for the extraction of non-QuEChERS-amenable pesticide residues, in other words, the highly polar residues, in plant-based food products as well as honey (Anastassiades et al., 2017). Extraction can be followed (or not) by a cleanup step depending on the matrix. This technique simply uses water content adjustment depending on the moisture of the matrix, and acidified methanol as organic solvent for the extraction of the compounds. Figure 13 below overviews the general protocol of QuPPE proposed by EURL (Anastassiades et al., 2017).

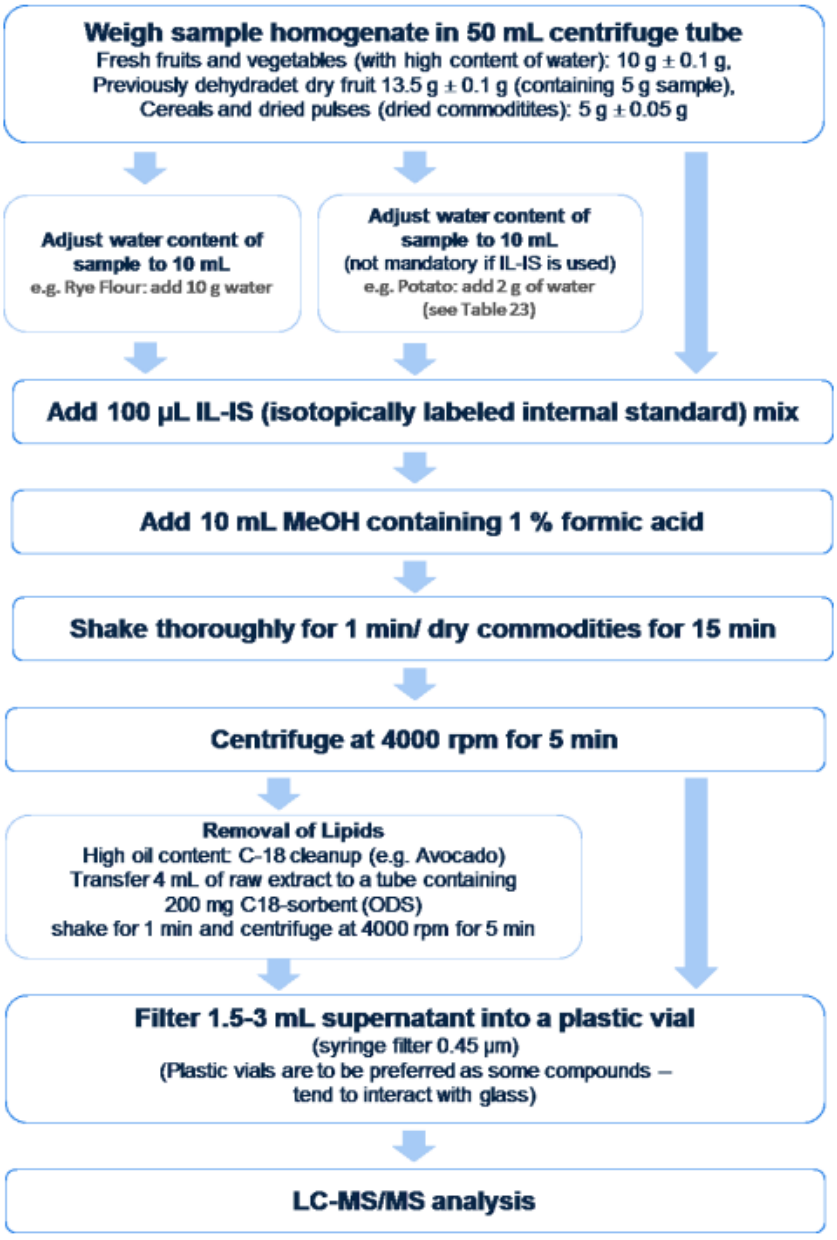

Fig.13. QuPPE method (from Anastassiades et al., 2017)

In litterature, Kaczyński (2017) used a modified QuPPE method following by a d-SPE with C_{18}, GCB, Florisil, chitosan and graphene, for the analysis of ten highly polar herbicides including well-known glyphosate and its metabolites, in various plant-based foodstuffs. Extracts were analysed using LC-MS/MS. High recoveries (64-97%) could be achieved with this simple and fast technique. In 2022, Jang et al. (2022) proposed a QuPPE method including

a cleanup step using C_{18} prior to LC-MS/MS analysis, for the determination and quantification of 30 multiclass veterinary drugs in feed. This method has shown very fast and efficient with recoveries between 71-118%.

However, application of QuPPE is limited to polar and highly polar compounds, because the use of methanol is much less appropriate for other medium polar or non-polar organic contaminants.

1.9.7. The "Mega-methods"

Recently was introduced the concept of so-called "mega-methods", which were designed to improve efficiency of laboratories, and cover a broader spectrum of contaminants that any other extraction methods, including QuEChERS. Indeed, to gain for efficiency and robustness, laboratories wish for such a single multiclass sample preparation technique to avoid the multiplication of methods needed to cover all the monitored contaminants. Here, will be presented two methods that can be defined as "mega-methods": (i) the Quick Easy Cheap Effective Rugged, Safe, Efficient and Robust (QuEChERSER), (ii) and the QuEChUP method.

a. The QuEChERSER mega-method

The QuEChERSER mega-method is an "update" of the well-established QuEChERS method, and enables to cover contaminants in a wider dynamic range of polarity, including polar and non-polar compounds for which QuEChERS can be limited (Lehotay, 2022). Although the names of both methods are close, there are still distinct differences between QuEChERS and newly introduced QuEChERSER. First, in comparison with QuEChERS, the QuEChERSER mega-method implies a comminution of bulk food matrices using cryogenic grinding with dry ice (-78°C) or liquid nitrogen (-196°C), allowing for obtaining representative test portion ≤ 5 g. Reducing test portion size enables to gain in efficiency during extraction, as explained by (Lehotay, 2022; Lehotay et al., 2020). While QuEChERS generally uses 1 mL of organic solvent per gram of sample to avoid analyte dilution and to fit with the containing capabilities of 50-mL centrifuge tubes, the reduced test portion size in QuEChERSER allows using 5 mL of acetonitrile:water (3:1, v/v) per gram of sample. This enables for the extraction of lipophilic compounds in fatty matrices, which could not be extracted using QuEChERS, as explained by (Lehotay, 2022). Otherwise, for LC analysis, QuEChERSER method does not require salting-out and purification, and 200 µL of the initial extract are collected after centrifugation. This allows preventing the loss of polar analytes and carboxylic acid compounds after salting-out and purification using PSA, respectively (Lehotay, 2022). Furthermore, to enhance peak shape of polar compounds, solvent exchange is performed to re-suspend the extract in a mixture corresponding to the initial mobile phase conditions (Lehotay, 2022). After, ultracentrifugation (13,000 rcf) is carried-out to precipitate lipophilic compounds rather than using purification or filtration, which could retain some analytes of interest or add more impurities than it supposed to remove (Lehotay, 2022). For GC analysis, the rest of the initial extract is subject to salting-out as the compounds of interest are non-polar. Furthermore, following the salting-out partitionning, µSPE using $MgSO_4$/PSA/C18/CarbonX is performed for cleaning (Lehotay, 2022). Overall, QuEChERSER allows for expanding the analytical scope to polar and non-polar analytes non-QuEChERS-amenable, while increasing extraction efficiency.

In the litterature, QuEChERSER method was already reported for the multiresidue analysis of several classes of contaminants in food. For example, Monteiro et al. (2021) successfully applied the QuEChERSER mega-method for the residual determination of 259 pesticides, veterinary drugs, metabolites and PBCs in beef. The methods has shown excellent recoveries for 85% of the targeted analytes (70-120%). Michlig and Lehotay (2022) used QuEChERSER for the efficient extraction of 252 pesticide residues and environmental contaminants in hemp, spinach, avocado, milk, egg and lamb samples, with acceptable recoveries achieved for most of the analytes (80-120%). As QuEChERSER was barely introduced less than five years ago, no publication has yet identified the potential drawback of this technique, but it appears as a next generation sample preparation method for the multiresidue analysis of contaminants in food.

b. The QuEChUP method

The QuEChUP method was introduced and published this year (2023) by our research team from the laboratory for food safety of Anses (Maisons-Alfort, France). This mega-method was set-up to overcome the drawback of QuEChERS of not being suitable for polar and hydrophilic analytes such as veterinary drug residues, due to the use of acetonitrile as extraction solvent, as well as the use of PSA during cleanup step. The principle of this method relies on a sequential extraction on the same sample portion using QuEChERS and QuPPE, respectively, followed by a purification of the combined extracts using EMR-lipid (Diallo et al., 2023). This method was optimized on fatty samples, and validated on seafood. The QuEChUP mega-method has shown exceptional capabilities of screening, with the wide-scope analysis of 850 multiclass contaminants, including pesticide residues, metabolites, industrial contaminants and more than 150 veterinary drug residues (Diallo et al., 2023). As the development of QuEChUP method was a part of this thesis, it will not be discussed more in depth in this section. However, it is a promising sample treatment technique and can easily be used to extend the analytical field and better characterize contaminants in food matrices.

As a final note on sample preparation as a crucial step for the extended analysis of contaminants in food matrices, Table 4 below summarizes the advantages and disadvantages of each of the techniques mentioned.

Table 4. Summary of main advantages and drawbacks for each sample preparation technique.

Sample preparation technique	Advantages	Drawbacks / limitations
LLE	(1) low-cost	(1) time-consuming (2) tedious (3) consumption of highly toxic solvents (4) possible loss of analytes due to emulsion (5) not very suitable for multiresidue extraction of contaminants in wide range of polarities
SPE	(1) lower organic solvent consumption (2) fast	(1) high-cost per analysis (2) difficult to master

Sample preparation technique	Advantages	Drawbacks / limitations
	(3) high recoveries	(3) requires in-depth optimization, especially for multiresidue analysis
	(4) good repeatability	(4) possible clogging of adsorbent materials
	(5) automatable	(5) requires high sample volume
SPME	(1) Easy-to-use	(1) fragility of the fibers
	(2) Low time of extraction	(2) instability of the coating
	(3) Solvent-free	(3) high instrumentation cost
	(4) automatable	(4) mainly limited to non-polar analytes
	(5) high recoveries	
ASE (PLE)	(1) high extracion efficiency	(1) co-extraction of numerous impurities
	(2) automated process	(2) requires additional cleaning of the extracts
	(3) increased reproductibility	(3) high instrumentation cost
	(4) Low time of extraction	
	(5) low solvent consumption	
	(6) suitable for various organic contaminants	
QuEChERS	(1) Easy-to-use	(1) can be inadapted for highly polar and hydrophilic compounds
	(2) Fast	(2) can be inadapted for highly lipophilic compounds in fatty samples
	(3) low-cost	
	(4) high recoveries	
	(5) good reproductibility	
	(6) suitable for the multiresidue analysis of hundreds of various contaminants with a different physio-chemical properties in food	
	(7) low organic solvent consumption	
	(8) easy-to-optimize	

Sample preparation technique	Advantages	Drawbacks / limitations
QuPPE	(1) Easy-to-use	(1) much less appropriate for other organic contaminants with a more dynamic range of polarity.
	(2) Fast	
	(3) low-cost	
	(4) adapted for highly polar and hydrophilic analytes (non-QuEChERS-amenable)	
	(5) high recoveries	
QuEChERSER	(1) high extracion efficiency	(1) possibly high cost instrumentation for communition using dry ice or liquid nitrogen?
	(2) increased reproductibility	
	(3) easy-to-follow	
	(4) covers a wider range of polarity than QuEChERS	
	(5) adapted for multiresidue and large-scale analysis of hundreds of contaminants	
QuEChUP	(1) easy-to-follow	(1) twice as much in solvent consumption than QuEChERS
	(2) covers the hydrophilic and polar compounds in comparison with QuEChERS	
	(3) adapted for multiresidue and large-scale analysis of hundreds of contaminants	

The need for laboratories to develop methods capable of monitoring a wide spectrum of contaminants at very low levels in food requires not only the development of suitable preparation methods, but also increasingly robust and sensitive analytical tools. The remainder of this state-of-the-art will introduce the analytical instruments officially used for the routine analysis of pesticides in food, their advantages and drawbacks, as well as more sophisticated tools that could improve food safety and provide data for the exposome.

1.10. The analytical instruments used for the multiresidue analysis of contaminants in food

In the last two decades, multiresidue analysis of pesticides and other contaminants in food has developed considerably with the introduction of new methods and the development of increasingly sensitive and resolving equipments. Historically, GC was one of the most widespread and effective techniques for analyzing compounds of interest in various fields of analytical chemistry, including the detection and monitoring of pesticide residues in foods (Soler et al., 2008). Indeed, GC offers the advantage of being selective, precise and highly sensitive for the detection of low-level residues. This technique was frequently used for the detection of organochlorine pesticide residues, and more generally, for the analysis of non-polar, thermally stable and volatile compounds (Soler et al., 2008).

However, the introduction of new pesticide active substances on the market with far more varied physico-chemical properties rapidly limited the effectiveness of multi-residue analysis methods using GC as a technique (Soler et al., 2008). For moderately polar, polar and thermally unstable compounds, LC emerged as a complementary tool of choice, which was rapidly adopted in routine official analysis. LC often used ultraviolet, fluorescence or electrochemical detectors for residue detection. However, these methods were not suitable for low-level multi-residue detection in matrices as complex as food matrices, due to the low sensitivity obtained with these detectors (Alder et al., 2006; Jansson et al., 2004; Klein and Alder, 2003).

The great complexity of samples and the wide variety of compounds to be analyzed have prompted the need to develop more selective and robust methods. The introduction of mass spectrometry to the market, and its coupling with separative methods such as LC or GC, has considerably improved the search for a large number of contaminants with varied physico-chemical properties, in a single analysis, with high sensitivity and selectivity (Alder et al., 2006). The coupling of LC and GC with mass spectrometers has brought a second analytical dimension to the analysis, with the possibility of characterizing the structure of species using mass spectrometry, and thus leading to more reliable identification. Since then, GC/LC-MS/MS techniques have established themselves today as the most effective tools for conventional and multi-residue monitoring of residues in food matrices in routine (Villaverde et al., 2016; Alder et al., 2006). In this configuration, the compounds of interest are first separated in a chromatographic system, before being introduced directly on mass spectrometric detection.

1.10.1. Chromatographic separation techniques

The advantage of chromatographic coupling is the efficiency of LC and GC techniques in separating the constituents of a complex mixture, thus considerably increasing the selectivity of mass spectrometry analysis. In addition, and particularly in the case of LC, separation reduces co-elution of matrix impurities with the analytes of interest, and limits competition in the mass spectrometer source with possible signal suppression (Soler et al., 2008). LC and GC techniques are both based on the separation of mixture constituents according to their affinity for a mobile phase and a so-called stationary phase.

a. Gas chromatography

In GC, the mobile phase corresponds to an inert gas (hydrogen, helium, argon, etc). This technique relies on the separation of compounds of a mixture based on their difference of boiling point and vapor pressure, as well as their polarity (Bartle and Myers, 2002). The sample to be separated is vaporized at the entrance of a chromatographic column, constituted by liquid or solid stationary phase. The carrier gas (mobile phase) transports the mixture through the column, on which they are adsorbed. An increasing gradient of temperature is then applied and the analytes are separated depending on their boiling point (Bartle and Myers, 2002). The most volatile compounds are eluted at the beginning of the gradient, and the less volatile compounds, over time of analysis with the increased temperature. Thus, molecules are characterized by a specific chromatographic retention time (t_R). GC-based analyses are commonly conducted in case the analytes of interest are non-polar, thermostable and volatile, or made volatile by chemical derivatization (Bartle and Myers, 2002). GC is often used to analyze lipophilic organochlorine pesticide residues (Hasan et al., 2022; Ye et al., 2020; Fernandes et al., 2012; Santhi et al., 2012). Once eluted from the column, the molecules are introduced into the mass spectrometer source through a heated transfer line.

b. Liquid chromatography

In LC, the mobile phases are aqueous (phase A) and organic (phase B). A pump system deliveries a flow rate ($\mu L.min^{-1}$) allowing the mobile phases to drive the sample through a column (stationary phase) filled with small particles onto which chemical functions are grafted for adsorption (Zhou, 2011; Bird, 1989). For the analysis of chemical residues, the separation is most commonly carried out following the principle of reversed-phase LC (RP-LC) (Stachniuk and Fornal, 2016; Soler et al., 2008). RP-LC allows the separation of most of the neutral (non-ionic) pesticides, accounting for >90% of the residues (Soler et al., 2008). In RP-LC, the particles of the column are mainly composed of silica, on which are grafted alkyl chains, in most case with 18 carbon atoms. During analysis, the proportion of aqueous and organic mobile phases is gradually modified (Bird, 1989). Thus, the polar and hydrophilic compounds are eluted at the beginning of the gradient, as they have more affinity with water, and the hydrophobic and less polar compounds are eluted when the proportion in organic phase increase as the gradient processes (Stachniuk and Fornal, 2016; Bird, 1989). At the end, compounds can be characterized by a specific t_R, which corresponds to the time for an analyte to be eluted from the column. Figure 14 below overviews a schematic diagram of LC system.

One major advantage of LC lies in the separation of compounds occurring in a wide range of polarity, as it is the case for pesticides and other contaminants (Stachniuk and Fornal, 2016), while reducing the matrix effects and the competition of analytes in the ionization source of the mass spectrometer. Thus, LC is highly suitable for multiresidue determination of various chemicals with different physiochemical properties.

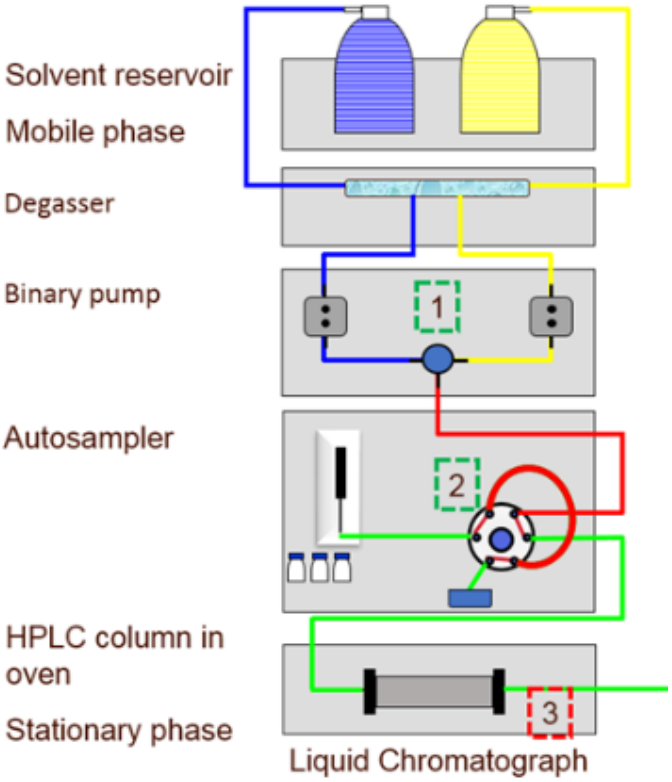

Fig.14. Schematic diagram of a LC system. (1) binary pump for aqueous and organic mobile phases, (2) autosampler, (3) stationary phase (from Liquid Chromatography – Including HPLC, UHPLC and LCxLC | Technology Networks).

1.10.2. Detection using tandem mass spectrometry

Mass spectrometry is a physical technique of analysis allowing for the detection and quantification of compounds of interest, as well as the characterization of their molecular structure. In mass spectrometry, the compounds eluted from the chromatographic column are first, ionized into positively or negatively charged ions. Then, the ions can be separated in the analyzers of the mass spectrometer according to their mass-to-charge ratio (*m/z*), before their final detection.

a. Interface and ionization

Once separated by the chromatographic system, the components of the sample are directly and progressively introduced in the ionization chamber of the mass spectrometer. For the analysis of pesticides in food using LC-MS/MS, the mass spectrometer is most commonly operating in electrospray ionization (ESI) (Stachniuk and Fornal, 2016). ESI is a soft ionization occurring at atmospheric pressure. The principle of ESI works as follows: the liquid enters a thin capillary, whose end is raised to a high potential (3-5 kV). Under this electrical-field, the liquid is transformed into a spray of fine droplets, charged depending on the ionization mode (protonation, cationisation or deprotonation) (Ho et al., 2003). The high temperature of source, as well as a heated gaz (nitrogen) induce desolvatation and evaporation of the droplets. The

density of charge of the droplets increase during evaporation. When the density of charge becomes equal to the surface tension (Rayleigh limit), the droplets explode into smaller microdroplets of charged analytes (Ho et al., 2003). The process is repeated until producing desolvated ions in gaz phase, which can be then, analyzed in the mass spectrometer, as illustrated in Figure 15. Electrospray ionization is widely used for the analysis of polar and medium-polar analytes, being very suitable for small compounds such as pesticides and organic contaminants.

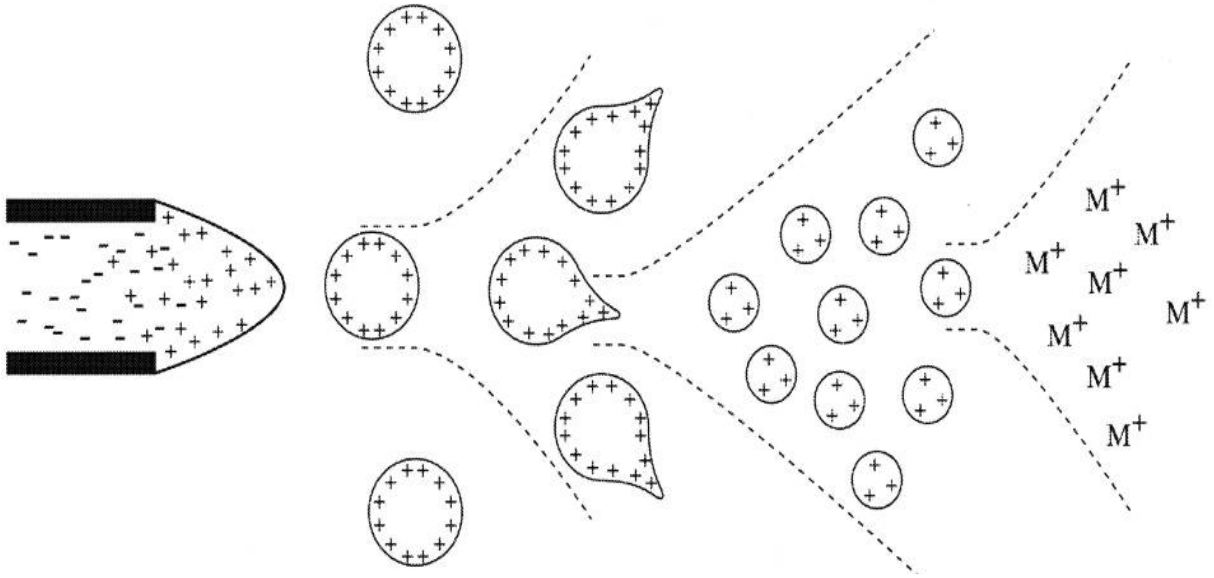

Fig.15. Principle of electrospray ionization (ESI) in mass spectrometry (from Ho et al., 2003).

Another possible ionization is the atmospheric-pressure chemical ionization (APCI). The working principle of APCI is similar to that of ESI, with the difference that ions are formed in the gas phase instead in solution (Stachniuk and Fornal, 2016). Although APCI is providing less matrix interferences, it also uses higher temperatures for vaporization of the in-coming liquid, which is can be limited for the analysis of thermally unstable compounds (Stachniuk and Fornal, 2016). In litterature, Klein and Alder (2003) compared the efficiency of APCI vs ESI using a mixture of 108 standard of pesticide residues. A much higher sensitivity was obtained for 103 pesticide standards and only five compounds provided better response using APCI. Another study conducted by Jansson et al. (2004) carried out this king of comparison. A mixture standard of 57 pesticide residues was injected using both APCI and ESI. The signals were 10 to 20-fold higher when using ESI for all tested compounds. Thus, ESI appears to be significantly more efficient for the ionization of multi-class pesticides than APCI. This may explain and justify the widespread use of ESI for the multiresidue analysis of pesticide residues and contaminants in food samples (Stachniuk and Fornal, 2016).

In GC-MS, the neutral analytes are mainly ionized using electronic impact (EI). A filament generates an electron, which is accelerated to 70 eV, allowing stripping an electron from the compound of interest, and produce *in fine*, a radical cation. Electronic impact is a so-called "hard" ionization process due to the high energy of the electrons (70 eV), and induces excessive in-source fragmentation (Sleeman and Carter, 2005). Consequently, there is only a little or no trace of the molecular ion. This process provides highly inter-reproductible results that can be compared between different GC-MS instruments using a common spectral database. However, in absence of the molecular ion, its structure can be difficult to determine, especially for the unknown compounds (Sleeman and Carter, 2005).

b. Separation and detection

The ions previously formed in the ionization source are then separated by the analyzer of the mass spectrometer according to their *m/z*. There are different analyzers in mass spectrometry, each operates following a specific physical principle. One of the most popular is the quadrupole analyzer. The quadrupole analyzer consists in an assembly of four parallel rod-shaped metal electrodes with a hyperbolic cross-section (Stachniuk and Fornal, 2016; Ho et al., 2003). The four electrodes are linked electrically in pairs. A direct voltage superimposed with a radio-frequency alternating voltage is applied to pair the opposite electrodes by a same potential difference. The adjacent electrodes are submitted to the same but opposite potential (Ho et al., 2003). This potential difference between each pair of electrodes results in an electrical field, carrying the ions forward and through the quadrupole following the z-axis, but with oscillatory movements in the x-y plane (Ho et al., 2003), as illustrated in **Figure 16**.

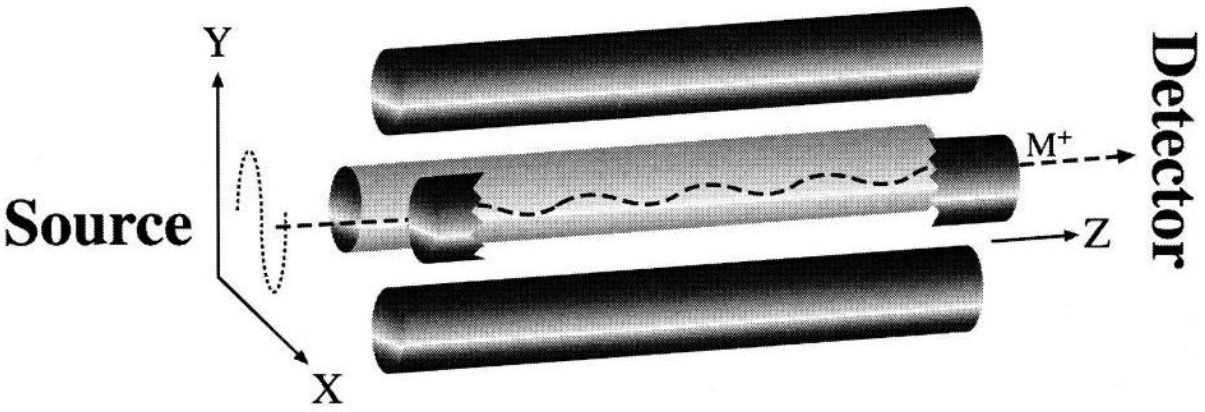

Fig.16. Trajectory of ions following an oscillatory pattern within the quadrupole analyzer (from Ho et al., 2003).

The oscillation amplitude depends on the *m/z* ratio of the ions. By adjusting the DC and AC voltages, the oscillation amplitude can be set to be stable within a given mass range. In this way, ions can move inside the quadrupole without hitting the electrodes. Ions outside the user-defined mass range of interest, on the other hand, will follow an unstable oscillation pattern and collide with the electrodes, and are neutralized from the analysis (Ho et al., 2003). Among other things, this reduces interference and increases the selectivity of the analysis method. As mentioned in the paper by Ho et al. (2003), quadrupole analyzers are robust, cost-effective and can be combined with various mass spectrometry interfaces.

In routine application, triple-quadrupole mass spectrometry (QqQ-MS) stands out as one of the most, if not the most, used mass spectrometer for determination and quantification of multiresidue contaminants in food (Stachniuk and Fornal, 2016). In QqQ-MS, there are three

successive quadrupole analyzers, usually disposed in a straight-line configuration, as shown in Figure 17 below.

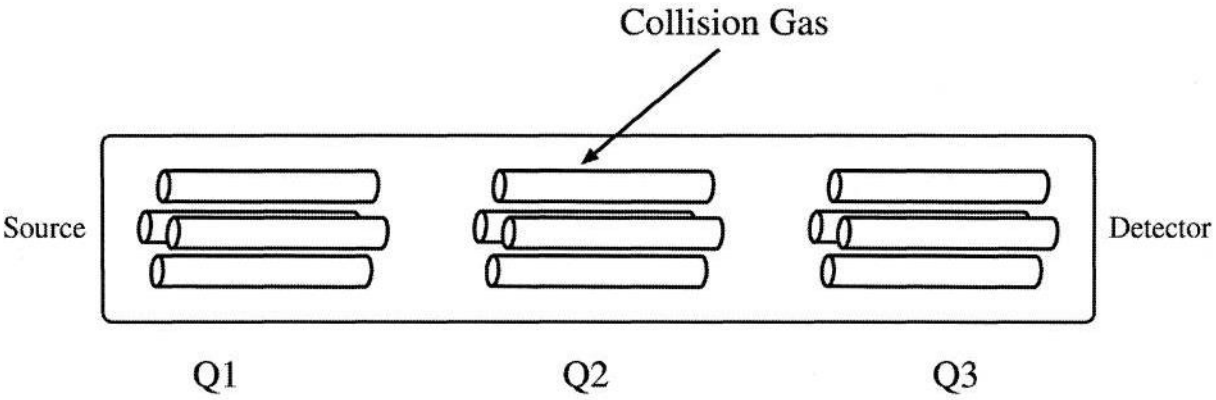

Fig.17. Configuration of a triple-quadrupole mass spectrometer (from Ho et al., 2003).

The first quadrupole filters the ions according to the mass range of interest, as described above. The filtered ions then reach a second, inactive quadrupole, where they are activated by collision with an inert gas (Fig.17). This collision results in ion fragmentation, otherwise known as collision-induced dissociation (CID) (Stachniuk and Fornal, 2016). Fragmentation ions, also known as product ions or daughter ions, are linked to the parent ion structure, and are separated at the last quadrupole before reaching the detector. They provide a wealth of information on the structure of molecules (Stachniuk and Fornal, 2016). The filtered ions finally reach a detector, usually an electron multiplier, which counts the ions and transforms the electrical signal into a computer signal, providing a mass spectrum

For multi-residue analysis and quantification of contaminants in foods, QqQ mass spectrometers most often operate in a mode known as "multiple reaction monitoring" (MRM). In MRM mode, the operator defines a list of molecules to be analyzed, as well as two transitions (parent ion or precursor → son ion), one for detection of the compound in the sample, the other for quantification. In this configuration, only the parent ion and the two defined daughter ions are correctly filtered by the quadrupole analyzers (Q1 and Q3), thus "purifying" unwanted ions from the analysis (Ho et al., 2003). Using this mode, several compounds can be monitored for analysis, each with two well-defined transitions. The QqQ-MS system operating in MRM is today the most widely used tandem mass spectrometer for conventional multi-residue analysis of pesticides in food (Stachniuk and Fornal, 2016).

1.10.3. Advantages and drawbacks of LC/GC-MS/MS

LC/GC-MS/MS is emerging as a first choice tool for the determination and quantification of multiple contaminants in food matrices. Operating in MRM mode, these methods are highly selective, achieving very high levels of sensitivity (Stachniuk and Fornal, 2016), on the order of picograms of residue per gram of sample. Moreover, they are easy to handle, and the costs associated with acquiring these instruments are relatively affordable for laboratories. These advantages justify their widespread use in control laboratories.

In the literature, numerous studies report the use of LC/GC-MS/MS with a QqQ-MS or other system, for the multiresidue analysis (>30 compounds) of pesticides (Lozowicka et al.,

2016; Uclés Moreno et al., 2015; Tran et al., 2012; Wong et al., 2010), veterinary drugs (Chen et al., 2016; Robert et al., 2015; Schneider et al., 2015) and toxins (Aguilera-Luiz et al., 2011) among others in food samples.

Nevertheless, despite all the advantages of LC/GC-MS/MS, these techniques have major limitations, not least the lack of completeness due to the MRM mode. In MRM mode, an initial list of molecules to be analyzed is defined by the operator, along with the associated transitions (precursor ion → two product ions). Any compound not included in the list will be excluded from the analysis, as the ions will not be filtered by the quadrupole analyzer, as described above. For this type of analysis, the compounds' analytical standards are therefore essential, otherwise they cannot be analyzed. This is known as targeted analysis (Kaufmann, 2012).

These analyses are conducted a priori, i.e. the operator knows what he is looking for. In general, the list of compounds specified is based on residues prioritized by the European Commission, or covered by the methods of the laboratory. This can pose serious problems in terms of food safety. A residue or contaminant found in the sample, but not included in the prioritized substances to be monitored, cannot be detected. Accidental contamination or misuse, as in the case of dioxin-contaminated pigs (Eskola et al., 2020) or fipronil-contaminated eggs (Authority (EFSA) et al., 2018), reminds us that no system is perfect. Moreover, given the huge diversity of chemical substances found in foodstuffs, LC/GC-MS/MS quickly becomes limited.

In addition, Kaufmann (2012) pointed out the difficulties using mass spectrometers operating in MRM for large-scale analysis. Indeed, operators have to make compromise between the number of transitions to be implemented, the dwell time, as well as the related number of chromatographic points per peak, which must comply with regulatory analytical guidelines (Kaufmann, 2012). This limits the number of compounds that can be analyzed in a single-run analysis. Furthermore, MRM-based methods require precise knowledge of retention time of every single compound analyzed, and adjustments are needed since retention time of certain analytes may shifted over time within long analytical sequences (Kaufmann, 2012). This make tedious the development of large-scale screening of several hundreds of contaminants. Nevertheless, multiresidue analysis is still possible with tandem mass spectrometry operating in MRM mode, such as reported by Lee et al. (2018), in which the authors used LC-MS/MS operating in MRM mode for the analysis of 310 multiclass pesticide residues in brown rice, orange and spinach samples.

Finally, tandem mass spectrometer analyzers are so-called low-resolution, as they only measure the nominal mass of the compounds. Distinguishing isobaric compounds (compounds with the same nominal mass) is therefore complicated, although chromatographic coupling can reduce these possibilities, without being able to avoid them altogether (Pérez-Ortega et al., 2016).

For the reasons given above, the wide diversity of substances present in food requires the food safety system to be upgraded, with the introduction of more exhaustive tools that can go far beyond the substances that are officially prioritized and monitored.

1.10.4. High-resolution mass spectrometry (HRMS)

The ongoing development of increasingly sophisticated, high-performance analytical tools has led to the advent of HRMS, which addresses the limitations of MS/MS. Indeed, this technique has given a new perspective to multi-residue analysis, with the possibility of

monitoring all substances present in a sample, without limit in number and without being constrained by a list, as long as they were correctly extracted and ionized. For the analysis of contaminants in foodstuffs, orthogonal time-of-flight (ToF) analyzers and Orbitrap are the most widely used (Feng, 2023). Their much greater resolving power (FWHM) than that of low-resolution analyzers, means that compounds can be separated more selectively, and their precise mass measured down to the fourth or fifth decimal place (Feng, 2023). In particular, this enables isobaric compounds to be distinguished.

a. Orthogonal time-of-flight (ToF) analyzer

Mass spectrometers incorporating time-of-flight analyzers are among the most widely used HRMS instruments. In a time-of-flight analyzer, ions with the same charge are accelerated to the same kinetic energy by a pulser, and then separated according to their m/z during their time-of-flight. Although the ions acquire the same momentum, their velocity differs. The time of flight, in other words the time taken for an ion to reach the detector, which is located at a known distance, is calculated (Stachniuk and Fornal, 2016). The precise measurement of the *m/z* ratio is a function of this time-of-flight. In the case of small, mono-charged molecules such as pesticides, the time-of-flight is a function of mass only. Lighter molecules will have a higher speed, while the time-of-flight will be greater for heavier molecules (Stachniuk and Fornal, 2016). In modern ToF analyzers, acceleration is orthogonal, and enabled by a reflectron that allows ions to be reflected back to the detector, thereby lengthening time-of-flight and improving resolving power (the power to separate ions with very close masses). There are three common ToF geometries, illustrated in Figure 18 below.

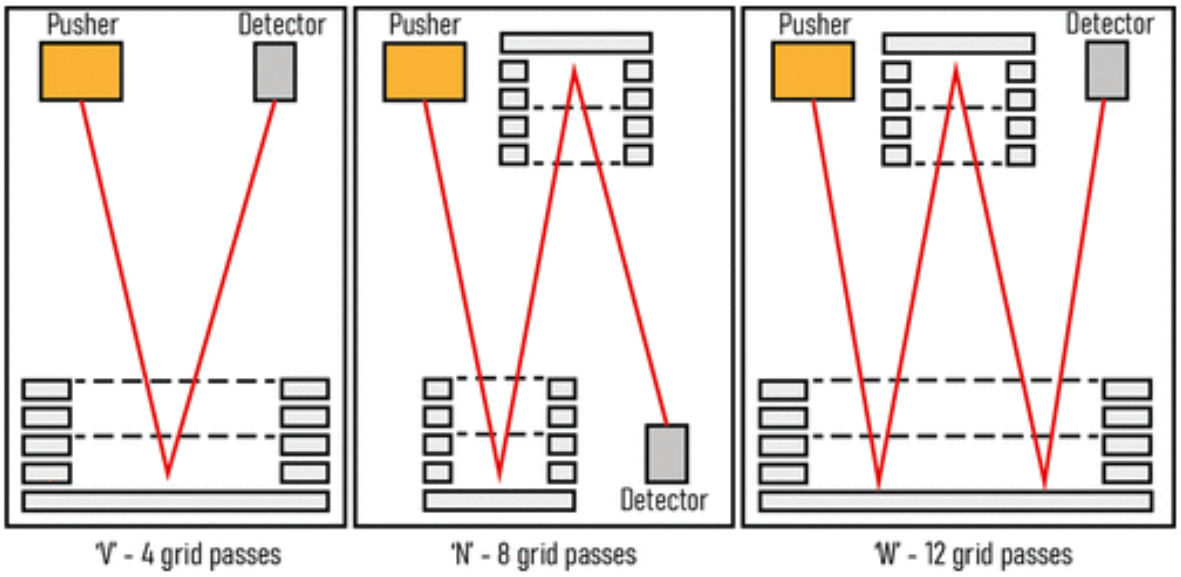

Fig.18. Diagram of the three common geometries of orthogonal time-of-flight analyzer (from Cooper-Shepherd et al., 2023).

The V-trajectory consists of four passes of incoming ions through mirror grids, giving optimum performances between resolving power and sensitivity. On the other hand, N and W-ion trajectories consist in more passes through the reflectron grids than in V-trajectory, resulting in an increase of resolving power but overall sensitivity may be affected (Cooper-Shepherd et al., 2023).

The orthogonal time-of-flight analyzer features a high acquisition frequency (Hz), is highly sensitive, and is capable of measuring ions in a mass range (small molecules, peptides, proteins, etc.). Furthermore, its high resolving power (between 20,000 and 40,000 FWHM, sometimes more) ensures excellent ions separation efficiency, thus providing accurate measurement of the measured mass.

b. Orbitrap analyzer

The Orbitrap is a high-resolution analyzer featuring very high mass resolving power and accurate mass measurement (to the fifth decimal place). It consists of a barrel-shaped outer electrode and a coaxial spindle-shaped inner electrode (Savaryn et al., 2016). Under the effect of an electrostatic field, ions are trapped in an orbital motion around the internal (coaxial) electrode, as shown in Figure 19. The ions have an axial oscillation frequency, measured for each ion, using two electrodes located on either side of the Orbitrap (Fig.19). These electrodes then detect the charge of the moving ions as they progress along an axial dimension. The frequency of each ion emits a signal that is collected, and which is specific to a given m/z ratio (Savaryn et al., 2016). The m/z ratios of the ions are calculated very precisely using the Fourier transform, based on the oscillation frequencies.

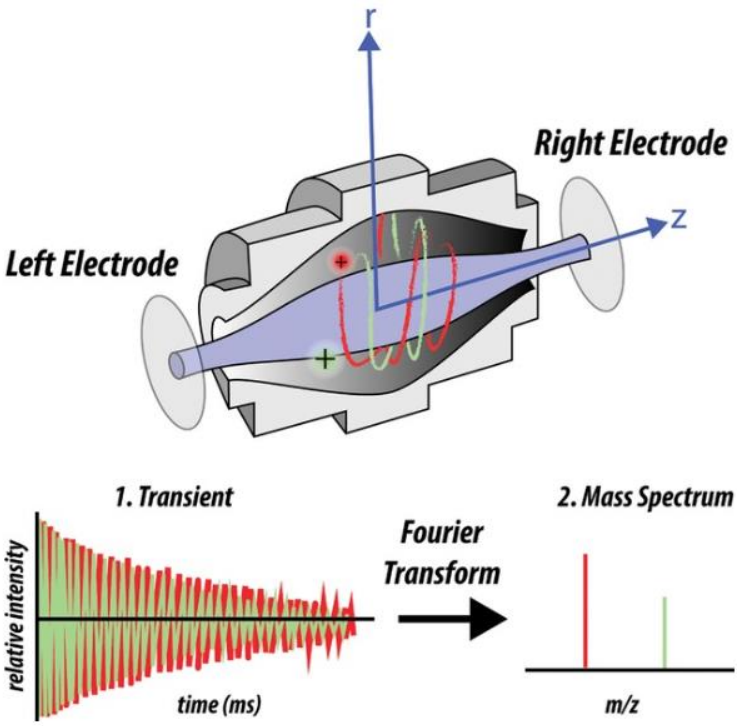

Fig.19. Diagram of an Orbitrap analyzer (from Savaryn et al., 2016).

c. High-resolution hybrid mass spectometers

In the field of pesticide and food contaminant analysis, the most commonly used high-resolution instruments are so-called hybrids, i.e. they combine different types of analyzers. For example, hybrid quadrupole time-of-flight (Q-ToF) or quadrupole Orbitrap (Q-Orbitrap) mass

spectrometers are among the most widely used. As with MS/MS, Q-ToF or Q-Orbitrap analyzers are arranged in series, sequentially. For example, in a Q-ToF, the first analyzer is a quadrupole acting as a mass filter (Stachniuk and Fornal, 2016). The filtered ions then reach a second quadrupole, this time passive, acting as a collision cell for ion fragmentation. The ions are then separated in a third analyzer, this time a high-resolution ToF analyzer (Stachniuk and Fornal, 2016). Figure 20 below, illustrates the architecture of a Q-ToF. These systems can be used to determine the elemental composition of the product ions produced by the fragmentation of the parent ion, in order to determine its structure.

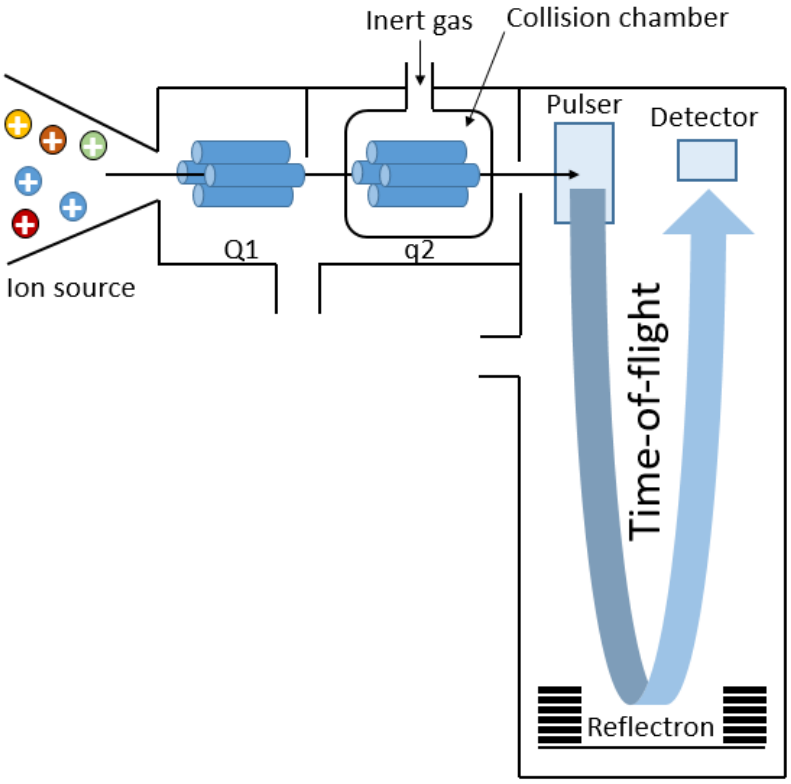

Fig.20. Diagram of a conventional Q-ToF mass spectrometer with V-ion trajectory.

It should be noted that recently, a new mass spectrometry hybrid system was developed based on time-of-flight separation. This is a hybrid quadrupole-multireflecting time-of-flight mass spectrometer. Unlike conventional Q-ToF-MS systems, this one includes a multireflecting (MRT) ToF analyzer, allowing to achieve resolving power >200,000 FWHM, high acquisition of mass spectra, as well as sub-ppm mass accuracy (Cooper-Shepherd et al., 2023). This new system is highly promising, and could further considerably improve performance and accuracy in the identification of compounds in complex matrices such as food.

1.10.5. Advantages of HRMS over MS/MS

For the screening of contaminants in foods, there is a fast-growing interest in the use of LC/GC-Q-ToF or LC/GC-Q-Orbitrap operating in full-scan mode. In this configuration, the operator defines a mass range of interest in which the compounds of interest are contained. For

the analysis of pesticide residues and other contaminants, this range is often between 100-1000 Da. All the ions within this mass range will be filtered out by the quadrupole analyzer, while others will be excluded from the analysis. This represents a considerable difference from MS/MS. Indeed, full scan mode in HRMS offers the possibility of accessing a much more exhaustive fingerprint of the sample, as all ions within the mass range of interest can be analyzed. In contrast, MS/MS operating in MRM mode specifically targets only operator-defined ion masses in the initial list, as explained in section 1.10.3.

The need to extend the scope of monitoring to an increasing number of contaminants lends credence to the usefulness of full-scan mode, which has made it possible post-acquisition data reprocessing, to search for unexpected contaminants, without the need to re-inject the sample. This can be very useful for conducting retrospective analyses and highlighting whether a newly identified contaminant was already present previously at the time of injection (Kaufmann, 2012).

Furthermore, as explained by Kaufmann (2012), the lack of availability of analytical standards for active substances and other contaminant residues can compromise their monitoring in foodstuffs. HRMS operating in full-scan mode has opened up new perspectives with the possibility of searching for unknown compounds, or known compounds but for which analytical standards are not available in the laboratory (Kaufmann, 2012). This type of approach is also known as suspect and non-targeted analysis, and is conducted without any a priori assumptions about what may be found in the samples analyzed. They considerably extend the scope of contaminant monitoring, although confirmation using the compounds' analytical reference standard is still required for unequivocal identification (Schymanski et al., 2014). Numerous studies report the use of suspect and non-targeted analyses in HRMS for the analysis of contaminants in foodstuffs (Anagnostopoulpou et al., 2022; Jansen et al., 2022; von Eyken and Bayen, 2019; Kunzelmann et al., 2018). In addition, these techniques are also frequently used for the targeted and simultaneous analysis of several hundred contaminants in foods (Oymen et al., 2022; J. Wang et al., 2019; Pérez-Ortega et al., 2017).

The potential of HRMS to improve food monitoring, along with the interest in its application, can be illustrated by the number of papers published (research articles and reviews) over the past 20 years. With this in mind, a quick search on the ScienceDirect database (Elsevier) was conducted using the following keywords: "HRMS, contaminants, food". At the time of the search, there were 3095 articles published over the last 20 years, with an upward trend over the years, as shown in Figure 21. Another significant indicator of the interest aroused by HRMS is related to the Human Biomonitoring for European Union (HBM4EU) initiative and its follow-up project "Partnership for the Assessment of Risks in Chemicals (PARC)", which aim to measure the exposure of Europeans to chemical substances and their effects on health, but also to provide more complete and exhaustive data to improve the scientific basis for risk assessment (Luijten et al., 2023). These projects incorporate HRMS as a modern tool for achieving these objectives.

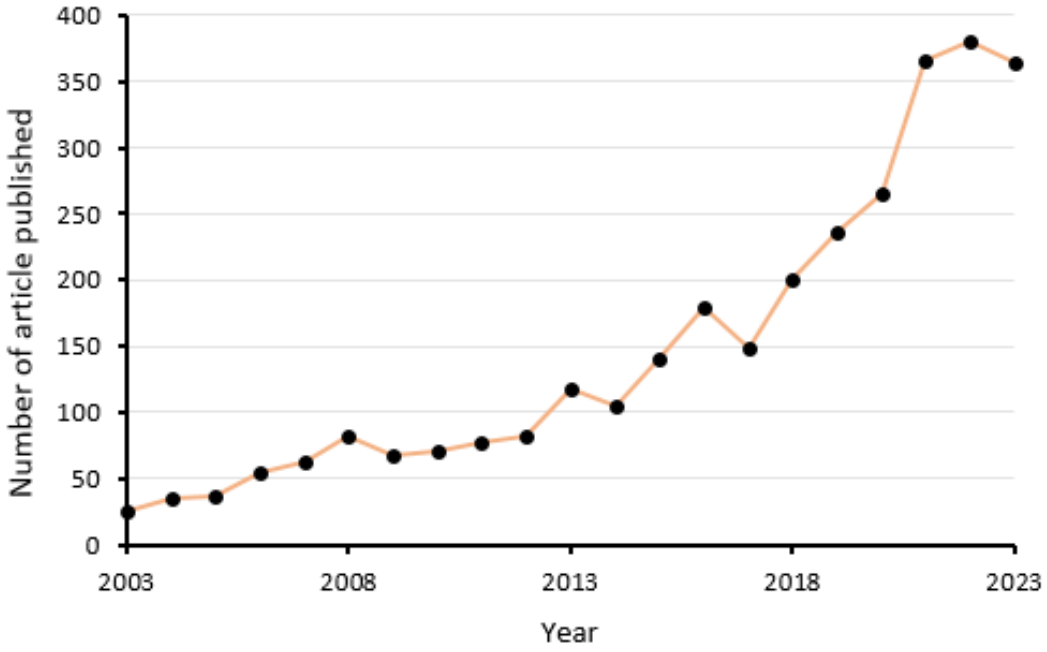

Fig.21. Evolving interest of researches related to analysis of contaminants in food using HRMS with the following key words: “HRMS, contaminants, food”.

HRMS is therefore a tool that has enhanced the concept of multiresidue analysis of contaminants, and seems much better suited than MS/MS to ensuring better monitoring of consumed products, and better characterizing the state of consumer exposure to chemicals.

1.11. Aim of the thesis

In the light of what was described in this state-of-the-art report, we intend to demonstrate the usefulness and relevance of HRMS for improving the concept of screening of contaminants and better characterizing the state of consumer exposure. The idea is to raise awareness of the need to integrate HRMS into routine laboratories, as a complement to MS/MS, in order to improve food safety. For this purpose, we need to develop methods for sample preparation, instrumental analysis and targeted, suspect and non-targeted data reprocessing, which are robust, reliable and suitable for the analysis of a very large number of contaminants (>500). In addition, the sensitivity of HRMS instruments may be one of the current issues surrounding the use of these modern, sophisticated tools. Therefore, it is also imperative to be able to develop HRMS methods that are sufficiently sensitive to search for substances well below their regulatory threshold (MRL), to highlight that this analysis system could very well be adapted to the needs and expectations of current jurisdictions

CHAPTER

Development of analytical methods for the multiresidue and large-scale screening of contaminants in food samples

2

Preamble

This chapter describes the analytical developments carried out as part of this thesis. The idea was to develop methods for the broad-spectrum analysis of different contaminants in a variety of food matrices. Indeed, the wide diversity of contaminants present in food products means that the monitoring system needs to be strengthened in order to better characterize the actual state of consumer exposure. This requires the development of reliable, generic and exhaustive methods, both for sample preparation and analysis. The methods were developed based on an LC-HRMS system to demonstrate that the tool can considerably extend the scope of contaminants monitoring, with sensitivity levels achieved that are high enough to search for substances well below regulatory limits. This chapter, and the work presented in it, represent the bulk of this thesis work, with the hope that they can help to further highlight HRMS as an effective and reliable tool for improving food safety.

Each study presented is complementary to the previous one, responding to specific needs or questions, and integrating a system of ongoing improvements. Indeed, as this thesis is mainly centered on the development of analytical methods, the project management of the various works was strongly inspired by the "Agile" methodology used in industry. These methods establish a holistic and iterative framework, and propose deliverables of the highest possible value. In this way, each work carried out during the course of this thesis adds value to the previous one, with the deliverable being the publication of the work in question in the form of a research article.

2.1. Development of a multiresidue method for the analysis of pesticides in baby foods

2.1.1. Context and aim of the study

We carried out a first development of a method for the multi-residue analysis of 204 pesticide residues in baby food. Baby food products are subject to stricter regulation by the European Commission, with MRLs set at 0.01 mg.kg-1 for all pesticide residues (European Commission, 2006). Some chemicals, such as pesticides, can be associated with toxicological risks for humans (Ntzani et al., 2013). Moreover, these risks are exacerbated in infants and young children, due to their low body weight and immature immune systems (Nougadère et al., 2020). Characterizing their exposure to pesticide residues is a major public health issue. However, data on the exposure of infants and young children to a broad spectrum of chemical contaminants is rather limited. Because of the importance and compositional and matrix diversity of these infant food products, we wanted to propose an optimized method that could be properly adapted to the multi-residue analysis of different types of baby foods.

2.1.2. Key points of the study

As part of this study, we were able to:

- Optimize a sample preparation method for multi-residue analysis of pesticides in baby food purées.
- Evaluate tolerance thresholds on criteria used for detection and identification in HRMS. In the literature, tolerance thresholds applied to criteria such as chromatographic retention time, mass error or MS/MS similarity scores vary according to official guides and authors, with no established consensus.
- Evaluate different algorithms for calculating similarities between experimental and reference MS/MS spectra, proposed by AB Sciex data processing software and used for HRMS identification.
- Evaluate the impact of an inclusion list on the fragmentation rate in information-dependent acquisition (IDA) mode.
- Search for anthropogenic contaminants using a suspect approach (without analytical standards).

2.1.3. Article 1 (Makni et al., 2022)

The following article details experiments on the optimization and validation of a method for the analysis of 204 pesticides in baby food samples . This article was published in the journal Food Chemistry. Due to Elsevier copyright restrictions, only the title and abstract of the paper were included in published format. The rest of the paper is inserted in Word-type format, and is available online using the following DOI: https://doi.org/10.1016/j.foodchem.2022.133573.

The references associated to this paper are displayed there: References section (Article No. 1)

The electronic supplementary materials (Annexes) associated to this article are displayed here: Article 1 (Makni et al., 2022): “Improving the monitoring of multi-class pesticides in baby foods using QuEChERS-UHPLC-Q-TOF with automated identification based on MS/MS similarity algorithms”

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Improving the monitoring of multi-class pesticides in baby foods using QuEChERS-UHPLC-Q-TOF with automated identification based on MS/MS similarity algorithms

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ABSTRACT

A screening method was developed for the multi-residue analysis of pesticides in baby foods using QuEChERS and UHPLC-Q-TOF. For sample preparation, the two-buffered versions of QuEChERS and different purification procedures were studied. False negatives and false positives were determined using different thresholds mentioned in the literature on the retention time and accurate mass measurement detection criteria. To reach unequivocal identification, the fragmentation spectra of the pesticides were used. The information-dependant-acquisition (IDA) mode was optimized with a precursor-inclusion list (PIL) to limit the loss of MS/MS data. Then, the experimental fragmentation spectra were compared to those included in a homemade library, by assessing different MS/MS algorithms and similarity scores. The optimised method was validated according to SANTE/11312/2021 guidelines. 95% and 73% of the pesticides presented a screening detection limit (SDL) and a limit of identification (LOI) ≤ 0.1 $mg.kg^{-1}$. One plasticizer was found in the investigated samples by a suspect-screening approach.

1. Introduction

In 2005, C. Wild introduced the concept of exposome as the total environmental and non-genetic exposure sources and factors that an organism undergoes throughout their lifetime, potentially associated with multifactorial disorders (Wild, 2005). In the context of dietary exposure, non-genetic factors to which humans can be exposed include microbiological agents and chemicals, such as pesticides. Pesticides represent a wide-range of bioactive chemical compounds of low molecular weight, intensively used in modern agriculture to control pest organisms and increase crop yields. During the past few decades, their widespread use has caused serious concerns worldwide regarding food quality and safety aspects. Importantly, their application to crops and use in livestock may result in chemical pollution in food products (Pang et al., 2021, which exposes the population to a wide array of pesticides occurring in a dynamic range of concentrations. Another important aspect is that exposure to mixtures of pesticide residues at different levels may enhance their harmfulness or, on the contrary, reduce it through potentiating effects and synergistic agonistic or antagonistic interactions, also known as

"cocktail effects" (Lukowicz et al., 2018; Rizzati et al., 2016). As a result, due to their known or potential adverse effects on human health (Ntzani et al., 2013), there is a need to assess the risks of chronic exposure to pesticides through diet.

The risks to health are even higher in infants below 3 years of age, who represent a more vulnerable group (Nougadère et al., 2020; Aguilera-Luiz et al., 2012). In Europe, the European Food Safety Authority (EFSA) has set maximum residue levels (MRLs) of individual pesticide residues in common animal and plant-based food products for human consumption (European Commission, 2005). Baby foods, a term used to designate mixtures of different matrices formulated for infants, including fruits and vegetables, animal and cereal-based food products (Hercegová et al., 2007), follow a standardised MRL of 0.01 $mg.kg^{-1}$ (European Commission, 2006).

In recent years, multi-residue screening of pesticides has developed significantly with the introduction of new methods, especially regarding sample preparation. The Quick, Easy, Cheap, Efficient, Rugged and Safe (QuEChERS) procedure stands out as one of the most commonly used methods for extraction of multi-class pesticides in food samples (González-Curbelo et al., 2015)**,** including baby foods (Pérez-Ortega et al., 2017; Jia et al., 2014; Aguilera-Luiz et al., 2012). The QuEChERS procedure involves extraction using acetonitrile and partitioning salts, followed by a clean-up step (Anastassiades et al., 2003). Although the QuEChERS procedure is well suited to extraction of multi-class pesticides with high yields in various matrices, there is no appropriate one-size-fits-all method. Therefore, prior optimisation may be required to improve extraction efficiency.

Regarding analytical techniques, gas and reversed-phase liquid chromatography coupled with tandem mass spectrometry (LC/GC-MS/MS) operating in multiple reaction monitoring (MRM) mode are the most developed technique for routine pesticide determination (Villaverde et al., 2016; Alder et al., 2006). Although these methods are very sensitive and robust, a major limitation is that they are limited to a predetermined list of targeted compounds to be searched *a priori*. These targeted approaches are blind to any compound outside this list.

The rise of high-resolution mass spectrometry (HRMS) has made it possible to overcome this limitation. Unlimited determination of compounds without a pre-defined list has become possible using high-resolution mass spectrometers such as the time-of-flight (TOF) or Orbitrap instruments operating in full-scan MS mode (Weng et al., 2020a). This feature improved the concept of screening methods and allowed for the development of suspect and non-targeted screening approaches, which extend the analytical scope (Dubocq et al., 2021; Phillips et al., 2018). Furthermore, retrospective analysis of acquired full-MS data is possible when a new contaminant was not characterised at the time of injection (Gómez-Pérez et al., 2015a).

Detection of pesticides in food using HRMS operating in full-scan mode is based on the retention time (t_r) and accurate mass measurement of a precursor ion. To date, there is no established consensus on the thresholds to be used for these criteria, even though analytical guidelines (SANTE, 2021; FDA, 2015) provide various recommendations. For instance, SANTE guidelines recommend a t_r tolerance of ± 0.1 min and accurate mass measurement ± 5 ppm for screening of pesticides in food, whereas some authors prefer to use wider thresholds (Wang et al., 2019; Pérez-Ortega et al., 2017; Luz Gómez-Pérez et al., 2015). This is a crucial parameter to consider as the data processing parameters may influence the balance between false negatives and false positives (López et al., 2014a). Given this consideration, an assessment on the thresholds to be used should be carried out at the time of method development, to provide for efficient and reliable automated-based data processing, which is a key for implementation of HRMS in routine use.

To reach a higher degree of confidence and limit the occurrence of false positives, screening of pesticides may also include MS/MS data for unequivocal identification (Schymanski et al.,

2014). In HRMS, full-scan MS mode is often followed by MS/MS data acquisition in the same run-analysis, which can be performed in two ways: full-scan mode followed by either information-dependent-acquisition (IDA) or data-independent acquisition (DIA). IDA mode provides MS/MS spectra of high quality, but all the analytes of interest are not systematically fragmented (Guo et al., 2020). To overcome this limitation, a precursor-inclusion list (PIL) can be included to prioritize the compounds to be fragmented in targeted analysis. Another option is the use of DIA mode, in which all the precursor ions are fragmented, providing more complex spectra (Diallo et al., 2022). There are no requirements on the mode to be used for identification. In guidelines (SANTE, 2021; FDA, 2015), identification entails the use of t_r and accurate mass measurement of a precursor ion and corresponding product ion(s). However, not all instrumental software supplies a mass error (ppm) on product ions, and the identification then relies on the similarity of the whole MS/MS spectrum of a compound, against its reference spectrum included in a home-made library. The degree of similarity is displayed by scores (%) measured using MS/MS search algorithms. Nevertheless, this approach is not covered by the guidelines, which may be detrimental if this is the only option provided by the software. In the literature, few studies have reported the use of automated identification based on MS/MS spectra similarity for multi-residue screening of pesticides in food (Wang et al., 2016).

The aim of this work was to develop a simple and reliable method for the screening of 204 pesticides in baby food samples using UHPLC-Q-TOF analysis. The sample preparation conditions were optimised based on a QuEChERS protocol that can be used for baby food of heterogeneous and varied composition. To the best of our knowledge, this study is the first evaluating different QuEChERS methods and clean-up procedures to analyse multi-class pesticides in such heterogeneous matrices as baby foods. False negatives and false positives were determined using different thresholds mentioned in the literature on the t_r and accurate mass measurement criteria.. Another part of the work focused on the identification of the pesticides. Thus, the impact of a PIL during data acquisition was evaluated on the performances of identification. Furthermore, this study is the first to evaluate the impact of different MS/MS search algorithms and similarity scores, regarding the performances of identification of multi-class pesticides in baby food samples. The method was validated based on the SANTE guidelines (SANTE, 2021). The screening detection limit (SDL) of each of the studied pesticides was thus established. Although there is no requirement for meeting identification criteria, the limit of identification (LOI) was also considered as a validation parameter. The versatility of the method was tested using an expanded list of organic contaminants in suspect-screening analysis.

2. Material and Methods

2.1. Chemicals and reagents

A kit of 204 LC pesticide standards, divided into ten mixtures (100 $mg.L^{-1}$ of each compound in either acetonitrile (MeCN) or methanol (MeOH)), was obtained from Restek Corporation (Ulis, France). HPLC–MS-grade MeCN and formic acid (FA) were obtained from Thermofisher Scientific Corporation (Illkirch, France). Ultrapure water (18.2 MΩ.cm) used for reagent and sample preparation was obtained through a Millipak 40 Gamma Gold Filter (pore size 0.22 µm) and using a Milli-Q Ultrapure and Pure water system purchased from Merck Millipore (Saint-Quentin-en-Yvelines, France). A QuEChERS extraction kit, based on the AOAC Method and containing 4.0 g of magnesium sulphate ($MgSO_4$) and 1.0 g of sodium acetate, was purchased from Agilent (Santa Clara, CA, USA). A QuEChERS extraction kit based on EN Method 15662 and containing 4.0 g of $MgSO_4$, 1.0 g of sodium chloride (NaCl), 1.0 g of sodium citrate and 0.5 g of sodium citrate sesquihydrate, was purchased from Agilent (Santa Clara, CA, USA). A Dispersive solid phase extraction (d-SPE) kit containing 150 mg of

primary and secondary amines (PSA) and 900 mg of $MgSO_4$ was purchased from Agilent (Santa Clara, CA, USA). A kit of d-SPE containing 400 mg of PSA, 1200 mg of $MgSO_4$, 400 mg of octadecylsilyl silica (C18) and 45 mg of Graphitized Carbon Black (GCB) was obtained from Agilent (Santa Clara, CA, USA). An SPE Oasis Prime HLB purification cartridge was acquired from Waters (Milford, MA, USA).

2.2. Equipment and apparatus

IKA Utra-Turrax T25 mixer used for sample extraction was obtained from Retsch Technology GmbH (Haa, Germany). A Genie 2 vortex used for sample extraction procedure was purchased from Scientific Industries (Bohemia, USA), and an Eppendorf 5810 centrifuge was purchased from Eppendorf (Hamburg, Germany).

The UHPLC-Q-TOF system used for analysis consisted of a Dionex UltiMate-3000 system with a binary pump and autosampler (ThermoFisher Scientific, Waltham, USA), coupled with a Q-TOF mass spectrometer (TripleTOF 5600^{TM}, AB Sciex, Darmstadt, Germany) equipped with an electrospray ionization source (ESI).

2.3. Preparation of standard solutions

The ten different mixtures (#1 to #10), 100 $mg.L^{-1}$, were transferred and stored in screw-capped amber glass tubes at –20°C. There were 13 pesticides in mix #1, 16 pesticides in #2, 38 in #3, 63 in #4, 30 in #5, 28 in #6, 7 in #7, 1 in #8, 7 in #9, and finally 1 pesticide in mix #10. A mixture of the 204 pesticides (2 $mg.L^{-1}$) was prepared by a suitable dilution of the 10 individual mixtures with MeCN, and stored in screw-capped amber glass tubes at –20°C. The composition of each mix is supplied in electronic supplementary materials (ESM) (Table S1).

2.4. Pesticides selected

The 204 pesticides included in this study were selected in view of their worldwide occurrence in food samples. The wide range of physicochemical properties of these pesticides make them a relevant model for a multi-residue method. Among these compounds, only the 63 pesticides belonging to mix #4 (Table S1) were selected for the fortification of baby food in the sample preparation optimisation-stage. They were selected as they cover the dynamic range of polarity (LogP) of the rest of the studied pesticides. The complete mixture of 204 pesticides was used for the fortification of the baby food samples for the following parts: (i) impact of different criteria thresholds on the performances of the method, (ii) impact of a PIL and different MS/MS algorithms on the performances of the method, and (iii) method validation.

2.5. Matrices selected

Fourteen baby food commodities of various matrix compositions were purchased from local markets (Maisons-Alfort, France), and stored in a freezer at −20 °C. The composition of each baby food is supplied in ESM (Table S2). Four of the fourteen baby food samples (#1 to #4), representative of the remaining foods in terms of matrix composition, were selected for optimisation of sample preparation. The ten remaining baby food samples (#5 to #14) were used for the other parts of the study: (i) impact of different criteria thresholds on the performances of detection, (ii) impact of a PIL and different MS/MS algorithms on the performances of identification, (iii) method validation, and (iv) suspect screening analysis.

2.6. UHPLC-Q-TOF analysis

Reversed-phase gradient liquid chromatography separation was performed using an Aqua® C18 column (150 x 2 mm, 3-µm particle size, 125 Å pore diameter; Phenomenex Inc, USA) equipped with an Aqua® pre-column (4.0 mm x 2.0 mm, 3-µm particle size, Phenomenex Inc, USA). The column temperature was thermostatted at 50°C. The mobile phase composition consisted of ultrapure water (eluent A) and MeCN (eluent B), both containing 0.01% of FA. The gradient profile was started with 10% B (0 min); increased linearly to 100% B for 9 min (0-9 min); fixed for 3 min (9–12 min), returned to the initial conditions for 0.1 min (12.1 min), and then followed by a re-equilibration step for 3.9 min. The total run time was 16 min. The autosampler was thermo-regulated at 15°C. The injection volume was 10 µL and the gradient flow rate was constant and set at 0.5 $mL.min^{-1}$.

Before each batch, the TripleTOF 5600™ system was systematically tuned and calibrated manually using the APCI positive calibration solution (AB Sciex technology) in TOF MS and TOF MS/MS in high-resolution mode. Furthermore, the automated calibration device system (CDS) was scheduled to perform automatic calibration every five samples during the run-analysis. ESI+ parameters were as follows: ion spray voltage floating (ISVF) was set at 5.5 kV, source temperature (TEM) 500°C, curtain gas (CUR) 30 psi, nebulising gas (GS1) 40 psi, and heater gas (GS2) 45 psi. In this study, two methods based on IDA mode were carried out using the UHPLC-Q-TOF system:

− **Method A** was a combination of full scan TOF-MS / IDA mode. Five experiments were conducted in a single-run analysis. The first experiment was a full-scan TOF-MS acquisition that covered a mass range of 50-1000 Da. The declustering potential was set at 80 eV and the collision energy (CE) was set at 10 eV. The accumulation time was set at 490 ms. The experiments 2-5 consisted in MS/MS data acquisition using IDA mode. The accumulation time was set at 100 ms for each IDA experiment, and the CE was set at 40 eV with a spread of ± 20 eV (20, 40 and 60 eV) in high-resolution mode. The collision-induced dissociation gas used was nitrogen. Dynamic background subtraction was turned on. The total cycle time was about 900 ms. Considering that the chromatographic peak width was approximatively 15 s, the obtained number of points per peak was about 16-17 which is quite enough according to the SANTE guidelines.

− **Method B** consisted in the same full scan TOF-MS / IDA acquisition mode than Method A, with the same parameters. However, in this method, a PIL of the 204-targeted pesticides was implemented to avoid the possible non-fragmentation of analytes. PIL comprised the 204 precursor ion masses in forms of $[M+H]^+$, $[M+Na]^+$, $[M+NH4]^+$, or in-source fragments, as well as their corresponding chromatographic t_r. These informations are supplied in ESM (Table S1).

Data acquisition was performed using Analyst® software (version 1.7) of AB Sciex (Les Ulis, France). The resulting extracted ion chromatograms (XICs) were reconstructed using PeakView® software, version 2.2 comprising the MasterView™ module of AB Sciex.

2.7. Development of a homemade MS/MS library

A homemade MS/MS library of 204 pesticides was built using the convenient LibraryView™ software, version 1.0.3 of AB Sciex. The library was built by injecting separately each of the ten mixtures diluted to 0.2 $mg.L^{-1}$ in MeCN. Exact mass, the CAS number and the MS/MS fragmentation spectrum of each of the studied pesticides were recorded. The fragmentation spectra included in the homemade library are considered as reference spectra.

2.8. Optimisation of sample preparation

Optimisation of extraction was performed comparing the two-buffered variants of QuEChERS, the AOAC 2007.01 (Lehotay, 2007) and CEN 15662 (Anastassiades et al., 2007) methods. In this study, these methods were modified including a hydrating strategy and without extraction solvent acidification.
Sample preparation optimisation is presented in Fig. 1. Before use, the samples were thawed at 4°C overnight. No sample pre-preparation was required. For the enrichment experiment, 15 µL of mix #4 diluted to 2 $mg.L^{-1}$ was added to 50 mL-polypropylene centrifuge tubes, which contained 3.0 g of blank sample ± 0.2 g, to provide a spiking level at 0.01 $mg.kg^{-1}$ of pesticides. A volume of 7 mL of ultrapure water was added to each tube, and then ground using an IKA Ultra-Turrax mixer for 3 min at 5000 rpm. Then, 10 mL of MeCN was added to each centrifuge tube to perform the extraction of pesticides, which were vortexed again for 1 min. Then, either AOAC or CEN extraction salts were added to the fortified samples, and the resulting mixture was centrifuged for 5 min at 4000 rpm. 1 mL of the resulted supernatant was deposited into a 2 mL-amber vial for injection in the UHPLC-Q-TOF system operating with **Method A.**

Sample preparation optimisation also included a comparison of different protocols of purification after the extraction-stage, in addition to the protocol without purification (Fig. 1). When a purification step was performed, 6 mL of the supernatant was recovered and deposited/percolated into either:

- A 15-mL centrifuge tube containing 900 mg of $MgSO_4$ and 150 mg of PSA;
- A 15-mL centrifuge tube containing 1200 mg of $MgSO_4$, 400 mg of PSA, 400 mg of C18 and 45 mg of GCB;
- An Oasis HLB cartridge, without prior conditioning.

Finally, 1 mL of the supernatant was deposited into a 2 mL-amber vial prior to injection in the UHPLC-Q-TOF system operating with **Method A**.
All protocols (Fig. 1) were performed in triplicate. The assessment was carried out considering the false negative rates of each procedure. A pesticide was considered a false negative when a pesticide did not fit a t_r variation ± 0.1 min and/or accurate mass measurement± 5 pm (SANTE, 2021).

2.9. Impact of different detection criteria thresholds on the performances of detection

In this section, the term "detection" was used to define the screening of pesticides using t_r and accurate mass measurement criteria on the precursor ions. In this study, an assessment of the criteria of detection was carried out using the following thresholds: (i) t_r variation ± 0.1 min, accurate mass measurement ± 5 ppm (SANTE, 2021); (ii) t_r variation ± 0.5 min, accurate mass measurement ± 5 ppm (Wang et al., 2019; FDA, 2015); (iii) t_r variation ± 0.25 min, accurate mass measurement ± 10 ppm (Pérez-Ortega et al., 2017).

Each of the studied thresholds was evaluated regarding the false negative and false positive rates obtained. A false negative was defined when a pesticide did not fit the expected thresholds for t_r and/or mass measurement criteria. In contrast, a false positive was defined when the software reported a positive hit, i.e., when a pesticide fitted both t_r and accurate mass

measurement criteria thresholds, in the non-spiked samples. The same list of 204 pesticides was used for the calculation of false negatives and false positives.

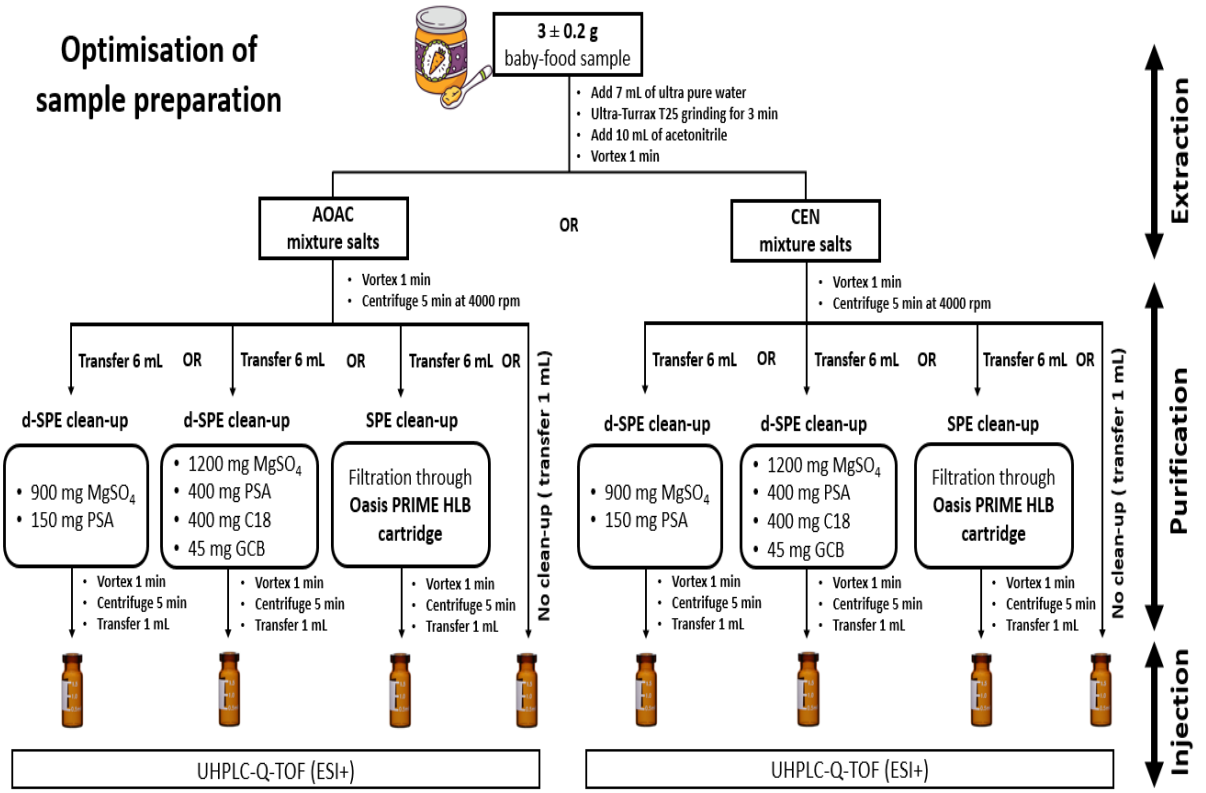

Fig.1. Comparison of different QuEChERS-based procedures for sample preparation optimisation.

2.10. Impact of a precursor ion list and different MS/MS similarity algorithms on the performances of identification.

In this section, the term "identification" was used to define the screening of the 204 pesticides using t_r variation ± 0.1 min and accurate mass measurement ± 5 ppm on the precursor ion, as well as the characteristic MS/MS fragmentation spectra. In this part of the work, the baby food samples were acquired using Method A and Method B, in order to evaluate the impact of the PIL on the performances. Then, the generated files were processed using MasterView™ software. The experimental fragmentation spectra obtained were compared to those included in the homemade library. This comparison was automatically computed by the software using MS/MS search algorithms. Three algorithms are available in the software, and were assessed in this study:

- The *purity algorithm* (PUR) measures the similarity between the experimental and reference spectra. All fragment ions from both spectra and their relative abundance are used for calculation;
- The *fit algorithm* (FIT) measures the degree to which the library spectrum is contained in the experimental spectrum, disregarding additional fragment ions present in the experimental spectrum but absent in the reference spectrum. All the expected fragment ions and their relative abundance are used for calculation;
- The *Reverse Fit* algorithm (RFIT) measures the degree to which the experimental spectrum is contained in the library spectrum, disregarding the fragment ions present in

the library spectrum but absent in the experimental spectrum. All the experimental fragment ions and their relative abundance are used for calculation.

These algorithms automatically calculate a degree of confidence characterised by a similarity score (%), allowing for fast and reliable identification, as illustrated in ESM (Fig. S1). Two similarity scores: (i) >50% and (ii) >70%, used elsewhere (Ogawa et al., 2020; Wang et al., 2016), were considered as the thresholds to be fulfilled. A pesticide that was not fitting the above mentionned criteria or not fragmented was reported a false negative.

2.11. Method validation

The method was validated according to the SANTE guidelines for screening methods. Method validation was conducted at 0.01 and 0.1 $mg.kg^{-1}$ to establish the screening detection limits (SDL) (SANTE, 2021) and the limits of identification (LOI). Experiments were carried out in triplicate for repeatability assessment. Each replicate was injected in a single batch, on three different days, to include inter-batch and instrumental over-time variabilities.. The SDL was established as the lowest concentration for which a compound was detected following (i) t_r variation ± 0.1 min and (ii) accurate mass measurement ± 5 ppm, in at least 95% of the samples (SANTE, 2021), i.e., in at least 29 out of the 30 baby food samples. In addition, the LOI was established as the lowest concentration for which a pesticide was correctly identified in at least 95% of the samples, i.e., in at least 29 out of the 30 baby food samples. The LOI used the same criteria as for the SDL, plus a comparison between experimental and reference fragmentation spectra using FIT algorithm with a similarity score >70%.

3. Results and discussion

3.1. Sample preparation optimisation

The sample preparation was studied and optimised regarding different extraction and purification procedures as explained in Section 2.7. The results for the four baby foods are displayed in Fig. 2.

When using AOAC mixture salts, false negative rates ranged from 22–32%, 19–33%, 21–32% and 13–22% in baby food 1 to 4, respectively regardless of the purification procedure used. Then, when using CEN mixture salts, false negative rates varied from 29–38%, 32–39%, 29–38% and 21–29% in baby food 1 to 4, respectively regardless of the purification procedure used.

Regarding the purification following AOAC-based extraction, false negatives varied from 19–27%, 13–22%, 22–33% and 19–32% using no purification, $MgSO_4$/PSA, $MgSO_4$/PSA/C18/GCB and the Oasis PRIME HLB cartridge, respectively. Regarding the purification following CEN-based extraction, false negatives varied from 23–34%, 21–32%, 21–36% and 29–39% using no purification, $MgSO_4$/PSA, $MgSO_4$/PSA/C18/GCB and the Oasis PRIME HLB cartridge, respectively. According to the results, purification using $MgSO_4$/PSA was the most effective to clear the extracts achieved with the AOAC or CEN methods.

The results obtained separately from the four baby foods (Fig. 2) were grouped together to increase the statistical power and to evaluate the overall performances, irrespective of the matrix composition. The results are displayed in ESM (Fig. S2). Average false negative rates ranged from 19–30% for the AOAC method against 28–36% for the CEN method, regardless of the purification procedure. Performances of detection were better when using the AOAC method, which was statistically confirmed (two-way ANOVA: p-value < 0.01). Therefore, the acetate-buffered version of QuEChERS was retained for the extraction of pesticides. This was

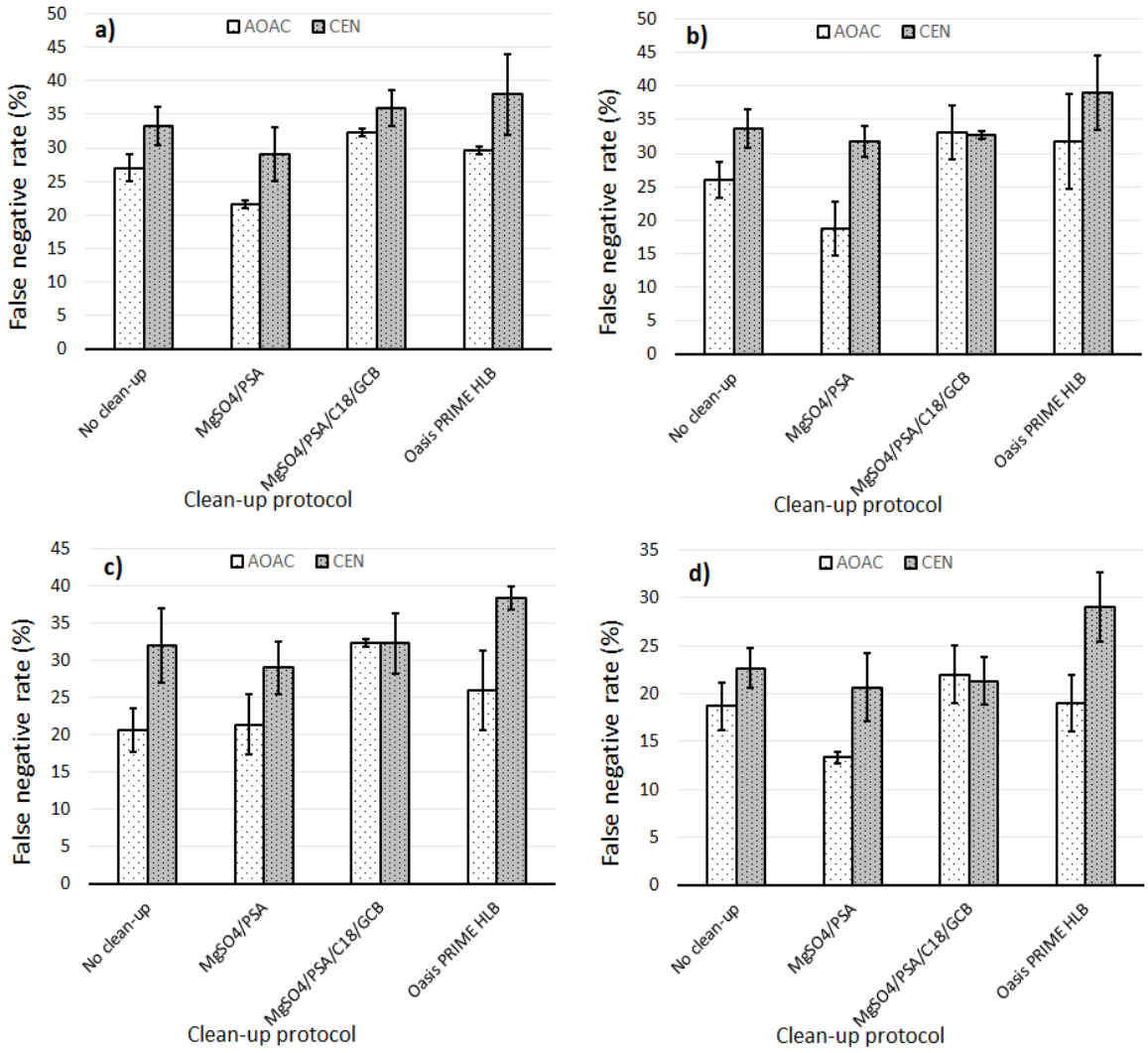

Fig.257. Impact of different extraction and purification procedures on the false negative rates (%) obtained for (a) baby food 1; (b) baby food 2; (c) baby food 3; and (d) baby food 4. The error bars correspond to the standard deviation for the response measured (Mean ± SD, n=3).

consistent with other studies in which AOAC mixture salts were used for screening of multi-class contaminants in baby foods (Pérez-Ortega et al., 2017; Aguilera-Luiz et al., 2012).
Then, the four purification protocols were assessed for the retained AOAC method. On average, false negative rates were 23%, 19%, 30% and 27% when using the procedure without purification, $MgSO_4$/PSA, $MgSO_4$/PSA/C18/GCB and the Oasis PRIME HLB cartridge, respectively. Standard deviations (SD) were equivalent overall. Purification using $MgSO_4$/PSA appeared to be the most efficient protocol to remove matrix interferents and improve compound detectability. $MgSO_4$ acts as a desiccant as it dries out the water to improve the partitioning process (Li et al., 2021), whereas PSA is commonly used in various food as a sorbent to remove co-extractives sugars, organic acids, fatty acids and certain pigments (Walorczyk et al., 2015). Nevertheless, there was no significant difference between this protocol and the protocol without a purification step.

Thus, to be able to select the most suitable protocol ($MgSO_4$/PSA vs no purification), the signal-to-noise ratio (S/N ratio) was considered. The results are supplied in ESM (Fig. S3). The

average S/N ratios were 371 and 476 without purification and with $MgSO_4$/PSA, respectively. On average, pesticide signals were better when using a clean-up step with $MgSO_4$/PSA, which was statistically confirmed (t-test, *p*-value < 0.05). Purification using $MgSO_4$/PSA was the most efficient protocol to improve the S/N of the pesticides and was therefore retained for the method. The lower S/N ratio in the samples without purification can be explained by the higher amount of co-extracted compounds (sugars, organic acids, fatty acids, pigments, etc.), which could lead to signal suppression of pesticides during the ionisation process (Petrarca et al., 2022). The use of $MgSO_4$/PSA as a purification method was also conducted by Pérez-Ortega et al., (2017) on a list of more than 600 contaminants in various matrices, including baby foods.

This sample preparation protocol could be further transposed to matrices other than baby foods, only requiring minor adjustments, as baby foods are mixtures of various food commodities of plant and animal origin. Moreover, the AOAC 2007.01 QuEChERS method as well as $MgSO_4$/PSA are widely used for multi-residue screening of organic pollutants in various food samples (Kim et al., 2019; Musarurwa et al., 2019). Furthermore, the low-starting sample amount (3 g) coupled to a hydrating strategy enable its further application to matrices with low-water content (≤ 25%), for which hydration is crucial to ensure effective extraction (Zhang et al., 2019).

3.2. Impact of different detection criteria thresholds on the performances of the method

There is no established consensus on the thresholds to be used for t_r variation and accurate mass measurement criteria. Moreover, an assessment of these detection criteria is required to obtain the best compromise between the false positives and false negatives reported by the software, as explained by (Gómez-Ramos et al., 2013). As a result, different thresholds detailed in section 2.9. were evaluated. Results regarding the false negative rates are displayed in Table 1. When t_r ± 0.1 min and accuracy mass measurement ± 5 ppm were used, the false negative rates ranged from 13% to 21% with an average of 16% at 0.01 $mg.kg^{-1}$, and from 3% to 9% with an average of 5% at 0.1 $mg.kg^{-1}$. When varying only the t_r threshold to ± 0.5 min, the false negative rates ranged from 13% to 20% with an average of 16% at 0.01 $mg.kg^{-1}$, and from 3% to 9% with an average of 5% at 0.1 $mg.kg^{-1}$. Finally, when setting the t_r threshold to ± 0.25 min and accuracy mass measurement to ± 10 ppm, the false negative rates varied from 9% to 13% with an average of 11% at 0.01 $mg.kg^{-1}$, and from 3% to 4% with an average of 3% at 0.1 $mg.kg^{-1}$. These results demonstrate that a wider t_r variation with unchanged accurate mass measurement (5 ppm) did not impact the average detectability, regardless of the concentration level. However, a larger accurate mass measurement threshold (± 10 ppm) slightly improved pesticide detection, especially at 0.01 $mg.kg^{-1}$. These findings are consistent with the study of López et al. (2014) which shown the same trends on 199 pesticides in fruits and vegetables. Otherwise, SDs for each baby food were all ≤ 7%, suggesting relatively good inter-batch repeatability. The total inter-batch and inter-matrix SDs were ≤ 4%, regardless of the thresholds used, suggesting good comprehensiveness of the method.

Table 1. Impact of different thresholds on the t_r and accurate mass measurement criteria regarding the false negatives (%), in a set of 10 baby food samples in triplicate, at 0.01 and 0.1 mg.kg^{1}.

	False negative (%)* ± SD (%)					
	Reported criteria for detection					
	(t_r ± 0.1 min; ME ± 5-ppm)[1]		**(t_r ± 0.5 min; ME ± 5-ppm)[2]**		**(t_r ± 0.25 min; ME ± 10-ppm)[3]**	
	Concentration (mg.kg^{-1})					
Sample (n=3)	**0.01**	**0.1**	**0.01**	**0.1**	**0.01**	**0.1**
Baby food 5	**16** ± 1	**6** ± 2	**16** ± 1	**6** ± 1	**12** ± 2	**4** ± 1
Baby food 6	**17** ± 2	**5** ± 2	**17** ± 2	**5** ± 2	**11** ± 2	**4** ± 2
Baby food 7	**15** ± 4	**9** ± 7	**14** ± 4	**9** ± 7	**12** ± 3	**3** ± 1
Baby food 8	**21** ± 1	**5** ± 1	**20** ± 1	**5** ± 1	**12** ± 3	**3** ± 1
Baby food 9	**17** ± 5	**6** ± 2	**16** ± 5	**6** ± 2	**10** ± 3	**4** ± 2
Baby food 10	**16** ± 7	**5** ± 1	**15** ± 7	**5** ± 1	**11** ± 5	**3** ± 1
Baby food 11	**15** ± 5	**5** ± 2	**14** ± 4	**5** ± 2	**9** ± 5	**3** ± 1
Baby food 12	**13** ± 4	**4** ± 0	**13** ± 1	**4** ± 0	**9** ± 3	**3** ± 0
Baby food 13	**17** ± 6	**5** ± 2	**16** ± 6	**5** ± 2	**13** ± 4	**3** ± 1
Baby food 14	**15** ± 4	**3** ± 0	**15** ± 2	**3** ± 0	**10** ± 4	**3** ± 0
Average (n = 30) ± SD (%)	**16** ± 4	**5** ± 3	**16** ± 4	**5** ± 3	**11** ± 3	**3** ± 1

False positives should also be considered as a criterion for evaluating the effectiveness of a screening method in HRMS. As there is no requirements in official guidelines (SANTE, 2021; FDA, 2015) on the false positive rates not to be exceeded, the proposed automated screening method must be able to provide false positive rates as low as possible, to avoid time-consuming manual inspections. Results on the false positives are displayed in ESM (Table S3). When using t_r ± 0.1 min and accuracy mass measurement of ± 5 ppm, the false positive rates ranged from 3% to 6% with an average of 5%, and an SD of 2%. When increasing the t_r threshold to ± 0.5 min, while keeping the same accurate mass measurement of ± 5 ppm, the false positive rates varied from 4% to 8% with an average of 6%, and an SD of 2%. Finally, when t_r ± 0.25 min and accuracy mass measurement ± 10 ppm were used, the false positive rates varied from 9% to 15%, with an average of 13%, and an SD of 5%. Thus, the false positive rates depended more heavily on the accurate mass measurement used than on the t_r variation threshold. These results are consistent with the findings of Pérez-Ortega et al. (2017) and López et al. (2014) regarding the influence of wider accurate mass measurement on false positives. However, the results were different considering the t_r criteria, as these authors showed higher false positives with the widening of the t_r threshold (Pérez-Ortega et al., 2017; López et al., 2014). In conclusion, the thresholds recommended in SANTE guidelines (t_r ± 0.1 min, accurate mass measurement ± 5

ppm) (SANTE, 2021) allowed us to obtain the best balance between false negative and false positive rates, and were therefore selected for pesticide detection.

To the best of our knowledge, this study is the first to provide both false negative and false positive rate results for multi-residue screening of pesticides in baby food samples. However, data of this type are available for similar related matrices, such as fruits and vegetables. For instance, López et al. (2014) proposed a method for the screening of almost 200 pesticides in a set of 22 fruit and vegetable samples using a QuEChERS procedure followed by UHPLC-Q-TOF (ESI+) analysis. They were able to detect from 61% to 94% of pesticides with an average of 84% at 0.01 mg.kg^{-1}, i.e., 16% false negatives, when using t_r of ± 0.2 min and accurate mass measurement of ± 5 ppm. The performances of detection in the present study and in the one of López et al. (2014) were equivalent (16% false negatives), but considering a tighter t_r threshold. On the other hand, they found up to 15 false positives on average against a library of 504 entries, i.e., a false positive rate of about 3%, which was equivalent to that in the present work (5%). In the study conducted by López et al. (2014), a QuEChERS extraction-based protocol was performed using equivalent sample amounts and extraction solvent volumes, making it possible to obtain 1 g of sample per mL of final extract. In contrast with the present study, the starting sample mass (3 g) was lower than the subsequently added MeCN (10 mL), providing about 0.3 g of sample per mL of final extract, which may decrease co-extractive compounds but also increase analyte detection limits. The overall method provided satisfactory detection performances with low-related variability and low false positive rate, even at low-level of concentration and given the complex nature of baby food samples.

3.3. Impact of a PIL and different MS/MS algorithms on the performances of the method

To achieve a simple and reliable automated screening method with unequivocal identification (level 1 confidence), it is necessary to consider both information regarding precursor ion and its characteristic fragment ions (Schymanski et al., 2014). For this purpose, the methods detailed in section 2.5 and the protocols detailed in section 2.10 were evaluated regarding pesticide identification. The results are displayed in Table 2.

Table 2. Impact of a PIL and different algorithm-score combinations on the false negatives (%), in a set of 10 baby food samples in triplicate, at 0.01 and 0.1 mg.kg^{-1}.

		False negative (%)* ± SD (%)			
		Concentration (mg.kg^{-1})			
		0.01 (MRL)		**0.1**	
MS/MS Algorithm	**Similarity score**	**Method A**	**Method B**	**Method A**	**Method B**
PUR	>50%	**52** ± 8	**36** ± 7	**27** ± 4	**14** ± 1
PUR	>70%	**55** ± 8	**42** ± 8	**28** ± 4	**17** ± 2

		False negative (%)* ± SD (%)			
		Concentration ($mg.kg^{-1}$)			
		0.01 (MRL)		0.1	
MS/MS Algorithm	**Similarity score**	**Method A**	**Method B**	**Method A**	**Method B**
FIT	>50%	**50** ± 8	**33** ± 7	**26** ± 4	**14** ± 1
FIT	>70%	**51** ± 8	**37** ± 8	**27** ± 4	**15** ± 2
RFIT	>50%	**50** ± 9	**29** ± 6	**26** ± 4	**13** ± 1
RFIT	>70%	**52** ± 8	**32** ± 6	**26** ± 4	**14** ± 1

Method A provided false negative rates from 50% to 55% at 0.01 $mg.kg^{-1}$, and from 26% to 28% at 0.1 $mg.kg^{-1}$, depending on the algorithm-score combination used. The false negatives were higher than those found at detection-stage (Table 1), which is consistent because for identification, additional parameter, comparison between experimental and library fragmentation spectra, is taken into account. **Method B** provided false negative rates from 29% to 42% at 0.01 $mg.kg^{-1}$, and from 13% to 17% at 0.1 $mg.kg^{-1}$, depending on the algorithm-score combination used. **Method B** always provided the lowest false negative rates at both concentration-levels, which can be explained by the use of a PIL, giving priority to the pesticides to be fragmented and limiting the loss of MS/MS data. Regarding the fragmentation triggering rate, it was found that 31% and 19% of the detected pesticides were not fragmented at 0.01 and 0.1 $mg.kg^{-1}$, respectively with **Method A**. When using **Method B**, the rates of detected but unfragmented pesticides dropped on average to 8% and 7% at 0.01 $mg.kg^{-1}$ and 0.1 $mg.kg^{-1}$, respectively. Interestingly, the PIL did not completely avoid the loss of information on MS/MS data, preventing these compounds from being unambiguously identified. However, it considerably overcame this limitation when compared with **Method A**. As a result, **Method B** was retained for data acquisition.

Regarding algorithm-score combinations (**Method B**), the false negative rates ranged from 36% at 0.01 $mg.kg^{-1}$ to 14% at 0.1 $mg.kg^{-1}$ using PUR, from 33% at 0.01 $mg.kg^{-1}$ to 14% at 0.1 $mg.kg^{-1}$ using FIT, and from 29% at 0.01 $mg.kg^{-1}$ to 13% at 0.1 $mg.kg^{-1}$ using RFIT, at a similarity score >50%. With a more restrictive similarity score (>70%), the false negative rates varied from 42% at 0.01 $mg.kg^{-1}$ to 17% at 0.1 $mg.kg^{-1}$ using PUR, from 37% at 0.01 $mg.kg^{-1}$ to 15% at 0.1 $mg.kg^{-1}$ using FIT, and from 32% at 0.01 $mg.kg^{-1}$ to 14% at 0.1 $mg.kg^{-1}$ using RFIT. This demonstrated that pesticide identification was strongly impacted by the concentration-level of analytes in the baby food samples. This was expected, since a higher concentration-level of analyte in the sample leads to better response of precursor and fragment ions, enhancing pesticide identification. Regarding the different algorithms, the results showed equivalent performances at 0.1 $mg.kg^{-1}$ regardless of the similarity score used. With lower concentrations, the PUR and FIT algorithms provided equivalent results with a similarity score >50%, whereas RFIT made it possible to slightly improve the performances. When using a similarity score >70%, the PUR algorithm showed the worst performances and RFIT the best. Nevertheless, RFIT is the least restrictive algorithm, because even if expected fragment ions are not present in the experimental spectrum, they are not taken into account in the calculation.. On the other hand, PUR is the most restrictive algorithm, as it uses the fragment ions of both

unknown and reference spectra, and their relative abundance for similarity calculation. This explains why this algorithm provided the highest false negative rates at low-concentration. The FIT algorithm appeared to be a compromise as it provided results close to those obtained using RFIT, while providing a higher level of confidence. The FIT algorithm presents the advantage of considering the entire expected fragmentation spectrum of the library in the calculation, excluding the interfering fragment ions that can be found in the experimental spectrum. As an example, the pesticide epoxiconazole ($[M+H]^+$, *m/z* 330.08039, t_R = 6.36 min) was identified with a similarity score of 100% using the FIT algorithm, but with lower scores (67%) using the PUR and RFIT algorithms due to unexpected fragment ions (Fig. S4). Thus, the RFIT and PUR algorithms were both discarded in favour of the FIT algorithm for the identification of pesticides. When using **Method B** and the FIT algorithm, false negative rates were close either using similarity score >50% or >70% (Table 2). Thus, a similarity score >70% was retained for the method, as it provides greater confidence in the automated identification process.

The optimised parameters of identification enabled us to discard all the false positives that were initially detected with only t_r variation ± 0.1 min and accurate mass measurement ± 5 ppm. However, the fungicide difenoconazole ($[M+H]^+$, *m/z* 406.07197, t_r = 7.31 min) initially considered a false positive, was confirmed to be a true positive at the identification-stage. It was found in non-spiked baby foods 5 and 6. Fig. 3 shows the unexpected identification of difenoconazole in the non-spiked baby food 5. The mass error was 0.2 ppm, the t_r variation was 0 min, the chlorinated-type isotope ratio difference was about 3%, and the similarity score of

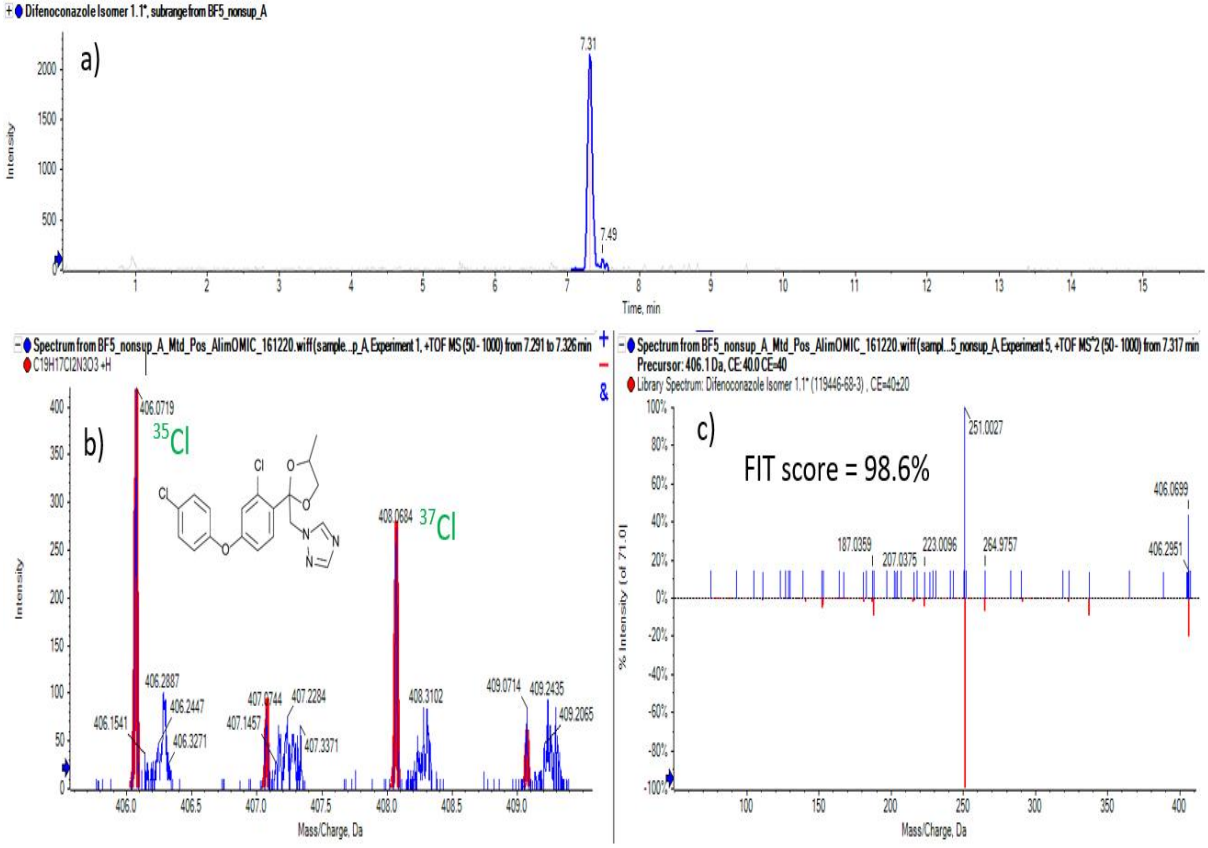

Fig.3. Unexpected identification of difenoconazole in non-spiked baby food 5, with corresponding (a) extracted ion chromatogram; (b) isotopic pattern; and (c) experimental and reference fragmentation spectra comparison using FIT algorithm.

identification was about 99% using the FIT algorithm. This demonstrates the reliability of the developed automated identification method, and how important MS/MS fragmentation spectra are for unequivocal identification (Schymanski et al., 2014).
Considering the literature, López et al. (2014) used a QuEChERS-UHPLC-Q-TOF method to screen almost 200 pesticides in fruits and vegetables. As an identification strategy, the authors used t_r variation ± 0.1 min and accurate mass measurement ± 5 ppm on the precursor ion, plus accurate mass measurement ± 10 ppm on corresponding product ion(s). The average identification rate was 64% at 0.01 $mg.kg^{-1}$, which was equivalent to our results (37% false negative rate, i.e., 63% identification rate). Despite the demanding nature of the identification approach proposed in this study and the complexity of the baby food matrices, the method showed satisfactory performances for a large-scale screening purpose, even at low-level of concentration

3.4. Method validation

The last part of this work consisted in validation of the complete optimised method, inspired by SANTE guidelines for screening methods (SANTE, 2021). SDL and LOI, detailed in section 2.11., were used as criteria of validation. However, as difenoconazole was found in baby foods 5 and 6, these samples were discarded. The results are displayed in ESM (Table S4) and are summarized in ESM (Fig. S5). Regarding the SDL, it was established at 0.01 $mg.kg^{-1}$ for 141 pesticides (71%), and at 0.1 $mg.kg^{-1}$ for 48 pesticides (24%). Overall, 95% of the pesticides had an SDL ≤ 0.1 $mg.kg^{-1}$. These validation results demonstrated the very good detection capabilities of the method, and its ability to act as an alert system if a pesticide found in a baby food sample significantly exceeds the MRL. However, 10 pesticides (5%) were not detected in at least 29 of the 30 baby food samples. Therefore, their SDL was established as > 0.1 $mg.kg^{-1}$.

Regarding the LOI, it was established at 0.01 $mg.kg^{-1}$ for 77 pesticides (39%), and at 0.1 $mg.kg^{-1}$ for 68 pesticides (34%). Overall, 73% of the pesticides had an LOI ≤ 0.1 $mg.kg^{-1}$. However, 54 pesticides (27%) could not be properly identified in at least 29 of the 30 baby food samples. Therefore, their LOI was established as > 0.1 $mg.kg^{-1}$ (Fig. S5).
In the literature, Luz Gómez-Pérez et al. (2015) used t_r variation ± 0.5 min and mass error < 5 ppm on the precursor and one of its fragment ions, for the screening of more than 300 pesticides in baby foods. The LOI was established at 0.01 $mg.kg^{-1}$ for about 61% of the compounds. In this study, the authors explained that analytes at low-concentration in complex matrices may provide fragment ions at low sensitivity, which make the identification process difficult (Luz Gómez-Pérez et al., 2015). This aspect may have a greater impact on the performances in the case of our presented study. Indeed, the FIT algorithm used for identification takes into account all the expected fragment ions of a compound in the calculation, and not only the most abundant fragment ion(s). At 0.01 $mg.kg^{-1}$, some expected fragment ions were missing in the experimental fragmentation spectra, which lowers the similarity scores computed by the software. This could explained the difference in the performances observed in both studies. In addition, another factor should be highlighted. Luz Gómez-Pérez et al. (2015) used DIA mode for their screening and identification. In our study, not all pesticides were fragmented with IDA-PIL mode, preventing them from being validated. Thus, it would be necessary in a future work to evaluate DIA mode that allows all precursor ions to be fragmented. Nevertheless, the use of DIA mode would require optimisation as it provides more interferences and complex spectra that reduce the confidence into the identification process (Diallo et al., 2022).

Regarding validation at the identification stage, the approach proposed in the present study is not covered by the analytical guidelines, being limited by the options provided in MasterView™ software. In this sense, manufacturers should be able to provide compliant identification strategies regarding guidelines and the literature. In parallel, there is a need to improve existing official guidelines (SANTE, 2021; FDA, 2015) to include the identification approach using MS/MS similarity in addition to the approach already proposed. Furthermore, there are no requirements regarding false positives for method validation currently. There is also a need to indicate the false positive rate not to be exceeded to be able to use a screening method in a high-throughput sample analysis-based context with a high confidence and to avoid time-consuming manual verifications.

3.5. Suspect screening analysis

HRMS not only offers the possibility of conducting targeted analyses, but also of reprocessing retrospectively acquired data (Phillips et al., 2018), in order to broaden the analytical scope and optimize monitoring in an exposomic-based context. Thus, the versatility and feasibility of the method was also demonstrated performing post-acquisition suspect-screening analysis on the analysed baby food samples. For this purpose, an expanded list of over 500 organic contaminants including pesticides and metabolites, flame retardants and plasticizers, was included in the database on the basis of their elemental formula and corresponding exact mass (Table S5). . Compound identification in suspect-screening analysis was conducted according to the identification confidence levels proposed by Schymanski et al. (2014). In the first instance, only the accurate mass measurement ± 5 ppm was used as a filter (confidence level 5). Among the positive results, if the compound was not fragmented, it was not considered anymore as a positive result as it was not feasible to identify the contaminant. If the compound was fragmented, the resulting fragmentation spectrum was compared to the spectra available in online databases. If the experimental spectrum matched with external spectrum, the compound was then considered as putatively identified (confidence level 2). Using this workflow, a flame retardant and plasticizer, tris(2-chloroethyl) phosphate (TCEP), was putatively identified in some baby food samples. Afterwards, the analytical standard of TCEP was purchased and injected for confirmation. The criteria used were the t_r variation ± 0.1 min and accurate mass measurement ± 5 ppm on the precursor ion, as well as the spectral similarity between the reference and experimental MS/MS fragmentation spectra, using FIT algorithm with a similarity score > 70%. Thus, the presence of TCEP was confirmed at the confidence level 1 of identification, as shown in Fig.4. The t_r variation was 0.01 min, the mass error was -2.5 ppm and the FIT score was 95.7%.

The proposed method is a qualitative method acting as an alert system, i.e., it is able to detect and identify the presence or absence of a contaminant. Nevertheless, it would be important to quantify TCEP, either through a semi-quantitative approach, or precisely through conventional tandem mass spectrometry to determine whether its presence in the baby food samples exceeds the MRL.

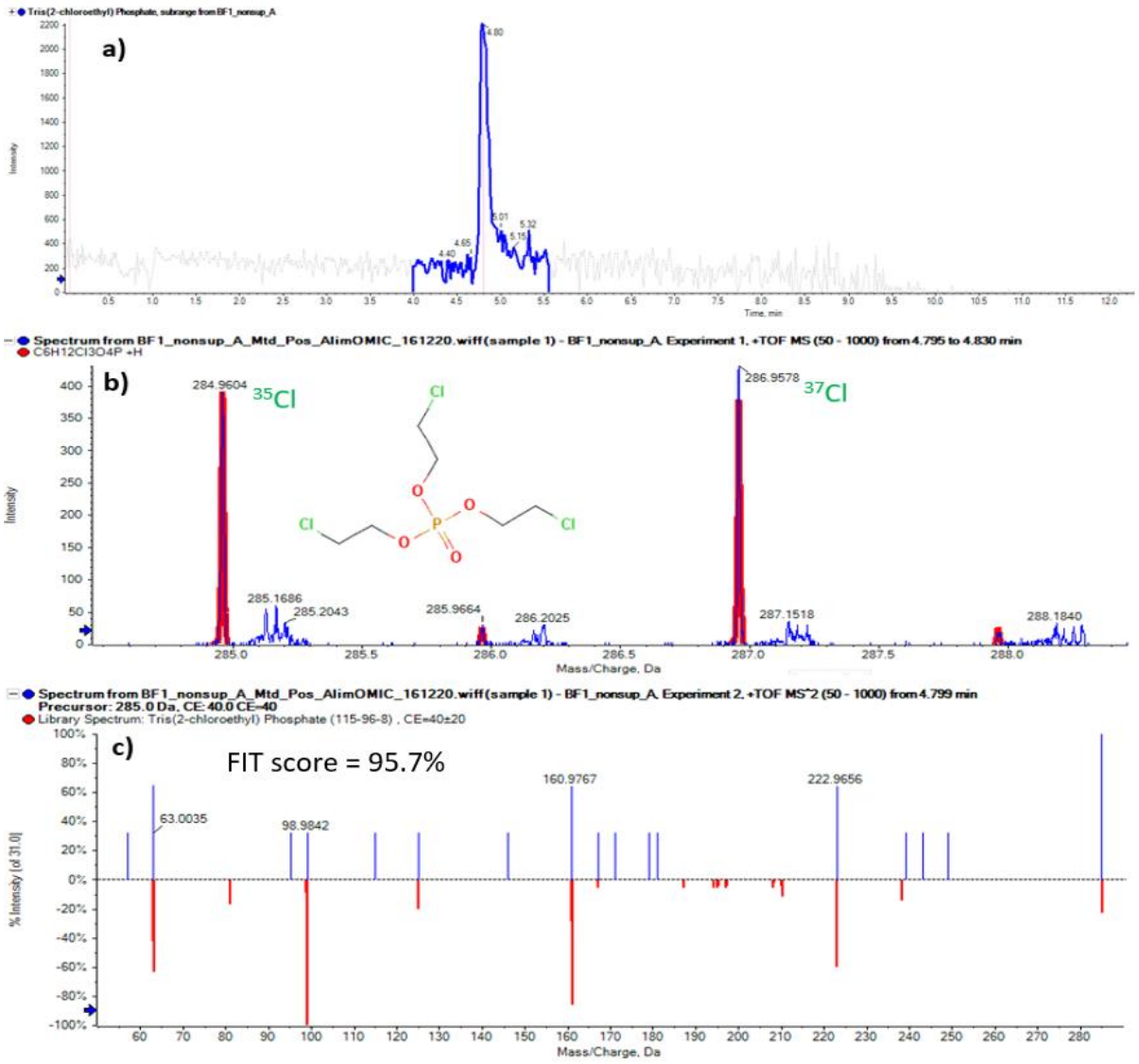

Fig.4. Identification of tris(2-chloroethyl) phosphate in non-spiked baby food 1, with corresponding (a) extracted ion chromatogram; (b) isotopic pattern; (c) experimental and reference fragmentation spectra comparison using FIT algorithm.

4. Conclusion

In this study, a QuEChERS-based protocol coupled to UHPLC-Q-TOF MS (ESI+) analysis enabled the screening of 204 pesticides in baby foods. The extraction procedure was optimized based on QuEChERS methods, to set-up a sample preparation protocol that can be adapted to various baby foods. The QuEChERS based on the AOAC method followed by a purification using $MgSO_4$/PSA, provided the less false negatives and the better signal-to-noise ratio. Screening of pesticides in baby food samples was performed at the detection and identification stages using a homemade t_r-MS/MS library, allowing for fast, automated and unequivocal compound identification. As there is no standardisation, different thresholds on the t_r and accurate mass measurement were assessed on the performances of detection. SANTE guidelines criteria (t_r ± 0.1 min, accurate mass measurement ± 5 ppm) showed the best balance between false negatives with 16% and 5% at 0.01 $mg.kg^{-1}$ and 0.1 $mg.kg^{-1}$, respectively, and false

positives with a low rate of 5%. Regarding identification, IDA and IDA-PIL modes as well as different MS/MS algorithms-score combinations were evaluated. IDA-PIL mode and identification using the FIT algorithm and similarity score >70% were selected for the method, and demonstrated good performances with 37% and 15% false negative rates, at 0.01 $mg.kg^{-1}$ and 0.1 $mg.kg^{-1}$, respectively. The method was then validated based on the SANTE guidelines for screening methods: 95% and 73% of the pesticides had a screening SDL and LOI $\leq$ 0.1 $mg.kg^{-1}$, respectively. The proposed method enabled the unequivocal identification of the pesticide difenoconazole and a plasticizer, TCEP, in some of the investigated samples.
Looking forward, the DIA mode should be further evaluated for pesticides and similar contaminants as it makes it possible to overcome the loss of MS/MS data and the related false negatives obtained in IDA mode. As the MS/MS spectral similarity is not yet integrated in analytical guidelines, there is a need to consider this type of identification.

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Declaration of competing interest

The authors declare that they have no conflicts of interest

2.1.4. Summary & main results

In this work, we optimized the QuEChERS preparation method to minimize false-negative rates, i.e. the number of pesticides present in the matrix but not detected/identified. We were also able to evaluate the criteria used for contaminant screening in HRMS, to define optimal tolerance thresholds and keep the false negative and false positive rates obtained as low as possible. We also opened a discussion on the use of algorithms for calculating similarity between a reference MS/MS spectrum vs. an experimental MS/MS spectrum. This is an identification method that we wanted to highlight through this paper, and which is not officially described in analytical guides, although very effective due to its high reliability. An inclusion list had to be used to compensate for the non-fragmentation of certain analytes of interest, inherent in the IDA mode, to enhance identification performances (down to MS/MS level). The optimized method was validated in compliance with European Commission guidelines. We were able to apply it and identify a triazole fungicide, difenoconazole, in carrot-based baby food. Retroactive suspect analysis using a list of contaminants of interest revealed a flame retardant, TDCPP, in two samples of meat-based baby food. This compound was then confirmed by targeted analysis after acquisition of the analytical standard.

2.1.5. Limitations and prospects for improvements

Although it lays the foundations for a broad-spectrum HRMS screening method, certain limitations emerge from this initial analytical development. First, optimization of the QuEChERS method has only focused on the composition of the extraction salts and purification materials used. Design-of-experiment optimization methodologies could be useful to assess more efficiently several parameters that affect the performances of the method and by saving time and experiments required. Another limitation concerns the acquisition mode used. In this first work, we exclusively used the IDA MS/MS acquisition mode. However, it would be important to carry out a comparative study of its efficiency with that of the SWATH-MS mode (= DIA on Orbitrap), to define the most relevant MS/MS acquisition method for broad-spectrum screening with a high level of confidence. Finally, in this paper, only 204 pesticide residues were included, which is a good start, but still limited. We need to broaden the spectrum of contaminants to demonstrate the robustness of HRMS for very broad-spectrum and efficient targeted screening.

More generally, an effort is also needed to improve the overall performance of the method, particularly up to the identification level (MS+MS/MS).

2.2. Development of a multiresidue method for the analysis of pesticides in bivalves

2.2.1. Context and aim of the study

This second project involved the development of a method for multi-residue analysis of pesticides in bivalve samples. These matrices are of major ecological and economic interest. Bivalves are sentinel species for environmental quality. In addition, abnormally high mussel mortality rates were observed in the Pertuis-Charentais (France), and this area of interest represents 22% of French bivalve production. Mussel mortality therefore represents a major economic issue. This work was mainly led by my colleague Thierno Diallo, a doctoral student at the laboratory for food safety of Anses, whose subject is the elucidation of this excess mussel mortality in the Pertuis-Charentais area (France). The main objective of this study was to optimize an efficient extraction method for the analysis of pesticide residues in bivalves, and to apply it to field samples in an attempt to shed light on any chemical contamination involved in mussel mortality.

I contributed to this work by supporting Thierno in the experiments, the optimization of the QuEChERS extraction method, and the use of SWATH-MS methods.

2.2.2. Key points of the study

As part of this method development, we were able to:

- Evaluate the efficiency of experimental designs using the Taguchi method (Narenderan et al., 2019) to reliably optimize the QuEChERS extraction protocol, while reducing the cost and experimental time required.
- Evaluate the performance of the main acquisition modes in HRMS. Indeed, the challenge of satisfactorily identifying the contaminants of interest lies not only in the fragmentation of the analytes, but also in the quality of the MS/MS spectra generated. It was important to be able to compare the two main methods, IDA and SWATH-MS. Indeed, although the proposed methods are developed using analytical standards, they are also intended to be used for suspect and non-target retro-analysis. If non-fragmentation rates are too high, or MS/MS spectra are marred by too much interferences, this could affect the annotations of other potential contaminants for which analytical standards are not available.

Fig.1 below describes and summarizes the major improvements compared with the previous work (Makni et al., 2022), following an iterative process of continuous improvement.

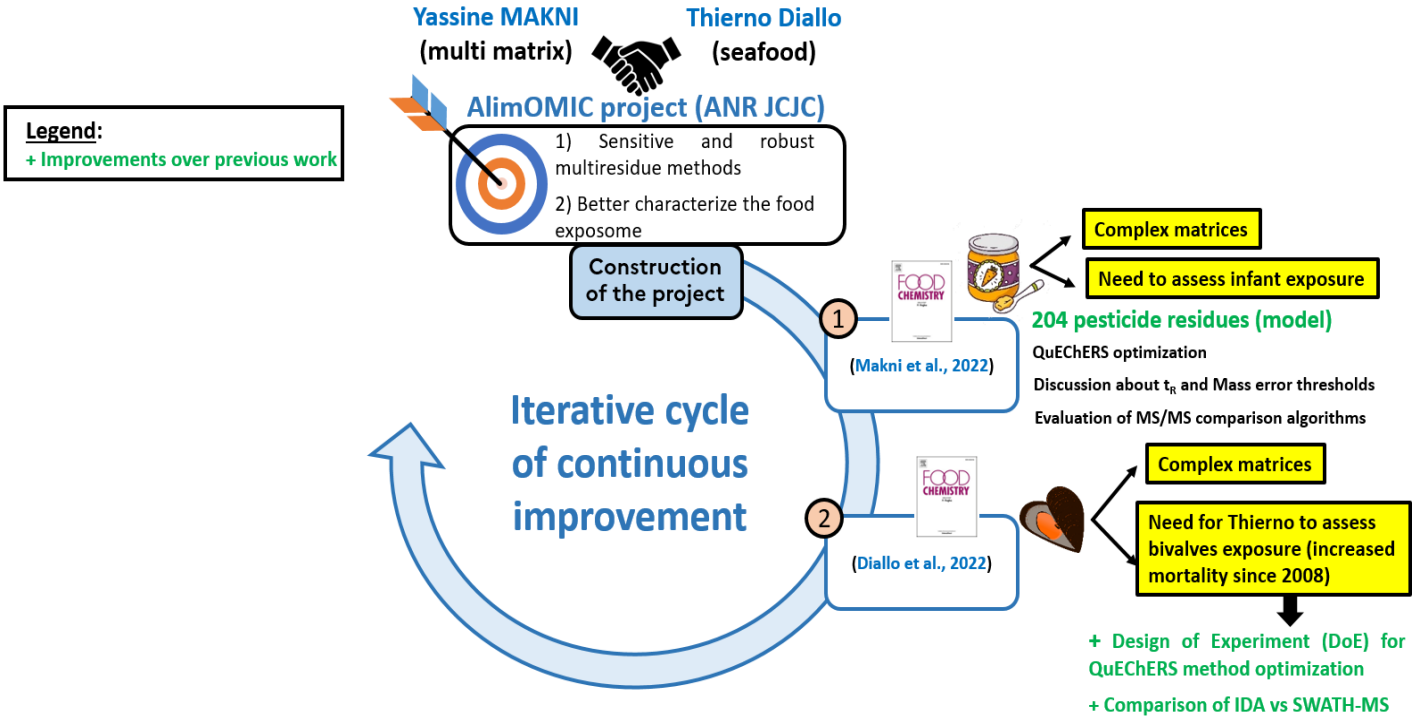

Fig.1. Cycle of iterative and continuous improvement – part 1

2.2.3. Article 2 (Diallo et al., 2022)

The following article details experiments on the optimization and validation of a method for the analysis of 204 pesticides in bivalves. This article was published in the journal Food Chemistry. Due to Elsevier copyright restrictions, only the title and abstract of the paper were included in published format. The rest of the paper is inserted in Word-type format. The published paper is available online using the following DOI

https://doi.org/10.1016/j.foodchem.2022.132871

The references associated to this article are displayed here: References section (Article No. 2).

The electronic supplementary materials (Annexes) associated to this article are displayed here: Article 2 (Diallo et al., 2022): "Development and validation according to the SANTE guidelines of a QuEChERS-UHPLC-QTOF-MS method for the screening of 204 pesticides in bivalves"

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Development and validation according to the SANTE guidelines of a QuEChERS-UHPLC-QTOF-MS method for the screening of 204 pesticides in bivalves

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ABSTRACT

A qualitative screening high resolution mass spectrometry method was developed and validated according to the EU SANTE/12682/2019 guidelines for the analysis of 204 pesticides in seven commercial bivalve species spiked at three concentrations (0.01, 0.05 and, 0.1 $mg.kg^{-1}$). Samples were extracted using QuEChERS and analysed using ultra-high-performance liquid chromatography coupled to quadrupole time-of-flight mass spectrometry. The QuEChERS method was optimised by the Taguchi Orthogonal Array approach. The best conditions were obtained with pure ACN, $MgSO_4$/NaCl as extraction salts, $MgSO_4$/PSA/C18 as clean-up, and the non-dilution of extracts. The impact of different HRMS acquisition modes on detection and identification rates were also evaluated. The screening detection limits were determined to be 0.01 $mg.kg^{-1}$ and 0.1 for 66% and 87% of pesticides, respectively. These screening procedure was finally applied to different bivalve samples using target and suspect analysis. This allowed the identification of diuron and its metabolite 1-(3,4-dichlorophenyl)-3-methylurea in the investigated samples.

1. Introduction

During the last few decades, the use of pesticides to protect crops has facilitated mass food production. However, the use of pesticides can lead to chemical pollution in water located near crop fields due to transport into surface and groundwater (Tudi et al., 2021). Once in water, pesticides and their metabolites become bioavailable to aquatic organisms and can bioaccumulate in their tissues via the skin, gills and/or diet, depending on their solubility (van der Oost et al., 2003). Biomagnification of chemicals through the food chain can lead to toxic effects to predators and humans (van der Oost et al., 2003). Therefore, the use of pesticides near surface waters poses a high risk to the aquatic ecosystem and potentially to consumers.

Bivalves are indicator species of environmental quality. They filter large volumes of water and concentrate xenobiotics, allowing for the assessment of pollutant concentrations in their ecosystems (Breitwieser et al., 2018). Moreover, bivalves are a reliable source of information on human exposure to contaminated seafood (Rodríguez-González et al., 2015). Bivalves are also crucial in aquatic environment since they provide habitats for other organisms (algae, macroinvertebrates) and contribute to nutrient cycling and storage (Vaughn and Hoellein, 2018). In addition, bivalves accounted for 17.7 million tons of coastal and marine animal

aquaculture in 2018, with an estimated market value of USD 34,6 billion (FAO, 2020). For all these reasons, high mortality of bivalves such as oysters (Vohmann et al., 2010) and mussels (McFarland et al., 2016) worldwide is not only a major ecological issue but also an economic concern.

Analytically, whole-body bivalves are complex matrices. The presence of proteins and lipids in high concentrations (between 2 to 10% and between 10 to 18% of lipids and proteins, respectively) makes it difficult to analyse compounds such as pesticides with lower concentrations in the sample (US Department of Agriculture, 2016). This matrix effect needs to be reduced to avoid bias in the overall analysis. Sample preparation of bivalves normally requires time-consuming steps to remove these lipids and proteins in order to obtain acceptable recoveries for the target compounds. The most commonly used extraction techniques for bivalve samples are accelerated solvent extraction (Galvao et al., 2012), pressurized liquid extraction (Rodrigues et al., 2016), and microwave extraction (Uluturhan et al., 2019). Extraction methods based on these techniques are usually followed by solid phase analysis (SPE). The Quick, Easy, Cheap, Effective, Rugged and Safe (QuEChERS) extraction method is a preferable alternative to these different methods due to its fast protocol, reliable results, and affordable cost. This method has already been successfully applied for the analysis of pesticides in bivalves (Cruzeiro et al., 2016; Álvarez-Muñoz et al., 2019).

Despite the advantages of QuEChERS, to achieve the best extraction efficiency, many parameters need to be optimised, including sample amount, extraction solvent, solvent pH, partition salt, dispersive-SPE (dSPE) sorbent, concentration to increase sensibility of the compounds, and dilution of extracts to reduce matrix effects. Because of the high number of parameters that can influence the analysis, the possible interactions between them, and the time needed to process data, it is not feasible to analyse all of them independently. As a result, it is recommended to use so-called split factorial design methods to save time. One of these methods, called Taguchi Orthogonal Array (TOA), is characterized by its simplicity and efficiency in designing parameter combinations and in evaluating each parameter. Taguchi proposed a design matrix that allows the study of all parameters with selectively reduced experimental size (Narenderan et al., 2019a). This matrix can be used to determine the influence of each designed parameter and to identify the best combination of parameters to obtain the best result (Narenderan et al., 2019a). The TOA method was recently used to optimise the QuEChERS method for wide-scope multi-residue analysis of pesticides in beef (Pang et al., 2021b).

Following the sample preparation optimisation step comes the analytical step, to highlight the presence or absence of target compounds and to quantify them in the reference matrices. To determine pesticides in bivalves, gas chromatography (GC) and liquid chromatography (LC) coupled to triple quadrupole mass spectrometry operating in multiple reaction monitoring (MRM) mode are the most common techniques, due to their selectivity and sensitivity (Cruzeiro et al., 2016). However, these low-resolution (LR) techniques are limited to the target compounds, so compounds not included in the method are not analysed. In addition, the number of compounds that can be screened simultaneously is limited (López et al., 2014b). More recently, there has been increasing interest in the benefits of high-resolution mass spectrometry (HRMS) (Rajski et al., 2019). This is partly due to its ability to perform simultaneous target, suspect, and non-target analyses to increase the number of analytes (the scope) that can be included in multi-residue methods (Rajski et al., 2019). HRMS increases selectivity needed to overcome interferences in more complex matrices (Rajski et al., 2021a). It also allows for retrospective analysis by reprocessing the acquired data for potential new compounds discovered without reinjection of the sample (Arroyo-Manzanares et al., 2021a), which limits sample stability problems. Although HRMS, such as time-of-flight (TOF) instruments, has

emerged as a conventional means for pesticide detection and identification (López et al., 2014b), it is still a major challenge to analyse low-level and trace pesticides in matrices as complex as bivalves. Therefore, the quality of MS/MS spectra is critical to obtain high confidence in the identification of small molecules (Schymanski et al., 2014b). Currently, the main methods for acquiring a simultaneous MS-MS/MS mass spectrum are data-dependent acquisition (DDA) and data-independent acquisition (DIA) methods. DDA and DIA are also referred to as IDA (information-dependent acquisition) and SWATH® (sequential window acquisition of all theoretical fragment ion spectra) in Sciex instruments, respectively. The MS/MS data for the SWATH® produce more fragments due to the ability of SWATH® to fragment all ions, including isotopes. This results in spectra that are richer in information but also more complex. In IDA mode, only the most intense ions are fragmented. The number of most intense ions (*top-n*) to be fragmented is set by the user. The MS/MS spectra in IDA mode are less rich than those obtained in SWATH, but clearer and easier to interpret (Álvarez-Ruiz and Picó, 2019a).

The aim of this study was to develop a simple, rapid and wide-scope QuEChERS sample extraction method, followed by a UHPLC-QTOF-MS comprehensive target screening analysis for 204 pesticides in bivalves. The list of target compounds included pesticides from different families with very distinct physicochemical properties, which therefore serve as a template to prepare the analysis in suspect screening. To our knowledge, this study is the first to perform HRMS analysis for such a comprehensive list of pesticides in bivalves. So far, only one study determined pesticides (12 in total) in bivalves by HRMS (Álvarez-Muñoz et al., 2019), while others have used LR mass spectrometers to analyse up to 60 pesticides in bivalves (Cruzeiro et al., 2016). The TOA method was used to evaluate optimum parameters for the sample extraction step. To the best of our knowledge, this is the first time that the TOA method has been used to optimise a QuEChERS extraction for the analysis of pesticides in bivalves. Moreover, different IDA and SWATH methods were tested to optimise detection and identification rates. The selected method was also validated according to the European Union SANTE/12682/2019 guideline (European Commission, 2019). For each pesticide, the screening detection limits (SDLs) was established in bivalve samples. Although it is not required for the qualitative screening method validation according to the SANTE guidelines, the limit of identification (LOI) was also established. The number of false positives was assessed using blank bivalve samples out of the 204 pesticides. Once validated, the screening method was applied to the analysis of different bivalve samples, including mussels and oysters by target and suspect analysis.

2. Materials and methods

2.1. Chemical substances and analytical standards

Acetonitrile (ACN), obtained from Fisher Scientific (Illkirch, France), and ultrapure water (18.2 MΩ.cm), obtained by purifying distilled water with a Milli-Q system from Merck Millipore (Saint-Quentin-en-Yvelines, France), were used for the mobile phases and sample preparation. Formic acid (FA) and acetic acid (AA) were supplied by Fisher Scientific (Illkirch, France), to prepare LC-MS mobile phases and the extraction solvent. QuEChERS extraction pouches based on the original method (4.0 g of magnesium sulphate ($MgSO_4$), 1.0 g of sodium chloride (NaCl)), AOAC Method 2007.1 (6.0 g anhydrous $MgSO_4$, 1.5 g sodium acetate) and EN Method 15662 (4.0 g of $MgSO_4$, 1.0 g of NaCl, 1.0 g of sodium citrate, and 0.5 g of sodium citrate sesquihydrate) were provided by Agilent Technologies (Santa Clara, CA, USA). A dispersive solid phase extraction (d-SPE) kit containing 900 mg of $MgSO_4$, 150 mg of Primary and Secondary Amines (PSA) and 150 mg of octadecylsilane (C18), and Enhanced Matrix Removal-Lipid (EMR-lipid) d-SPE was obtained from Agilent Technologies (Santa Clara, CA,

USA). Zirconium-based Z-Sep/C18 (120 mg Z-Sep, 300 mg Discovery DSC-18) was supplied by Supelco (Bellefonte, PA, USA). The standard consists of 204 pesticides (Table S1) divided into ten mixtures (100 $mg.L^{-1}$ of each compound in ACN). The ten pesticide standard stock solutions were obtained from Restek Corporation (Les Ulis, France), transferred and stored in screw-capped amber glass tubes at -20 °C. A mixture working solution (2 $mg.L^{-1}$) was prepared through suitable dilution of the ten intermediate solutions with ACN, and stored in screw-capped amber glass tubes at -20 °C.

2.2. Equipment and apparatus

A Genie 2 vortex mixer (Scientific Industries, Bohemia, NY, USA) was used for the extraction procedure. An IKA Ultra-Turrax T25 digital homogenizer and a GM 200 Grindomix (Retsch Technology GmbH, Haan, Germany) were used for the extraction procedure. A Mettler Toledo (Columbus, USA) XS 204 analytical balance was used to weigh the samples.

An UHPLC Thermo Fisher Scientific U3000 system composed of a binary pump and autosampler (Waltham, MA, USA) coupled with a 5600 Q-TOF AB Sciex mass spectrometer (Darmstadt, Germany) with an electrospray ionization source (ESI) was used for analyses.

2.3. Orthogonal array design for optimisation of QuEChERS extraction and clean- up

Four factors (extraction solvent acidification, extraction salts, dSPE and dilution ratio) were considered for the optimisation of QuEChERS extraction and clean-up. Three levels were used for each factor (Table 1).

To optimise these four factors simultaneously, a Design of Experiment (DoE) was performed using L9 TOA. As shown in Table S2, nine experiments with three replicates for each were performed to evaluate responses such as pesticide detection rates (%) and signal-to-noise (S/N) of the 204 pesticides.

Table 1. Control factor and levels in the QuEChERS extraction and clean-up.

Level	Factor			
	Solvent acidification	**Salt**	**dSPE**	**Dilution**
1	ACN (1% AA)	AOAC Method*	$MgSO_4$/PSA/ C18	Non-dilution
2	ACN (1% FA)	EN Method**	Z-sep/C18	1:2
3	ACN	Original Method***	EMR lipid	1:4

2.4. Bivalve samples

The bivalve samples (oysters, mussels, cockles, clams, sea almonds and two types of scallops) used for method optimisation and validation were purchased from local markets (Maisons-Alfort, France). To test the screening method applicability, a total of fourteen bivalves (seven mussels and seven oysters) were collected at three sites located in the Pertuis Charentais littoral area (southwest France) in May 2019, September 2019 and January 2020 and frozen at -20 °C. Before shucking, the oysters were stored at 4 °C overnight and then brought to room

temperature. The samples were homogenized with a GM 200 Grindomix (Retsch Technology GmbH, Haan, Germany) and kept at -20 °C until analysis.

2.5. Sample preparation

Extraction solvent acidification, extraction salts, dSPE and dilution ratio were simultaneously optimised using L9 TOA. For the enrichment experiment, 7.5 µL of the mix working solution were added to 50-mL polypropylene centrifuge tubes, which contained 1.50 ± 0.05 g of blank oyster sample, to provide a supplementation at 0.01 $mg.kg^{-1}$ of pesticides. A contact time of 24 h at 4 °C was allowed for the pesticides to bind to the matrix. Then, 8.5 mL of Milli-Q water were added to each tube, and the sample was then ground using an IKA Ultra-Turrax mixer for 3 min at 5,000 rpm. Then, 10 mL of extraction solvent were added to each centrifuge tube to perform pesticide extraction, and tubes were vortexed again for 1 min. After that, the salts were added to the fortified samples, and the resulting mixture was centrifuged for 5 min at 4,000 rpm.

When EMR lipid was used as the dSPE reagent, 5 mL water was added to a 15-mL centrifuge tube containing the EMR-Lipid and vortexed for 3 s to activate the sorbent. Then, 5 mL of the supernatant (50-mL polypropylene centrifuge tube) were transferred to activated 15-mL centrifuge tube. The mixture was vortexed immediately for 1 min. The tube was centrifuged at 4,000 rpm for 5 min, and 5 mL of the supernatant was transferred to the polishing tube containing $MgSO_4$ to remove excess water. When using the other dSPE reagents, 6 mL of the supernatant were transferred to a 15-mL centrifuge tube containing the dSPE reagent. The tube was vortexed for 1 min, and then centrifuged for 5 min at 4,000 rpm. The supernatant was then combined with ACN according to the dilution ratio. The mixture was then vortexed, filtered, and deposited into a 2-mL auto-sampler vial for injection in the UHPLC-QTOF system.

To determine background contamination, matrix-free ACN was subjected to the same extraction and purification protocols as previously described.

2.6. UHPLC-QTOF-MS conditions

Reversed-phase liquid chromatography separation was performed using A Phenomenex Aqua® C18 column (150 x 2 mm, 3 µm particle size, 125 Å pore diameter; Phenomenex Inc, Torrance, CA, USA). A gradient using Milli-Q water (Solvent A) and acetonitrile (Solvent B) with both containing 0.01% of FA was used at a constant flow rate of 0.500 $mL.min^{-1}$. The gradient profile started with 10% B (0 min); increased linearly to 100% B for 9 minutes (0-9 min); fixed for 3 minutes (9–12 min) and returned to the initial conditions in 0.1 min (12.1 min), followed by a re-equilibration step for 3.9 minutes. The total run time was 16 min. The auto sampler was thermo-regulated at 15 °C to avoid sample degradation during analysis-runs. The injection volume was 10 µL and the column temperature was set at 50 °C. The detection was carried out in positive (ESI+) ionization mode. The instrument was tuned and calibrated before each batch, in high-resolution mode. The automated calibration device system (CDS) was scheduled to perform automatic calibration every five injections using APCI Positive Calibration Solution for the 5600 system (AB Sciex technology). ESI+ parameters were as follows: the ion spray voltage floating (ISVF) was set at 5.5 kV, the source temperature (TEM) was 500 °C, the curtain gas (CUR) was set at 30 psi, the nebulizing gas (GS1) at 40 psi, and the heater gas (GS2) at 45 psi.

2.7. Evaluation and comparison of IDA and SWATH® workflows for pesticide detection and identification

In this study, four acquisition methods were implemented using the UHPLC-QTOF-MS system for pesticide detection and identification in spiked sample at 0.01 mg.L^{-1} of the target 204 pesticides. The source condition was the same for all methods as well as the mass range of 50–1,000 Da for TOF MS and TOF MS/MS.

Method A consisted in implementing the IDA method. The accumulation time for the TOF MS full scan was set to 490 ms, while in TOF MS/MS it was set to 100 ms. For the product ion scan, the parameters were set as follows: collision energy (CE) was fixed at 40 eV with ± 20 eV and declustering potential (DP) was 80 eV (+). Isotope exclusion was switched off. The 4 most intense ions (*Top4*) following precursor ion intensity greater than 50 cps with ion tolerance ≤ 10 ppm were monitored per cycle, and dynamic background subtraction was turned on. The total cycle run time was 940 ms.

Method B used IDA-PIL (Precursor Ions List). The parameters were the same as the IDA but with an inclusion list of the 204 target pesticides.

Method C and method D consisted in using the fixed (F-SWATH) and variable (V-SWATH) methods, respectively, with the specific settings listed in Table S3. Different numbers of SWATH® windows (20, 30, 40, and 50) were evaluated with F-SWATH (F-SWATH20, F-SWATH30, F-SWATH40 and F-SWATH50) or V-SWATH (V-SWATH20, V-SWATH30, V-SWATH40 and V-SWATH50) window width for Q1 isolation (overlap 1 Da). F-SWATH selects and fragments all detected precursor ions with an m/z window size Q1 that is uniform throughout the LC-MS run. For V-SWATH, the m/z windows are variable depending on the density of precursor ions by adjusting the isolation window to the number of precursor ions in the window (Álvarez-Ruiz and Picó, 2019a).

Different acquisition methods were evaluated and compared using the pesticide detection rates and identification rates. For the latter, two different MS/MS search algorithms (*purity score* and *fit score*) at two levels (>70% and > 50%) were evaluated according to the literature (Gómez-Romero et al., 2011).

2.8. Method validation

The QuEChERS-LC-HRMS qualitative screening method was validated according to the European Union SANTE/12682/2019 guidelines (European Commission, 2019). For this purpose, seven species of commercial bivalves were used: oysters, mussels, cockles, clams, sea almonds and two types of scallops (*Pecten maximus* and *Mimachlamys varia*). For each species, four groups were randomly formed. Individuals from each group were pooled, then 1.5 g of each was weighed and transferred into 50-ml polypropylene centrifuge tubes. Sub-samples were spiked before extraction with a mixture containing 204 pesticides at 0.01, 0.05, and 0.1 mg.kg^{-1}, (to a total of 28 samples for each concentration level). The SDL was established as the lowest concentration level at which a compound was detected (not necessarily meeting the MS-identification criteria) in at least 95% of the samples (i.e., 27 out of 28 samples analysed) (European Commission, 2019). SDL was estimated as the concentration level at which the thresholds of (i) T_R (variation ± 0.1 min) and (ii) mass accuracy (± 5 ppm) of the precursor ion were satisfied (European Commission, 2019). The LOI (not required according to SANTE guidelines) was established as the lowest concentration tested for which a compound was satisfactorily identified in at least 95% of the samples. LOI used the same thresholds as for SDL, as well as an MS/MS library score. Non-spiked (blank) samples were also extracted and analysed to assess the number of false positives out of the 204 targeted pesticides.

2.9. Software and statistical analysis

Analyst® 1.7 software (AB Sciex, Les Ulis, France) was used for equipment control and data acquisition. Data were processed and evaluated using PeakView® software version 2.2 comprising the AB Sciex MasterView™ module (Les Ulis, France), with intensity > 50 cps and S/N > 3. Pesticide detection was performed using a previously developed home-made database containing information on molecular formulae, retention time (T_R), accurate *m/z*, and isotopic pattern for 204 target pesticides (see Fig. S1). Pesticide identification was performed by MS/MS spectral matching and not by mass accuracy of the product ions as recommended by SANTE guidelines (European Commission, 2019). Indeed, MasterView™ software allows to obtain automatically the mass error only on the precursor ions and not on the product ions. The MS/MS spectral library of 204 pesticides was built using AB Sciex LibraryView™ software, version 1.0.3 (Les Ulis, France). The library was acquired in IDA mode by injecting separately each of the ten standard intermediate solutions diluted to 0.2 $mg.L^{-1}$ in ACN. It should be noted that LibraryView™ software does not enable creation of a SWATH® spectral library. Different MS/MS search algorithms were used for pesticide identification, including *purity score* (Purity) and *fit score* (Fit). Purity is guaranteed in the range of 0–100 and is a measure of the similarity between the library spectrum and the acquired spectrum (Gómez-Romero et al., 2011). Fit reflects the degree of agreement between the masses and intensities of the library spectrum and those found in the acquired spectrum, ignoring other masses contained in the acquired spectrum (Gómez-Romero et al., 2011). A high Fit and low Purity indicate that the acquired spectrum is likely impure but contains the library compound.

The SWATH™ Variable Window Calculator tool (version 1.1) was used to calculate V-SWATH using an IDA total ion chromatogram (TIC).

Statistical analyses were performed using RStudio (Boston, MA, USA). The normality of the data was verified by the Shapiro–Wilk test. According to the distribution of the data, analysis of variance (ANOVA) with Tukey's multiple comparison post-hoc test or Kruskal–Wallis's test with Dunn's post-test were used (confidence limit of 95%, $p < 0.05$).

3. Results and discussion

3.1. Optimisation of sample preparation using the TOA method

Several parameters can have an impact on the efficiency of a QuEChERS extraction. This is the case for the sample amount, the extraction solvent, the acidification of the solvent, the partition salt, the clean-up, the concentration and the dilution of the extracts. To simplify the optimisation of the QuEChERS method, the Taguchi approach was chosen to simultaneously optimise the acidification of the extraction solvent, extraction salts, dSPE and dilution ratio. Responses evaluated were detection rates (%) and S/N of the 204 pesticides. The sample amount was not tested in this study as the aim of this work is to apply the optimised method to analyse a large number of bivalve samples (in particular oysters and mussels) pooled and individually (to test inter-individual variability). As the flesh of a mussel can weigh between 1 and 2 g, the choice of a sample weight of 1.5 g was considered appropriate.

The values of the mean detection rates oscillated between 56% and 86% (Table 2) and the S/N between 97 and 190 (Table 3) for all experiments. Overall, the best performances were found with experiment 9 and 1 for detection rates and S/N, respectively. The performance of each experiment depends on the pesticide considered as shown in the chromatograms of fenpropimorph, methoprotryne, hydramethylnon and azoxystrobin in Fig. S2. According to the R values for the mean detection rates and S/N, the most impactful factor is dilution (R=28.55 and 56.76), followed by extraction solvent acidification (R=3.98 and 9.69) or dSPE (R=2.39 and 43.19), and finally the extraction salts (R=1.40 and 8.92). The effects of the four studied factors on the pesticide detection rates and S/N are also shown in Fig. S3. Detection rates and

S/N graphs can be read in two different ways depending on whether the levels are represented by column chart or connected by curves. When the levels are connected by curves (as in the case of dilution), the flatter the slope, the less significant the factor on the response studied. Conversely, the steeper the slope, the more significant the factor. When the detection rate and S/N ratio are represented by column chart (as in the case of extraction solvent acidification, extraction salts and dSPE), the greater the difference between the best and worst performing level, the more significant the factor. Only dilution was a significant factor ($p < 0.05$) for the detection rates, while all factors were significant for the S/N (Table 2 and 3).

Table 2. Pesticide detection rates of L9 TOA (3^4) for the optimisation of QuEChERS extraction and clean-up.

Experiment	Extraction solvent acidification	Extraction salts	dSPE	Dilution	Mean of Detection Rates (%)	Relative SD (%)
1	1	1	1	1	84.98	2.36
2	1	2	2	2	75.29	3.88
3	1	3	3	3	55.97	3.50
4	2	2	1	3	55.65	8.09
5	2	3	2	1	82.10	4.93
6	2	1	3	2	72.82	3.34
7	3	3	1	2	80.06	9.80
8	3	1	2	3	56.13	12.40
9	3	2	3	1	86.33	4.39
K1*	72.08	71.31	73.56	84.47		
K2	70.19	72.42	71.17	76.06		
K3	74.17	72.71	71.71	55.92		
R**	3.98	1.40	2.39	28.55		
F-value	1.75	0.24	0.69	95.09		
p*-value**	0.20	0.79	0.51	< 0.001		

* The average detection rate for each level (Ki) in different factors. It is used to select the best level for each factor.
** The range of detection rates for different factors. It is used to rank the factors by their impacts on the detection rate. The higher this value, the greater the impact of the given parameter on the detection rate.
*** One-way ANOVA test.

Table 3. Pesticide S/N of L9 TOA (3^4) for the optimisation of QuEChERS extraction and clean-up.

Experiment	Extraction solvent acidification	Extraction salts	dSPE	Dilution	Mean of S/N	Relative SD (%)
1	1	1	1	1	189.73	6.57
2	1	2	2	2	117.11	1.42
3	1	3	3	3	96.87	4.20
4	2	2	1	3	127.81	14.36
5	2	3	2	1	150.95	1.63
6	2	1	3	2	114.99	2.48
7	3	3	1	2	174.95	6.09
8	3	1	2	3	96.79	1.48
9	3	2	3	1	151.07	0.21
K1*	134.57	133.83	164.16	163.92		
K2	131.25	132.00	121.62	135.68		
K3	140.94	140.93	120.98	107.16		
R**	9,69	8,92	43,19	56,76		
F-value	4.80	4.40	121.44	159.65		
p*-value**	0.0213	0.0277	< 0.001	< 0.001		

* The average detection rate for each level (Ki) in different factors. It is used to select the best level for each factor.
** The range of detection rates for different factors. It is used to rank the factors by their impacts on S/N. The higher this value, the greater the impact of the given parameter on the S/N.
*** One-way ANOVA test.

3.1.1. Extraction solvent acidification

For the extraction solvent, only ACN was tested as extraction solvent because the use of ACN leads to much less interference from compounds such as lipophilic compounds, lipids and pigments than other extraction solvents such as acetone, ethyl acetate (Anastassiades et al., 2003). In addition, ACN is the most widely used organic solvent for QuEChERS extraction due to its ability to extract a wide polarity range of pesticides from several animal and plant foodstuffs. Due to its miscibility with water, it is able to penetrate the aqueous fraction of the sample matrices, allowing for easy separation of the two phases upon salt addition. In order to increase the extraction efficiency of certain pesticides (e.g., acidic compounds), ACN can be acidified with acetic acid (AA) or formic acid (FA), for instance (Pang et al., 2021b). For this study, we therefore chose to evaluate the impact of ACN with 1% (v/v) FA or 1% (v/v) AA on the detection rates of target pesticides and their S/N. The best detection rates and S/N were obtained with pure ACN as extraction solvent (Fig. S3).

3.1.2. Extraction salts

In the QuEChERS method, $MgSO_4$ and NaCl are the original salts used for liquid-liquid phase separation by binding to water (Anastassiades et al., 2003). $MgSO_4$ has good water absorption and allows the release of acetonitrile, while NaCl affects the polarity of the extraction solvents and, therefore, increases the selectivity of the extraction (Kim et al., 2019). To avoid ionization or degradation of pesticides due to pH changes during extraction, two modifications of the original QuEChERS method were developed: (1) AOAC Method (acetate buffer) (Lehotay, 2007) and (2) EN Method 15662 (citrate buffer) (Anastassiades et al., 2007). Both methods stabilize the pH at 5–5.5, which facilitates the extraction of pesticides sensitive to low pH or those with stability problems. However, the ability of the primary secondary amine PSA (used as a sorbent) may decrease to retain the co-extractives at this pH level, especially for samples with high fat content (Kim et al., 2019). As shown in Fig. S3, a mixture of $MgSO_4$ and NaCl without buffer yielded better results in terms of detection rates and S/N than the methods using buffers.

3.1.3. dSPE

As illustrated in Fig. S3, the best detection rates and S/N were obtained with a mixture of $MgSO_4$/PSA/C18 as dSPE reagent. As mentioned in the previous paragraph, $MgSO_4$ is commonly used as a drying salt for ACN extraction because it effectively removes residual water. PSA has been shown to remove many polar organic acids from the extract, as well as polar pigments, sugars and fatty acids, whereas C18 can retain fats, vitamins, and minerals (Kim et al., 2019). Z-Sep/C18 is composed of zirconium oxide and C18. This mixture reduces fat and pigment levels in matrices and it is recommended for matrices with >18% of lipid (Álvarez-Ruiz et al., 2021), which is not the case for bivalve samples, whose lipid content is usually below 10%. EMR-Lipid, whose structure is a proprietary secret, removes lipids from sample matrices (Álvarez-Ruiz et al., 2021; Pang et al., 2021) but its ability to remove other interferents such as proteins has not yet been described in literature.

3.1.4. Dilution

As observed in Fig. S3, non-dilution was necessary to obtain the best detection rates and S/N. Dilution combined with extraction and purification steps showed decreased matrix effects in apple, tea and broccoli during analysis (Guo et al., 2019a). However, sample dilution reduces the overall sensitivity of the method, thus a compromise is needed to reduce matrix effects while maintaining high method sensitivity. In addition to the dilution of extracts, the concentration of the sample can be important on the sensitivity of the target compounds and on matrix effects. To have a simple, reliable and not time-consuming method to apply it to a large number of bivalve samples, the sample concentration was not considered in this work. However, this aspect should be tested in a future research to obtain a good compromise between increasing sensitivity and minimising matrix effects.

The conclusion based on the R values associated with the K1, K2, and K3 values and the main effects plot for both responses is that the optimal QuEChERS extraction conditions were obtained with pure ACN, Original QuEChERS method, $MgSO_4$/PSA/C18 as dSPE, and the non-dilution of extracts.

3.2. Evaluation and comparison of IDA and SWATH® workflows for pesticide detection and identification

As shown in Fig. 1a, detection rates ranged from an average of 75% to 96% for all methods, with the IDA and IDA-PIL methods being the most effective with detection rates of 96% on average, for both modes. The detection rates of F-SWATH mode ranged from an average of

75% for F-SWATH50 to 94% for F-SWATH20 and the detection rates of V-SWATH ranged from an average of 77% for V-SWATH50 to 94% for V-SWATH20. The detection similarity between IDA and IDA-PIL is expected because they have the same TOF-MS conditions. PIL only affects TOF-MS/MS (identification). The same observation was made with F-SWATH and V-SWATH which have the same detection rates when the number of windows is the same. For the SWATH® methods, the detection rates decreased with the increase of the number of windows. This is because, for the same accumulation time, if the number of windows increases, the number of cycles and points per peak decreases, which reduces the sensitivity of the precursor ions. In terms of detection, the performance of the IDA modes is equivalent to that of the best SWATH modes.

The TOF-MS used gave information on the accurate *m/z* of the targeted pesticides. However, pesticides were only considered identified in cases where the characteristic MS/MS of the compound was obtained. As can be seen in Fig. 1b-e, the IDA-PIL mode achieved a better identification rate than the IDA mode. This is due to the fact that in the IDA-PIL mode, the targeted precursor ions have the highest priority for MS/MS data acquisition, even though these precursor ions were not the most intense. For the IDA mode, only the *top n* most intense precursor ions are fragmented, which can be problematic in case of complex matrix or low concentration. The IDA modes were slightly impacted by the decrease of the MS/MS score threshold (from > 70% to > 50%) with an average increase of 5% of pesticides identified for both IDA and IDA-PIL. The same observation is made for the impact of the MS/MS search

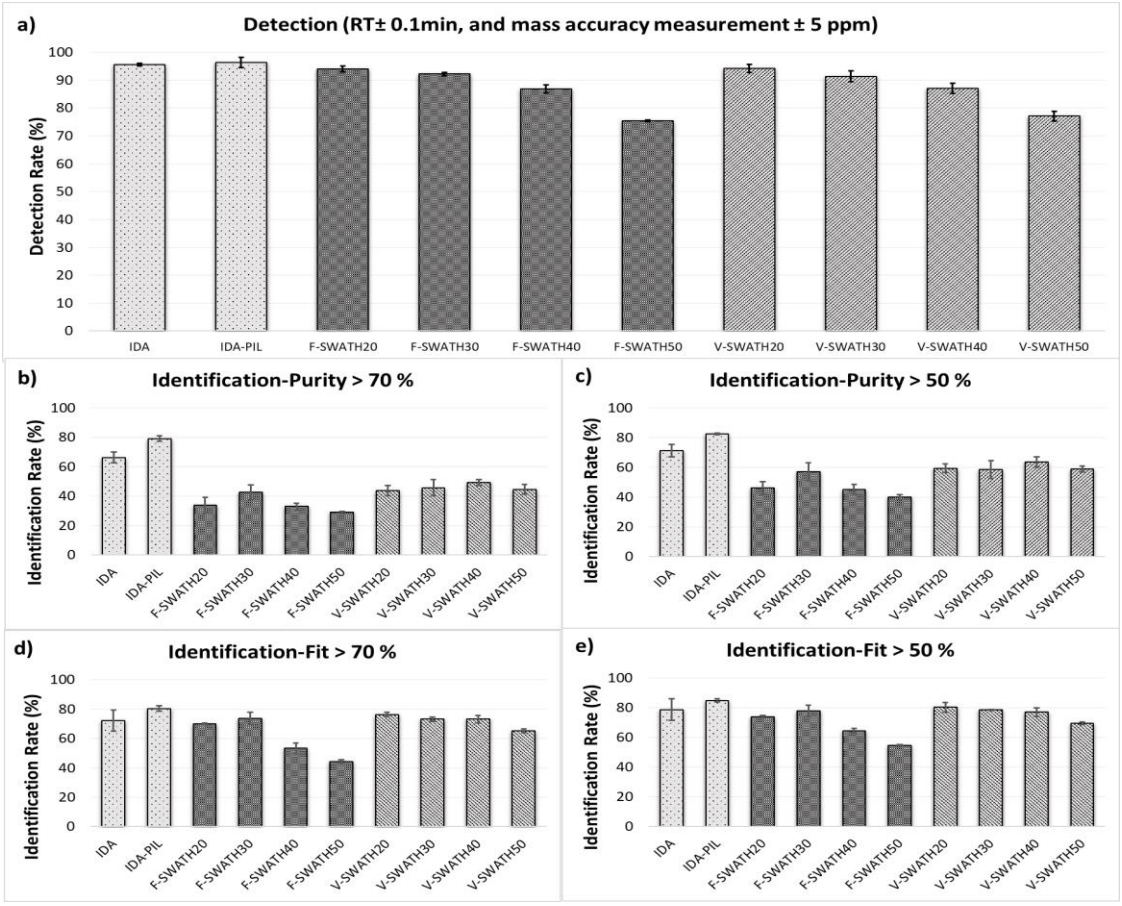


Fig.1 Evaluation and comparison of IDA, IDA-PIL, F-SWATH and V-SWATH methods with 20, 30, 40 and 50 windows for pesticide detection (a) identification rates using Purity > 70% as search algorithm (b), identification rates using Purity > 50% as search algorithm (c), identification rates using Fit > 70% as search algorithm (d), and identification rates using Fit > 50% as search algorithm (e) at 0.01 µg.mL^{-1} in ACN of the target 204 pesticides.

algorithm. From Purity to Fit, an average increase in pesticide identification rates of 2 and 6% was observed for the IDA-PIL and IDA modes, respectively.

For SWATH modes, V-SWATH achieved overall higher identification rates than F-SWATH because it adjusts the isolation window to the number of precursor ions in the window. For F-SWATH, the *m/z* Q1 window size is uniform throughout the LC-MS run. Compared to IDA modes, SWATH modes are more affected by the decrease of the MS/MS score threshold (from >70% to >50%), especially for the Purity algorithm with an average increase of 15% of identified pesticides (Fig. 1b-c). For MS/MS search algorithms, the impact was even more pronounced. From Purity to Fit, an average increase of 20% in pesticide identification rates was observed. The Fit algorithm was therefore found to be the best for identifying compounds in SWATH modes.

Unlike what was observed for detection rates (Fig. 1a), which decrease with increasing the number of SWATH® windows (decreasing precursor ion sensitivity), this is not always the case for identification rates (Fig.1b-e). Increasing the number of SWATH® windows with narrower widths, allows fewer precursor ions to be selected for MS/MS fragmentation, resulting in higher specificity and selectivity (Demianova et al., 2017). A compromise is therefore necessary to increase sensitivity while maintaining high precursor ion specificity and selectivity for confident pesticide identification.

In terms of identification, the best performance was obtained with IDA-PIL, regardless of the algorithm or MS/MS threshold chosen, which demonstrates the importance of adding PIL to increase the probability of fragmenting the desired precursor ions. A previous study by Álvarez-Ruiz and Picó (2019) also compared the IDA mode (without PIL) with the F-SWATH and V-SWATH modes. In this mentioned study, the SWATH modes performed better than the IDA mode.

For the identification of pesticides in complex matrices such as bivalves, the quality of the MS/MS spectrum is also crucial. It was therefore taken into account in this work. As an example of the difference between the IDA modes and SWATH® methods, Fig. 2 shows the results obtained with IDA-PIL and V-SWATH methods for zoxamide in spiked sample at 0.01 mg.L^{-1}. The MS spectra showed the two characteristic signals of zoxamide (one with ^{35}Cl and one with ^{37}Cl) (Fig. 2a). The MS/MS data of the SWATH® acquisition showed zoxamide product ions with ^{35}Cl and ^{37}Cl (Fig. 2b). In the IDA acquisition, only the monoisotopic ion (zoxamide with ^{35}Cl) was selected and fragmented (Fig. 2c), so the MS/MS data lose isotopic abundance but with a cleaner spectrum than that obtained in SWATH®. These results are consistent with the study conducted by Álvarez-Ruiz and Picó (2019) who found that the quality of MS/MS spectra is lower in SWATH than in IDA and more complex to interpret. Indeed, not all MS/MS data acquired with SWATH is useful as it may come from several precursor ions that are not all of interest. Thus, some fragments of other precursors may interfere with the signal of the analyte of interest, leading to additional verification by the user. Despite these described drawbacks, SWATH modes have shown good performance for the analysis of small molecules such as pharmaceuticals and personal care products in complex matrices, although these modes are more commonly used for protein analysis (Álvarez-Ruiz and Picó, 2019a; Baduel et al., 2015).

For the search algorithm, the library scores (Fig. 2b-c) showed that the Purity algorithm does not adapt the SWATH® data, especially when compared to a home-made library in IDA. Of note, LibraryView™ does not allow for the implementation of a home-made spectral library in SWATH® mode, which is an issue. It is therefore necessary to find ways in the future with improved software to take better advantage of SWATH modes. Indeed, SWATH modes have

interesting unique features, namely the generation of chemical fingerprints (MS and MS/MS spectra) of the sample that can be exploited retrospectively as new knowledge is gained and the possibility of using samples in multiple studies. According to the results obtained in terms of detection, identification rates and quality of MS/MS spectra, the IDA-PIL mode was selected for the validation method. The identification rates obtained with the evaluated algorithms being similar in the IDA-PIL mode, the Purity algorithm was chosen because it allows to evaluate the quality of the obtained spectra in terms of interfering peaks. As the score used does not have a great influence on the identification rates in the IDA-PIL mode, the score threshold > 70% was set to increase identification confidence. Furthermore, for IDA-(PIL) modes, the Purity > 70%

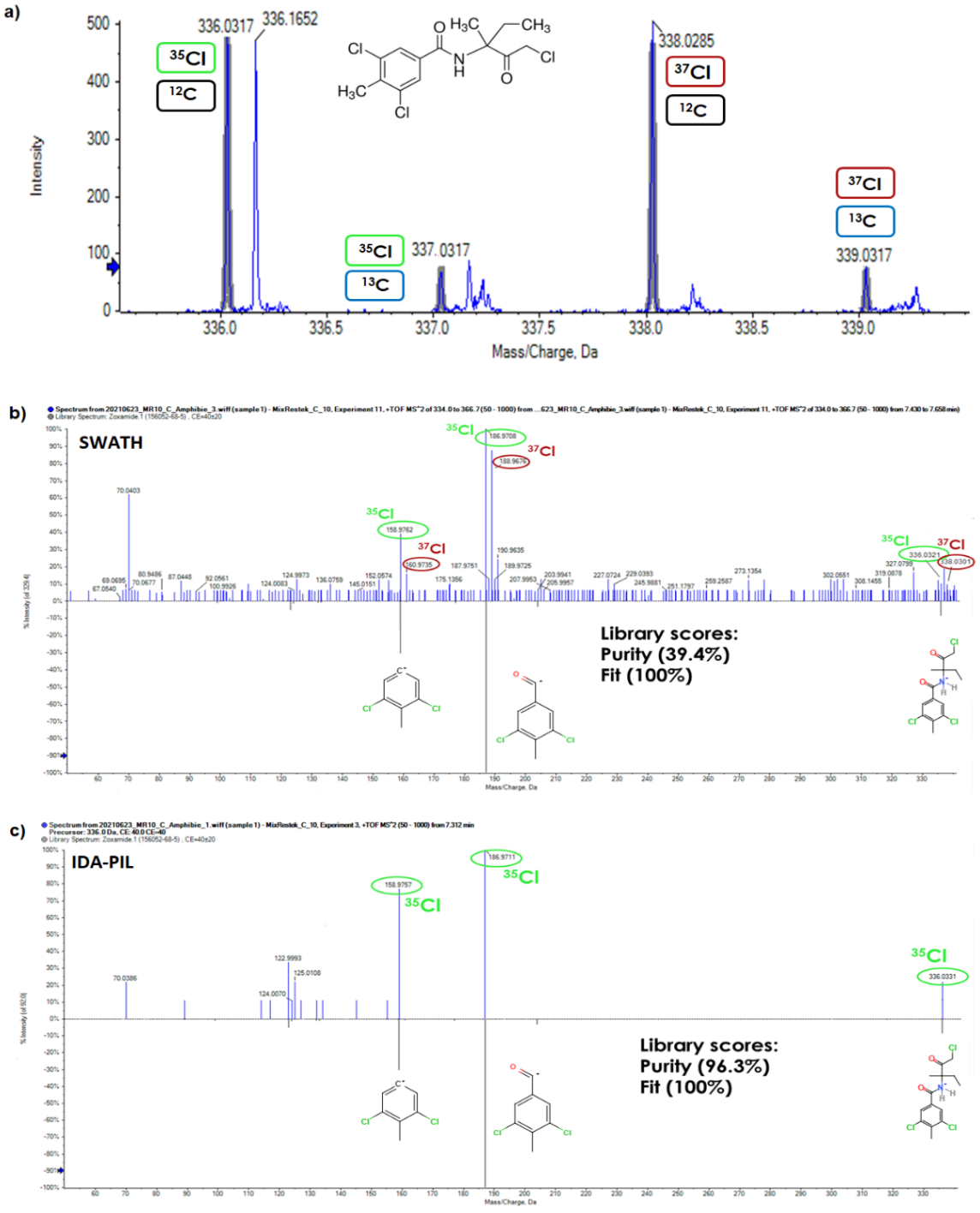


Fig.2. Zoxamide MS spectrum with isotopic profile pattern (a), MS/MS spectrum acquired in SWATH® (b) and IDA-PIL mode (c) in spiked sample at 0.01 µg.mL^{-1}.

is most often used in the literature by authors working with the 5600 Q-TOF AB Sciex mass spectrometer (Baduel et al., 2015; Romera et al., 2018).

3.3. Selectivity of the screening method

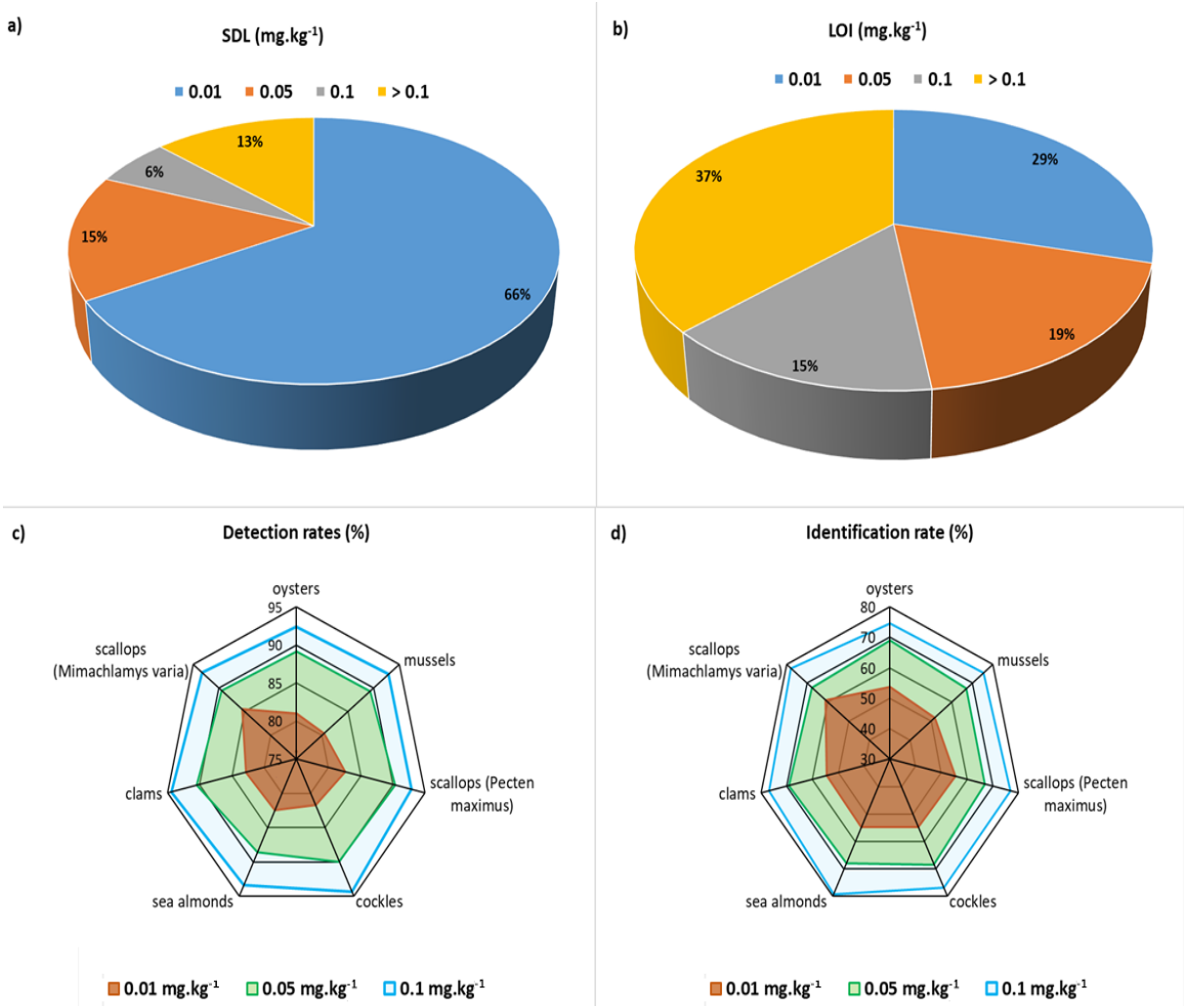
In order to determine the selectivity of the chosen screening method, the possible presence of false positives was also checked. In the SANTE guideline no criteria have been set with respect to the occurrence of false positives. However, it is important that the selectivity of the method is such that it reduces them to a sufficiently low number to avoid manual verification or confirmatory analysis that may reduce the effectiveness of the screening methods. The number of false positives was checked by analysing blank samples of each of the seven bivalve species prepared in triplicate. According to the results, a total of 5 false positives (2.5% of the 204 target pesticides) were obtained across all blank samples, when applying tolerances of ± 5 ppm and ± 0.1 min for mass accuracy and T_R, respectively. False positive pesticides for fenpropimorph ($C_{20}H_{33}NO$) and formetanate-HCl ($C_{11}H_{16}ClN_3O_2$) were each detected once across the different blank samples, whereas false positives for spiroxamine ($C_{18}H_{35}NO_2$), aminocarb ($C_{11}H_{16}N_2O_2$) and propham ($C_{10}H_{13}NO_2$) were observed in two, three and five samples, respectively. When additional criteria were set, such as the MS/MS library score (Purity > 70%) the number of false positives dropped to zero. These results demonstrate the good selectivity of the method both in terms of detection and identification.

3.4. Method validation

The objective of this work was to develop and validate an analytical methodology according to the SANTE guidelines for the simultaneous detection and identification of 204 pesticides (used as model compounds) in bivalve matrices. Therefore, the validation of the qualitative screening methodology included the determination of SDL. Although it is not required for the SANTE guidelines, the LOI was also established. Seven species of bivalves were tested for method validation: oysters, mussels, cockles, clams, sea almonds and two species of scallops (*Pecten maximus* and *Mimachlamys varia*). Four groups of each species were spiked at three concentration levels (0.01, 0.05, and 0.1 $mg.kg^{-1}$). For each individual pesticide, the number of positive detections and identifications at each concentration level was recorded and the SDL and LOI were established. Table S4 shows the number of detections and identifications for each compound in the 28 samples and the corresponding SDL and LOI. A summary of this table is also shown in Fig. 3.

As it can be seen, about 93% of the pesticides could be detected at 0.1 mg kg^{-1} in bivalves, while the percentage of identification decreased down to 77% at this same concentration level. The SDL was determined to be equal to or less than 0.1 $mg.kg^{-1}$ for 87% of the pesticides, whereas the percentage of pesticides with an LOI equal to or less than 0.1 $mg.kg^{-1}$ decreased to 63%. The criteria of SDL and LOI were therefore not reached for 13 and 37% of pesticides, respectively. However, the proposed screening method was able to detect and identify them in most of the samples at the highest concentration level. In this regard, it is worth noting the complexity of bivalve matrices, which generally present a significant amount of co-extractives, even after sample clean-up, which may increase SDLs and LOI compared to other simpler matrices. For 50 pesticides (representing 25% of the selected pesticides), it was possible to establish the SDL at least at one of the three concentration levels, but not the LOI. For these compounds, validation was limited to detection (only SDL could be set-up). Regarding maximum residue limits (MRLs), no values have yet been established in bivalves for any of the pesticides studied, so the SDLs obtained, in most cases 0.01 $mg.kg^{-1}$, can be considered satisfactory and the proposed methodology suitable. In addition, no qualitative pesticide screening was performed on bivalves by QuEChERS-LC-HRMS to

compare our results. Previous work has been done on other matrices such as fish fillet (Munaretto et al., 2016a), salmon feed (Regueiro et al., 2017), and fruits and vegetables (López et al., 2014b) for qualitative screening of 182, 156, and 199 pesticides, respectively. In these three studies, the percentage of pesticides with an SDL of 0.05 mg.kg^{-1} ranged from 79% to 84%. In our study, the SDL was determined to be equal to or less than 0.05 mg.kg^{-1} for 81% of



the pesticides which is quite similar to the literature and done on more complex matrix like

Fig.3. Percentage of pesticides presenting SDL (a) and LOI (b) at 0.01, 0.05, 0.1 and > 0.1 mg.kg^{-1} under optimised conditions. Detection (c) and identification rates (d) across different bivalve samples spiked at 0.01, 0.05 and 0.1 mg.kg^{-1}.

bivalves.

As described above, this study is the first to perform a qualitative multi-residue analysis of pesticides in bivalves. The other studies performed so far were quantitative analyses. This is the case for the studies carried out by Álvarez-Muñoz et al. (2019) and Cruzeiro et al. (2016) for the quantitative analysis of 13 and 55 pesticides, respectively. The authors of these two works obtained LOD and LOQ values below 0.01 mg.kg^{-1} for all the pesticides studied. Of all the pesticides investigated in the two studies mentioned above, nine (acetamiprid, azoxystrobin, difenoconazole, dimethoate, imidacloprid, metribuzin, simetryn, terbutryn and thiabendiazole) are included in the list of 204 pesticides analysed in the present study. For all of these nine pesticides, the SDL was established at least at one of the three concentration levels tested in the

present study and only one of these pesticides (simetryn) had an LOI greater than 0.01 $mg.kg^{-1}$.

3.5. Application to real samples

3.5.1. Target screening analysis

To evaluate the applicability of the proposed method, 14 bivalve samples (seven mussels and seven oysters) from three sites (Ile de Ré, Sèvre Niortaise and Charente) located in the Pertuis Charentais littoral area were analysed. For target screening, the home-made database of the 204 target pesticides (with information on T_R, MS, isotopic pattern, and MS/MS spectra) was used. Pesticides were detected and identified using the criterion applied in this work. Table S5 summarizes pesticides detected and identified in mussel and oyster samples. Diuron was the most frequently detected and identified compounds (in 8 of the 14 bivalve samples). Although it has been banned in France since 2008, diuron is still detected at high concentrations in coastal and fresh waters (Caquet et al., 2013). Other pesticide such as fungicide (fenpropimorph) was also detected and identified in one mussel sample in Sèvre Niortaise estuary in January 2020. To best our knowledge, this study is the first to show the presence of fenpropimorph in bivalves.

3.5.2. Suspect screening analysis

In target screening, most of the peaks resulting from sample analysis are ignored during data processing. The feasibility of the developed method has also been demonstrated on "known unknown" compounds in bivalve real samples. Post-acquisition data processing was carried out using a suspect screening of accurate masses. The database of compounds (with information of exact mass and molecular formula) has been expanded to include approximately 545 organic contaminants, including many pesticides and their metabolites as well as some flame retardants and plasticizers. A total of five additional compounds were tentatively identified. The identification obtained from the suspect screening was considered tentative (level 3) until confirmed by a standard compound to reach identification confidence level 1 (Schymanski et al., 2014b). As in the case of diuron in the target analysis, its metabolite 1-(3,4-dichlorophenyl)-3-methylurea was the most frequently tentatively identified. Other pesticide such as fungicide (diphenylamine) and personal insect repellent (N,N-diethyl-*m*-toluamide (DEET)) were also tentatively identified. Diphenylamine has been frequently detected in environmental waters because, in addition to its wide use as a fungicide, it is an important intermediate used in the chemical and pharmaceutical industries (Chen et al., 2014). DEET has previously been reported in mussels collected in San Francisco Bay, California with a concentration (mean 0.014 $mg.kg^{-1}$) positively correlated with their lipid content (Klosterhaus et al., 2013). The organophosphate flame retardant and plasticizer (2-ethylhexyl diphenyl phosphate (EHDPP) and tris(2-chloroethyl) phosphate (TCEP)) were tentatively identified. EHDPP and TCEP have previously been detected in bivalves collected on several points along the northern coast of Spain and along the Korean coast, with a concentration of around 0.002 $mg.kg^{-1}$ for both (Castro et al., 2020; Choi et al., 2020). As shown in Table S6, all tentatively identified compounds were subsequently confirmed with their respective reference standard with MS, MS/MS and T_R matching.

4. Conclusion

The development and validation of a QuEChERS-LC-HRMS method using IDA-PIL mode enabling screening of 204 pesticides in bivalves was carried out according to the European Union SANTE/12682/2019 guidelines. The list of target compounds included pesticides from different families with very distinct physicochemical properties. The use of L9 TOA for QuEChERS parameter optimisation greatly simplified the method development process and

made it scientifically sound. We evaluated the impact of the different IDA and SWATH® modes on a QTOF 5600 on detection and identification rates and demonstrated the effectiveness of the IDA-PIL approach, especially since LibraryView™ software does not allow for building of a SWATH library, only an IDA library. Most of the target list compounds were detected at all three concentration levels (0.01, 0.05 and 0.1 $mg.kg^{-1}$) with false positives averaging 2.5% on blank matrices. Unequivocal identification was problematic at the lowest concentration (0.01 $mg.kg^{-1}$) due to the lower abundance of product ions but was possible for most analytes at the highest concentration level (0.1 $mg.kg^{-1}$). The SDL and LOI were equal to or less than 0.1 $mg.kg^{-1}$ for 87% and 67% of pesticides, respectively.

The applicability of this approach for pesticide screening was finally demonstrated by analysing several samples of mussels and oysters collected in southwestern France. Diuron and fenpropimorph were the only identified analytes in the investigated samples using target analysis. The method also demonstrated its versatility to identify other organic contaminants (pesticides or other compounds) than those included in the method validation by suspect screening. This allowed the identification of diuron metabolite 1-(3,4-dichlorophenyl)-3-methylurea and other contaminants such as flame retardants and plasticizers.

Although the proposed methodology is very suitable, it is still necessary to develop workflows on different open-source software to follow SANTE guidelines regarding identification (product ion mass accuracy ± 5 ppm). Importantly, MasterViewTM software can be used to automatically obtain the mass error only on the precursor ions and not on the product ions. Another important point will be to find ways to realize an MS/MS library in SWATH methods in order to better exploit the advantages of these acquisition methods, especially on the richness of the generated MS/MS spectra and the retrospective analysis of the data.

Acknowledgements

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Declaration of competing interest

The authors declare no conflicts of interest.

2.2.4. Summary & main results

In the present study, we optimized the QuEChERS extraction/purification protocol using a Taguchi fractional factorial experimental design methodology. This enabled us to evaluate different parameters of the protocol simultaneously, with high statistical robustness. This is a pragmatic approach, because in addition to the reliable results generated, the savings in terms of experimental time and costs are not negligible.

In addition, we compared SWATH-MS acquisition methods, with the IDA mode that was used exclusively in the first study (Makni et al., 2022a). Following this evaluation, the IDA mode was selected, as the spectra generated were of much higher quality, enabling us to obtain higher identification rates (MS+MS/MS) than with the SWATH-MS mode. The entire method, optimized for bivalve analysis, was validated according to the European commission guidelines for HRMS screening (European Commission, 2021). It was then used for the analysis of bivalves purchased on the market, enabling us to identify diuron (a herbicide banned by the European Commission) by targeted analysis, as well as its metabolite 1-(3,4-dichlorophenyl)-3-methylurea by suspect analysis, in several bivalve samples.

2.2.5. Limitations and prospects for improvements

Although the acquisition modes were optimized, the IDA mode selected as a result of this work was still limiting with regard to the non-fragmentation rate, which remained high, as well as the low sensitivity obtained on fragmentation ions. This directly affects the identification of compounds of interest in food matrices, since if an analyte is not fragmented, it cannot be unequivocally identified. Moreover, even if the analyte is fragmented, if the sensitivity levels achieved for fragmentation ions are too low, this can make it difficult to compare MS/MS spectra. These limitations were therefore considered in order to improve the overall performances of the method. The developed methods also aim to be used for suspected and non-targeted analyses, to screen other chemicals for which the analytical standards are not available in the laboratory. In this case, it is impossible to generate inclusion lists for prioritized fragmentation.

As a complement to this work, the IDA acquisition mode was further optimized to overcome the above-mentioned limitations. The results of this additional optimization are presented in the following section, but were not published in an article.

2.3. Optimization of IDA mode

2.3.1. Context of optimization

As mentioned in previous papers (Diallo et al., 2022; Makni et al., 2022), non-fragmentation rates in IDA mode can be problematic. This can be reduced by an inclusion list for targeted analyses, but when analyzing compounds for which analytical standards are not available, non-fragmentation can compromise contaminant annotation. Moreover, low-level identification can also prove difficult, due to a lack of sensitivity on fragmentation ions. Thus, the optimization presented in this section aimed to overcome these limitations, to be able to use the IDA mode for both targeted analysis, as well as suspect and non-targeted analysis, with higher levels of sensitivity.

Fig.2 below describes and summarizes the major improvements compared with the previous works (Diallo et al., 2022; Makni et al., 2022), following an iterative process of continuous improvement.

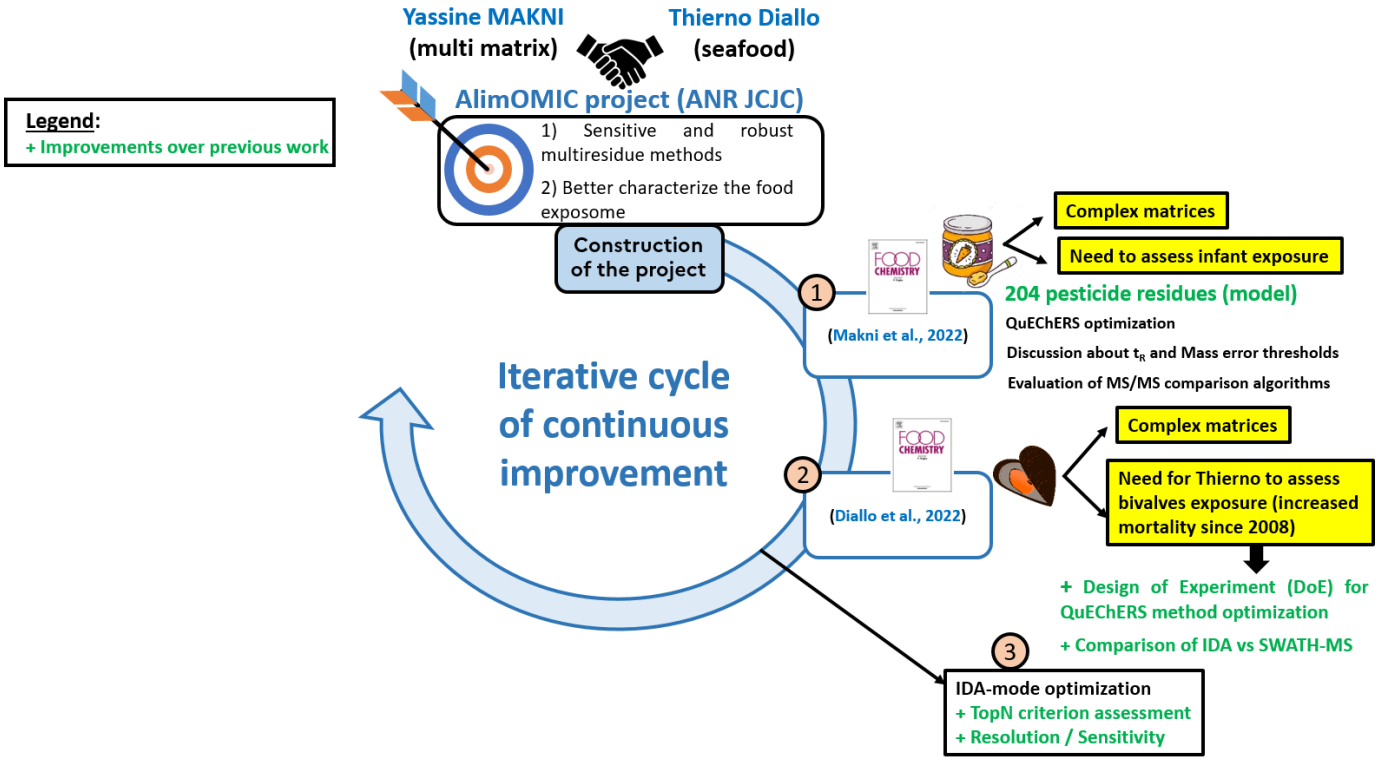

Fig.2. Cycle of iterative and continuous improvement – part 2

2.3.2. Materials & Method

a. Materials

This optimization was carried out on a pool of fishery product samples (mussels, oysters, scallops, sea almonds, scallops, cod, sol, tuna, anchovies, salmon), to reflect the large and highly complex matrix variability. This not only enables the methods to be properly tested, but also reduces the volume of experiments, saving time and consumables. An aliquot of 1.5 ± 0.05

g of this pool was weighed into 50 mL polypropylene tubes. This aliquot was supplemented to 0.01 mg.kg-1 with the mix of 204 pesticides used in the first two studies. The sample was then prepared using the QuEChERS method, and injected in positive polarity (ESI+) in triplicate into the UHPLC-Q-ToF system.

b. Optimization of topN and MS/MS accumulation time parameters

In this section, two IDA mode parameters were optimized:

- The "*topN*" parameter, which corresponds to the number of MS/MS experiments and defines the "N" most intense precursor ions to be fragmented for each scan, and which has a direct impact on the non-fragmentation rate. Indeed, if the precursor ion of an analyte of interest is not among the most intense, it will not be fragmented.
- Accumulation times (ms), which correspond to the time the instrument spends accumulating data for each scan and for each candidate precursor ion. This parameter impacts the sensitivity and quality of the MS/MS spectra generated.

These two parameters need to be optimized in conjunction with each other, because as the "*topN*" increases, so does the total cycle time. A cycle time that is too high has a negative impact on the number of points per peak, as well as on peak shape and sensitivity. These observations were made during the evaluation of the SWATH-MS mode (Diallo et al., 2022). It was found that an increase in the number of SWATH-MS windows, and consequently in total cycle time, resulted in a decrease in the number of points per peak and in the sensitivity obtained.

As part of this optimization, and taking into account the observations made for the SWATH-MS mode, we optimized the IDA mode by evaluating 4 methods with different "*topN*". For each method, MS/MS accumulation times were initially kept constant, resulting in a gradual increase in total cycle time and a decrease in the number of points per peak. In a second step, for each method, we adjusted the MS/MS accumulation times to maintain a constant total cycle time and number of points per peak. Table 1 below summarizes the different methods and the parameters evaluated.

Table 1**.** Paramètres d'évaluation du mode IDA.

	Accumulation time (ms)		
topN	**ToF-MS (precursor ions)**	**MS/MS (fragment ions)**	**Total cycle time (s)**
4	490	100	940
10	490	100 or 40	1540 or 940
15	490	100 or 27	2040 or 940
20	490	100 or 20	2540 or 940

c. Optimization of the resolution and sensitivity of MS/MS ions

In this section, the resolution and sensitivity on fragmentation ions were optimized. AB Sciex TripleToF5600^{TM} offers either high-resolution or high-sensitivity during MS/MS acquisition. The former offers higher resolution (32,000 FWHM at *m/z* 415.2728), while the latter offers lower resolution (20,000 FWHM at *m/z* 415.2728) but two to five times greater sensitivity. Both modes were therefore tested in triplicate. Indeed, in high-sensitivity mode, the ion optics of the Q-ToF compress the ion beam to get higher throughpout, which brings ions

back into the accelerator which would normally (in high-resolution) be blocked from entering the accelerator. However, there are more ions but they are not aligned as good on “starting line” in the accelerator, due to the focussiong process, so the starting position has a higher deviation, reducing the resolution.

2.3.3. Results of the optimization of IDA mode

a. Results of the optimization of topN and MS/MS accumulation time parameters

The results of this optimization are shown in Figure 1. When MS/MS accumulation times were kept constant (Fig.1a), lower detection rates were observed as “*topN”* increased. Indeed, as the "*topN*" increased, the total cycle time increased and the number of points per peak decreased, resulting in lower signals. However, there was also an increase in the identification rate of pesticides from *top4* to *top10* (63% and 71%, respectively), followed by a decrease in these percentages to 66% and 52% with *top15* and *top20*, respectively (Fig.1a). When looking at non-fragmentation rates, there were 26% of unfragmented compounds with a *top4*, 15% and 17% with a *top10* and *top15*, respectively (Fig.1a). However, with a *top20*, the non-fragmentation rates were similar to those obtained with a *top4* (25%), as the precursor ion signals were so weak that they were not fragmented. When the MS/MS accumulation times were adjusted to keep the total cycle time and the number of points per peak constant, detection rates were the same (91%) for all four methods (Fig.1b). As for identification rates, they were lowest with the *top4* method, and equivalent between the *top10*, *top15* and *top20* methods, at 72%, 71% and 69%, respectively (Fig.1b). Looking at unfragmented compounds, the results shown a significant decrease in rates with 26% with a top4 method, and around 8% with a *top10*, *top15* and *top20* (Fig.1b). Looking at unfragmented compounds, the results shown a significant decrease in rates with 26% with a top4 method, and around 8% with a top10, top15 and top20 (Fig.1b).

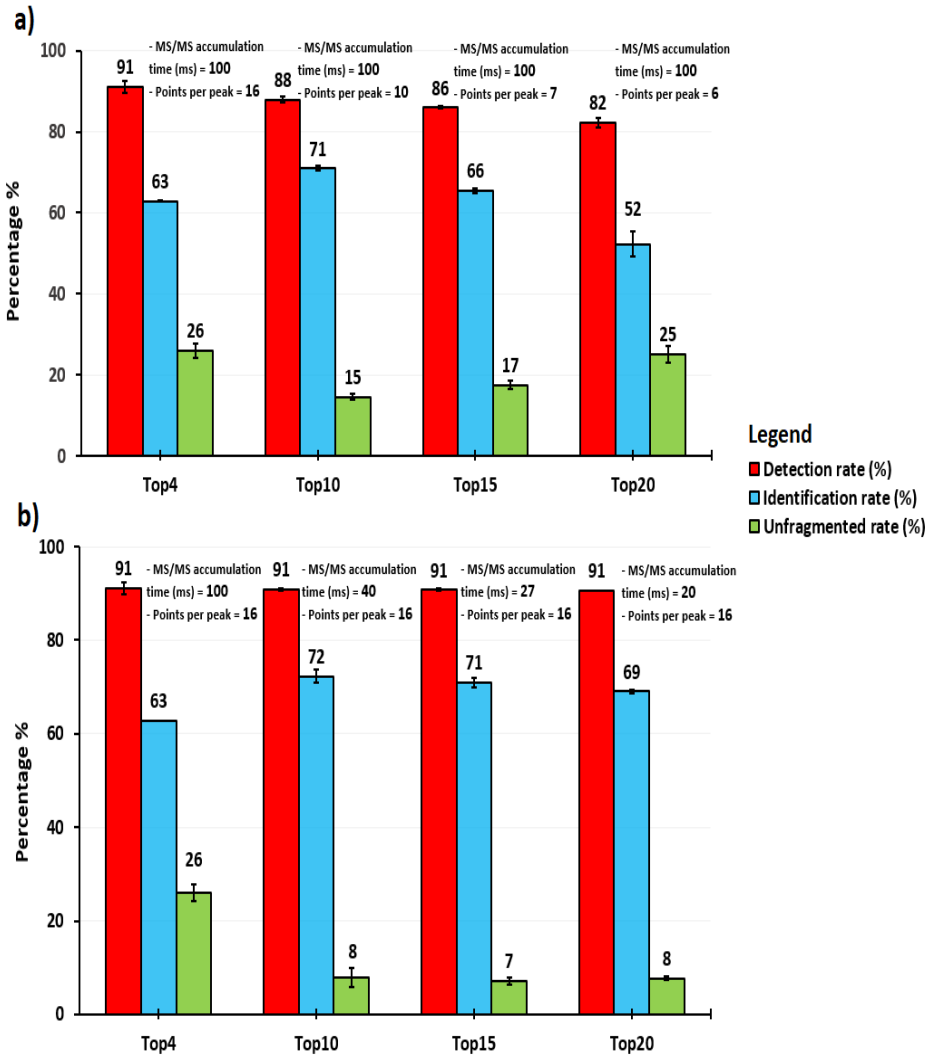

Fig.1. Variation in the detection, identification and non-fragmentation rates of 204 pesticides using (a) different IDA methods constant MS/MS accumulation time (b) different IDA methods with adjusted MS/MS accumulation time.

In view of these results, the increase in "*topN*" is therefore correlated with lower non-fragmentation rates, if the total cycle time is not too great. Nevertheless, despite this optimization, low-level identification may still prove difficult. Indeed, even if non-fragmentation rates were considerably reduced, signal of fragment ions was sometimes too low, leading to spectral matching with similarity <70%.

b. Results of the optimization of resolution and sensitivity of MS/MS ions

The results of this optimization are shown in Figure 2. The identification rates obtained were higher using the high-sensitivity mode (80%) than the high-resolution mode (72%). Figure 3 shows the example of Fuberidazole, a fungicide, acquired in high-resolution mode (Fig.3a) and high-sensitivity mode (Fig.3b). In high-resolution mode, the maximum fragmentation ion height was only 31 counts, making spectral comparison difficult, with a similarity of 54% (<70% required for identification) (Fig.3a). However, in high-sensitivity mode, the fragmentation ion signal increased by a factor of around five, from a maximum of 31 counts to

153 (Fig.3 b). This facilitated identification with a similarity score of 100% (Fig.3 b), without affecting the mass accuracy on fragment ions.

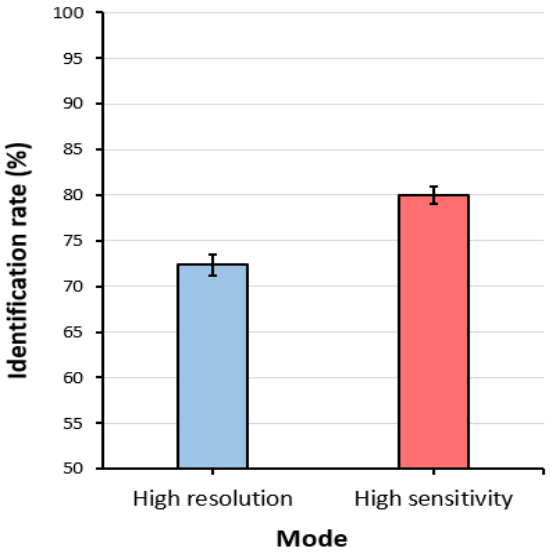

Fig.2**.** Identification rates obtained in high-resolution, high-sensitivity fragmentation ion mode over 204 pesticides.

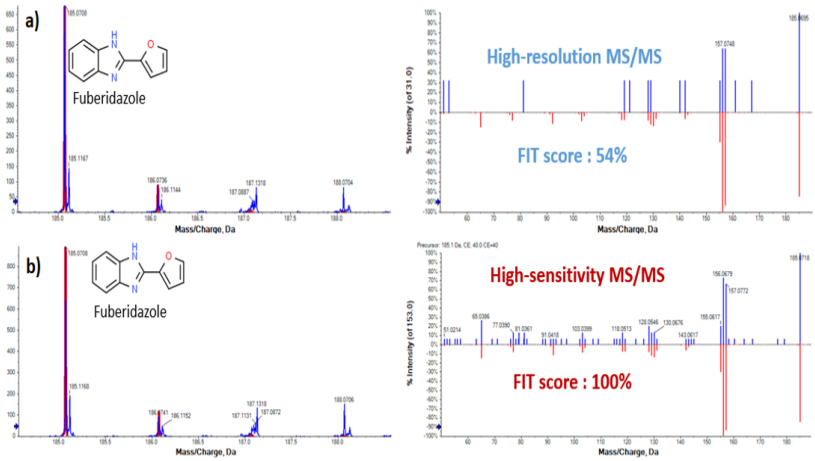

Fig.3**.** Identification of the fungicide fuberidazole in high-resolution mode (a) and in high-sensitivity mode (b).

2.3.4. Conclusion

In conclusion, the increase in "*topN*" is correlated with a decrease in the non-fragmentation rate of the analytes of interest, for a given total cycle time. Thus, as a result of this optimization, the *top4* IDA mode with MS/MS accumulation times of 100 ms, used in our first two studies (Diallo et al., 2022; Makni et al., 2022), evolved into a *top10* with MS/MS accumulation times adjusted to 40 ms.

In addition, evaluation of the resolution and sensitivity of fragmentation ions showed much better identification performances when resolution was reduced in favor of sensitivity. As a result, we modified the resolution on fragmentation ions from 32,000 FWHM to 20,000 FWHM (m/z 415.2728), to improve the sensitivity levels and identification performances of our methods.

2.4. Development of a method for the multiresidue analysis and semi-quantification of 694 contaminants in sugary products

2.4.1. Context and aim of the study

This third study focused on the development of a method for the very broad-spectrum analysis of 694 contaminants and chemical substances in sugary products, using time-of-flight mass spectrometry. Sugary products such as honey, jams, jellies and syrups are very popular and, as a result, widely consumed by adults and children alike. However, apart from honey, which is widely studied, there are few published contamination data for other sugar-rich products such as jams and jellies, which are unregulated intermediate products. There is therefore a real need to be able to provide data that will support the characterization of the risk associated with exposure to chemical contaminants in this type of highly popular and consumed food product. This would also serve to alert us to the need to regulate certain intermediate consumer products (jams, jellies, syrups, etc.). To achieve these goals, the aim of the study was to optimize a sample preparation method suited to the multiresidue analysis of several hundred contaminants in products belonging to the group of very high sugar and low water content matrices. In addition, we also wanted to develop our screening methods towards those offering the possibility of semi-quantifying targeted compounds of interest, more simply than with conventional quantification methods, to go further in characterizing the risk associated with chemicals exposure.

2.4.2. Key points of the study

As part of this study, we were able to:

- Optimize the QuEChERS extraction protocol, using Taguchi fractional factorial experimental designs (Narenderan et al., 2019), to achieve high method performance in these complex food matrices, at lower cost and limiting the time required for experiments.
- Significantly broaden the spectrum of contaminants analyzed (204 pesticide residues in previous works, compared with 694 in the present study).
- Propose new, low-cost, easy-to-implement semi-quantification methods for estimating the concentrations of chemical compounds found in the food matrices analyzed.

Fig.3 below describes and summarizes the major improvements compared with the previous works (Diallo et al., 2022; Makni et al., 2022), following an iterative process of continuous improvement.

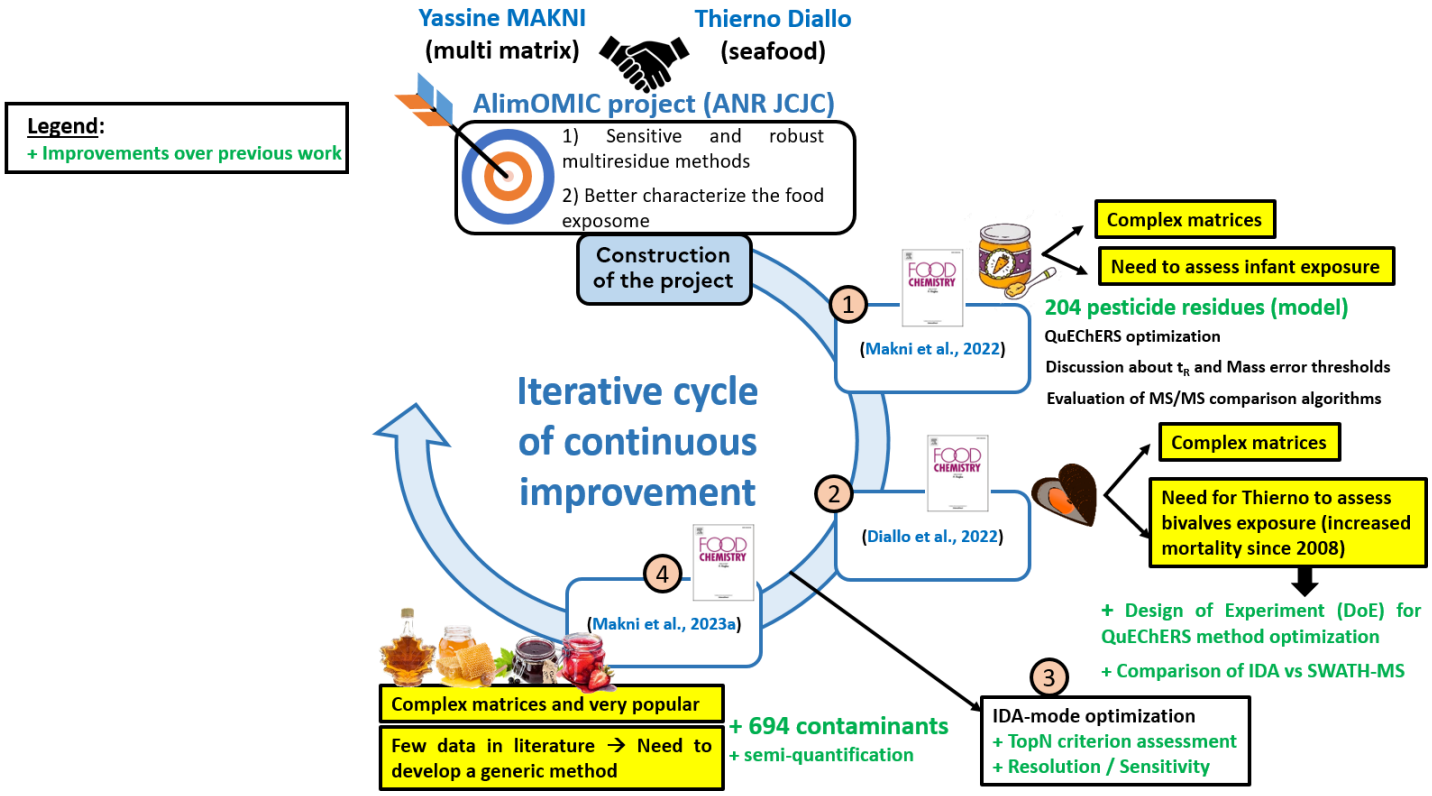

Fig.3. Cycle of iterative and continuous improvement – part 3

2.4.3. Article 3 (Makni et al., 2023a)

The article below details experiments on the optimization and validation of a method for the analysis and semi-quantification of 694 contaminants in various sugary products. This article was published in the journal Food Chemistry. Due to Elsevier copyright restrictions, only the title and abstract of the paper were included in published format. The rest of the paper is inserted in Word-type format, and is available online using the following DOI: https://doi.org/10.1016/j.foodchem.2023.136448

The references associated to this paper are displayed there: References section (Article No. 3)

The electronic supplementary materials (Annexes) associated to this article are displayed here: Article 3 (Makni et al., 2023a): "Optimisation and implementation of QuEChERS-based sample preparation for identification and semi-quantification of 694 targeted contaminants in honey, jam, jelly, and syrup by UHPLC-Q/ToF high-resolution mass spectrometry"

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Optimisation and implementation of QuEChERS-based sample preparation for identification and semi-quantification of 694 targeted contaminants in honey, jam, jelly, and syrup by UHPLC-Q/ToF high-resolution mass spectrometry

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ABSTRACT

A screening and semi-quantitative method was developed for the analysis of 694 various contaminants in honey, jam, jelly and syrup samples by ultrahigh-performance liquid chromatography and quadrupole time-of-flight mass spectrometry. Sample preparation, which was optimised using split factorial design, was based on acetate-buffered version of QuEChERS, followed by a clean-up step and a concentration step to enhance sensitivity of analytes. The method was validated according to SANTE/11312/2021 guidelines. The screening detection and limits of identification were established as being less than or equal to 0.05 $mg.kg^{-1}$ for 89% and 74% of the contaminants, respectively. The validated screening method was applied to 50 concentrated sugary products. Overall, 46% of the samples were positive to pesticide residues. Most of the positive samples (78%) contained mixtures of pesticide residues. Three time-and-cost saving convenient strategies suitable for high-throughput analysis were proposed for the targeted semi-quantification of the previously contaminants identified in samples.

1. Introduction

The increasing demand for concentrated sugary products such as honey, jam and jelly implies the need to pay growing attention to food safety aspects. Honey is a natural and very nutritious beehive product, consumed worldwide for its therapeutic benefits (Oymen et al., 2022; Tette et al., 2016) or its sweet taste, leading to its use either as a sugar substitute or an added sweetener in different foodstuffs. Jams and jellies are concentrated sugary products incorporating what are known as "processed" fruits because they are obtained following several industrial food procedures (Valera-Tarifa et al., 2020; Reichert et al., 2015).

Honey and processed fruits can be contaminated by contaminants such as pesticides from agricultural activities (El-Nahhal, 2020; Valera-Tarifa et al., 2020) and diverse environmental pollution. As a result, consumers may be exposed to mixtures of different hazardous substances through their diet, which raises serious public health concerns. In a food exposome-based context, it is crucial to take into consideration the exposure of consumers to cocktails of contaminants occurring in a dynamic range of concentrations, and not only to individual substances (Juan-Borrás et al., 2016). Indeed, different chemicals in food can act synergistically, even when their concentrations are low, resulting in the potentiation of

toxicological hazardous effects also known as “cocktail effects” (Juan-Borrás et al., 2016; Rizzati et al., 2016).

To protect the consumer, the European Food Safety Authority (EFSA) has established maximum residue levels (MRLs) for individual pesticide residues in food products, including honey and raw fruits (Regulation (EC) No 396/2005). To date, there are no established MRLs for pesticide residues in processed fruits such as jams and jellies (Valera-Tarifa et al., 2020). Therefore, in order to better describe the range and mixtures of chemical compounds to which the consumer may be exposed, occurrence data would need to be generated for various organic contaminants. Occurrence of contaminants associated with processing factors data in intermediate and processed products such as jams and jellies could provide sound data to better support risk assessment and regulate these type of food products (Scholz et al., 2018).

According to the document SANTE/11312/2021, honey and processed fruits belong to the same group of high-sugar and low-water content food commodities and are considered as very complex (European Commission., 2021; da Silva et al., 2016; Reichert et al., 2015). The complexity of these matrices, as well as the wide array of chemicals applied on farmland, lead to the need to develop sensitive multiresidue methods to detect a broad range of contaminants at low concentrations. To address this requirement, multiresidue sample preparation methods were developed to cover a wide range of contaminants in food samples. The Quick, Easy, Cheap, Efficient, Rugged and Safe (QuEChERS) method, introduced by Anastassiades et al. (2003), is among the most generic and well-known sample preparation techniques for the simultaneous determination of a large number of contaminants in food, and especially pesticide residues and environmental contaminants (González-Curbelo et al., 2015). Other methods, which are so-called « mega-methods » were also introduced to expand the analytical scope by covering more families of contaminants. For example, Mol et al. (2008) proposed a method to cover for 136 pesticide residues, 36 natural toxins and 86 veterinary drugs (VDs) in feed samples and honey samples. More recently, the QuEChERSER mega-method was introduced to cover for a broader spectrum of polar and nonpolar compounds, and for example, (Monteiro et al., 2021b) were able to analyse 161 pesticide, 63 veterinary drugs, 24 metabolites and 14 polychlorinated biphenyls in bovine muscle samples. However, although these mega-methods were developed, QuEChERS technique remains of a first choice, and it is currently widely disseminated and used in official laboratories to effectively screen for pesticide residues in food, and were previously successfully employed in honey (Oymen et al., 2022; Lozano et al., 2019; Tette et al., 2016). Regarding processed fruits such as those in jams, Reichert et al. (2015) and Valera-Tarifa et al. (2020) used QuEChERS-based methods to determine 107 and 250 pesticide residues, respectively. Nevertheless, with prior consideration to these works, QuEChERS methods may differ and be modified according to the authors, and to date, there is no single QuEChERS-based method optimised to cover hundreds of contaminants in a wide variety of concentrated sugary products.

Even though the QuEChERS sample preparation technique is suitable for determining a large number of pesticide residues in food, it first needs to be tailored to improve extraction efficiency regarding the target matrix composition. Indeed, various QuEChERS parameters such as the pH of the matrix, partition salts, clean-up, concentration of the extracts to improve method sensitivity or on the contrary, dilution of extracts to reduce potentially strong matrix effects, may affect the efficiency and sensitivity of the global method (Diallo et al., 2022a). Nevertheless, it is time-consuming and inefficient to optimise these parameters independently. Therefore, the use of practical split factorial experimental designs appears to be a robust method for simplifying the optimisation process. These experimental designs enable the simultaneous

study of several parameters while reducing cost and the number of experiments required (Diallo et al., 2022; Pang et al., 2021).

Along with sample preparation, appropriate analytical methods should be developed to overcome the drawbacks associated with the complexity of concentrated sugary products. Liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) operating in multiple-reaction-monitoring mode (MRM) has demonstrated satisfactory performance for the multiresidue determination of contaminants in concentrated sugary products (Valera-Tarifa et al., 2020; Tette et al., 2016; Reichert et al., 2015). In addition to LC-MS/MS, gas chromatography coupled with MS/MS (GC-MS/MS) allows for the complementary analysis of non-polar (non LC-amenable) contaminants, and was already employed to screen for pesticide residues in honey (Oymen et al., 2022). These techniques have the advantage of being selective and sensitive to a predefined list of prioritized chemicals to be searched for. However, they also have the disadvantage of overlooking compounds not on the predefined list (Makni et al., 2022a).

Thus, in recent years, high-resolution mass spectrometry (HRMS) in laboratories with Orbitrap or time-of-flight (ToF) instruments has made it possible to broaden the analytical scope. Indeed, these instruments operating in full-scan MS mode may be used for the theoretically unlimited determination of eluted compounds in a sample, without being restricted to a list of targeted chemicals or by the number of compounds to be analysed (Mezcua et al., 2009). Such analytical instruments have improved the concept of multiresidue screening methods, and several studies have reported the use of GC or LC coupled with HRMS for the multi-class determination of contaminants in various food samples (Gómez-Ramos et al., 2013b). For example in honey, Gómez-Pérez et al. (2012) successfully used Orbitrap mass spectrometry to screen more than 350 pesticide and VD residues. However, to the best of our knowledge, there is no study reported the use of HRMS instruments for the multiresidue screening of hundreds of contaminants in other concentrated sugary products.

Such instruments also introduced the suspect and non-targeted approaches, allowing to expand the analytical scope (Parinet, 2021; Phillips et al., 2018). The non-targeted and suspect-screening analyses has made it possible the semi-quantification of compounds for which analytical standards are not available, based on chemical similarity strategies (Malm et al., 2021) (Kalogiouri et al., 2017). In case the analytical standards being available in laboratory, accurate quantification of contaminants relies on the preparation of calibration curves (Sun et al., 2022). Quantification strategies such as example, multi-point external calibration curve (MPC) provide accurate quantitative results, by preparing different blank matrices spiked with different concentration-level (Sun et al., 2022). However, this strategy presents some drawbacks as the MPCs have to be prepared in each batch of samples, and this could be tedious in case hundreds of contaminants are included in the scope of the method, as mentionned by the author. Another method is the use of labeled internal standards to compensate for possible sources of variability and errors during the analytical process. However, as mentionned by Sun et al. (2022), the available labeled internal standards could be very expensive, limiting its application for large-scale and multiresidue quantitative analyses. Another strategy is the single-point calibration (SPC), more adapted for high-throughput analysis of hundreds of contaminants as one concentration-level is required, but also provides much less accurate quantitative results (Sun et al., 2022). It would be useful to configure a strategy for targeted analyses in HRMS that is easy to operate, time-and-cost saving, suitable for high-throughput semi-quantitative multiresidue analysis, while providing accurate concentrations of analytes.

The objective of this work was to develop an efficient method based on QuEChERS sample preparation and HRMS to improve the hazard characterisation associated with the presence of

mixtures of contaminants in various concentrated sugary products. To the best of our knowledge, this study is the first proposing a single screening and semi-quantitative method suitable for high-throughput analysis of 694 various targeted contaminants in different concentrated sugary products using UHPLC-Q/ToF.

2. Material and Methods

2.1. Chemicals and reagents

A 746-contaminant mix of analytical standards, divided into five mixtures (5 $mg.L^{-1}$ of each compound in solvent) was purchased from LGC Standards (Molsheim, France). Acetic acid (AA, LC-MS grade, ~ 98%), formic acid (LC-MS grade, ~ 98%) and acetonitrile (ACN, HPLC-MS grade, ~ 98%) were purchased from Thermo Fisher Scientific (Illkirch, France). A Milli-Q ultrapure water system and a Millipak 40 Gamma Gold filter (pore size 0.22 µm), obtained from Merck (Saint Quentin-en-Yvelines, France), were used to produce ultrapure water (18.2 MΩ.cm). Extraction kits based on the original QuEChERS method and containing 4.0 g of magnesium sulphate ($MgSO_4$) and 1.0 g of sodium chloride (NaCl) were purchased from Agilent (Santa Clara, USA). Extraction kits based on official EN Method 15662, containing 4.0 g of $MgSO_4$, 1.0 g of NaCl, 1.0 g of sodium citrate and 0.5 g of sodium citrate sesquihydrate, were obtained from Agilent (Santa Clara, CA, USA). Extraction kits containing 4.0 g of $MgSO_4$ and 1.0 g of sodium acetate (NaOAc) were purchased from Agilent (Santa Clara, CA, USA). Dispersive solid phase extraction (d-SPE) kits containing 900 mg of $MgSO_4$ and 300 mg of primary and secondary amines (PSA) were purchased from UCT (Bristol, PA, USA). Kits of d-SPE containing 900 mg of $MgSO_4$, 150 mg of PSA and 150 mg of octadecylsilyl silica (C18), were obtained from Agilent (Santa Clara, CA, USA).

2.2. Equipment and apparatus

A cooled centrifuge Universal 320R model and a Genie 2 vortex, used during sample extraction, were purchased from Hettich Lab Technology (Tuttlingen, Germany) and Scientific Industries (Bohemia, USA), respectively. A single-block heating and stirring module (Reacti-Therm™, model 18971) and an evaporating unit (Reacti-Vap, model 18780), used to evaporate the extracts, were purchased from Thermo Fisher Scientific (Waltham, USA).

Chromatographic separation was carried out using a Dionex UltiMate-3000 UHPLC system from Thermo Fisher Scientific, equipped with a binary pump and autosampler. The UHPLC system was coupled with a hybrid Q-ToF mass spectrometer from AB Sciex (TripleToF 5600™, Darmstadt, Germany), operating in electrospray ionisation mode (ESI).

2.3. Selection and use of the contaminants

Out of the 746 initial contaminants, only 694 could be successfully detected in solvent at 0.1 $mg.L^{-1}$, so these were selected for the present work (Table S1).

To optimise sample preparation, 204 pesticides were selected, including 187 from the above-mentioned mixture (Table S1). They were selected as representative of other compounds of the above-described mix in terms of retention time (t_R), mass-to-charge ratio (*m/z*) and range of polarity (LogP).

Once the method was optimised, the mixture of 694 contaminants — including mainly pesticide residues (acaricides, algaecides, fungicides, herbicides, insecticides, nematicides and rodenticides), but also transformation products (TPs), some pharmaceuticals (antibiotic, antimicrobial agents, anti-inflammatory drug), dual-use substances, environmental and industrial contaminants — was used to validate the screening method.

2.4. Selection and use of the samples

This work focused on the analysis of concentrated sugary products that are frequently consumed. In total, 54 honey, processed fruit and syrup samples of various types and origins were purchased from local markets (Maisons-Alfort and Créteil, France) then stored at 4°C. Metadata for the samples used in this study are provided in Table S2. Firstly, six honey samples were pooled and used as a representative and model sample for optimising sample preparation (Table S2). This pooled honey was used to optimise the method with the most complex matrix composition, as honey is among the matrices with the highest sugar content (~80%) and the lowest water content (~18%). This efficient process also led to time and cost savings by reducing the number of extractions and injections into the UHPLC-Q/ToF system. Secondly, 20 different honey, fruit jam and syrup samples were selected to validate the method (Table S2). Thirdly, 50 concentrated sugary products were selected and analysed in that part of the study dedicated to applying the method to provide occurrence data (Table S2) and to estimate concentrations.

2.5. UHPLC-Q-ToF parameters and data acquisition

The UHPLC conditions — including the column and pre-column used, mobile phase composition, gradient profile and some other liquid chromatography-linked parameters — were as previously described (Makni et al., 2022). The injection volume used for analyses was 10 µL.

The TripleToF 5600^{TM} system was operated in both positive and negative modes (ESI^+ / ESI^- in separate injections), using the following parameters: ion spray voltage floating (ISVF), 5.5 kV (-4.5 kV in ESI^-); source temperature (TEM), 500°C; curtain gas (CUR), 30 psi; nebulising gas (GS1), 40 psi; heater gas (GS2), 45 psi. Data acquisition consisted in a combination of a full-scan ToF-MS and information-dependent acquisition (IDA) mode:

- The full-scan ToF-MS acquisition covered a mass range of 50-1000 Da in high-resolution mode. The declustering potential (DP) was 80 eV (-80 eV in ESI^-) and the collision energy (CE) was 10 eV (-10 eV in ESI^-). Mass resolving power was 32,000 FWHM (*m/z* 415.2728). The accumulation time was 490 ms.
- The IDA mode (MS/MS data acquisition) included ten experiments (*top10*) in high-sensitivity mode, with a pre-selection of the ions to be fragmented as a priority using a precursor ion list (PIL). The PIL included the retention time (t_R) and the mass-to-charge ratio (*m/z*) of the targeted compounds (Table S1). For each of the ten IDA experiments, the CE was set at 40 eV (-40 eV in ESI^-) with a spread of ± 20 eV; nitrogen was used as the collision-induced dissociation gas; the mass resolving power was 20,000 FWHM (*m/z* 415.2728); the accumulation time was set at 40 ms and the total cycle time was 940 ms.

Before each batch, the system was systematically tuned and calibrated manually using the APCI positive or negative calibration solutions. Moreover, automated calibrations were performed within the batch every five samples. The UHPLC-Q/ToF system was controlled using Analyst® software (version 1.7), AB Sciex (Les Ulis, France).

2.6. Development of a homemade LC-MS/MS compound database

A homemade compound database (HCDB), including the reference MS/MS fragmentation spectra of the studied compounds, was developed and used for automated identification. The HCDB was built by injecting, in both ESI^+ and ESI^- modes, the analytical standards divided between mixtures and diluted to 0.1 $mg.L^{-1}$ in acetonitrile. The fragmentation spectra obtained in solvent were recorded for each compound and were considered as the reference spectra for the automated identification process in samples. In total, 610 and 139 spectra in ESI^+ and ESI^-

, respectively, were recorded with LibraryView™ software (version 1.0.3, AB Sciex). Among the 749 spectra recorder in LibraryView™ software, there were 55 compounds with spectra recorder in both ESI^+ and ESI^- modes.

2.7. Data processing and screening criteria

Data were processed using PeakView® software (version 2.2, AB Sciex) that includes the easy-to-use MasterView™ module, thus enabling fast, automated screening of samples against a list of compounds. The MasterView™ module is inter-connected to LibraryView™ software and allows the experimental fragmentation spectra to be compared with those recorded in the HCDB, as shown for example in Fig. S1.

Samples were screened for contaminants at detection and identification levels. The term detection was employed when the screening was based on the precursor ion with the following criteria: (i) experimental t_R maximum variation ± 0.1 min compared to the t_R obtained using the standard in solvent that was injected in the same batch; (ii) mass error tolerance ± 5 ppm. For unequivocal identification (Schymanski et al., 2014), characteristic fragment ions of the precursor ion were also used. Thus, the identification of the compounds was based on: (i) experimental t_R maximum variation ± 0.1 min compared to the t_R obtained using the standard in solvent that was injected in the same batch; (ii) mass error tolerance ± 5 ppm on the precursor ion; and (iii) spectral similarity >70% between the experimental and reference MS/MS fragmentation spectra using an FIT algorithm (Makni et al., 2022). This algorithm measures the degree to which the reference spectrum included in the HCDB is contained in the experimental spectrum, without being impacted by interfering fragment ions. The algorithm provides a similarity score (%).

2.8. Optimisation of sample preparation using an orthogonal array design

The sample preparation was optimised through a design of experiment (DoE) that consisted of an L18 Taguchi orthogonal array (TOA). Five factors were simultaneously optimised in triplicate (volume of water added, acidification of acetonitrile, extraction salts, d-SPE and dilution/concentration ratio) at three different levels (Table 1). The detection rates (%) as well as the signal-to-noise ratio (S/N) of the 204 pesticides selected were used as responses for evaluation.

Table 1. Factors and levels used for the optimisation of sample preparation.

Level	Factor				
	Volume of water (mL)	**Solvent acidification**	**Extraction salts**	**Clean-up**	**Dilution / Concentration**
1	2	ACN	AOAC 2007.01[a]	No clean-up	No dilution or concentration
2	5	ACN (0.1% AA)	EN 15667[b]	900 mg $MgSO_4$ / 300 mg PSA	Dilution 1:1
3	8	ACN (1% AA)	Original[c]	900 mg $MgSO_4$ / 150 mg PSA / 150 mg C18	Concentration ×10

[a] 4.0 g $MgSO_4$ / 1.0 g NaOAc
[b] 4.0 g $MgSO_4$ / 1.0 g NaCl / 1.0 g sodium citrate / 0.5 g sodium citrate sesquihydrate
[c] 4.0 g $MgSO_4$ / 1.0 g NaCl

2.9. Sample preparation

The sample preparation depended on the experiment of the L18 TOA. First, 2.0 ± 0.1 g of blank sample was weighed into a 50 mL-polypropylene centrifuge tube. Then, 20 µL of a mix working solution (1 $mg.L^{-1}$ of each compound in solvent) was added to the sample to provide supplementations at 0.01 $mg.kg^{-1}$. The matrix was left in contact with the mix working solution for 2 h at room temperature. Ultrapure water was then added to the tube, which was vortexed at full speed (2 min). Next, 10 mL of non-acidified or acidified ACN was added to the centrifuge tube, which was again vortexed at full speed (1 min). Afterwards, one of the three compositions of extraction salts (Table 1) was added to the centrifuge tube, and the resulting mixture was vortexed again at full speed (1 min). The tube was then centrifuged at -20°C, at 1842 relative centrifugal force (rcf) (5 min).

When a clean-up step was performed, 6 mL of the supernatant was recovered and deposited into either: a 15-mL centrifuge tube containing 900 mg $MgSO_4$ / 300 mg PSA or a 15-mL centrifuge tube containing 900 mg $MgSO_4$ / 150 mg PSA / 150 mg C18.

The tube was vortexed at full speed (1 min) and centrifuged at -20°C, at 1842 rcf (5 min). If no dilution/concentration step was performed, 1.5 mL of the supernatant was directly poured into a 2-mL amber vial prior the injection in UHPLC-Q/ToF system. The equivalent sample concentration of final extract was 0.2 $g.mL^{-1}$. If a dilution step was performed, 750 µL of the supernatant was diluted into 750 µL of ACN (dilution 1:1) into a 2-mL amber vial. In this case, the equivalent sample concentration of final extract was 0.1 $g.mL^{-1}$. When a concentration step was performed, 1.5 mL of the supernatant was poured into a 2-mL amber vial. The purified extract was then evaporated to near dryness at room temperature, and re-suspended in 150 µL of ACN to concentrate the contaminants. In this case, the equivalent sample concentration of final extract was 2 $g.mL^{-1}$.

If no clean-up step was performed after salting-out step, the non-purified extract was either directly poured into a 2-mL amber vial (0.2 $g.mL^{-1}$ equivalent concentration of sample), or diluted (0.1 $g.mL^{-1}$ equivalent concentration of sample), or concentrated (2 $g.mL^{-1}$ equivalent concentration of sample), following the same steps as those described above for purified-extracts.

2.10. Method validation

The optimised method was validated according to SANTE/11312/2021 guidelines for screening methods (European Commission, 2021). In this work, the method was validated using honey (n=13), fruit jam (n=5) and syrup (n=2) samples (Table S2). Syrup samples were also selected for validation as they also belong to the same group of high sugar and low water content commodities, thus introducing more matrix variability. Each non-spiked sample was first screened for the 694 studied contaminants (Table S1) in order to determine the compounds already present so as to exclude them from the validation process. Samples were then spiked at 0.001 $mg.kg^{-1}$, 0.01 $mg.kg^{-1}$ and 0.05 $mg.kg^{-1}$ with the mixture of the 694 contaminants to establish the screening detection limit (SDL) and the limit of identification (LOI). The SDL was established as the lowest concentration for which a compound was considered to have been successfully detected, by fulfilling (i) t_R variation ± 0.1 min and (ii) accurate mass measurement ≤ 5 ppm, in at least 95% of the samples (i.e. 19 out of 20 samples). The LOI, not required in SANTE/11312/2021 guidelines, was established as the lowest concentration for which a compound was considered to have been identified in at least 95% of the samples (i.e. 19 out of 20 samples). The criteria used to estimate the LOI were the same as those used for the SDL, but considering in addition a spectral similarity >70% between the reference and experimental MS/MS fragmentation spectra.

2.11. Application of the method to provide occurrence data

2.11.1. Target screening

The method was applied to 50 concentrated sugary products (Table S2) to provide occurrence data. The samples were screened at the level of detection and up to identification for confirmation (section 2.7.).

2.11.2. Semi-quantification

The concentrations of identified contaminants in the samples were estimated and compared using the following three semi-quantification methods:

Method A: Procedural calibration curves were constructed by re-using data from the 20 samples analysed during method validation and spiked at 0.001, 0.01 and 0.05 $mg.kg^{-1}$ with the mixture of 694 contaminants. To account for the inter-day signal variability, a 2-mL amber vial containing the mixture of 694 contaminants in solvent at 0.1 $mg.L^{-1}$ that was injected in the same batch as the validation samples was also used. The area values obtained for the spiked samples were divided by the area value of the corresponding compounds obtained in solvent. For each level of supplementation, an average ratio was calculated using the ratios obtained for the 20 individual samples. The average ratios (n = 20) obtained for the three levels of supplementation were used to construct the calibration curves. Only curves showing an acceptable coefficient of determination (r^2), i.e. higher than 0.99, were retained.

Method B: Similar to method A, but this time the procedural calibration curves were specific to each product family. When a compound was unequivocally identified in a honey or jam / jelly sample, only the 13 honey samples or the five jam samples were selected to construct the calibration curves, respectively.

Method C: Similar to method A, but this time the procedural calibration curves were specific to each type of sample. When a compound was unequivocally identified in a sample, only the same type of sample was selected to construct the calibration curve.

For the compounds found in the non-spiked samples, because the context is semi-quantification and not quantification, the area ratios obtained were subtracted from the area ratios obtained for the same compounds in the samples spiked at 0.001, 0.01 and 0.05 $mg.kg^{-1}$, whatever the method used.

3. Results and discussion

3.1. Sample preparation optimisation

To develop a wide-range extraction method for various contaminants in concentrated sugary products, several parameters of the QuEChERS protocol that may affect the efficiency of extraction were simultaneously optimised using an L18 TOA (Table 1).

Overall, the detection performance ranged from 73 to 91% (Table S3). The highest detection rates were obtained for experiments 2, 3 and 15, whereas the lowest performance was obtained for experiments 10 and 11 (Table S3). The factors with the highest impact on performance are reflected by the R-values (Table S3), which are used to rank the factors by their impact on the detection rate in this case. The higher this value, the greater the impact of the given parameter on the detection rate. The dilution / concentration ratio factor provided the greatest impact on the detection rates (R = 11), followed by the clean-up parameter (R = 3), extraction salts and solvent acidification (R = 2) and volume of water added (R = 0). The S/N ranged from 155 to 855 (Table S4). Overall, it was again experiments 2, 3 and 15 that gave the highest

performances, and experiments 10 and 11 the lowest. The factor with the highest impact on performance, as reflected by the R-values, was again the dilution / concentration (R = 516), followed by the extraction salts (R = 89), clean-up (R = 36), volume of water added (R = 27) and the solvent acidification factor (R = 19) (Table S4). According to these results, the only factor that appears to have a significant impact on performance is the dilution / concentration factor.

3.1.1. Volume of water added

The QuEChERS method was originally designed for the analysis of samples with a high water content of 75% (Tette et al., 2016). For matrices with a low water content (<25%), the sample amount can be diluted using water to achieve effective extraction of contaminants (Kolberg et al., 2011). Therefore, the sample amount was set at 2 ± 0.1 g and the volume of water to be added to the sample was tested (Table 1). According to the results, the three levels tested provided detection rates around 82% (Fig. S2) and a S/N value of 408, 389 and 381, respectively, with equivalent variability (Fig. S3). Even though the volume of water added did not have any major impact on performance, level 1 (2 mL) was selected for the method, as it provided on average the highest S/N.

3.1.2. Solvent acidification

In the QuEChERS method, ACN is the most widely used organic solvent for its ability to cover compounds with a wide polarity range. ACN is often acidified using AA or formic acid to protect and stabilise the base-sensitive compounds (Alcântara et al., 2019b). Thus, pure ACN was compared with acidified ACN as mentioned in Table 1. The detection rate performances (Fig. S2) were equivalent (81-83%). In addition, there was no major difference in S/N values between the three levels tested (386-405), even though slightly higher signals were obtained with ACN (0.1% AA v/v) (Fig. S3). As a result, acidified ACN (0.1% AA v/v) was selected for the method.

3.1.3. Extraction salts

The original QuEChERS method used a combination of $MgSO_4$ / NaCl for the salting-out process (Anastassiades et al., 2003a). $MgSO_4$ is a desiccant that binds and dries out water, thus improving the liquid-liquid partitioning and the transfer of compounds to the organic layer, while NaCl increases the recovery of polar compounds (Kim et al., 2019c). Nevertheless, recovery rates can be low using these original salts for pH-sensitive compounds. The original QuEChERS method had two official buffered variants, one with sodium acetate (Lehotay et al., 2007) and the other with citrate salts (Anastassiades et al., 2007b), which stabilise the pH of the medium around 5-5.5 and allow higher recoveries for pH-dependent compounds (Santana-Mayor et al., 2019b). In this study, the three compositions of salts (Table 1) were tested. As shown in Fig. S2, the detection performances were equivalent (81-83%). However, regarding the S/N obtained, the performances were slightly better using sodium acetate salts (level 1) with an average S/N of 441 compared with 384 and 383 for the other two levels, respectively (Fig. S3). Thus, the combination of salts using $MgSO_4$ / NaOAc was selected for the method under development.

3.1.4. Clean-up step

The cleaning up of honey extracts appears to be a crucial step in sample preparation due to the complexity of the matrix, which mainly includes co-extractive sugars of various types but also vitamins, enzymes, lipids and waxes (Gaweł et al., 2019a). Previous studies have reported the use of PSA to clean honey extracts due to its ability to remove sugars, pigments and organic acids (Oymen et al., 2022; Nadaf et al., 2015). However, it has also been reported that PSA

alone might not be sufficient for the cleaning of honey samples (Oymen et al., 2022). Indeed, several studies have highlighted the relevance of combining PSA with other sorbents such as C18, which removes non-polar co-extractive compounds, to improve the clean-up efficiency for honey extracts (Gaweł et al., 2019; Abdallah et al., 2017). Therefore, this study tested not only this aspect but also the efficiency of not having a clean-up step (Table 1). As shown in Fig. S2, detection rates ranged from 80 to 83% and average S/N ranged from 373 to 409 (Fig. S3). Surprisingly, the absence of any clean-up of honey extracts has no major impact on the method's performance. The use of ACN in QuEChERS could explain these results, as major co-extractive compounds such as sugars are not very soluble in this organic solvent and would therefore not be completely extracted. Regarding the use of $MgSO_4$ / PSA alone, the results were equivalent to those using a combination of $MgSO_4$ / PSA / C18. Although this study did not demonstrate any major impact of a clean-up step on performance, the combination of $MgSO_4$ / PSA was selected for the method. This is because it was observed during analyses that the non-purified extracts could lead to traces of dirt due to the caramelisation of sugars following exposure to high temperatures in the source of the mass spectrometer. This could damage the system in the long-term, especially when the extracts are concentrated.

3.1.5. Dilution / concentration ratio

Due to the high sugar content, pigments and phenol (Yang et al., 2022), honey matrix effects may be strong, potentially affecting ionisation and the detectability of analytes. Diluting the extract may reduce potential matrix effects and enhance the signal from analytes but it could also reduce the method overall sensitivity, as observed in other food matrices (Diallo et al., 2022a). In contrast, concentrating the extract could be a way of improving the signal of analytes of interest, especially when the instrument lacks of sensitivity to achieve satisfactory performances as it was the case in this work. However, it could also lead to stronger matrix effects and signal suppression. This study therefore tested these two aspects in comparison with a condition in which the extract is neither diluted nor concentrated (Table 1). As shown in Fig. S2, detection performances were generally higher when the extracts were concentrated (88%) rather than diluted (77%), in comparison with the extracts that were neither diluted nor concentrated (81%). The S/N values were also higher when the extracts were concentrated (709) than either diluted (193) or neither diluted nor concentrated (276) (Fig. S3). Thus, the concentration of honey extracts following a clean-up step in QuEChERS appears to be a key parameter with a strong positive impact on the performances obtained, without damaging the instrument. Therefore, it was decided to concentrate honey extracts as part of the method.

The complete and optimised sample preparation protocol is summarised in Fig. 1.

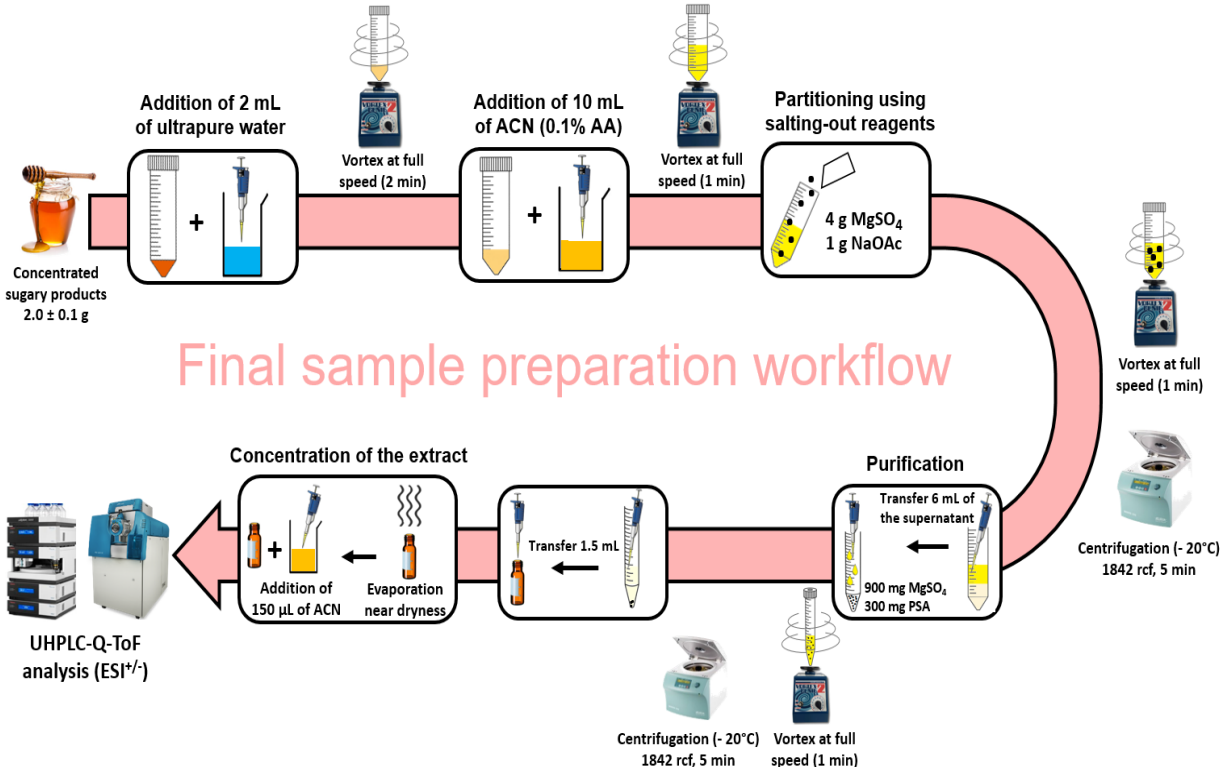

Fig.1. Final sample preparation workflow for determining contaminants in concentrated sugary products.

3.2. Method validation

The method was validated according to SANTE/11312/2021 guidelines (European Commission, 2021). The SDL and LOI (see section 2.10.) were used for validation purposes. However, acetamiprid, azoxystrobin, coumaphos, cyprodinil, difenoconazole, flonicamid, fluopyram, fuberidazole, prothioconazole-desthio, spinosyn A and thiacloprid were found in non-spiked samples, and were therefore excluded from validation. Thus, the SDL and LOI were established for 683 contaminants instead of 694.

The detection rates ranged from 66 to 78%, 87 to 93% and from 91 to 96% depending on the sample, at 0.001, 0.01 and 0.05 mg.kg^{-1}, respectively (Fig. 2a). As shown by the results, the detection rates were high and equivalent at 0.01 and 0.05 mg.kg^{-1}. At trace level (0.001 mg.kg^{-1}), the performances decreased but were still satisfactory as at least two thirds of the contaminants were correctly detected (Fig. 2a). Furthermore, regardless of the concentration, there was no difference in performance between honey, fruit jam and syrup samples, which highlights the robustness and efficiency of the optimised method for analysing concentrated sugary products. The SDLs were established at 0.001 mg.kg^{-1} for 352 contaminants (52 %), at 0.01 mg.kg^{-1} for 191 contaminants (28%), and at 0.05 mg.kg^{-1} for 63 contaminants (9%) (Table S5 and Fig. S4). Overall, 89% of the contaminants had an SDL ≤ 0.05 mg.kg^{-1} (Fig. S4) and only 78 compounds (11%) had an SDL > 0.05 mg.kg^{-1} (Fig. S4).

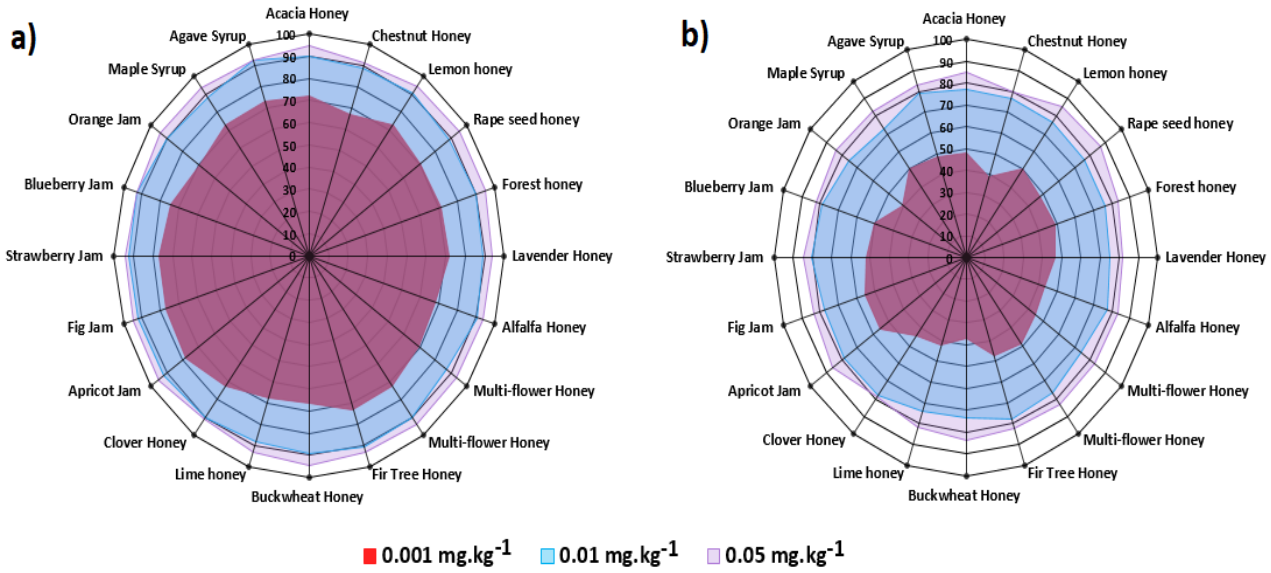

Fig.2. Analytical performances of the optimised method with **(a)** detection rates and **(b)** identification rates obtained in 20 concentrated sugary products at 0.001, 0.01 and 0.05 mg.kg^{-1}.

Depending on the sample, the identification rates ranged from 37 to 56%, 73 to 81% and 79 to 86% at 0.001, 0.01 and 0.05 mg.kg^{-1}, respectively (Fig. 2b). The performances were high and equivalent at 0.01 and 0.05 mg.kg^{-1}, and satisfactory at trace level (0.001 mg.kg^{-1}). The LOI was established at 0.001 mg.kg^{-1} for 148 contaminants (22%), at 0.01 mg.kg^{-1} for 268 contaminants (39%) and at 0.05 mg.kg^{-1} for 88 contaminants (13%) (Table S5 and Fig. S4). Overall, 74% of the contaminants had an LOI ≤ 0.05 mg.kg^{-1} (Fig. S4). However, 180 compounds (26%) were not successfully identified in at least 19 of the 20 samples. Thus, their LOI was established at > 0.05 mg.kg^{-1} (Fig. S4). In the present study, the approach used to identify a compound did not only involve the mass error calculation on one specific fragment ion, as recommended by European Commission (2021). Indeed, the identification process performed and detailed in section 2.7.1. is more restrictive, as it involves using the whole fragmentation spectrum of a given compound. However, it also generates a higher level of confidence in identification, as explained in our previous study (Makni et al., 2022a).

Among the 683 contaminants included in the method validation, 187 compounds were also analysed by Gómez-Pérez et al. (2012) using a dilute-and-shoot sample preparation protocol and Orbitrap mass spectrometry. For these compounds only, the LODs (established as the lowest tested concentration for which a compound provided a signal higher than 1×10^3 counts and ranging from 0.001 to 0.05 mg.kg^{-1}) provided by Gómez-Pérez et al. (2012) were compared with the SDLs established in the present work. The results showed that 39 compounds (21%) had an SDL < LOD, 81 compounds (43%) had an SDL equal to the LOD and 67 compounds (36%) had an SDL slightly higher than the LOD, but remained in the same order of magnitude (Table S6 and Fig. S5). Overall, 64% of the compounds had an SDL equal to or below the LODs found by Gómez-Pérez et al. (2012) (Fig. S5). However, even if a compound has an SDL of a given concentration, its theoretical LOD may be even lower. Fig. S6 shows as an example the extracted ion chromatogram (EIC) of five compounds (bromuconazole, bupirimate, fenarimol, tebufenozide, tetraconazole) validated with an SDL of 0.001 mg.kg^{-1} (Table S5). Even at this trace level, the peak shapes were satisfactory and well distinguishable from background noise (Fig. S6), suggesting that their theoretical LODs were even lower.

All of these results highlighted the excellent analytical performances achieved by the method and its efficiency for screening a broad spectrum of contaminants in various concentrated sugary products with high confidence. However, some considerations should be raised. First, some of the contaminants included in this work were weakly detected in LC, and are much better analysed in GC because of their non-polar and lipophilic character. In this sense, the use of GC in complementary to LC techniques appears essential to achieve the most complete chemical coverage possible. Regarding the sample preparation, QuEChERS-based methods may not be very effective for the analysis of highly polar compounds (Lehotay, 2022). Also, the use of PSA during the clean-up step retains some analytes of interest, especially carboxylic acids compounds (Lehotay, 2022). The proposed method did not compel with the class of VDs, for which the use of high amount of PSA in QuEChERS may not work well. Because of their high interest in honey, it would be useful to assess the efficiency of the method on various classes of antibiotics. However, it should be kept in mind that it is still not feasible to date to cover all the contaminants using a single method, and often a complementarity of methods is necessary, although this aspect is improving with the recent introduction of mega methods (Monteiro et al., 2021b). Nevertheless, despite these considerations, the present method proved to be highly effective and sensitive for the screening of LC-amenable contaminants with wide polarity range even at low-levels in concentrated sugary products.

Regarding the 11 compounds excluded during method validation, even though the analytical performances could not be determined, they were kept within the analytical scope so their potential presence in concentrated sugary products could still be monitored.

3.3. Application of the method to provide occurrence data

3.3.1. Target screening

The method was finally applied to 50 different concentrated sugary products to detect the potential presence of the 694 targeted contaminants. It was found that 23 out of the 50 samples (46%) were positive for a single contaminant or a mixture of them (Table 2). There were 14 positive honey samples out of 33 (i.e. 42%), seven positive jams out of 12 (i.e. 58%) and two positive jellies out of two (i.e. 100%). No contaminant was identified in the three syrup samples tested (Table 2). Among the 23 positive samples, five (22%) were positive for one pesticide residue, while the other 18 (78%) were positive for a mixture of pesticide residues (Table 2). Overall, the jams and jellies containing red berries were the samples with the highest number of pesticide residues (Table 2). In these food commodities, mixtures could range from two pesticide residues in a strawberry jam sample to nine in strawberry jam and in currant jelly (Table 2). For jams without berries, only one apricot jam was positive for a mixture of four pesticide residues, while all the others were free of residues (Table 2). These results confirm the need to monitor and regulate processed fruits for the presence of pesticide residues, especially as they are submitted to thermal treatment reducing water content during processing, which could concentrate non-volatile residues (Valera-Tarifa et al., 2020). Additionally, active substances may be degraded during thermal processes, leading to the formation of degradation by-products that it would be beneficial to monitor. In positive honey samples, the occurrence varied from one pesticide residue (in alfalfa, buckwheat, chestnut, forest and an unspecified type of honey) up to five in a lemon tree honey (Spain) and a multi-flower honey (France) (Table 2).

Table 2. Contaminants identified in the 50 sweet products.

Sample	Type	Origin	Compounds unequivocally identified
Honey	Acacia	France	
	Alfalfa	France	fluopyram
	Buckwheat	France	fluopyram
	Cactus	Morocco	
	Chestnut	France	
	Chestnut	Spain	coumaphos
	Clover	France	azoxystrobin, flonicamid, fluopyram
	Eucalyptus	Madagascar	
	Eucalyptus	Mexico	
	Fir	France	
	Forest	France	fuberidazole
	Forest	France	
	Forest	Chile	
	Lavender	France	
	Lavender	France	
	Lemon tree	Spain	acetamiprid, coumaphos, flonicamid, fluopyram, thiacloprid
	Lime	France	
	Mountain	Chile / Spain	acetamiprid, fludioxonil, pyrimethanil
	Multi-flower	France	azoxystrobin, difenoconazole, flonicamid
	Multi-flower	France	
	Multi-flower	France	azoxystrobin, cyproconazole, fluopyram, metconazole, prothioconazole-desthio
	Multi-flower	Madagascar	
	Multi-flower	Kyrgyzstan	
	Niaouli	Madagascar	
	Orange tree	Spain	acetamiprid, coumaphos
	Rapeseed	France	azoxystrobin, fluopyram, prothioconazole-desthio
	Rapeseed	France	prothioconazole-desthio, tebuconazole
	Rapeseed	France	
	Sunflower	France	
	Unspecified	France	fluopyram
	Unspecified	France	dimoxystrobin, fluopyram, metconazole

Sample	Type	Origin	Compounds unequivocally identified
	Unspecified	France	
	Unspecified	Ukraine	
Jam	Apricot	France	
	Apricot	France	cyprodinil, difenoconazole, fludioxonil, imazalil
	Blueberry	France	
	Cherry	France	carbendazim, difenoconazole, fenbuconazole, fluopyram, tebuconazole, thiacloprid
	Fig	France	
	Orange	France	
	Orange	France	
	Raspberry	France	azoxystrobin, boscalid, cyprodinil, difenoconazole, fenhexamid, fludioxonil, trifloxystrobin, spinosyn A
	Strawberry	France	cyprodinil, spinosyn A
	Strawberry	France	carbendazim, cyprodinil, difenoconazole, fludioxonil, fluopyram, penconazole, pyrimethanill, trifloxystrobin, spinosyn A
	Strawberry	France	carbendazim, difenoconazole, fludioxonil, fluopyram, imazalil, pyrimethanil, thiabendazole, spinosyn A
	Strawberry	France	azoxystrobin, carbendazim, cyprodinil, fludioxonil, fluopyram, pyrimethanil, spinosyn A, tetraconazole
Jelly	Currant	France	boscalid, carbendazim, cyprodinil, difenoconazole, fludioxonil, fluopyram, pyrimethanil, tetraconazole, thiacloprid
	Currant/Raspberry	France	carbendazim, cyprodinil, fludioxonil, tebuconazole, pyrimethanil
Syrup	Agave	Non-EU	
	Maple	Canada	
	Maple	Canada	

In total, 25 pesticide residues (20 fungicides and five insecticides) and one TP were found through the screening of the 50 concentrated sugary products. Their frequency of appearance (FoA) is indicated in Table 3. The most frequently identified compound was the fungicide fluopyram with an FoA of 26%, followed by the fungicides fludioxonil (FoA 16%), cyprodinil and difenoconazole (FoA 14%), azoxystrobin, carbendazim and pyrimethanil (FoA 12%), and the bio-insecticide spinosyn A (FoA 10%) (Table 3). Fig. 3 shows as an example, unequivocal identifications of azoxystrobin, fluopyram and pyrimethanil in multi-flower honey, cherry jam and currant / raspberry jelly. It can be highlighted that carbendazim, cyprodinil, difenoconazole, fludioxonil, fluopyram, pyrimethanil and spinosyn A were prevalent in the mixtures found in

red berry jams and jellies (Table 2). These results support previous studies reporting these same compounds in processed fruits (Valera-Tarifa et al., 2020; Reichert et al., 2015), except for fludioxonil which was not reported, but for which the occurrence in jam and jelly samples remains consistent as it a fungicide approved to be used for certain small fruit and berries. The presence of two cyano-substituted neonicotinoids, acetamiprid and thiacloprid (FoA 6%), should also be noted, as should the dual-use substance coumaphos (FoA 6%) in honey samples from Spain (Table 3). Neonicotinoids are well-known as they are implicated in the excess mortality of bee colonies (Andrione et al., 2016), while coumaphos, an acaricide and organophosphate insecticide, is legally approved as a veterinary product to treat hives against the *Varroa* mite (Lozano et al., 2019).

Table 3. Frequency of appearance (%) of contaminants identified in 50 sweet products.

Type of xenobiotic	Compound	Class	%FoA
Pesticide residues	acetamiprid	insecticide	6
	azoxystrobin	fungicide	12
	boscalid	fungicide	4
	carbendazim	fungicide	12
	coumaphos	insecticide	6
	cyproconazole	fungicide	2
	cyprodinil	fungicide	14
	difenoconazole	fungicide	14
	dimoxystrobin	fungicide	2
	fenbuconazole	fungicide	2
	fenhexamid	fungicide	2
	flonicamid	insecticide	6
	fludioxonil	fungicide	16
	fluopyram	fungicide	26
	fuberidazole	fungicide	2
	imazalil	fungicide	4
	metconazole	fungicide	4
	penconazole	fungicide	2
	pyrimethanil	fungicide	12
	spinosyn A	insecticide	10
	tebuconazole	fungicide	6
	tetraconazole	fungicide	4
	thiabendazole	fungicide	2
	thiacloprid	insecticide	6
	trifloxystrobin	fungicide	4
TP	prothioconazole-desthio		6

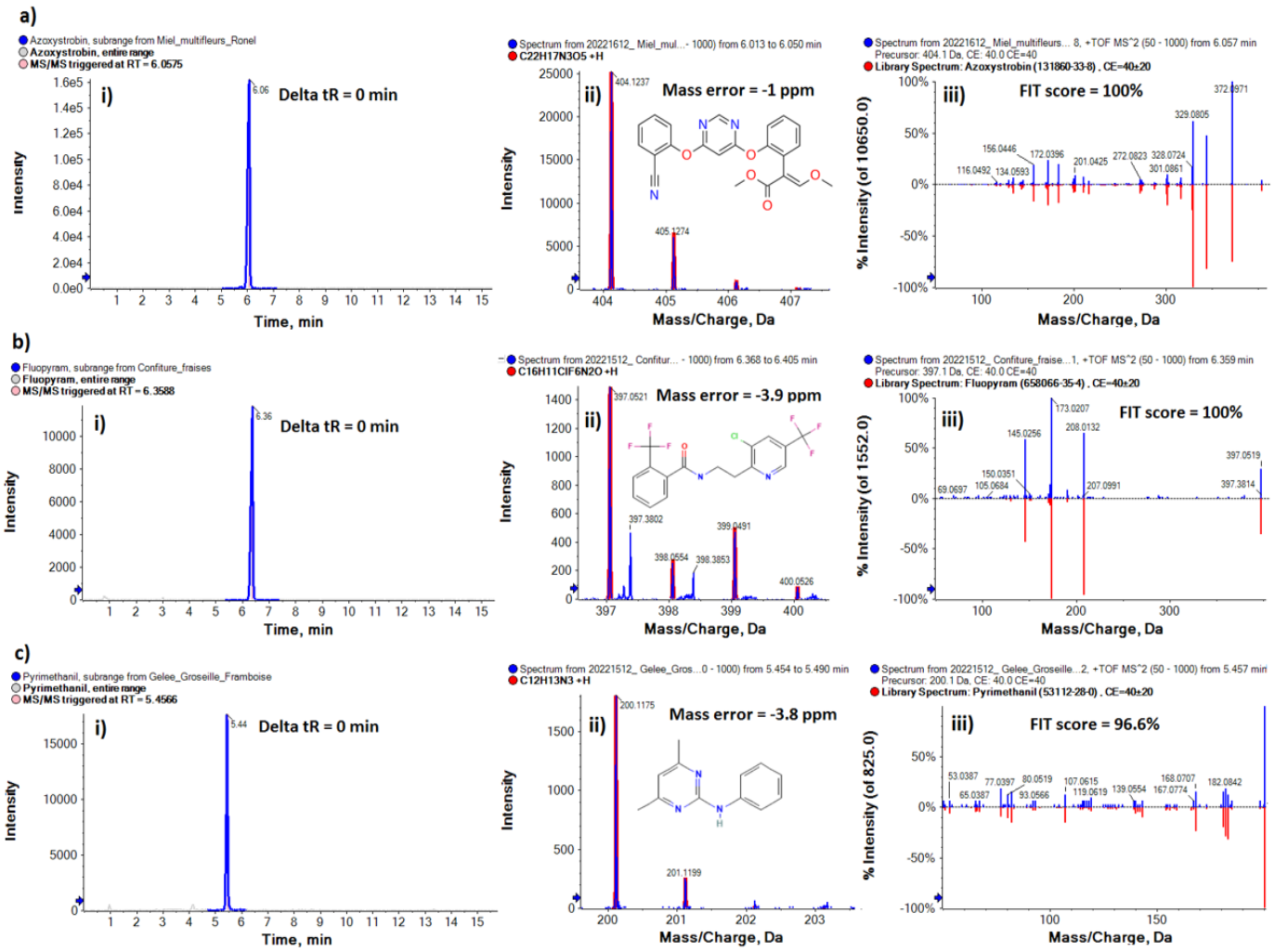

Fig.3. Unequivocal identification of **(a)** azoxystrobin in multi-flower honey; **(b)** fluopyram in cherry jam and **(c)** pyrimethanil in current/raspberry jelly. **(i)** Extracted ion chromatogram; **(ii)** Isotopic pattern and mass error of the precursor ion; **(iii)** Experimental fragmentation spectrum (in blue) matched against the library spectrum made by injecting standard in solvent (in red).

3.3.2. Semi-quantification of the identified contaminants

The quantification of identified compounds remains necessary to check compliance with current regulations, as well as to provide data for hazard characterization in this type of food products. However, it would be tedious and expensive to implement a full accurate quantification method, not very compatible with high-throughput quantitative multiresidue analysis. Thus, an easy-to-implement semi-quantification strategy compatible with high-throughput multiresidue targeted analyses was used to semi-quantify the previously identified pesticides and TP, by comparing the three methods described in section 2.11.2.

The estimated concentrations calculated with the three methods were equivalent or within the same order of magnitude, especially when the compound was found in lower concentrations (Table S7). For example, the fungicide cyprodinil was found at concentrations from 0.001 up to 0.003 $mg.kg^{-1}$ whatever the method used (Table S7). Another example, the fungicide difenoconazole occurred at an equivalent range of concentrations, from 0.001-0.008 $mg.kg^{-1}$ with method a, 0.001-0.007 $mg.kg^{-1}$ with method b and 0.002-0.006 $mg.kg^{-1}$ with method c

(Table S7). When a compound was found in higher concentrations in a sample, the concentrations found with the three different methods remained in the same order of magnitude. This was notably the case for the fungicides azoxystrobin (0.030-0.041 $mg.kg^{-1}$) and cyproconazole (0.027-0.036 $mg.kg^{-1}$) in multi-flower honey, fluopyram (0.015-0.023 $mg.kg^{-1}$) in cherry jam, and pyrimethanil (0.011-0.015 $mg.kg^{-1}$) in strawberry jam (Table S7). Nevertheless, the difference was more marked in the case of fenhexamid, occurring in raspberry jam at concentrations estimated from 0.040 to 0.066 $mg.kg^{-1}$ depending on the method used (Table S7). Overall, there was no pesticide residue found that exceeded the MRL in honey (Table S7). There is no established MRL to date for processed fruit.

These results suggest that the use of average calibration curves reflecting the matrix variability of an entire group (method a) or family (method b) could be considered for the semi-quantification of contaminants. These methods would present the major advantage of using composite calibration curves in different sugary products or in different honey/processed fruits/syrups, without having to establish the calibration curves on the same type of sample than the contaminated one. However, the inter-matrix variability may be significant, which could result in concentration values far from the real concentration in the sample. The use of a calibration curve specific to the type of matrix (method c) in which a compound was identified would be in theoretical more accurate. However, it would be necessary to evaluate the selectivity of a given matrix to ensure that there is little variability in this product purchased from different markets and areas. Such an evaluation was not conducted in this study and will be the research topic for further works to improve the semi-quantification aspect of screening methods. It would save time and costs as the calibration curves would be established only once for a large panel of contaminants then re-used during sample analysis. Despite the potential benefit of these approaches, it would remain essential to more precisely quantify the contaminant found using an appropriate validated quantitative method, in order to confirm the concentrations found through semi-quantification. Such a comparison would be very useful for assessing the relevance and accuracy of the targeted semi-quantification approaches proposed in this work, and to what extent they could be applicable for high-throughput multiresidue analysis of samples in food safety laboratories.

4. Conclusion

The study conducted presented a single method for the multiresidue screening contaminants in different and popular sugary products. The implementation of a generic QuEChERS-based method with a concentration step of the final extracts shown to be very effective to cover a wide range of contaminants with high sensitivity. The use of UHPLC-Q/ToF as analytical system allowed for the simultaneous analysis of 694 LC-amenable contaminants (pesticide residues mainly but also TPs, some pharmaceuticals, veterinary drugs and environmental / industrial contaminants), with high confidence using automated detection and identification processes. The use of HRMS instruments offers the possibility to significantly broad the analytical scope, which is needed bearing in mind the objective of improving hazard characterisation associated with the occurrence of mixture of chemicals in food, in a food exposome-based context. Indeed, occurrence of mixtures of pesticide residues and TPs were identified in honey and processed fruits, supporting the need to monitor these products to ensure consumer protection and safety. In addition, novel semi-quantification strategies were proposed based on the configuration of procedural calibration curves of entire group of sugary products (method a), family (method b) or sample specific (method c). They are configured one time and reusable afterwards to provide estimation of quantitative results of contaminants in samples. These methods present the advantage of being easy to implement, time-and-cost saving, and suitable for high-throughput

analysis, which is not necessarily the case of traditional accurate quantitative method. However, the efficiency and accuracy of these methods need to be used in parallel with conventional quantitative methods for comparison to confirm their relevance.

In routine applicability, the present method could be used upstream as a realistic early-warning system to bring to light non-prioritised and emerging contaminants, or the misuse of chemicals and unexpected pollution, with estimation of the concentrations in order to improve hazard characterization and food safety. Traditional GC or LC-MS/MS with well-established quantitative strategy would then be used to confirm the results.

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Declaration of competing interest

The authors declare they have no conflicts of interest.

2.4.4. Summary and main results

The QuEChERS extraction method was first optimized by fractional factorial design of experiment using the Taguchi method (Narenderan et al., 2019). This optimization was carried out on a pool of samples of different honeys, as this hive product is among the most complex sugary products, due to its very high sugar content (~80%) and low water content (~20%). This honey pool was supplemented with 204 pesticide residues at low levels (0.01 mg.kg-1). This enabled us to optimize the sample preparation method under harsh and highly complex conditions, and on a pesticide pool representative of the rest in terms of LogP, chromatographic retention time and mass. The method was then validated according to European Commission recommendations (European Commission, 2021) on 20 different sweet products (honeys, jams and syrups) supplemented with a mix of 694 various contaminants, including pesticide residues, processing products, industrial contaminants, etc. The correctly validated method was then applied to analyze 50 commercially-bought sugary products. Overall, 25 pesticide residues were reliably and unequivocally identified. We were also able to develop and apply a semi-quantification method to estimate the concentrations of contaminants identified in the sweet products previously analyzed. The semi-quantification method proposed in this work is based on traditional quantification methods, while being more compatible with multiresidue and high-throughput sample analysis, easy to implement and inexpensive. The estimated and found concentrations of analytes in honeys complied with the regulatory thresholds set by EFSA, whereas for jams and jellies, these products are not regulated, which poses a problem.

2.4.5. Limitations and prospects for improvements

Despite the quality of the work carried out, several limitations stand out and may suggest certain avenues of improvement for our methods. Firstly, the need to diversify the contaminants used for analytical developments. Indeed, for cost and practical reasons, pesticide residues are the main contaminants included in this work, although transformation products and industrial contaminants were also included in method validation Nevertheless, it would be essential to be able to integrate another family of highly regulated chemical substances, veterinary drugs, which are at the heart of certain public health concerns. In addition to this food safety and public health aspect, veterinary drugs are generally more polar compounds than pesticide residues. Thus, the use of acetonitrile as an extraction solvent may not be suitable for the analysis of this type of contaminant, hence the need to evaluate and adapt methods to cover them.

In addition, it would also be essential to further develop suspect analysis with a view to demonstrating the full capabilities of HRMS to broaden the spectrum of contaminants and highlight emerging, and varied mixtures of chemical substances. All this would serve the initial objective of demonstrating the relevance and value of HRMS in improving the food safety system.

Finally, as HRMS is an "omics" technique, i.e., one that generates massive amounts of data, the implementation of non-targeted workflows is a major point missing from our current work.

2.5. Development of a method for the multiresidue analysis and semi-quantification of 850 contaminants in seafood

2.5.1. Contexte and aim of the study

This fourth study is part of a project undertaken by my colleague Thierno Diallo, who is working on the elucidation of excess mussel mortality in the Pertuis-Charentais area of France. Indeed, resolving mussel mortality in this region of France presents major economic and ecological stakes, central to the interests of local oyster farmers. The aim of this study was therefore to develop a new sample preparation method, covering a broader spectrum of contaminants than conventional QuEChERS methods, for the broad-spectrum analysis of 850 contaminants in seafood products. This method will subsequently be used by Thierno, to characterize the exposure of possible contaminants that could be implicated in the over-mortality of mussels in the Pertuis-Charentais area (France). This method is also intended to be used to characterize consumer exposure to chemical substances present in a variety of seafood products widely consumed by the population, hence their inclusion in the study in addition to bivalve species.

I contributed to this work by assisting Thierno in optimizing the new sample preparation method, validating the method, and setting up a semi-quantification method. Indeed, the semi-quantification of chemical substances found in the seafood products analyzed was the fruit of joint reflection, and was already introduced in the previous article on sugary products (Makni et al., 2023a).

2.5.2. Key points of the study

In the course of this work, we were able to:

- Develop a new sample preparation method capable of covering contaminants with a very wide range of polarity. At present, the QuEChERS protocol is highly effective, but has limitations when it comes to polar compounds that are difficult to extract with acetonitrile, such as veterinary drugs.
- Implement a semi-quantification method to provide quantitative data on chemical contamination in fish products.
- Introduce an extended search for contaminants via a suspect-screening approach using open-access software and external databases.

Fig.4 below describes and summarizes the major improvements compared with the previous works (Makni et al., 2023a; Diallo et al., 2022; Makni et al., 2022), following an iterative process of continuous improvement.

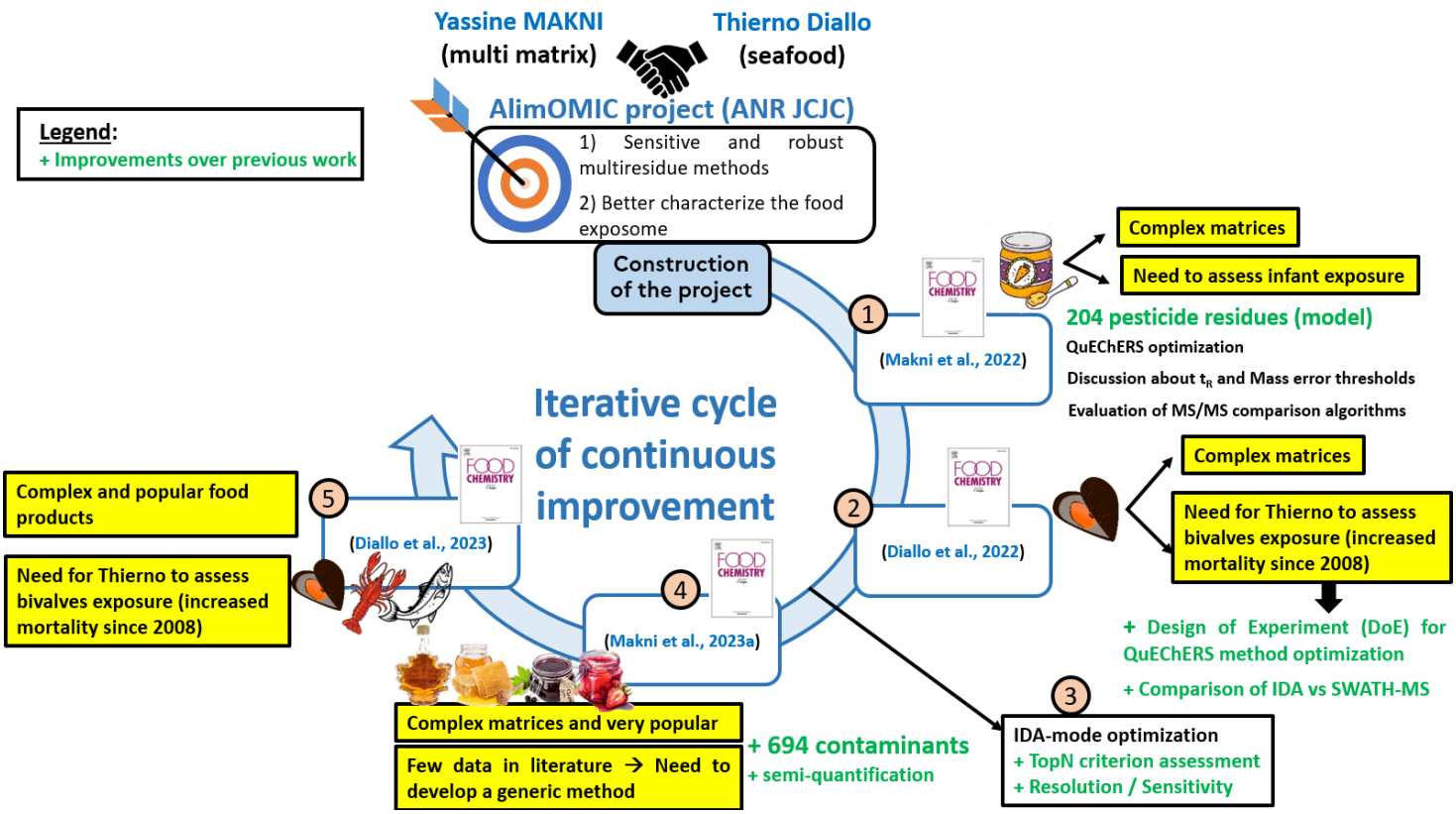

Fig.4. Cycle of iterative and continuous improvement – part 4

2.5.3. Article 4 (Diallo et al., 2023)

The following article details experiments on the development and validation of a new sample preparation method for the analysis and semi-quantification of 850 contaminants in seafood. This article was published in Food Chemistry. Due to Elsevier copyright restrictions, only the title and abstract of the paper were included in published format. The rest of the paper is inserted in Word-type format. The published paper is available online using the following DOI: https://doi.org/10.1016/j.foodchem.2023.136572

The references associated to this article are displayed here: References section (Article No. 4).

The electronic supplementary materials (Annexes) associated to this article are displayed here: Article 4 (Diallo et al., 2023): "Wide-scope screening of multi-class contaminants in seafood using a novel sample preparation (QuEChUP) procedure coupled with UHPLC-Q-TOF-MS: Application for semi-quantitation of real seafood samples"

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Wide-scope screening of multi-class contaminants in seafood using a novel sample preparation (QuEChUP) procedure coupled with UHPLC-Q-TOF-MS: Application for semi-quantitation of real seafood samples

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ABSTRACT

A high-resolution mass spectrometry screening method was developed and validated based on EU SANTE/11312/2021 guidelines for the analysis of 850 multi-class contaminants in commercial seafood samples. Samples were extracted using a novel sequential QuEChUP preparation method that combines the QuEChERS and QuPPe procedures. The screening detection limits (SDLs) and limits of identification (LOIs) were equal to or lower than 0.01 $mg{\cdot}kg^{-1}$ for 92% and 78% of contaminants, respectively. This screening procedure was ultimately applied for a target screening analysis of 24 seafood samples. The concentrations of identified contaminants were assessed using semi-quantitative approach. Two identified contaminants, diuron and diclofenac, showed the highest estimated average concentrations: 0.076 and 0.068 $mg{\cdot}kg^{-1}$ respectively in mussel samples. Suspect screening was also performed. Target and suspect screening led to the identification of mixtures of contaminants (pesticides, veterinary products, industrial chemicals and personal care products) and the assessment of their frequencies of appearance (FoA).

1. Introduction

Currently, there is heightened awareness of the toxicity of certain chemical compounds, such as pesticides, whose presence in the environment has been or is regulated by various legislation (Teysseire et al., 2021). Along with pesticide use, veterinary drug use has increased dramatically in recent years (Casado et al., 2019). This latter group of substances, which includes antimicrobials, hormones and non-steroidal anti-inflammatory drugs (NSAIDs), is one of the major classes of emerging contaminants (Samal et al., 2022). The main route of entry of veterinary drugs into the aquatic environment is via wastewater (including urban, industrial, agricultural and livestock wastewater), whereas pesticides enter the aquatic ecosystem via runoff, vaporisation into the atmosphere, agricultural returns, intrusion into groundwater or by adsorption or uptake by plants (Tudi et al., 2021). Once pesticides, veterinary drugs and various mixtures of contaminants enter the water, aquatic species absorb them — e.g. fish take them up through their gills — and they can accumulate and undergo metabolism in tissues (van der Oost et al., 2003). In addition, other species such as bivalves filter a large volume of water and can bioaccumulate xenobiotics in their digestive glands, making bivalves good sentinel species of environmental quality (Breitwieser et al., 2018) and therefore relevant for eco-exposome assessment. Pesticides, veterinary drugs and other contaminants that enter the food chain

through aquatic ecosystems can indirectly threaten human health (Breitwieser et al., 2018b; van der Oost et al., 2003). Contaminant residues in seafood are therefore a critical public health issue that needs to be addressed not only in the context of the advocated 'One Health' approach but also to amend the limited information available on the mixtures of contaminants to which humans are exposed. Nevertheless, few maximum residue limits (MRLs) have been set for currently employed contaminants to ensure safe seafood consumption.

Seafood contains a large quantity of lipids (up to 17%) and proteins (up to 27%) (Anses, 2020) that can affect the analysis of target contaminant compounds, especially because when the analytes are present at low concentrations. These usually result in signal suppression or enhancement, which affects the accuracy of the results obtained (Diallo et al., 2023a). Therefore, appropriate extraction and clean-up methods must be developed to limit the presence of matrix interferents during analysis. The current popular generic solid-phase extraction method is the QuEChERS (which stands for 'quick, easy, cheap, effective, rugged and safe') method, owing to its rapid protocol, reliable results and affordable cost (Barbieri et al., 2019). Acetonitrile is the most widely used organic solvent for QuEChERS extraction, because it can extract a wide range of non-polar and medium polar pesticides from several animal and plant foodstuffs (Kim et al., 2019). Some extraction methods use methanol as the extraction solvent, such as the quick polar pesticides (QuPPe) method (Jansons et al., 2021). This method, which was originally designed to extract polar and highly polar pesticide residues — i.e. non-QuEChERS-amenable — , has already been tested for the analysis of antiviral drugs (Douillet et al., 2022).
Food sample preparation for the analysis of pesticides and veterinary drugs normally involves an extraction and purification step. To achieve the best extraction performance, many parameters need to be optimised, including sample amount, extraction solvent, pH, partition salt, clean-up, and concentration/dilution of the extracts, which makes optimisation complex and time consuming. The orthogonal array design, also known as the Taguchi orthogonal array (TOA) design, is a simple and effective strategy for the simultaneous optimisation of multiple experimental conditions at multiple levels (Narenderan et al., 2019c). It can greatly simplify the experimental optimisation without reducing the quality of the results. The TOA method has been used to optimise the QuEChERS method for wide-scope multi-residue analysis of 129 and 204 pesticides in beef (Pang et al., 2021) and bivalves (Diallo et al., 2022), respectively.

Most current analytical methods for the separation and detection of pesticides and veterinary drug in seafood are based on liquid or gas chromatography coupled to triple quadrupole mass spectrometry (LC-MS/MS or GC-MS/MS, respectively) operated in multiple reaction monitoring (MRM) mode due to their selectivity and sensitivity (Barbieri et al., 2019). However, the use of these instruments has proven to have some limitations, including the limited number of target compounds that can be included in the analysis. For large-scale screening purposes, an alternative to MRM is the application of full-scan techniques based on high-resolution mass spectrometry (HRMS), using Orbitrap MS-based instruments and time-of-flight (ToF) MS systems (Rajski et al., 2021). This analytical technique can perform simultaneous (*via* data treatment) target, suspect and non-target analyses to increase the number of analytes that can be included in multi-residue approaches (Rajski et al., 2021). In addition, retrospective analyses are possible because data can be reprocessed and the digitised samples (mass spectra) can be used in future studies without having to re-inject them (Arroyo-Manzanares et al., 2021).

One of the greatest challenges of HRMS is to obtain good quality MS/MS spectra for unequivocal identification of contaminants in complex matrices. The HRMS acquisition mode that provides the best quality and easiest-to-interpret spectra is the data-dependent acquisition (DDA) mode, also called information-dependent acquisition (IDA), in Sciex instruments

(Diallo et al., 2022). However, only the most intense precursor ions selected by the user (Top*N*) are fragmented in IDA mode, which can lead to difficulties in complex matrices or low concentrations. The Top*N* must therefore be optimised to avoid or minimise the loss of pertinent MS/MS data, especially for suspect and non-targeted analyses. For targeted analyses, a precursor inclusion list (PIL) can be added. In IDA-PIL mode, the targeted precursor ions have the highest priority for fragmentation, regardless of whether these precursor ions are the most intense (Diallo et al., 2022; Makni et al., 2022).

The aim of this study was to develop a wide-scope screening approach for 850 multi-class chemical contaminants in 12 different commercial seafood products using a novel sample preparation method combining QuEChERS and QuPPe (called QuEChUP), followed by UHPLC-QTOF-MS analysis. The list of target contaminants included pesticides, veterinary drugs, their transformation products (TPs) and industrial chemicals from different families with very distinct physicochemical properties, used as a templates for suspect screening. To our knowledge, this study is the first to perform simultaneous analysis by HRMS for such a comprehensive list of contaminants in so many different seafood species. The TOA method was used to evaluate the optimal parameters for the sample extraction step. The developed method was validated in accordance with the criteria set by European Union SANTE/11312/2021 guidelines for qualitative multi-residue methods (European Commission, 2021). For each contaminant, screening detection limits (SDLs) were established. Although not required for the validation of the qualitative screening method according to SANTE guidelines, the limits of identification (LOIs) were also established. The number of false positives was assessed using non-spiked seafood samples. To test its applicability, the screening method was applied to the analysis (target screening) of real seafood samples, including mussels, oysters, sole, horse mackerel, spiny lobster and crayfish from South-West France and the French West Indies. The concentration of the identified contaminants was estimated using different semi-quantitative strategies. To test the versatility of the method on contaminants other than those included in the validation, a suspect screening approach was also performed. This study reports the first comprehensive data on the occurrence of a large number of multi-class chemical contaminants in real seafood samples.

2. Materials and methods

2.1. Chemical substances and analytical standards

A kit of 745 pesticide and industrial chemical standards, divided into five mixtures (5 $mg.L^{-1}$ of each compound in either acetonitrile (ACN) or methanol (MeOH)), was obtained from LGC Standards (Molsheim, France). The analytical standards of 180 veterinary drugs, divided into 10 mixtures (10 $mg.L^{-1}$ of each compound in either ACN or MeOH)), was obtained from the ANSES Fougères Laboratory (France). ACN, MeOH, purchased from Fisher Scientific (Illkirch, France), and ultrapure water (18.2 MΩ.cm), obtained by purifying distilled water with a Milli-Q system from Merck Millipore (Saint-Quentin-en-Yvelines, France), were used for the mobile phases and sample preparation. Formic acid (FA) was supplied by Fisher Scientific to prepare the LC-MS mobile phases and the extraction solvent. QuEChERS extraction pouches based on the original method (4.0 g of magnesium sulphate ($MgSO_4$), 1.0 g of sodium chloride (NaCl)) was provided by Agilent Technologies (Santa Clara, CA, USA). A dispersive solid-phase extraction (dSPE) kit containing 900 mg of $MgSO_4$, 150 mg of primary and secondary amines (PSA) and 150 mg of octadecylsilane (C18), Enhanced Matrix Removal-lipid (EMR-lipid) dSPE, and a dispersive kit for veterinary drugs containing 900 mg Na_2SO_4, 50 mg PSA and 150 mg C18 end-capped (C18EC), were obtained from Agilent Technologies. Ethylenediaminetetraacetic acid disodium salt dihydrate ($Na_2EDTA.H_2O$), citric acid (≥99.5% purity) and disodium phosphate (HNa_2PO_4; ≥99.0% purity) were obtained from Fisher

Scientific. $Na_2EDTA.H_2O$ (37.18 g), citric acid (12.9 g) and HNa_2PO_4 (10.9 g) were dissolved in 1 L of ultrapure water to prepare a 0.1 $mol.L^{-1}$ Na_2EDTA-McIlvaine buffer solution.

2.2. Equipment and apparatus

A Genie 2 vortex mixer (Scientific Industries, Bohemia, NY, USA) and an Eppendorf 5810 centrifuge (Eppendorf, Hamburg, Germany) were used for the extraction procedure. An IKA Ultra-Turrax T25 digital homogeniser and a GM 200 Grindomix (Retsch Technology GmbH, Haan, Germany) were also used for the extraction procedure.

An UHPLC Thermo Fisher Scientific U3000 system with a binary pump and autosampler (Waltham, MA, USA) coupled with a 5600 Q-TOF AB Sciex mass spectrometer (Darmstadt, Germany) with an electrospray ionisation source (ESI) was used for analyses.

2.3. Selection and use of the contaminants

Of the initial 920 contaminants, 850 could be analysed in solvent at 0.2 $mg.L^{-1}$ and were therefore selected for this study (Table S1); of these 364 (204 pesticides and 160 veterinary drugs) were used for (i) optimisation of sample preparation and (ii) optimisation of the IDA mode. These substances are representative of the rest of the contaminants in terms of retention time (t_R), mass-to-charge ratio (*m/z*) and range of polarity (LogP) (Table S1). The optimised method was then validated on 850 contaminants to demonstrate its relevance and applicability on a wide scope of multi-class contaminants. The contaminants used for method validation included pesticides, veterinary drugs and industrial chemicals, as well as their TPs (Table S1).

2.4. Selection and use of seafood samples

Twelve of the most widely consumed seafood species in France, namely oysters, mussels, scallops (*Pecten maximus* and *Mimachlamys varia*), clams, cod, salmon, sole, anchovies and tuna, as well as spiny lobster and crayfish, used to optimise and validate the method (including to asses false positives), were purchased from local markets in March and April 2022 (Maisons-Alfort, France). These 12 seafood samples were pooled and used to optimise sample preparation. To validate the method, two groups were randomly formed for each of the 12 seafood species, for a total of 24 seafood samples. To test the applicability of the screening method using target and suspect screening, two species of bivalves (mussels (n = 6) and oysters (n = 6)) and two species of fish (sole (n = 3) and horse mackerel (n = 3)) were collected in the Pertuis-Charentais area (South-West France), and two species of crustaceans (lobster (n = 3) and crayfish (n = 3)) were collected in Martinique (French West Indies). Before shucking (bivalves) or dissection (fish), the seafood samples were stored at 4°C overnight and then brought to room temperature. The samples were homogenised and kept at -20°C until analysis.

2.5. Development of a homemade LC-MS/MS compound database and MS/MS library

A homemade MS/MS library of 850 contaminants was built using AB Sciex LibraryView™ software, version 1.0.3 (Les Ulis, France). The library was acquired in IDA mode by injecting mixtures of compound analytical standards, diluted to 0.1 $mg.L^{-1}$ in ACN. The injections of the standards were performed in both ESI^+ and ESI^- mode. The information on molecular formulae, retention time (T_R), accurate m/z of the precursor ion, isotopic pattern and the MS/MS fragmentation spectrum of each of the studied contaminants were recorded and taken as reference for the automated detection and identification process in matrix samples. In total, 744 and 247 spectra in ESI^+ and ESI^-, respectively, were recorded. Data were processed and evaluated using PeakView® software version 2.2 comprising the AB Sciex MasterView™ module. The MasterView™ module is inter-connected to LibraryView™ software and

compares the experimental fragmentation spectra to those recorded in the homemade database. The term 'detection' was employed when a contaminant did not exceed the following thresholds: (i) T_R variation ± 0.1 min and (ii) mass accuracy ± 5 ppm on the precursor ion (European Commission, 2021). The term 'identification' was based on the same thresholds as detection, and also satisfied an MS/MS library score of spectral similarity of >70% between the experimental and reference MS/MS fragmentation spectra using the Fit MS/MS search algorithm (Makni et al., 2022). The Fit algorithm represents the degree of similarity of the peaks and intensities of the reference spectrum with those of the experimental spectrum, ignoring the other interfering peaks in the experimental spectrum.

2.6. Orthogonal array design for optimisation of sample preparation

The factors affecting the detection rates (%) were simultaneously optimised by adopting an analysis of mean (ANOM) approach, using the Taguchi method. Three factors (extraction solvent, dSPE and dilution ratio) were considered for extraction and clean-up optimisation. Three levels were defined for each factor, as described in Table 1.

In the conventional full-factorial method of optimisation, the total number of experiments for three parameters with three levels is 27. If each experiment is replicated three times, the total number of experiments would be equal to 81 (i.e. 3 × 27). Taguchi method of optimisation significantly reduces the number of experiments using orthogonal arrays. Using an L9 orthogonal array, with each experiment replicated three times, the total number of experiments reduces to 27 (i.e., 9 × 3). The L9 orthogonal array (Table S2) was used to design the experiments. The response assessed was the detection rate (%) of the contaminants.

Table 1. Control factors and levels in the sample preparation process.

Level	Factor		
	Extraction solvent	**dSPE sorbent**	**Dilution**
1	ACN	$MgSO_4$/PSA/C18	Not diluted
2	MeOH/ACN (7:3)	EMR-lipid	1:2
3	MeOH (1% FA)	PSA/Na_2SO_4/C18EC	1:4

ACN, acetonitrile; MeOH, methanol; EMR, Enhanced Matrix Removal; PSA, primary and secondary amines

2.7. Optimisation of sample preparation

Extraction solvent, dSPE and dilution ratio were simultaneously optimised using L9 TOA. To obtain a pesticide supplementation at a concentration of 0.01 $mg.kg^{-1}$, 7.5 µL of the mix containing 364 contaminants were added to 50-mL polypropylene centrifuge tubes, which contained 1.50 ± 0.05 g of pooled seafood sample. The tubes were stored at 4°C for 24 h to allow the contaminants to bind to the matrix. Then, 8.5 mL of the aqueous phase (Na_2EDTA-McIlvaine buffer (0.1 $mol.L^{-1}$)) was added to each tube, and the sample was then ground using an IKA Ultra-Turrax mixer for 3 min at 5000 rpm. Then, 10 mL of organic solvent was added to each centrifuge tube and vortexed again for 1 min. After that, a mixture of 4.0 g of $MgSO_4$ and 1.0 g of NaCl were added to the fortified samples, and the resulting mixture was centrifuged for 5 min at 4000 rpm.

For the purification step, there were two cases. When EMR-lipid was used as the dSPE reagent, the sorbent was activated by adding 5 mL of water to a 15 mL centrifuge tube containing the EMR-lipid and vortexed for 3 s. Then, 5 mL of the extract supernatant (50 mL polypropylene centrifuge tube) was transferred to the activated 15 mL centrifuge tube. The mixture was immediately vortexed for 1 min. The tube was centrifuged at 4000 rpm for 5 min, and 5 mL of the supernatant was transferred to the polishing tube containing $MgSO_4$ to remove excess water. When using the other dSPE reagents, 6 mL of the supernatant was transferred to a 15-mL centrifuge tube containing the dSPE reagent. The tube was vortexed for 1 min, and then centrifuged for 5 min at 4000 rpm. The supernatant was then combined with ACN according to the dilution ratio. The mixture was then vortexed, filtered and deposited into a 2-mL autosampler vial for injection in the UHPLC-QTOF system.

To check for cross-contamination, matrix-free ACN was subjected to the same extraction and purification protocols as previously described.

2.8. UHPLC-Q-TOF-MS conditions

Reversed-phase liquid chromatography separation was performed using a Phenomenex Aqua® C18 column (150 × 2 mm, 3 µm particle size, 125 Å pore diameter; Phenomenex Inc, Torrance, CA, USA). The UHPLC-Q-TOF-MS conditions were the same as in previous work by Diallo et al. (2022), Makni et al. (2022) and are summarised in Table S3. The instrument was tuned and calibrated manually before each batch, in high-sensibility mode using the APCI positive or negative calibration solutions for the 5600 system (AB Sciex technology). The automated calibration device system (CDS) was scheduled to perform automatic calibration every five injections to avoid as much as possible a mass deviation over 5-ppm during the run analysis.

Data acquisition was performed using a combination of full scan TOF-MS and IDA mode. The mass range of full-scan TOF-MS acquisition was 50–1000 Da, the collision energy (CE) was 10 eV (-10 eV in ESI^-) and the accumulation time was set to 490 ms. In IDA mode, the declustering potential (DP) was 80 eV (-80 eV in ESI^-) and the collision energy (CE) was 40 eV with ±20 eV (-40 eV in ESI^- with ±20 eV). The 10 highest intensity precursors (i.e. ion intensity greater than 50 cps and ion tolerance ≤ 10 ppm) (Top10) were monitored in every cycle, and dynamic background subtraction was turned on. Data acquisition with the UHPLC-Q-TOF system was performed using Analyst® software (version 1.7) of AB Sciex.

2.9. Method validation

The screening method was validated according to EU SANTE/11312/2021 guidelines (European Commission, 2021). For this purpose, 24 commercial seafood samples were used (see section 2.4). Samples (1.5 g) were spiked before extraction with a mixture containing 850 contaminants at 0.001, 0.01, and 0.1 $mg.kg^{-1}$ (in a total of 24 samples for each concentration level). The SDL was established as the lowest concentration level at which a contaminant was detected in at least 95% of the samples (i.e., 23 out of 24 samples analysed) (European Commission, 2021). SDL was estimated as the concentration level at which the thresholds of (i) T_R (variation ±0.1 min) and (ii) mass accuracy (±5 ppm) of the precursor ion were satisfied (European Commission, 2021). The LOI (not required according to SANTE guidelines) was established as the lowest concentration tested for which a contaminant was satisfactorily identified in at least 95% of the samples. LOI used the same thresholds as for SDL, and also satisfied an MS/MS library score (Fit > 70%). Non-spiked samples were also extracted and analysed to assess the number of false positives out of the 850-targeted contaminants.

2.10. Data processing for real sample analysis

2.10.1. Target screening

For target analyses, data processing was performed using PeakView® software version 2.2 comprising the AB Sciex MasterView™ module. The contaminants were detected and identified using the previously developed homemade database for automated screening of samples against a target list of 850 contaminants. The criteria for detection and identification are the same as those described in Section 2.5.

The concentration of positively identified contaminants was estimated using a semi-quantitative approach. Calibration curves were constructed only for positively identified contaminants. To construct the calibration curve, the areas obtained for each contaminant in the 24 validation samples (spiked at 0.001, 0.01 and 0.1 $mg.kg^{-1}$) were used. For normalisation purposes, the areas obtained in the matrices for each contaminant were divided by the area of the same contaminant in solvent (injected in each batch) at 0.1 $mg.L^{-1}$ to obtain area ratios. Three calibration curves, constructed on general, broad and specific taxon groups, were established for each positive contaminant as follows.

Calibration strategy A: average area ratios for each contaminant were calculated using the values for all 24 samples. These average area ratios (n = 24) were used to establish the final calibration curve for each contaminant to estimate their concentration in the real seafood samples.

Calibration strategy B: average area ratios for each contaminant were calculated for each broad taxon group (bivalves, fish and crustaceans). These average area ratios for each species (n = 10, n = 10 and n = 4 for bivalves, fish and crustaceans, respectively) were used to establish the final calibration curve for each contaminant to estimate their concentration in the real seafood samples.

Calibration strategy C: average area ratios for each contaminant were calculated for each specific matrix (oysters, mussels, sole, spiny lobster and crayfish). These average area ratios for each matrix (n = 2 for all matrices) were used to establish the final calibration curve for each contaminant to estimate their concentration in the real seafood samples. When the matrix type of the real samples was not present in the validation samples, a calibration curve resulting from a similar matrix in terms of lipid and protein content was used. This was the case for horse mackerel; the most similar matrix in the validation samples was sole.

Only contaminants with a satisfactory linearity ($r^2 > 0.995$) were selected for semi-quantitation.

2.10.2. Suspect screening

For the suspect screening analyses, data processing was performed using the open-source software MSDial (version 4.7), which allows for large-scale screening and annotation of compounds of interest against external MS/MS libraries, and for which the analytical standards are not available. In this work, MSDial software was linked to the MS/MS spectra contained in the Mass Bank of North America (MoNA). In total, 98,000 and 46,000 LC-MS/MS spectra in positive and negative mode, respectively, were used in this approach.

The suspect screening of potential contaminants was performed using the following criteria: (i) mass accuracy ± 5-ppm of precursor ion, (ii) spectral similarity >70% between the experimental and external reference MS/MS fragmentation spectra. The spectral comparison was performed using the reverse DOT algorithm, which works on the same principle as the FIT algorithm in MasterView™ software. All the contaminants reported that fulfilled these criteria were considered as putatively identified (confidence level 2a) according to Schymanski et al. (2014).

3. Results and discussion

3.1. Optimisation of the sample extraction and purification steps

Although presenting a simple experimental layout, the efficiency of the QuEChERS/QuPPe method depends on certain factors and, in general, the performance of the extraction method can be improved. These factors include sample amount, extraction solvent, pH, partition salt, clean-up and concentration/dilution of the extracts. Thus, selection of the experimental conditions is a crucial step and must be considered. A TOA approach was applied to find the best conditions for detection rates (%) for pesticides and veterinary drugs. Three parameters were optimised: extraction solvent, dSPE and the dilution of the extracts.

The values of the mean detection rates for all contaminants ranged from 49% to 83% (Tables S4, S5) for all experiments. Overall, the best performances were found with Experiment 1 and 6 for pesticides and veterinary drugs, respectively. According to the R values, the factor with the greatest impact on pesticide detection was dilution (R = 23), followed by extraction solvent (R = 14) and finally the dSPE (R = 3). For veterinary drug detection, the most influential factor was solvent extraction (R = 18), then dilution (R = 17), and finally dSPE (R = 8). The effects of the three studied factors on the pesticide and veterinary drug detection rates are also shown in Fig. 1. The detection rates are represented in bar charts; therefore, the greater the difference between the best and worst performing levels, the more significant the factor is. All factors were significant ($p < 0.05$) for the veterinary drug detection rates, and solvent extraction and dilution were significant for the pesticide detection rates (Tables S4, S5).

3.1.1. Extraction solvent

Three extraction solvents, namely, 10 mL of ACN, 10 mL of MeOH with 1% FA and 10 mL of ACN/MeOH (7:3, v/v), were assessed. ACN is the most used solvent in the QuEChERS method for the extraction of medium polar pesticides. MeOH with 1% FA is frequently used for the extraction of polar contaminants in the QuPPe method (Anastassiades et al., 2015). ACN/MeOH was also assessed based on previous studies that analysed pharmaceuticals in fishery products (Kim et al., 2017). As shown in Fig. 1, ACN was provided the best detection rate for pesticides, followed closely by ACN/MeOH and MeOH with 1% FA. For veterinary drugs (generally more polar than pesticides), the best detection rates were obtained with ACN/MeOH as the solvent, followed by ACN and MeOH with 1% FA. This result shows that pure ACN is most effective for the extraction of targeted pesticides. ACN/MeOH was not only suitable for the extraction of veterinary drugs, but also successfully extracted pesticides, making it a more versatile extraction solvent. This may be due to the fact that the resulting polarity of this mixture is a suitable compromise between that of targeted pesticides and veterinary drugs.

3.1.2. dSPE

As illustrated in Fig. 1, the best pesticide detection rates were obtained with a mixture of $MgSO_4$/PSA/C18 as dSPE reagent, closely followed by EMR-lipid. $MgSO_4$ is commonly used as a drying salt for ACN extraction because it effectively removes residual water. PSA has been shown to remove many polar organic acids from the extract, as well as polar pigments, sugars and fatty acids, whereas C18 can retain fats, vitamins and minerals (Kim et al., 2019). For veterinary drugs, the best detection rates were obtained with EMR-lipid, followed by a mixture of PSA/Na_2SO_4/C18EC. EMR-lipid, whose structure is a proprietary secret, removes lipids from sample matrices (Pang et al., 2021). This sorbent allows a highly selective and efficient interaction with lipids, providing excellent extraction efficiency, precision and matrix effect

(Castilla-Fernández et al., 2021). Na_2SO_4 is also a drying agent, similar to $MgSO_4$. This salt performed better for veterinary drugs than $MgSO_4$, because the Mg^{2+} ions can also form complexes with some veterinary drugs, which reduces detection rates (Gros et al., 2019). Another difference is that Na_2SO_4 is a weak drying agent compared with $MgSO_4$, and when added to the organic extraction solvent, the amount of water is higher than when $MgSO_4$ is used, favouring the extraction of polar compounds, such as veterinary drugs (Munaretto et al., 2016b). The C18EC products are based on reversed phase, bonded and end-capped octadecylsilane silica gel particles. The non-polar sorbent is end-capped (EC), which reduces polar secondary interactions associated with surface silanol groups (Sobczak et al., 2021).

3.1.3. Dilution

As observed in Fig. 1, non-dilution led to the best detection rates for both pesticides and veterinary drugs. Dilution combined with extraction and purification steps can decrease matrix effects, as shown in apple, tea and broccoli samples during analysis (Guo et al., 2019b). However, sample dilution reduces the overall sensitivity of the method; thus, a compromise is needed to reduce matrix effects and nonetheless maintain high method sensitivity. In addition to the dilution of extracts, the concentration of final extracts can be important for the sensitivity of the target compounds and on matrix effects. To have a simple, reliable and time-effective method for application to a large number of seafood samples, the concentration of the sample was not considered in this study.

The conclusion based on the R values associated with the K1, K2, and K3 values and the main effects plot for detection is that the optimal extraction conditions for pesticides were obtained with pure ACN, $MgSO_4$/PSA/C18 for dSPE, and the non-dilution of extracts, which corresponds to a classical QuEChERS method, and consistent with previous results (Diallo et al., 2022b). For the detection of veterinary drugs, the optimal extraction conditions were obtained with ACN/MeOH, EMR-lipid as the dSPE sorbent and the non-dilution of extracts, which corresponds to a modified QuPPe method.

3.2. Comparison of optimal conditions for the detection of pesticides and veterinary drugs

In this study, the objective was to optimise a sample preparation method for the simultaneous analysis of pesticides and veterinary drugs, as well as other organic contaminants. To do so, the optimal detection conditions for pesticides (QuEChERS) and veterinary drugs (QuPPe) were compared for all 364 combined contaminants studied for method optimisation. The mixture of the final QuEChERS and QuPPe extracts (QuEChERS + QuPPe in Fig. 2) was also evaluated as well as the sequential method of QuEChERS and QuPPe (QuEChUP). This sequential method consists of a QuEChERS extraction followed by a QuPPe extraction of the same sample and subsequent purification. The protocol for these four methods (QuEChERS, QuPPe, QuEChERS + QuPPe and QuEChUP) is summarised in Fig. 2.

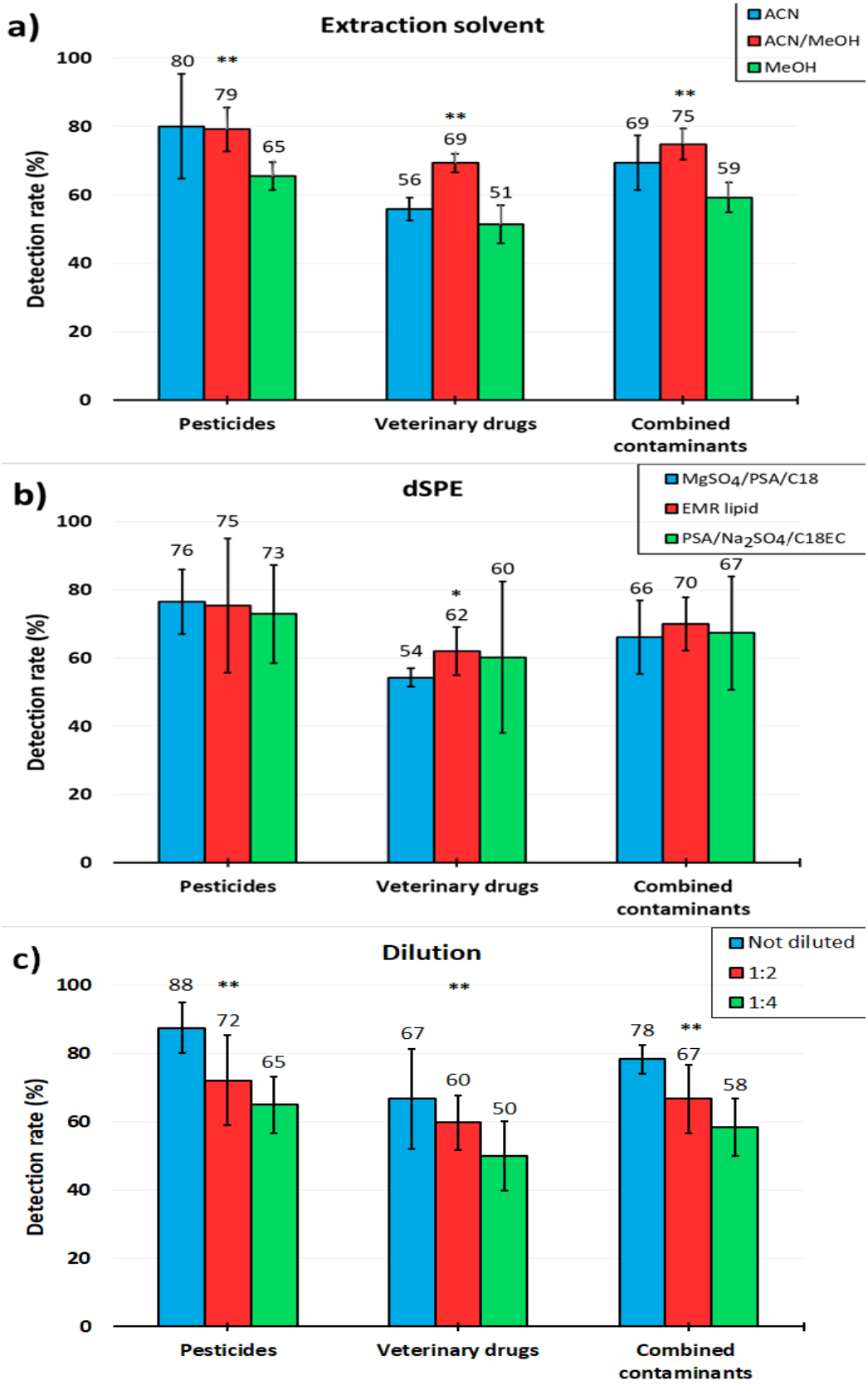

Fig.1. Effects of extraction solvent (a), dispersive solid phase extraction (dSPE) sorbent (b) and dilution (c) on the detection rates of pesticides and veterinary drugs, with the significance of the ANOVA test *p*-value < 0.05 (*) and *p*-value < 0.01 (**). The error bars correspond to the standard deviation (SD) for the response measured (Mean ± SD, n = 3).

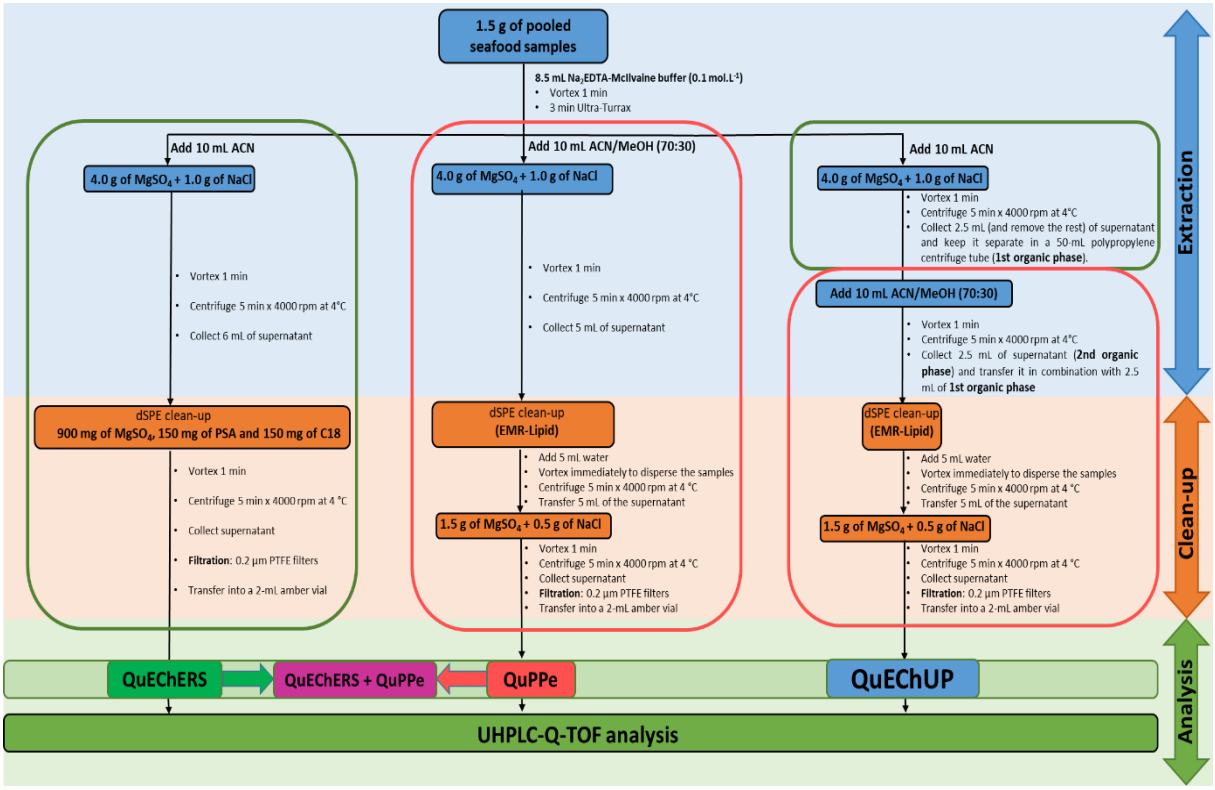

Fig.2. Protocol of the four different sample preparation methods (QuEChERS, QuPPe, QuEChERS + QuPPe and QuEChUP, see text for method definitions) for the simultaneous analysis of 364 organic contaminants.

As observed in Fig. 3, the QuEChERS method was more specific to pesticides, allowing a very high detection rate (97%) for pesticides, but low (54%) for veterinary drugs. The QuPPe method was more versatile, with a high detection rate for pesticides (84%) and veterinary drugs (86%). The best detection rates (90–91%) were obtained with the mixture of final extracts (QuEChERS + QuPPe) and the sequential method (QuEChUP) for all 364 contaminants combined. In addition, both methods can cover a wide range of polarity (LogP from -4.2 to 7.2), as illustrated in Fig. S1. Indeed, these two methods combine the advantages of QuEChERS and QuPPe for the extraction of pesticides (generally medium-polar) and veterinary drugs (generally polar), respectively. The QuEChUP method was ultimately preferred to the QuEChERS + QuPPe method, because it is faster and allows the simultaneous analysis of a wide range of contaminants in small seafood samples (e.g. mussels) individually, which could be very useful in the case of a metabolomic approach, for example. For these reasons, the QuEChUP method followed by EMR lipid clean-up was chosen for the subsequent analyses (Fig. 2).

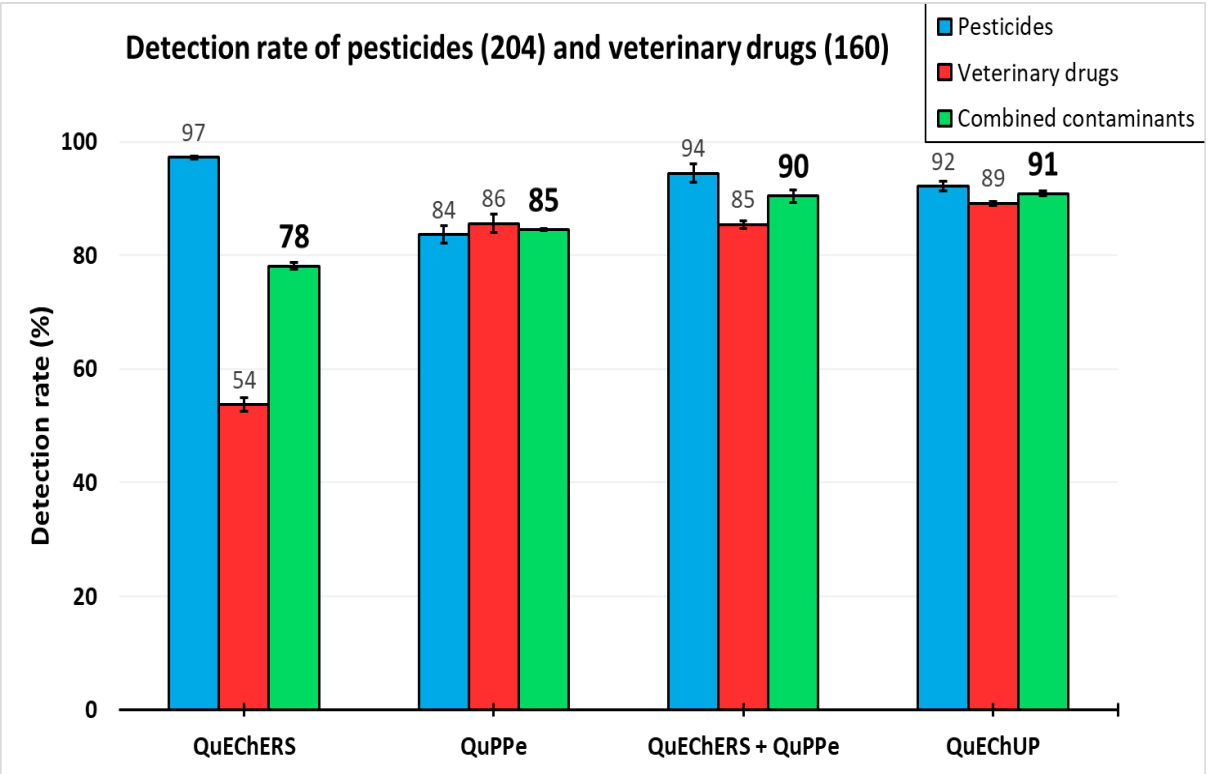

Fig.3. Comparison of the QuEChERS, QuPPe, QuEChERS + QuPPe and QuEChUP sample preparation methods for detection of pesticides and veterinary drugs. The error bars correspond to the standard deviation (SD) (Mean ± SD, n = 3).

3.3. Validation of the screening method

Twelve different seafood matrices were tested in the validation of the method: oysters, mussels, scallops (*P. maximus* and *M. varia*), clams, cod, salmon, sole, anchovies, tuna, spiny lobster and crayfish. Two groups of each type were spiked with the mixture of 850 contaminants at three concentration levels (0.001, 0.01 and 0.1 $mg.kg^{-1}$) and analysed with their respective non-spiked samples for qualitative validation.

3.3.1. Selectivity of the screening method

In SANTE guidelines, no criteria have been set with respect to the occurrence of false positives. However, the selectivity of the method must reduce the false positive rate to a sufficiently low level to avoid manual verification or confirmatory analysis that may reduce the effectiveness of the screening method. The number of false positives was checked by analysing 24 non-spiked seafood samples. According to the results, a total of 42 ± 7 (standard deviation, SD) false positives (5% of the 850 target contaminants) were obtained across all non-spiked samples, applying the detection criteria, i.e. tolerances of ±5 ppm and ±0.1 min for mass accuracy and T_R, respectively. To reduce this false positive rate and to obtain a more reliable detection of contaminants, an additional criterion on the signal-to-noise (SN) ratio was added for detection. When the S/N threshold was set to S/N>10 instead of S/N>3 (as was originally the case), the number of false positives dropped drastically to 17 ± 4 contaminants, representing only 2% of the 850 targeted contaminants. The addition of this extra criterion had no impact on the detection rates of contaminants, which remained unchanged. Finally, when the identification criterion was considered by adding the MS/MS library score (Fit > 70%), the number of false positives dropped to 2 ± 1 contaminants (0.24% of the 850 targeted contaminants). These false

positives were due to misattributions during automatic MS/MS matching. False positive contaminants for 1,2-benzisothiazol-3(2H)-one (C7H5NOS) and pipenonyl butoxide ($C_{19}H_{30}O_5$) were each detected in five non-spiked seafood samples, whereas false positives for (E)-metominostrobin ($C_{16}H_{16}N_2O_3$) were observed in nine samples. The other false positives were only detected once each in the different samples. These results demonstrated the good selectivity of the method both in terms of detection (with S/N > 10) and identification.

3.3.2. Determination of SDL and LOI

The validation of the qualitative screening methodology included the determination of SDLs (European Commission, 2021). Although it is not required to satisfy SANTE guidelines, the LOI was also established. A summary of the SDLs and LOIs assessed in the 24 seafood samples is presented in Fig. 4 (see also Table S6 for individual values obtained for each contaminant). The SDLs were determined to be equal to or less than 0.001, 0.01 and 0.1 $mg.kg^{-1}$ for 86, 92 and 94% of pesticides, respectively (Fig. 4a). The SDL criteria were therefore not reached for 6% of contaminants. However, the proposed method was able to detect them in most of the samples at all three concentration levels. As can be seen in Fig. 4b, about 96–97% of the contaminants could be detected at 0.01 $mg.kg^{-1}$ and 0.1 $mg.kg^{-1}$, but the detection rate decreased to 91–95% at 0.001 $mg.kg^{-1}$. No significant differences were observed between the matrices studied. Ten contaminants (alpha-cypermethrin, benfluralin, bentazon-methyl, butocarboxim, chlorthiamide, diafenthiuron, dioxathion, fluorodifen, omethoate and tridiphane) were not detected in any of the spiked samples. These compounds may not be stable under the extraction conditions assayed or may be highly sensitive to matrix effects.

The LOI was determined to be equal to or less than 0.001, 0.01 and 0.1 $mg.kg^{-1}$ for 67, 78 and 85% of pesticides, respectively (Fig. 4c). Thus, 16% of the contaminants could not be validated for identification because the criteria of LOI were not met. For 82 contaminants (representing 10% of the selected contaminants), it was possible to establish the SDL at least at one of the three concentration levels, but not the LOI. For these compounds, validation was limited to detection (only the SDL could be set). Overall, the reliable identification was likely for 89% of contaminants at 0.1 $mg.kg^{-1}$ (Fig. 4d). This value decreased to 87% and 80% at 0.01 and 0.001 $mg.kg^{-1}$, respectively.

To check the applicability of the screening method, the resulting SDLs must be compared with the MRLs in food, established by the European Commission to ensure consumer safety. The MRL is the highest level of a contaminant or residue that is legally tolerated in food and can therefore be used. To date, no MRLs have been established for the targeted residues in seafood matrices. A general default MRL of 0.01 $mg.kg^{-1}$ applies where a contaminant is not specifically mentioned. Thus, the SDL and LOI obtained, in most cases less than or equal to 0.01 $mg.kg^{-1}$, can be considered satisfactory and the proposed methodology adequately sensitive for suspect and non-targeted screening purposes. As shown in Table S7, as with the previous studies (Bai et al., 2022; Diallo et al., 2022; Munaretto et al., 2016), the present study also provided a thorough and complete validation of the qualitative method. The percentage of contaminants with SDLs equal to 0.01 $mg.kg^{-1}$ was higher than or equal to those of the previously reported methods in qualitative analysis (Bai et al., 2022; Diallo et al., 2022; Munaretto et al., 2016). Furthermore, none of these previous studies tested concentrations below 0.01 $mg.kg^{-1}$, but in the present study the lowest concentration level tested was 0.001 $mg.kg^{-1}$. It should be noted that most studies on multi-residue analysis of organic contaminants in seafood have been carried out using a quantitative method. In this case, SDLs have not been established and other criteria are used to assess the sensitivity of the method such as limits of quantification (LOQ). The percentage of contaminants with LOQs < 0.01 $mg.kg^{-1}$ in previous studies (Barbieri et al., 2019; Castilla-Fernández et al., 2021; Park et al., 2022) is also comparable to that of the SDLs

< 0.01 mg.kg^{-1} in this present study, signifying the good sensitivity of the sequential QuEChUP method followed by EMR lipid clean-up.

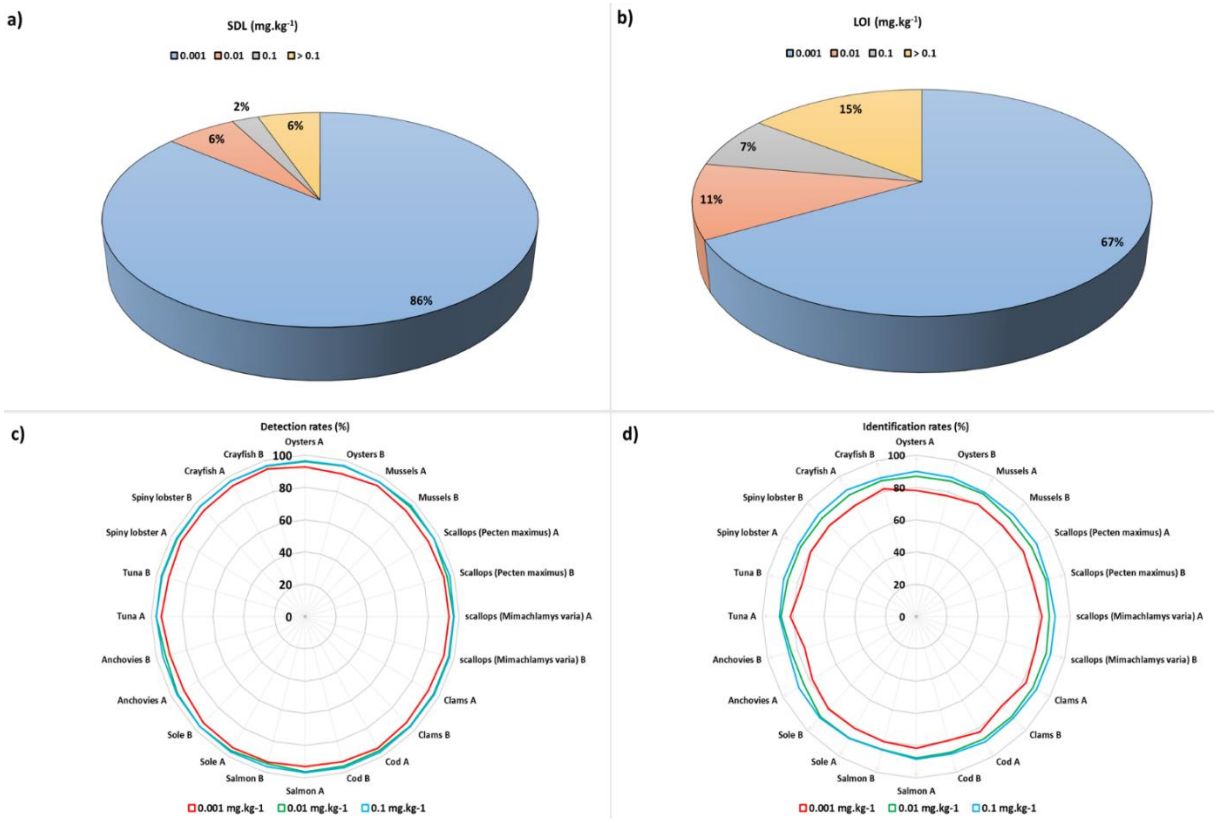

Fig.4. Percentage of pesticides presenting screening detection limits (SDLs) (a) and limits of identification (LOIs) (b) at 0.001, 0.01, 0.1 and > 0.1 mg.kg^{-1} under optimised conditions. Detection (c) and identification rates (d) across different seafood samples spiked at 0.001, 0.01 and 0.1 mg.kg^{-1}.

3.4. Target screening in real seafood samples

To evaluate the applicability of the QuEChUP method, it was employed in the analysis of the target contaminants in bivalves (mussels and oysters), fish (sole and horse mackerel) collected in the Pertuis-Charentais area (South-West France), and crustaceans (spiny lobster and crayfish) collected in Martinique (French West Indies).

Contaminants were identified using the criteria applied in this study (see sections 2.5 and 2.10.1). Fig. 5 showed an unequivocal identification of diuron and diclofenac in a mussel sample.

All samples analysed were positive for different mixtures of contaminants. The HRMS acting as a diagnostic system provides comprehensive and large-scale data on the occurrence of these mixtures. However, in an eco-exposure context, the concentration level of these contaminants must be at least estimated to ensure that the levels do not exceed the regulatory levels (e.g. provisional no-effect concentrations (PNECs) (Nikolopoulou et al., 2023). Semi-quantitation remains a relevant approach if the objective is to estimate the order of magnitude of the concentration level in a sample. However, to confirm the concentration levels, the subsequent use of a validated quantitative approach is necessary. Here, semi-quantitative approaches were used to estimate concentrations. To do so, three calibration curves were constructed. The aim

was to evaluate a more general method (Calibration strategy A) for all seafood products as well as a more specific method (Calibration strategy C) for a given matrix (e.g. estimating the concentration of a contaminant in oysters with a calibration curve on an oyster matrix). As observed, the concentration values were similar for most contaminants in the same sample, regardless of the calibration strategy used, suggesting that matrix effects are equivalent (Table S8). However, in contrast, diclofenac and vedaprofen increased from 0.057 to 0.068 mg.kg^{-1} in mussels and from 0.030 to 0.046 mg.kg^{-1} in crayfish respectively, depending on the calibration strategy used.

As depicted in Fig. S2, the most frequent contaminants were pesticides and their TPs (59%), followed by veterinary drugs and their TPs (26%) and industrial chemicals (15%). The list of

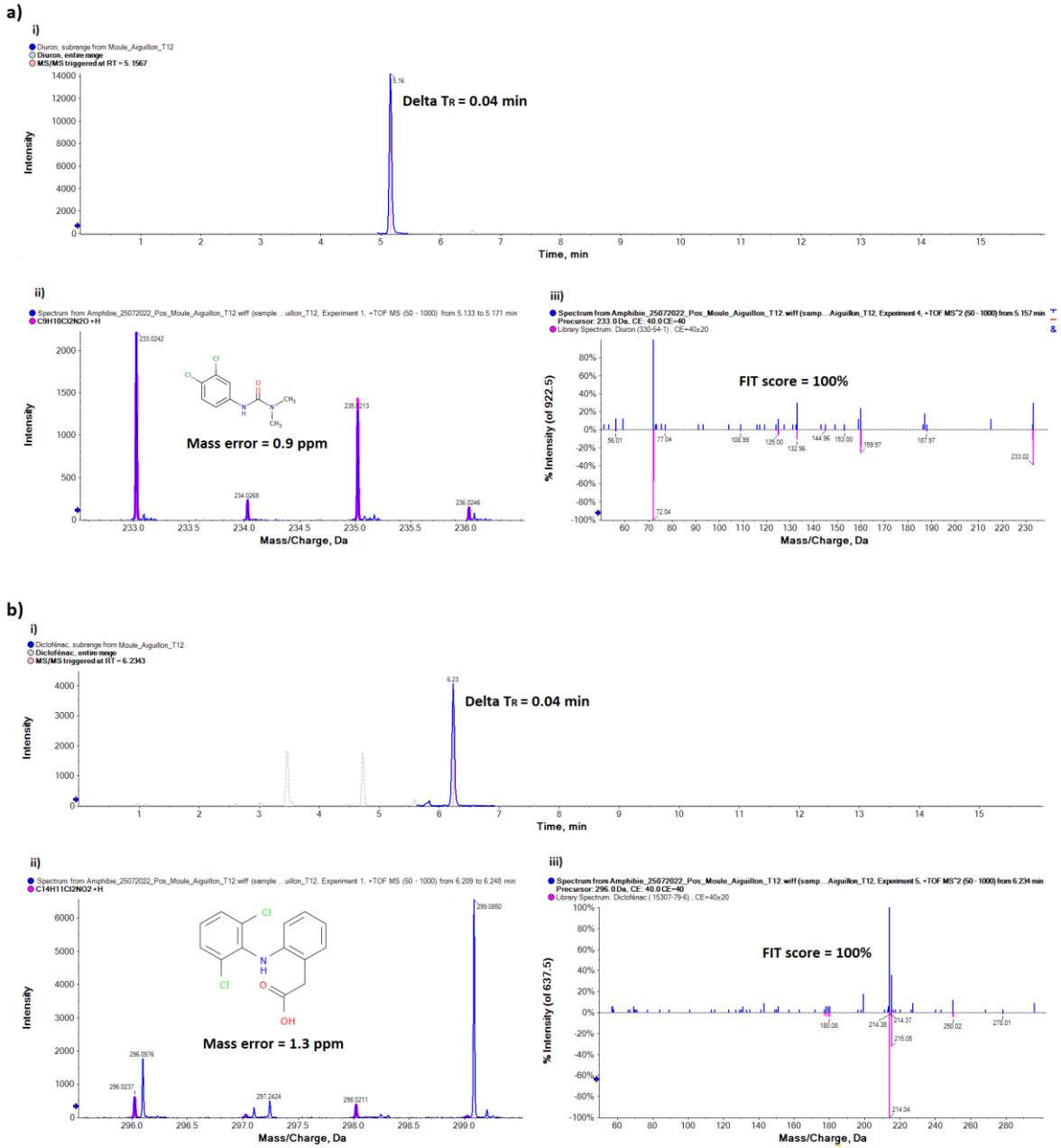

Fig.5. Positive finding of diuron (a) and diclofenac (b) in a mussel sample, with corresponding extracted ion chromatogram (i); isotopic pattern (ii); experimental and reference MS/MS spectra comparison using the Fit algorithm (iii).

identified contaminants as well as their frequencies of appearance (FoA) and estimated mean concentration in target screening can be found in Table S8 and are discussed briefly in the following sections.

3.4.1. Pesticides and their transformation products (TPs)

For all the seafood samples, the most identified pesticides were herbicides and fungicides, most of them in the bivalve samples. The pesticides identified with 100% FoA in all seafood samples were *N*,*N*-diethyl-*m*-toluamide (DEET) and diphenylamine, with an estimated average concentration of 0.016 and 0.007 $mg.kg^{-1}$, respectively. Diuron and its TP 1-(3,4-dichlorophenyl)-3-methyl urea) were identified with a 63% FoA, with an estimated maximum concentration of 0.078 to 0.086 $mg.kg^{-1}$ for diuron in mussels. Butroxydim, diazinon, diflufenicen, prosulfocarb and spiroxamine were identified in oysters and mussels (50% FoA), with an estimated average concentration ranging from below the SDL for diazinon to 0.016 $mg.kg^{-1}$ for butroxidim. The pesticides with the lowest FoA (13%) were azimsulfuron, bupirimate, pyroxsulam, tebuconazole and thiabendiazole, which were only identified in crustacean samples (spiny lobsters or crayfish) with an estimated maximum concentration of 0.009 $mg.kg^{-1}$ for azimsulfuron in crayfish. These pesticides found in this study have also been identified in previous reports (Diallo et al., 2022; Slaby et al., 2022).

3.4.2. Veterinary drugs

Generally, the categories of the seven identified veterinary drugs were antibiotics, NSAIDs and antihistamines. Of these, none had a FoA of 100%. Clarithromycin, dapsone and diclofenac were identified in oysters and mussels (50% FoA), with an estimated maximum concentration of 0.057 to 0.068 $mg.kg^{-1}$ for diclofenac in mussels. Vedaprofen was identified in crustacean and fish samples (50% FoA), with an estimated average concentration between 0.027 and 0.046 $mg.kg^{-1}$ in these samples. The veterinary drug with the lowest FoA (13%) was 4-dimethylaminoantipyrine, which was only identified in spiny lobster. These veterinary drugs have previously been detected in seafood and environmental samples (Daniele et al., 2016; Ramírez-Morales et al., 2021.

3.4.3. Industrial chemicals

Two industrial chemicals were identified with a FoA of 100%. This is the case for tris(2-chloroethyl) phosphate (TRCP) and tri-*o*-cresyl phosphate (TCP). Two other industrial chemicals triphenyl phosphorothioate (TPPT) and 2-ethylhexyl diphenyl phosphate (EHDPP) were identified with FoAs of 75 and 63%, respectively. Most of these compounds are commonly detected in seafood and environmental samples (Diallo et al., 2022; Nikolopoulou et al., 2023; Peng et al., 2018).

3.5. Suspect screening analysis in real seafood samples

The method was also tested for the analysis of other organic contaminants such as pharmaceutical and personal care products (PCPs) to demonstrate its versatility by performing suspect screening on the same seafood samples used for target screening. The suspect screening of potential contaminants was performed using the criteria described in the section 2.10.2. All reported contaminants that met these criteria were considered as putatively identified (confidence level 2a) according to Schymanski et al. (2014). The identification list contains various classes of emerging contaminants, especially pharmaceuticals (Table S9). For all the seafood samples, a total of 20 pharmaceuticals were identified, most of them in the bivalve samples. Generally, the categories identified were antiarrhythmic, anaesthetics, hormones, antibiotics, antihistamines and NSAIDs. Most of the pharmaceuticals identified in this study

have previously been reported in previous work, such as ibuprofen (50% FoA), norethindrone (50% FoA), propafenone (50% FoA), progesterone (25% FoA), fexofenadine (25% FoA) and methylprednisolone (13% FoA) (Dodder et al., 2014; Omar et al., 2019; Ramírez-Morales et al., 2021). Tetrahydrocannabinol (THC), an illicit drug, was also identified in oyster and mussel samples (50% FoA). It has previously been found in fish from Argentina (Carrizo et al., 2022). Two pesticide TPs (flufenacet-ethane sulfonic acid (ESA) and metamitron-desamino) were identified only in mussel samples (25% FoA). Flufenacet ESA has been reported in fish collected from north-eastern France (Slaby et al., 2022). Metamitron-desamino has been identified in Greece (Nika et al., 2020). A total of six PCPs (galaxolidone, dihydromuronic acid, 4-hydroxybenzoic acid, laurocapram, phenylacetaldehyde and Velvione®) were identified in all the seafood samples. Most of these PCPs have already been reported in seafood or environment samples in the literature (Gadelha et al., 2019; Nikolopoulou et al., 2023). Four industrial chemicals (bisphenol S, triethylene glycol bis(2-ethylhexanoate) (TEG-EH), tri-isobutylphosphate (TiBP) and tris(1-chloro-2-propyl) phosphate (TCPP)) were also identified in the seafood samples, as previously observed (Nikolopoulou et al., 2023; Peng et al., 2018).

The contaminants mentioned in the target and suspect screening were mainly identified in positive ionisation mode (ESI^+). However, several other contaminants were identified in negative ionisation mode (ESI^-) in seafood samples. This is the case for allopurinol (antigout agent) and its TP oxypurinol, dinoterb (herbicide), gemfibrozil (fibrate), prostaglandin E1 (vasodilator), salicylic acid (NSAID). Chlordecone (organochloride insecticide) and its metabolite chlordecole were identified in crayfish and spiny lobster from the French West Indies. A perfluorooctane sulfonic acid (PFOS) precursor, N-ethylperfluorooctane sulfonamidoacetic acid (N-EtFOSAA), was also identified. This shows the importance of using both ionisation modes for wide-scope screening of multi-class contaminants.

4. Conclusion

The development and validation of an original QuEChUP-LC-HRMS method to screen 850 organic contaminants in seafood were carried out according to European Union SANTE/11312/2021 guidelines. The list of target compounds included pesticides, veterinary drugs and industrial chemicals from different families with very distinct physicochemical properties. The use of L9 TOA for QuEChERS and QuPPe parameter optimisation greatly simplified the method development process. After obtaining an optimal method for each class of contaminants, their performance was evaluated on all contaminants. The QuEChUP (QuEChERS followed by QuPPe) procedure provided the best detection rates of the targeted contaminants. Moreover, this new method of extraction is very appropriate in an exposome context to extract the most diverse contaminants. QuEChUP is very suitable for metabolomic type studies where each individual is analysed separately and *a fortiori* when only small samples are available. Most of the target list compounds were detected and identified at all three concentration levels (0.001, 0.01 and 0.1 $mg.kg^{-1}$) with false positives averaging 0.24% on non-spiked matrices. The SDL and LOI were equal to or less than 0.01 $mg.kg^{-1}$ for 92% and 78% of targeted contaminants, respectively.

The applicability of this method for multi-class contaminants screening was demonstrated by analysing several samples of bivalves, fish and crustaceans. All samples analysed by target screening were exposed to mixtures of contaminants. Of these, 59% were pesticides, 26% veterinary drugs and 15% industrial chemicals. Diuron (herbicide) and diclofenac (NSAID) were the contaminants identified with the highest estimated average concentrations, especially in mussel samples with 0.076 and 0.068 $mg.kg^{-1}$, respectively. Vedaprofen (NSAID) was also found at concentrations well above the default MRL in fish and crustacean samples, and two

antibiotics such as clarithromycin and dapsone were found at concentrations slightly greater than the MRL in bivalve samples. The rest of the contaminants were found at concentrations equal to or lower than the default MRL. These concentrations were estimated using different semi-quantitation strategies. However, the use of a validated quantitative method may be considered in future work to confirm and compare the concentration levels obtained with an MRL, if available. The method also demonstrated its versatility to identify other organic contaminants than those included in the method validation by suspect screening. This allowed the identification of other mixtures of contaminants, mainly pharmaceuticals, as well as illicit drugs and PCPs.

In this study, the combined results of targeted and suspect screening allow a better estimation of all contaminants likely to be present in the analysed samples, in a single analytical method based on an optimised extraction step and on the enhanced capabilities of HRMS detection. This innovative method will allow a better assessment of the combined actions of contaminants (cocktail effects) in future studies and to better reflect the impact of environmental exposures.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

2.5.4. Summary & main results

In the course of this study, a new sample preparation method called "QuEChUP" was developed. This is a sequential method with an initial QuEChERS extraction, followed by a QuPPE extraction and purification of the two extracts mixed using EMR-lipid purification material. This method has proved highly effective for the analysis and validation of 850 contaminants, including residues of pesticides, transformation products, veterinary drugs, pharmaceuticals and industrial contaminants. This new method covers a broader spectrum of contaminants than conventional QuEChERS and QuPPE methods. In food exposome-based context, the use of methods capable of extracting a wide range of contaminants is crucial. The method was validated in compliance with European Commission guidelines (European Commission, 2021). It was then applied to the analysis of commercially purchased seafood products, enabling the identification of 26 residues of pesticides, transformation products, veterinary drugs and various industrial contaminants. The contaminants found could be semi-quantified, but none exceeded regulatory limits in seafood products. Finally, to extend the scope of monitoring and highlight emerging and little-researched contaminants, a robust, automated suspect analysis (without analytical standards) was carried out using the open-source MSDial software. This software allows the use of external MS/MS lists (in .msp format) of chemical substances, downloadable from external databases such as MassBank of North America. Suspect analysis has enabled the provisional identification (confidence level 2a according to Schymanski et al. (2014)) of a very large number of emerging contaminants (see article).

2.5.5. Limitations and prospects for improvements

A limitation of the present study was the inability to confirm contaminants found by automated suspect analysis with the purchase of analytical standards, for cost reasons. Although the automated suspect approach is robust thanks to the similarity scores assigned for comparison of MS/MS spectra, unequivocal identification still requires prior injection of an analytical standard. It would be interesting to be able to purchase these analytical standards, if only to confirm the effectiveness of the approach presented.

In the light of this study and all the work presented to date, one prospect for improvement would be the implementation of non-targeted analysis protocols, which represent a major element in HRMS and are missing from our work. Mastery of these tools would enable us to interrogate the overall footprint of the sample, in an attempt to highlight other chemical substances of interest without a priori (without the use of targeted or suspect lists).

CHAPTER 3

The versatility of HRMS: targeted, suspected and non-targeted analyses

Preamble

Nowadays, chromatographic separation (LC/GC) hyphenated with the benefit from technological improvements with HRMS to identify known and unknown compounds are one of the most promising and relevant strategies to be used for food analysis. The last chapter of this thesis is devoted to a study of the versatility of HRMS system as a whole. It gives an overview of its potential use through the structural and large-scale screening of multiclass contaminants in purchased honey samples, as well as the suspected and non-targeted approaches for the research of markers. Otherwise, this chapter also describes implementation of a simple, efficient and robust quality assurance and quality control procedures, based on previous recommendations, which ensures data reliability by controlling certain analytical biases that are not negligible in such analyses.

3.1. A proof-of-concept study on honey

3.1.1. Context and aim of the study

This study overviews the versatility of HRMS, and its ability to perform different types of analysis on food samples. The aim was to bring together and summarize in a single study, the main benefits offered by HRMS, and how this tool could be effectively used to improve official food safety and authenticity systems. Honey was selected because it is a very popular and consumed sweet product, with high economic potential, subject to numerous contaminations as well as fraudulent and misleading practices. It was therefore of interest to us to use honey for demonstrating the robustness of HRMS for broad-spectrum contaminant screening, but also to highlight differentiation markers in food samples. To carry out this work, we reused the QuEChERS method previously developed and published as part of the study on sweet products (Makni et al., 2023a).

3.1.2. Key points of the study

As part of this study, we were able to:

- Set up robust QA/QC procedures to attest to the quality of the data generated and the analytical system used
- Perform very broad-spectrum screening of contaminants: (i) targeted analysis using a database of 850 contaminants for which analytical standards are available in the laboratory; (ii) robust, automated suspect analysis of various families of anthropogenic chemicals and contaminants using the open-access software MSDial.
- Robust and automated suspect analysis of endogenous chemicals with MSDial software, for the detection of floral biomarkers of differentiation in honey samples.
- Non-targeted and multivariate analyses for the in-depth search for markers responsible for the differentiation of honey samples according to type (urban or rural), floral or geographical origin.

Fig.5 below describes and summarizes the major improvements compared with the previous works (Diallo et al., 2023; Makni et al., 2023a; Diallo et al., 2022; Makni et al., 2022), following an iterative process of continuous improvement.

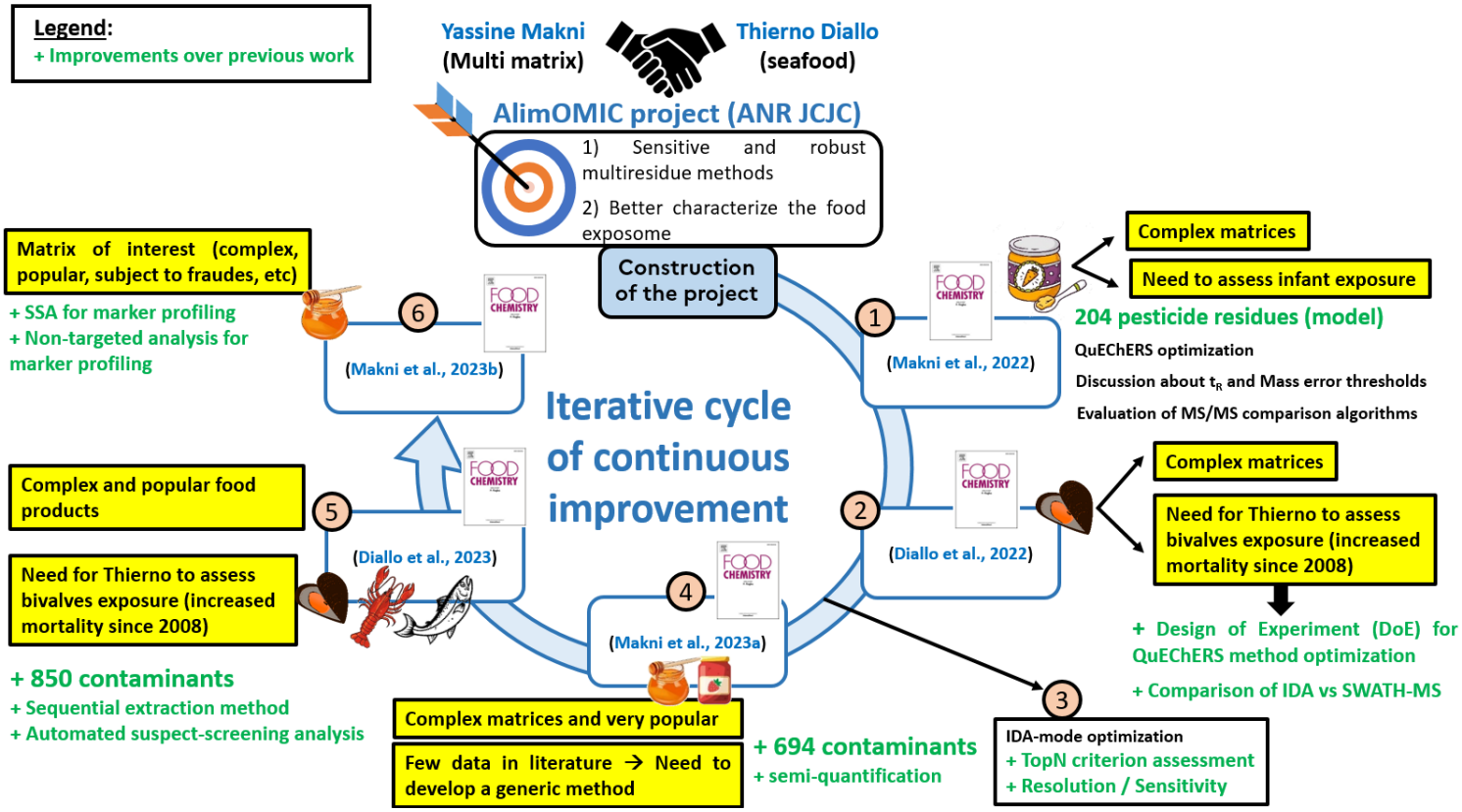


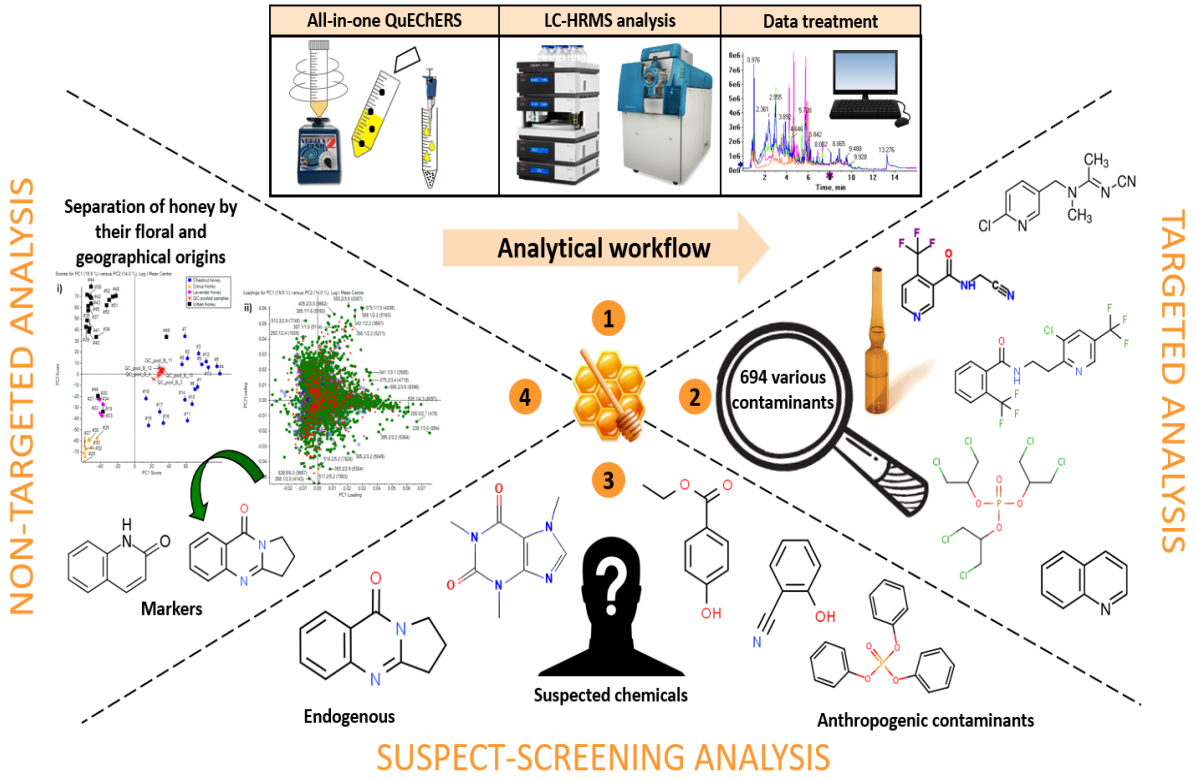
Fig.5. Cycle of iterative and continuous improvement – final 5

3.1.3. Article 5 (Makni et al., 2023b)

The following article details the experiments carried out as part of this study. Due to Elsevier copyright restrictions, only the title and abstract of the paper were included in published format. The rest of the paper is inserted in Word-type format. The published paper is available online using the following DOI: https://doi.org/10.1016/j.foodchem.2023.137720

The references associated to this paper are displayed there: References section (Article No. 5)

The electronic supplementary materials (Annexes) associated to this article are displayed here: Article 5 (Makni et al., 2023b): "A proof-of-concept study on the versatility of liquid chromatography coupled to high-resolution mass spectrometry to screen for various contaminants and highlight markers of floral and geographical origin for different honeys"



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A proof-of-concept study on the versatility of liquid chromatography coupled to high-resolution mass spectrometry to screen for various contaminants and highlight markers of floral and geographical origin for different honeys

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ABSTRACT

The high-resolution mass spectrometry is a powerful analytical tool for improving food safety and authenticity, but still underused in official control laboratories. The present work is a proof-of-concept study overviewing how liquid-chromatography coupled to high-resolution mass spectrometry could be used simultaneously for large-scale screening of contaminants and differentiation of honey samples. Within this study, the samples were extracted using all-in-one QuEChERS-based protocol that allowed for analysis of various anthropogenic contaminants and endogenous compounds. First, targeted-analysis of 52 honey samples led to unequivocal identification of 23 chemicals, including neonicotinoids, triazole fungicides and synergist. Then, suspect-screening using MSDial software allowed for tentative identification of 30 chemicals including plasticizers, flame-retardants and additives. Suspect-screening also made it possible to highlight tentative markers of chestnut honey (deoxyvasicinone, 2-quinolone, indoleacrylic acid and kynurenic acid) and citrus honey (caffeine, 2-oxindole and indole-3-carbinol). Lastly, non-targeted analysis enabled to separate honeys by their type, floral and geographical origins.

1. Introduction

The widespread use of pesticides in modern agriculture to increase crop yields and control pests can lead to residues that can contaminate food products. The exposure of consumers to pesticide residues via food raises serious concerns due to the potential adverse effects some of these chemicals may have on human health (Ntzani et al., 2013). In addition to the negative impact on human health, pesticide residues can also lead to environmental pressures on other species such as certain pollinating insects, particularly honeybees. For instance, certain neonicotinoid insecticides are thought to be involved in the excess mortality of pollinators (Auteri et al., 2017; Andrione et al., 2016). To protect the consumer, the European Food Safety Authority (EFSA) has set regulations for individual pesticide residues in various foodstuffs (Regulation (EC) No 396/2005). However, current regulations overlook possible agonist or antagonist interactions between different contaminants — i.e. cocktail effects — with potentially related sublethal adverse effects on human health (Rizzati et al., 2016). These potential cocktail effects are of major concern because consumers are not just exposed to individual substances, but to a wide variety of different contaminants through their diet. Pollinators are also affected by potential cocktail effects; for example, in honeybees, the simultaneous exposure to triazole fungicides or

synergist compounds along with neonicotinoid insecticides may enhance the toxicity of the latter (Gaweł et al., 2019; Iwasa et al., 2004).

In official routine analyses, pesticide residues in food samples are monitored using liquid or gas chromatography (LC/GC) coupled to tandem mass spectrometry (LC/GC-MS/MS) operating in multiple reaction monitoring (MRM) mode (Villaverde et al., 2016). The development of multiresidue sample preparation methods, such as the 'quick, easy, cheap, effective, rugged, and safe' (QuEChERS) method, has led to the coverage of a much larger panel of contaminants with a wide range of polarity and physico-chemical properties (Anastassiades et al., 2003; González-Curbelo et al., 2015). However, although traditional techniques for routine analysis are highly sensitive, LC/GC-MS/MS instruments operating in MRM have the drawback of being restricted to a predefined list of prioritised compounds for which analytical standards are available (Weng et al., 2020). Therefore, these techniques are blind to any other compounds not included in the list, which raises concern because unlisted, potentially dangerous compounds can unexpectedly contaminate food products.

In recent years, with the advent of high-resolution mass spectrometry (HRMS), research laboratories can now address issues associated with the blindness of low-resolution instruments. However, although these instruments offer many opportunities, they remain underused in food safety-based context, especially due to their high acquisition costs, which may represent a limitation for laboratories. The use of time-of-flight (ToF) or Orbitrap high-resolution instruments with full-scan mode-based methods has made it possible to search for a theoretically unlimited number of compounds, lifting the restriction to only target analyses of prioritised chemicals (Mezcua et al., 2009). Such instruments also offer the possibility of re-using acquired data to conduct retrospective analyses with suspect screening and non-targeted approaches. These approaches expand the scope of chemical analysis by screening for a broader spectrum of chemicals, without prior presumptions, and for which analytical standards are not available at the time of injection (Parinet, 2021; Phillips et al., 2018). As such, unexpected pollution, new and emerging contaminants, as well as contaminant mixtures to which consumers are exposed can be brought to light with the use of HRMS instruments (Ottenbros et al., 2023). Likewise, various recent studies have reported the use of HRMS instruments for the wide screening of contaminants in food samples (Diallo et al., 2023; Makni et al., 2023; Fu et al., 2017; Gómez-Ramos et al., 2013).

Nevertheless, HRMS is not limited to the screening of anthropogenic contaminants, because this tool can be used to conduct non-targeted analyses. The non-targeted approach is a powerful and holistic approach for the exploration of infinitely numerous endogenous and exogenous compounds in complex samples. Non-targeted approaches using multivariate statistical tools can be employed to evaluate food safety, food authenticity, as well as food traceability (Lacalle-Bergeron et al., 2021; Böhme et al., 2019; Cubero-Leon et al., 2014).

In the literature, various studies have reported the use of HRMS either for the screening of contaminants or for biomarker profiling applications in food, but less frequently for both simultaneously. Cotton et al. (2014) conducted a study to highlight the versatility of HRMS instruments using Orbitrap mass spectrometry for the analysis of 76 honey samples. They screened for 83 targeted pesticides, and carried out metabolomics-like analyses to search for unknown contaminants and to discriminate the samples according to floral origin (Cotton et al., 2014).

Here, a feasibility study was carried-out using ultra-high performance liquid chromatography (UHPLC) coupled to high-resolution mass spectrometry to highlight the versatility of these instruments for food safety and food authenticity purposes. This work was focused on honey,

because this food product perfectly demonstrates on how LC-HRMS tools can be easily used for various analytical applications. Honey is a highly nutritional quality product, with a complex composition and very popular within consumers (da Silva et al., 2016); furthermore, it is well known for its therapeutic properties (El-Nahhal, 2020) and sweet flavour. However, honey can be the source of various contaminations, which can raise food safety concerns. Moreover, honeybees can be contaminated during foraging and collecting nectar from blossoms to produce honey (El-Nahhal, 2020). This bee product may thus bear witness to contaminants occurring in the environment and affecting bee health. Finally, honey can also be subject to adulteration and misleading practices for economic benefits, underlining the need to ensure the authenticity and traceability of honey samples.

The present work followed and integrated appropriate quality assurance (QA) and control (QC) procedures inherited from the metabolomics field (Broadhurst et al., 2018) on 52 honey samples to conduct: (a) a large-scale targeted screening of more than 800 chemicals including 694 various contaminants related to a previous study (Makni et al., 2023), (b) suspect screening using MSDial software to expand the analytical coverage and search for hundreds of emergent and little sought-after chemicals, (c) original suspect screening of endogenous compounds to highlight floral-specific markers of honey, (d) non-targeted analyses to discriminate little-studied urban honeys and different monofloral honeys, as well as to discriminate among chestnut honey samples according to three different geographical areas.

2. Materials and Methods

2.1. *Chemicals and reagents*

A kit of 746 contaminants analytical standards (of which only 694 were correctly detected in solvent as explained in (Makni et al., 2023)) was purchased from LGC Standards (North Charleston, SC, USA). Acetonitrile (HPLC-MS grade ~ 98%) was purchased from ThermoFisher Scientific (Illkirch, France). Acetic acid (LC-MS grade ~ 98%) and formic acid (LC-MS grade ~ 98%) were also obtained from ThermoFisher Scientific. Extraction salts kits containing 4.0 g of magnesium sulphate (MgSO4) and 1.0 g of sodium acetate (NaOAc), were purchased from Agilent (Santa Clara, CA, USA). Dispersive solid-phase extraction (d-SPE) kits that contained 900 mg of MgSO4 and 300 mg of primary and secondary amines (PSA), and were obtained from UCT (Bristol, PA, USA).

2.2. *Honey samples*

A total of 52 honey samples, including 33 rural honeys (#1 to #33) and 19 urban honeys (#34 to #52) were examined in this study. The honey samples were selected based on their type (rural or urban), floral and geographical origins. Different groups were formed based on the type and floral origins of honey samples: urban honey (n=19); chestnut honeys (n=18); citrus (lemon tree + orange tree) honey (n=10); lavender honey (n=5). Furthermore, three groups were also formed based on geographical origins of the 18 chestnut honeys: chestnut honeys from France (n=8); from Italy (n=6); from Spain (n=4). All the honeys were purchased from local markets in Maisons-Alfort and Créteil (Île-de-France, France) and Montreal (Québec, Canada). The metadata associated with each sample and including the type, floral and geographical origins, texture and production method are given in Table S1. However, the sample production year of the honey samples was not indicated on the jars.

2.3. *Sample processing*

Sample processing was based on a modified acetate-buffered version of QuEChERS, which was optimised for the analysis of concentrated sugary products in a previous study (Makni et al., 2023). This optimization was performed on 2 g of sample for technical reason, to fit with the quantity of mix of contaminants that was available in the laboratory. The sample preparation procedure is fully detailed in Fig.S1. Analytical system and sample analysis

Samples were analysed using ultra-high performance liquid chromatography (UHPLC) coupled to high-resolution mass spectrometry (HRMS). The UHPLC system was a Dionex UltiMate-3000 system equipped with a binary pump and autosampler (ThermoFisher Scientific, Waltham, MA, USA). The mass spectrometer consisted of a Q-ToF from AB Sciex (TripleTOF 5600TM, Darmstadt, Germany). All the UHPLC-Q-ToF-MS parameters used for analysis are displayed in Table S2.

2.4. *Quality assessment and quality control*

In this study, various QA and QC procedures were implemented to meet standard requirements for quality and ensure the robustness of the whole analytical process. Before analysis, a series of procedures were implemented to avoid insofar as possible measurement bias, to control any potential contamination and to guarantee the quality of the generated data. These procedures involved (a) including extraction blank samples during sample preparation to control for any possible contamination during the experiments. The extraction blank sample was performed without using any honey matrice, but followed the same preparation with the same solvents, reagents and consumables; (b) two pooled/intra-study QC samples, one obtained by pooling 50 µL of each of the 18 chestnut honey extracts only (#A), and the other obtained by pooling 20 µL of each of the 52 honey extracts (#B); (c) a QA sample that consisted in a mixture in acetonitrile of 746 analytical standards of contaminants at 0.1 mg.L-1 (of which only 694 were correctly detected in solvent) (Table S3); (d) manual calibration of the Q-ToF-MS system before analysis using an external calibrant delivery system (CDS) that infuses a positive or negative APCI calibration solution.

During analysis, series of QA and QC measures were also implemented to assess the suitability of the LC-HRMS analytical system and quality of the generated data. The QA and QC measures consisted of (a) automatic calibration at the beginning of the sequence prior to the first injection and, in addition, every five injections to control for instrument signal drift and foster insofar as possible high instrument precision over time; (b) a blank vial of acetonitrile, injected twice after the first automatic calibration, once after the first QA sample, and then punctually throughout the whole analytical sequence to assess possible carry-over and memory effects of the analytical system; (c) an extraction blank was made without any honey matrice, but following the same preparation that the honey samples, with the same solvents, reagents and consumables. It was injected at the beginning of the sequence to control for any possible contamination during sample preparation or coming from the laboratory material used; (d) two pooled/intra-study QC samples (#A and #B) injected twice after the extraction blank and then punctually throughout the whole analytical batch to assess intra-study reproducibility; (e) a QA sample injected three times (at the beginning, middle and end of the sequence) to investigate the stability of the analytical system; and (f) randomisation of honey samples to minimise as much as possible the impact of any instrument drift on data quality.

The samples were extracted and injected in a single replicate. Indeed, the different groups of honey samples included in this work included various individuals, as mentionned in Section 2.2., allowing taking into account inter-individual variability within the same group. As so, in this work, individuals were considered as “replicates” for a given group of honeys. Furthermore, the injections of QC-pooled samples across the analytical batch already allow for assessing the

signal variability over time, so there was no need to make replicates of injection of the different honey samples.

Fig.S2 summarises the overall design of the sequence used in the study, and the set of QA/QC measures implemented during the analysis.

2.5. *Data processing and analysis*

The entire data mining workflow used in this study is summarised in Fig.1.

In this study, honey samples were investigated using targeted analysis, suspect screening analysis (SSA) and non-target analysis (NTA). For targeted analysis, samples were screened against a home-made database containing more than 800 contaminants, including the mixture of 746 contaminants of the QA sample (Table S3), as well as other contaminants for which the analytical standards were available in laboratory. Targeted analysis was conducted using PeakView® software (version 2.2, AB Sciex) with the integrated module MasterViewTM. MasterViewTM is user-friendly and allows for fast and automated screening of several compounds in samples, based on acceptance criteria defined by the user. Furthermore, this module is interconnected to LibraryViewTM software (version 1.0.3, AB Sciex), enabling the comparison of the experimental fragmentation spectrum of a compound and its reference fragmentation spectrum obtained by injecting the analytical standard in solvent at 0.1 mg.L-1. Unequivocal identification, i.e. confidence level 1 according to Schymanski et al. (2014), was based on the following acceptance criteria: (a) good peak shape (Gaussian and well-defined with respect to noise); (b) experimental mass error ± 5 ppm compared to theoretical exact mass; (c) experimental variation in retention times (tR) ± 0.1 min compared to the analytical standard in solvent injected in the same batch; (d) similarity score >70% between experimental and reference fragmentation spectra, computed using FIT algorithm, already used in previous studies (Diallo et al., 2023; Makni et al., 2023).

For SSA, the LC-HRMS files from the AB Sciex instrument (.wiff format) were converted to .mzML format using the conversion tool MSConvert GUI (64 bit) version 3.0.23143 (ProteoWizard, Palo Alto, California, USA). Afterwards, the files were uploaded in the open-source MSDial software (version 4.9.2). This easy-to-use software can connect with external databases, and was used in this study to search for:

- (i) Anthropogenic contaminants for which analytical standards were not available, to expand the analytical coverage in a food safety-based context. External LC-MS/MS lists were used and are available and downloadable in .msp format on the website of MassBank of North America (MoNA). There were 98,154 spectra in the list in positive mode, and 46,459 spectra in negative mode. Tentative identification, i.e. confidence level 2a according to Schymanski et al. (2014), was based on the following acceptance criteria: (a) good peak shape (Gaussian and well-defined with respect to noise); (b) experimental mass error ± 0.01 Da compared with theoretical exact mass to filter non-relevant features and simplify the dataset obtained; (c) manual calculation of experimental mass error obtained with a threshold ± 5 ppm not to exceed to limit for potential false positives; (d) similarity score >70% between experimental and external fragmentation spectra, using dot product (DP) and reverse dot product (RDP) algorithms; (e) absence of the tentatively identified compound in solvent blank and extraction blank samples, or presence but at significant lower signal than in honey samples.

- (ii) Endogenous and natural occurring substances, for marker profiling applications, using the same lists and criteria as described for anthropogenic contaminants. In this part, a QC-pooled sample was selected to generate an alignment file, highlighting expression profiles and

abundances of the tentatively identified compounds with respect to four defined groups of honey samples (Section 2.2.).

For the NTA, data were processed using MarkerViewTM software (version 1.2.1, AB Sciex), amenable to marker profiling applications using statistical analysis and simple graphical representations. To describe spontaneous and significant trends of the multivariate dataset, as well as to control the quality of data generated using QC-pooled samples, principal component analysis (PCA) was performed in ESI^+ and ESI^-. Principal component analysis (PCA) is a non-supervised chemometric analysis used to simplify multidimensional datasets (Earnshaw et al., 2010). Then, principal component discriminant analysis (PCA-Da) in ESI^+ and ESI^- mode was used to maximise the discrimination of the different groups of honey samples, and explore features that separate the floral and geographical origins. PCA-Da is a supervised statistical technique that takes into account user-supplied information about external variables (group information) when reducing the dimensionality of the honey dataset. PCA-Da is better suited than PCA to separate groups of individuals and for the clustering analysis (Earnshaw et al., 2010). However, in this work, the dataset was not divided into training and validation sets, as the number of honey samples included in this study was not enough to conduct further validation of the models. It was also the case in a previous study that used PCA-Da without validation due to the rather small number of samples (Lee et al., 2018). Prior to chemometric analysis, pre-processing steps consisted of log transformation of data and mean-centre scaling. Log transformation corrects for heteroscedastic noise and also provides a pseudo-scaling effect by reducing the predominance of large values (Engel et al., 2013). PCA and PCA-Da generate loading plots, which highlight the influence of the original variables on the principal components, and a score plot that shows the similarities and differences between samples. Finally, univariate analysis (comparison of groups using a t-test) was carried out to confirm or rule out the significance of any potential discriminating features reported, with a fold-change threshold of ≥ 10 and $\alpha = 1\%$ (p-value ≤ 0.01).

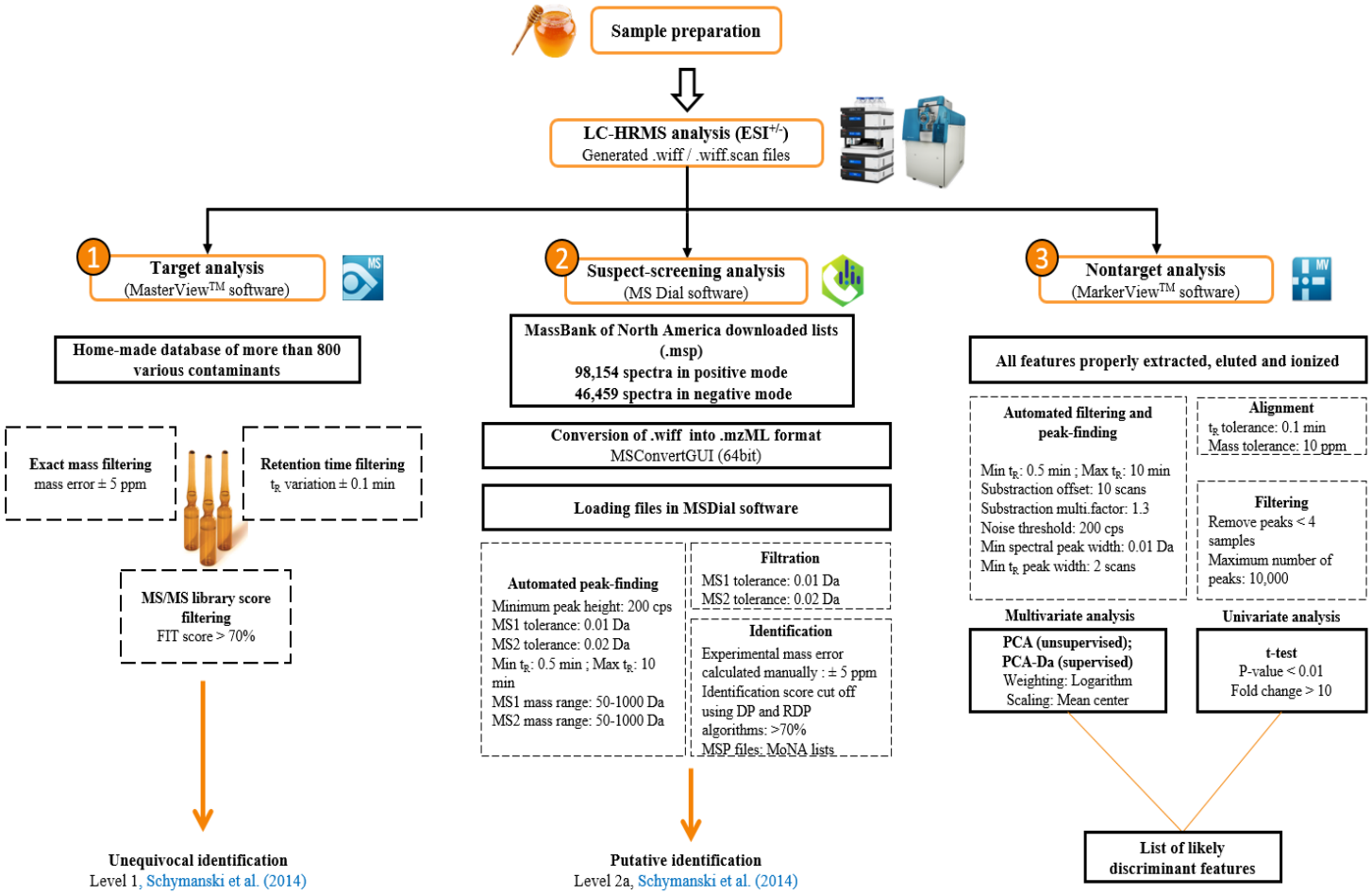

Fig.1. Data processing workflow used in this study.

3. Results and discussion

3.1. *Data quality and system suitability assessment*

For assessing the suitability of the analytical system and the quality of the data generated, QA and QC are two critical quality management practices to consider in the context of research and non-target or metabolomics-like studies (Broadhurst et al., 2018). The guidelines proposed by Broadhurst et al. (2018) were used as a foundation for the design of the analytical sequence with appropriate QA and QC measures in this study (Fig. S2). Results for quality data assessment are displayed in Fig. S3.

For quick control of instrument signal drift, the total ion chromatograms (TICs) of the automated calibrations were overlain together in ESI^+ (Fig. S3a) and ESI^- (Fig. S3b). In positive mode, the TIC intensities ranged from $6.5e^5$ to $8.5e^5$ cps, with an approximate average of $7.5e^5$ cps (Fig. S3a), which represents about 19% variation in the instrument signal over time. In negative mode, the instrument signal was nearly twice as stable, with the TIC intensities ranging from $6e^5$ to $7e^5$ cps and an approximate average of $6.5e^5$ cps (Fig. S3b), which represents about 11% variation over time. Overall, the variation in the instrument signal did not tend to towards a gradual decrease or increase over time, but randomly fluctuated around the mean. In effect, we did not observe any significant impact between the first and the last samples. This lack of decreasing or increasing trend attests to the satisfactory stability of the system with an acceptable variability of <20% in ESI^+ and ESI^- despite the injection of 52 concentrated honey

extracts during a run lasting more than 24 hours. In addition, the TICs of the 14 pooled QC samples (#A) injected across the batch were also overlain to take into consideration the chromatographic dimension in appraisal of the results and the signal variability. The results showed that the TICs of the pooled QC samples overlapped very well in both ESI^+ (Fig.S3c) and ESI^- (Fig.S3d), attesting to the good overall intra-study reproducibility of the method.

For chromatographic stability assessment, Figure S4 shows an example of six extracted ion chromatograms (EIC) including early-, middle- and later-eluted compounds, obtained in ESI^+ from a mixture of 746 contaminants (of which only 694 were correctly detected in solvent), injected three times in the batch. Retention time shift, peak symmetry and definition, as well as chromatographic resolving power in case of isomer compounds, were used for assessing the suitability of the system, as presented in Broadhurst et al. (2018). As shown in Figure S4, t_R values were very stable over time, with no or non-significant shifts between the first injection (Fig.S4a) and the following two injections (Figs. S4b and S4c). Peak shape of the six compounds was very good, with narrow, symmetric and well-defined peaks, without degradation over time (Fig. S4). Finally, the resolving power was sufficient to separate isomer compounds, as in the case of bromuconazole for example (Fig.S4).

These results attest to the robustness and the very satisfactory intra-reproducibility of the method and the analytical system used, ensuring robust data generation and results. These results also support the relevance of previous guidelines and recommendations for implementing QA and QC measures to evaluate the reliability of analytical methods and protocols in research and for the purposes of non-targeted studies (Broadhurst et al., 2018).

3.2. *Target screening of honey samples*

Targeted screening of the samples highlighted that 34 of the 52 honey samples (i.e. 65% of the samples) were positive for a single contaminant or a mixture of contaminants (Table S4), and a total of 23 different contaminants were identified. All of the Spanish honey samples (100%, n=11) tested positive, followed by French (88%, n=16), Italian (55%, n=11) and Canadian honey samples (21%, n=14) (Table S4). Furthermore, it was surprising to identify synthetic pesticide residues in honey samples from organic farming (#1, #10, #18 and #30 for example, Table S3). Indeed, organic farming normally excludes the use of synthetic pesticides, and only allows to use for fertilizers and pesticides of plant, animal, microbial or mineral origin. The fertilizers and pesticides allow to be used within organic farming are regulated by (Regulation (EC) No 889/2008). It could possibly highlight misuse or food fraud, or it could also be explained by the ability of certain pesticide residues to translocate into different environmental compartments. This would suggest that they might have been used on nearby land used for conventional farming, leading contamination of land used for organic farming.

The corresponding frequency of appearance (%FoA) of the identified contaminants is provided in Table S5. There were mainly pesticide residues or transformation products (TP). The most frequently identified compounds were N-(2,4- dimethylphenyl)formamide (DMF, FoA 44%) and 2,4-dimethylaniline (DMA, FoA 21%), both metabolites of amitraz, a veterinary drug legally approved for usage on beehives to fight against the *Varroa* mite, a bee pest (Regulation (EU) No 37/2010) (Lozano et al., 2019). The third most frequently identified contaminant was the dual-use substance coumaphos with an FoA of 21% (Table S5), also used as a legally approved veterinary treatment to control *Varroa destructor* (Lozano et al., 2019). Also, neonicotinoids were identified in some honey samples. This class of widely used insecticides is known to have adverse effects on non-target pollinators, and is involved in the excessive mortality of honeybee colonies (Andrione et al., 2016). However, only acetamiprid occurred

with a significant FoA (19%) among the samples tested, and flonicamid, imidacloprid and thiacloprid showed lower FoAs (Table S5). Other insecticides such as chlorfenvinphos, dimethoate, flupyradifurone, hexythiazox and tebufenozide were also identified but with relatively low FoAs (Table S5). It should also be noted the occurrence of triazole fungicides, such as propiconazole and tebuconazole, which could considerably potentiate adverse and toxic effects of neonicotinoid insecticides on honeybees (Gaweł et al., 2019; Iwasa et al., 2004). Figure S5 shows the automated and unequivocal identifications of the neonicotinoid insecticide flonicamid (Fig.S5a), occurring simultaneously with the triazole tebuconazole (Fig.S5b) in a lemon tree honey from Spain (Table S4, ID #27). The occurrence of synergist agents such as piperonyl butoxide in Spanish chestnut (#17, Table S4) and orange tree honeys (#33, Table S4), may also enhance the potency of some neonicotinoid insecticides (Iwasa et al., 2004). In addition to the above-mentioned compounds, a flame retardant, tris(1,3-dichloro-2-propyl)phosphate (TDCPP) was found, albeit with a low FoA of 4% (Table S5). Figure S5c highlights the unequivocal identification of TDCPP in a lemon tree honey from Italy (Table S3, ID #24).

These screening results underline the need of considering better the chemical mixtures to which a living organism may be exposed. Although maximum residue levels (MRLs) have been established for individual residues, risk assessments generally overlook the possibility of combined effects from mixtures or that some compounds may interact with each other resulting in toxicological effects at lower doses.

3.3. *Suspect screening analysis (SSA)*

3.3.1. Screening for anthropogenic contaminants

The SSA of the 52 honey samples enabled the tentative identification of 30 chemicals at confidence level 2a according to (Schymanski et al., 2014). Table S4 summarises the compounds found as well as their FoAs. Various plastic-related chemicals were tentatively identified, including in particular phthalate esters (PEs). These cost-effective additives are used in the polymer industry to impart flexibility, elasticity and durability to plastic materials, and are especially used for food-packaging materials and food processing (Lo Turco et al., 2016; Zhou et al., 2014). Phthalates are of concern as there can contaminate foodstuffs, and are suspected to have adverse effects on health and on reproductive capabilities. Among the PEs found, di-n-butyl phthalate (DBP) and diethyl phthalate (DEP) occurred at significant FoAs of 100% and 54%, respectively, whereas the other PEs were much less frequently identified with FoAs of ≤ 6% (Table S5). It should be noted the ubiquitous occurrence of di-n-butyl phthalate as it was also reported in blank samples, but at 2-3 fold lower signal than in honey samples. Additional plastic-related chemicals were also tentatively identified such as acetyl tributyl citrate (ATBC, FoA 10%), dibutyl sebacate (DBS, FoA 50%) and triphenyl phosphate (FoA 17%), among others (Table S5). The SSA also highlighted the tentative identification of some additives, personal care products and pharmaceuticals, as well as preservatives including ethyl and methyl paraben with non-negligible FOAs of 46% and 23%, respectively (Table S5). It should also be noted the high occurrence of 2-(4-morpholinyl)benzothiazole (24MoBT) and 2-hydroxybenzonitrile (2HBzN) with FOAs of 65% and 67%, respectively (Table S5). 24MoBT belongs to the benzothiazole class of chemicals, and is an impurity of the vulcanisation accelerator 2-(morpholinothio)benzothiazole found in automobile tyres. 2HBzN is a multi-use chemical that has pesticidal, preservative and disinfectant properties, and is also used as starting agent in the synthesis of pharmaceuticals (Binev et al., 2004). Among all the previous reported chemicals, some of the PEs found including BBP, DBP, DEP and DP, have already been characterised and found in honey samples, using GC-MS/MS instruments (Peñalver et al., 2021;

Lo Turco et al., 2016; Zhou et al., 2014). However, there is a lack of data regarding some of the other pollutants in environmental and food samples.

This may not necessarily reflect the low occurrence of such contaminants in food samples, but rather suggest that they are not included in the lists of prioritised contaminants or to be investigated. In this sense, LC-HRMS allowing for SSA clearly proves to be a very convenient and useful tool for providing data on the emergence of heretofore unconsidered pollutants. However, a crucial aspect of SSA involves the lists of compounds to be used in a food safety-based context to expand the current analytical coverage. These lists can be established manually and specifically by the analyst with regard to the literature, which can be tedious. External and online lists with available LC-HRMS spectra can also be used to be more exhaustive, as demonstrated in this study. In the field of food safety, it would be particularly useful if the community agrees to compile HRMS spectra of anthropogenic contaminants with associated analytical informations, into a single dedicated database, with the possibility to download lists in a format that can be used in open or private access software by all users. Another critical aspect of SSA is the interoperability in LC-ESI-HRMS. Indeed, it can be difficult to compare experimental and external MS/MS spectra acquired using different LC-HRMS instruments. These issues raise questions on how SSA analyses should be conducted. If correctly addressed, SSA could more effectively bring to light mixtures and contaminants of emerging concern, leading to a better understanding of the external exposome.

3.3.2. Screening of endogenous compounds for the determination of floral origin markers in honey samples

In addition to the use of SSA for more extensive food monitoring, the present study also aims to highlight how this kind of approach could be used and useful for the chemical characterisation of honey, and particularly for the discovery of markers of floral origin or type of honey.

First, for each honey sample, the compounds along with their abundance were represented in MSDial software using a heatmap with a hierarchical clustering analysis of the samples (Fig. 2). The results showed excellent hierarchical clustering of the samples by honey type in ESI^+ (Fig.2a). However, in ESI^-, the samples were less well grouped by type (Fig. 2b). For example, in ESI^+, the heatmap highlighted the relative overexpression of deoxyvasicinone (*m/z* 187.0868; t_R= 3.03 min) and 2-quinolone (*m/z* 146.0599; t_R= 2.95 min) in chestnut honeys, as well as caffeine (*m/z* 195.0879; t_R= 2.18 min) and 2-oxindole (*m/z* 134.0601; t_R= 2.96) in citrus honeys. Figures 3a and 3b show the expression in the chestnut honey group of tentatively identified deoxyvasicinone and 2-quinolone, respectively, and their absence in other groups. The experimental fragmentation spectrum was highly comparable with the external reference spectrum for both compounds. Interestingly, both compounds also occurred in urban honey #49. Likewise, Figures 3c and 3d show the tentative identification of caffeine and 2-oxindole, respectively, in the citrus honey group and their absence in other groups. These findings are consistent with a previous study that reported deoxyvasicinone and 2-quinolone as typical substances of chestnut honey, and caffeine as typical endogenous substance of orange tree honeys (Schievano et al. 2013). Here, caffeine was also tentatively identified in lemon tree honeys, as well as in orange tree honeys. Thus, our results as well as those published by Schievano et al. (2013) suggest using deoxyvasicinone and 2-quinolone as specific markers of chestnut honey, and caffeine as specific marker of citrus honey (lemon tree and orange tree honey). To the best of our knowledge, this study is the first to date that reported 2-oxindole in citrus honey.

Second, fold change (>10) and the *p*-values of an ANOVA (< 0.01) were used as filters in the ion table of the alignment file to highlight other endogenous substances that show potential for use as markers of floral origin. This complementary analysis led to the tentative identification of three other endogenous substances in ESI^+: indoleacrylic acid (*m/z* 188.0705; t_R= 2.73 min) (Fig.S6a), kynurenic acid (KYNA) (*m/z* 190.0497; t_R= 2.04 min) (Fig.S6b) in the chestnut honey group and in an urban honey (Table S1, #49), and indole-3-carbinol (*m/z* 130.0648; t_R= 4.43 min) in the citrus honey group (Fig.S6c). KYNA is a well-known metabolite of tryptophan, found to be occurring at very high levels in chestnut honey and flowers of the chestnut tree (Turska et al., 2022; Turski et al., 2016). KYNA also occurs in other types of honey or food samples, but at a much lower content (Turska et al., 2022). Indoleacrylic acid is another metabolite of tryptophan, but has never been reported in honey samples to date. Likewise, our study appears as the first to highlight indole-3-carbinol in honey samples and especially citrus honey. Further investigations of the presence/absence of both compounds in other types of honey are needed to confirm their use as markers of floral origin.

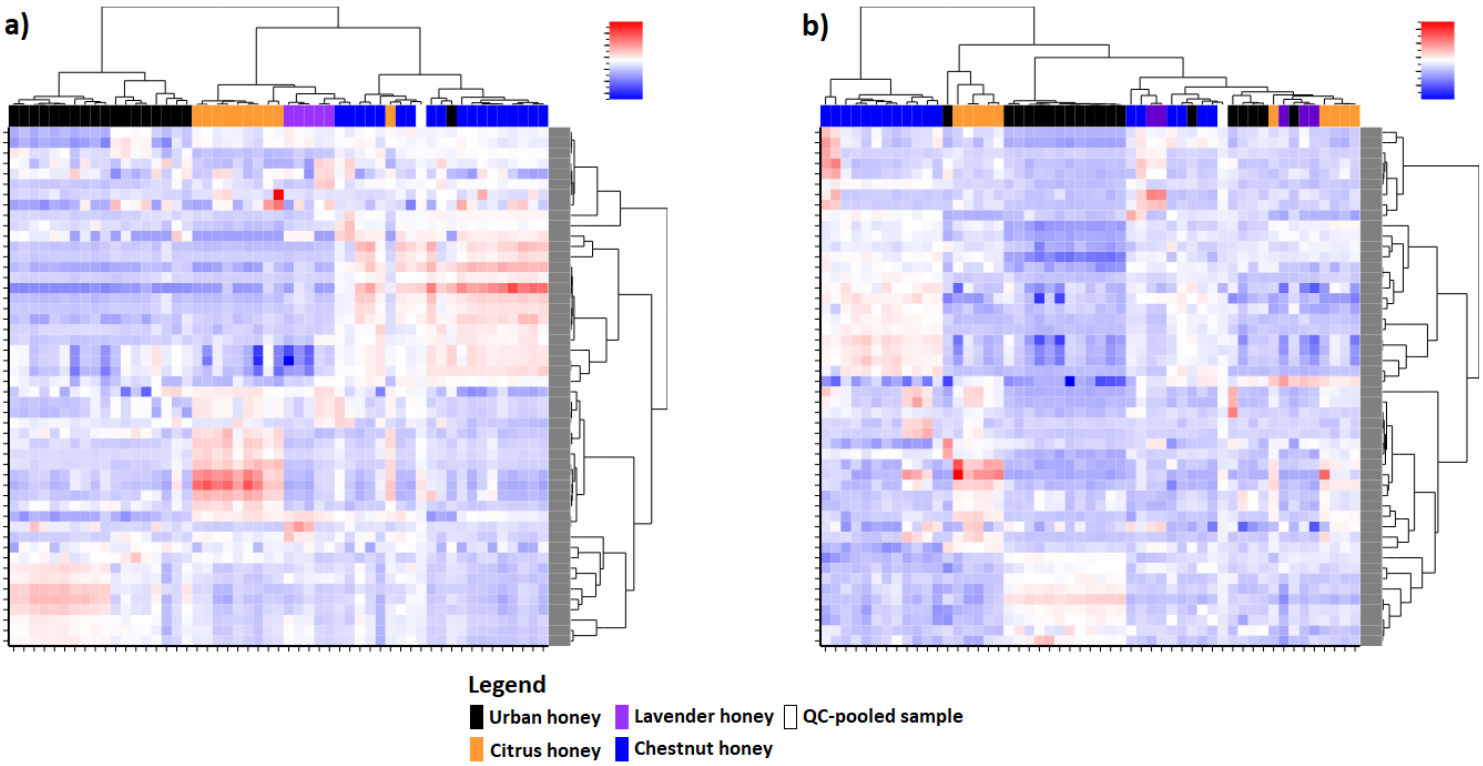

Fig.2. Generated heatmap using MSDial and showing various annotated compounds and their relative abundance in 52 honey and one QC-pooled sample which were hierarchical clustered. The scale of high to low relative abundance is shown in red and blue, respectively. Heatmaps were generated in (a) ESI^+ and (b) ESI^-.

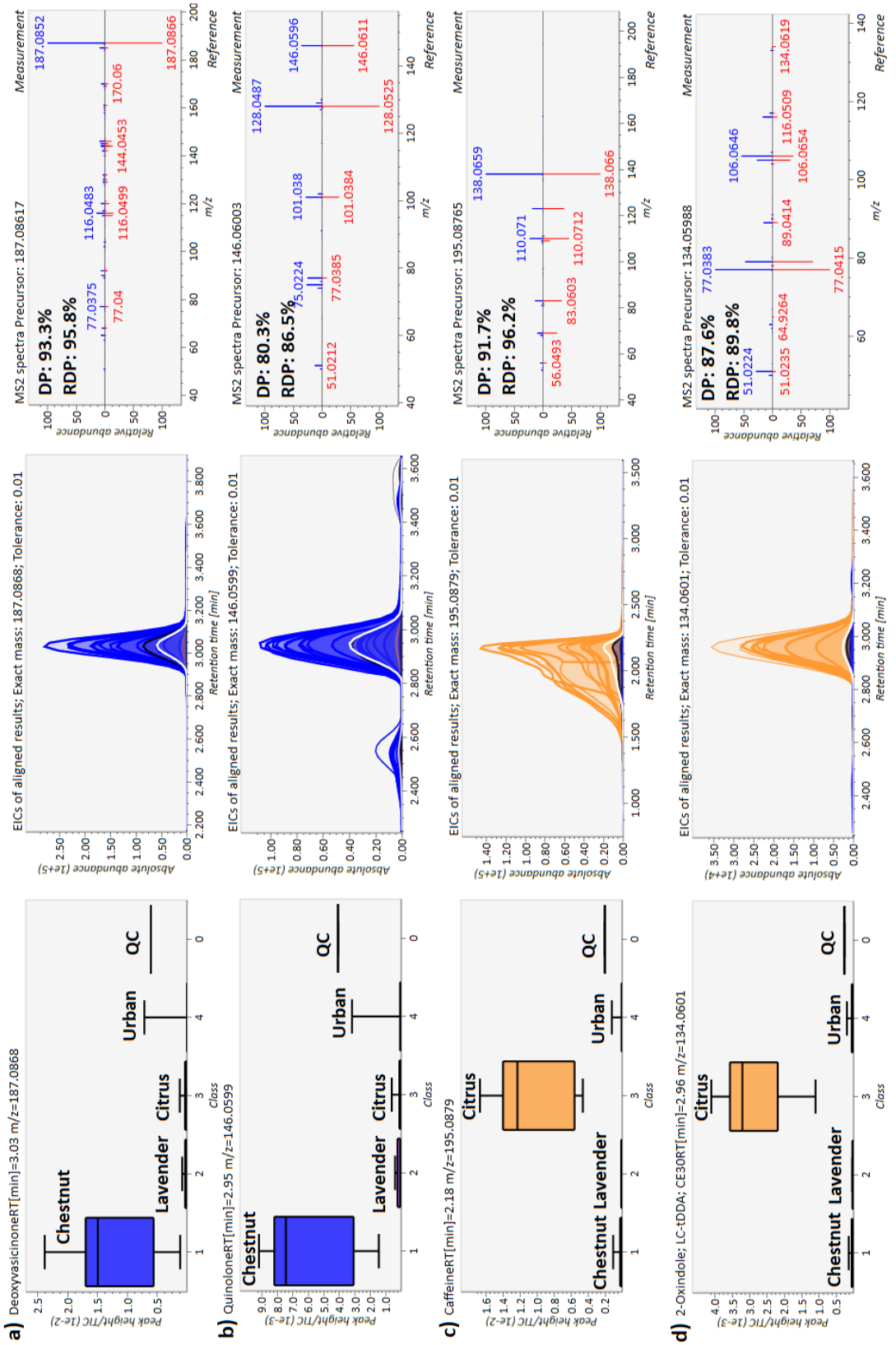

Fig.3. Tentative identification in ESI$^+$ of potential floral origin markers: (a) deoxyvasicinone in the chestnut honey group; (b) 2-quinolone in the chestnut honey group; (c) caffeine in the citrus honey group and (d) 2-oxindole in the citrus honey group. From left to right: the expression profile of the compounds in the honey groups and QC-pooled samples; the extracted ion chromatograms of the compound in the samples; experimental fragmentation spectrum (in blue) matched against an available external fragmentation spectrum acquired in other analytical conditions (in red).

3.4. *Non-targeted analysis to explore markers of floral and geographical origin in honey samples*

Suspect screening focused only on tentatively identified compounds. However, a large number of features could not be annotated because they were not included in the external database. Therefore, we carried out NTA to consider all the features extracted from the samples, thereby allowing for more in-depth marker profiling.

3.4.1. Application of NTA to explore markers of honey type and floral origin

Here, the first step consisted in mapping the whole dataset including the QC-pooled samples using PCA to assess the quality of data generated (Fig. 4). The PCA score plot showed excellent grouping of all QC-pooled samples, either in ESI^+ (Fig. 4a) or ESI^- (Fig. 4b), attesting to the high stability of the system throughout the whole analytical sequence. Furthermore, the PCA score plot highlights clear, spontaneous discrimination between all the different groups of honey based on their floral origin (chestnut, lavender or citrus honey) or type (urban honey). However, in the PCA score plot, urban honey #49 clustered near the chestnut honey group, and urban honeys #34 and #46 near the lavender honey group, in ESI^+ (Fig.4a) and ESI^- (Fig.4b). These results as well as the fact that all the tentatively identified markers of chestnut honey group in Section 3.3.2. were also found in urban honey #49, suggest that this honey sample was produced from chestnut tree blossoms.

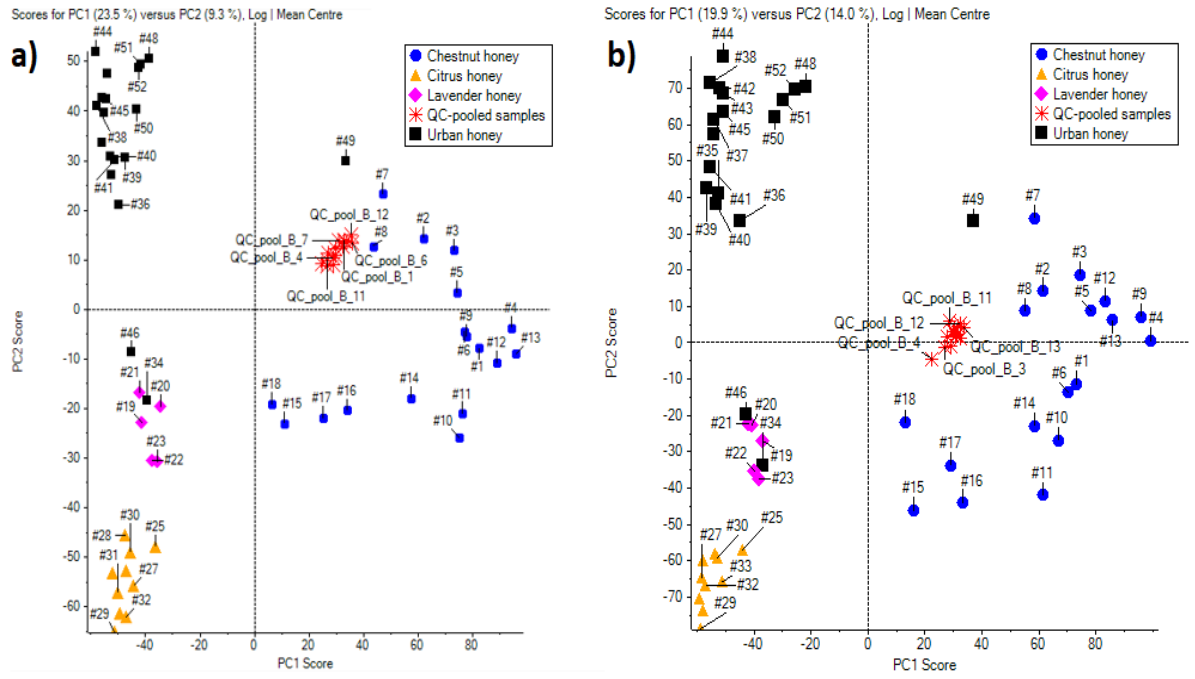

Fig.4. Principal component analysis (PCA) of the dataset of 52 honey samples with the quality control (QC)-pooled samples to assess data quality. (a) PCA generated in ESI^+ (b) PCA generated in ESI^-. (i) PCA score plots of honey samples (ii) PCA loading plots of honey samples.

When focused on the separation of the different groups of honey using PCA-Da (Fig.5), samples clearly clustered by honey type or floral origin. In ESI^+, we obtained a good discrimination among chestnut, citrus and urban honeys using D1 and D2 (Fig. 5a), whereas D1 and D3 clearly discriminated the lavender honey group from the others (Fig. 5b). In ESI^-, lavender, citrus and chestnut honey samples were well discriminated using D1 and D2 (Fig. 5c), whereas D1 and

D3 clearly separated the urban honey samples (Fig. 5d). The associated loading plots of PCA-Da provided the features preponderant in the separation of the different groups of honey samples. However, as explained in Section 2.6., the PCA-Da model could not be validate in this study as the number of honey samples constituting the dataset was not enough. As a result, further validation of PCA-Da model using another and independant honey dataset should be necessary to verify the relevance of the clustering analysis.

The significance of the features found using PCA-Da was confirmed by fold change and *t*-tests with $\alpha = 1\%$. Table S6 summarises the most discriminant features found for each honey group, with their *m/z*, retention times, fold change and *p*-values. The endogenous compounds tentatively identified in Section 3.3.2. using SSA were also found in NTA and were among the most discriminant features. Furthermore, the NTA highlighted various other discriminant features but that have not been annotated. Therefore, future investigations of these features can provide the opportunity to propose tentative annotations and better characterise honey according to its type and floral origin, which may be useful for honey authenticity and traceability purposes. NTA may also be useful in a food safety-based context if some of the annotated discriminant features responsible for the clustering of honeys by their floral origin are found to be anthropogenic contaminants.

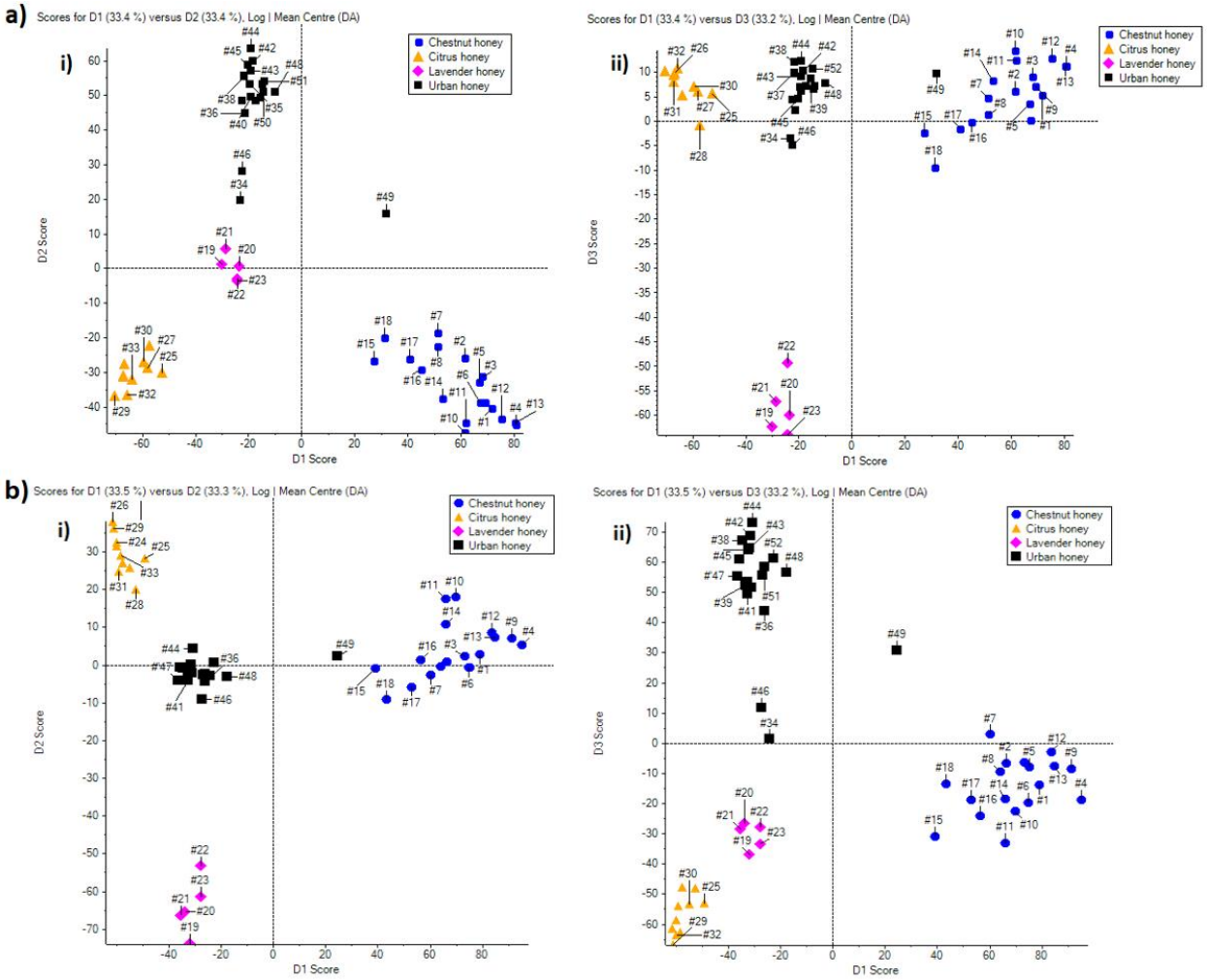

Fig.5. Separation of the groups of honey samples to identify potential markers of floral origin using principal component discriminant analysis (PCA-Da): (a) dimension 1 (D1) and D2 in ESI^+; (b) D1 and D3 in ESI^+; (c) D1 and D2 in ESI^-; (d) D1 and D3 in ESI^-.

3.4.2. Application of NTA to explore geographical origin markers of chestnut honeys

Non-targeted analysis were also conducted to highlight differences between honey samples with the same floral origin, but related to different geographical areas. In this study, chestnut honey samples originating from France, Italy and Spain were separated using PCA-Da (Fig. 6). The score plots showed excellent discrimination in both ESI^+ (Fig. 6ai) and ESI^- (Fig. 6bi). PCA-Da loading plots (Fig.6aii for ESI^+ and Fig.6bii for ESI^-) were then used to highlight the features responsible for the separation between these three groups. Their significance was verified and only features with fold changes of ≥ 10 and *p*-values of ≤ 0.01 were kept (Table S6). In ESI^+, three and two features were found to be discriminant for the separation of French and Italian chestnut honey, respectively (Table S7), and there was no feature that was significant for the separation of Spanish chestnut honey. Nevertheless, the analysis in ESI^- highlighted various features that were highly discriminant for the separation of Spanish chestnut honey (Table S7). However, the number of samples analysed was limited, especially for Spanish chestnut honey (n=4), which calls for additional studies with a larger panel of chestnut honey samples to confirm or reject the tentative markers highlighted in the present work, as well as to validate the PCA-DA model. Furthermore, all the potential markers found should also be tentatively annotated to describe and characterise the chemical constituents that discriminate chestnut honey originating from different locations. Because our study did not aim to annotate non-targeted features, future investigations need to be designed with the appropriate methodology for structure determination and annotation. This may be very helpful to ensure efficiently chestnut honey traceability. If some of the annoted features are found to be anthropogenic contaminants, this could help to highlight specific contaminations or treatments according to geographical origin, which may be useful in food safety-based context.

4. Conclusion

Here, we demonstrated the usefulness and the versatility of LC-HRMS by conducting a proof-of-concept study on 52 different honey samples. For the honey sample processing, we used a single method based on a QuEChERS protocol, optimised in a previous study for the specific screening of anthropogenic contaminants in sugary products (Makni et al., 2023). The samples were analysed using UHPLC and ESI-Q-ToF-MS. A single analytical batch in ESI^+ and in ESI^- was sufficient and designed with appropriate QA and QC procedures, complying with the requirements of quality standards for metabolomics and NTA studies. Using this method, we successfully carried out (a) the large-scale targeted analysis of 52 honey samples to screen for 694 various contaminants for which analytical standards were available; (b) SSA using open-access MSDial software to search for other anthropogenic contaminants to extend the analytical coverage, as well as endogenous compounds to identify markers of floral origin of the honey samples; (c) NTA using multivariate and univariate statistical tools for an in-depth investigation of features that could be floral and geographical origin markers of the honey samples.

This work was a feasibility study carried out on honey only, but the presented approaches and methodologies can be easily transposed to other foodstuffs. The critical merits of the method used here are the use of an ‘all-in-one’ sample preparation method to screen for anthropogenic contaminants and endogenous compounds, and how the same LC-HRMS data are easily re-used for various analytical applications using different approaches. HRMS is proving very useful for the determination of anthropogenic contaminants and markers. In routine testing laboratories, HRMS can be used in complement to LC/GS-MS/MS to extend the scope of the analysis, and highlight misuses, mixtures and contaminants of emerging concern. Moreover, for addressing issues of honey authenticity, this method can help to better trace honey to detect

fraud. In a food-safety context, our method can help highlight contaminants responsible for the separation of honey samples according to their floral or geographical origin, thereby potentially highlighting the use of treatments applied to a particular plant species or specific to a geographical area.

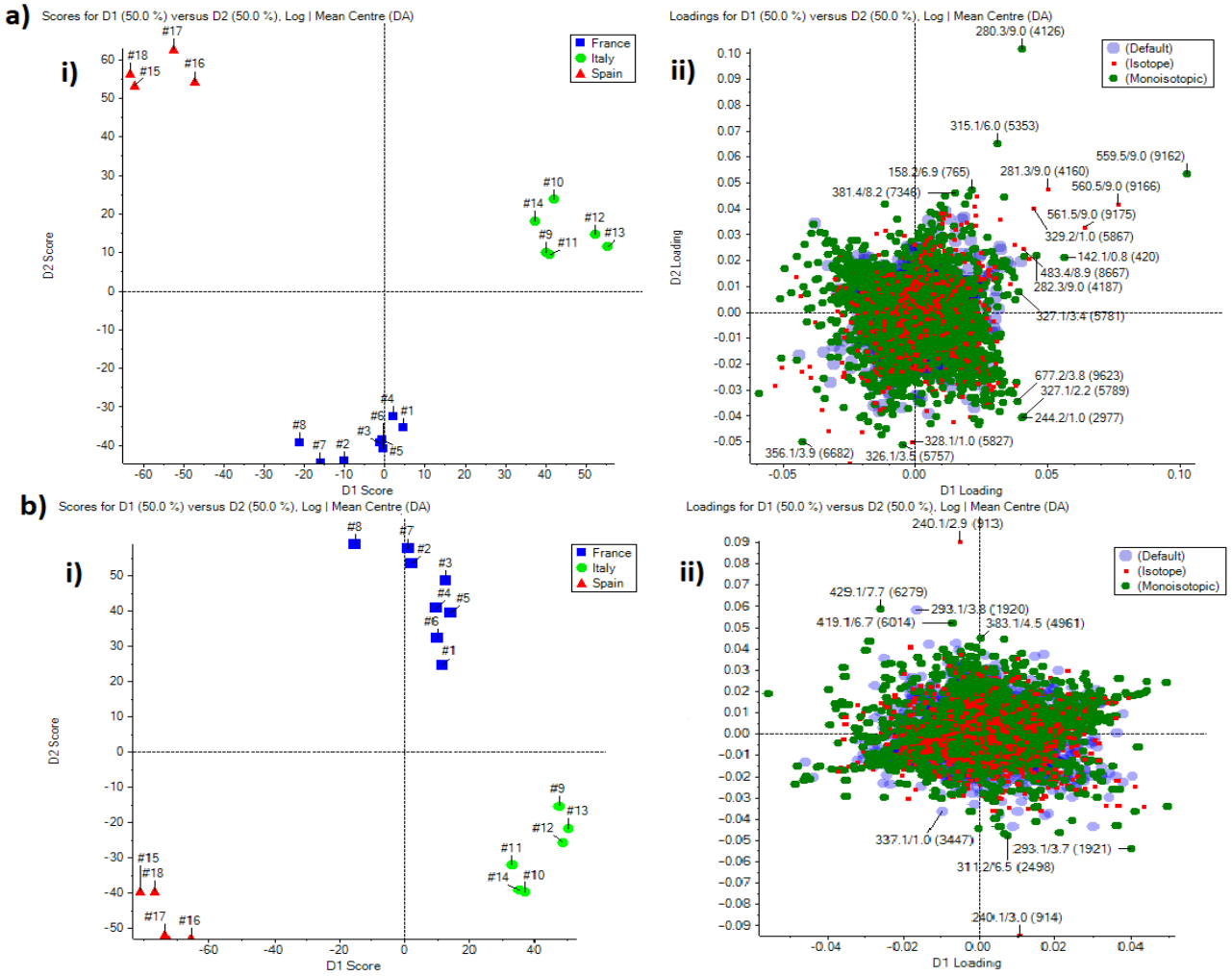

Fig 6. Separation of chestnut honey samples according to their geographical origin using principal component discriminant analysis (PCA-Da): (a) PCA-Da generated in ESI^+ (b) PCA-Da generated in ESI^-. (i) PCA-Da score plots of chestnut honey samples; (ii) PCA-Da loading plots of chestnut honey samples.

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Declaration of competing interest

The authors declare they have no conflicts and competing financial interest.

3.1.4. Summary and main results

In this work, we proposed a feasibility study on honey to highlight the versatility of HRMS. By integrating a robust and efficient quality control system, we were able to reliably carry out: (i) targeted broad-spectrum analyses using a database of 850 contaminants for which we had analytical standards. These targeted analyses enabled us to identify 23 contaminants, mainly pesticide residues, including neonicotinoid insecticides, as well as triazole fungicides and synergist compounds, which potentiate the toxicological effect of neonicotinoids. (ii) suspected analyses using MSDial open-access software and MS/MS lists from the MoNA database to broaden the spectrum of contaminants sought. These suspect analyses enabled the provisional identification of 30 emerging and little researched contaminants, some of which were never reported in honey. These results underline the importance of not only considering prioritized contaminants, but if possible, going much further. (iii) suspect analyses using MSDial software and MS/MS lists from MoNA database to search for endogenous compounds, markers of floral origin. We were able to highlight markers for chestnut and citrus honeys. (iv) non-targeted analyses for in-depth research of markers of honey type (rural vs. urban), as well as markers of floral and geographical origin.

3.1.5. Limitations and prospects for improvements

In the light of the presented work presented, certain important limitations stand out. Indeed, one of the main limitations was not being able to annotate the features highlighted using multivariate and non-targeted analyses, and responsible for the differentiation of honey samples according to their floral and geographical origins. It would be important to develop a methodology for annotation, as this would help to highlight chemical substances that would serve as specific markers of food samples. It could also enable the highlighting of contamination specific to a geographical area or floral origin.

Another limitation lies in the number of samples and varieties of honey included and used in this study. It would be useful to be able to include more samples of the same honey category, but also to include other widely consumed honey, such as acacia, eucalyptus or multi-flower honeys, for example. It would be interesting to be able to highlight floral markers of these honey typologies, with a sufficiently large data set to facilitate their statistical significance.

END

General conclusion and outlook

1. Conclusion

Faced with the scale of the increase in chronic and multi-factorial pathologies, some of which are associated with dietary exposure to chemicals, a change of approach is called for in the current food safety system, which is not sufficiently taking into account possible combined and "cocktail" effects of chemical mixtures. The aim of the works carried out during this thesis was to highlight the effectiveness of HRMS in improving the current food safety system, and to better characterize the French food chemical exposome. To this end, it was imperative to develop tools and methods capable of analyzing several hundred or even more than a thousand chemicals in a single analysis, accurately, precisely and automatically. In this context, various analytical developments and method optimizations were carried out, for the broad-spectrum and multiresidue analysis of contaminants in a variety of food products. Indeed, we succeeded in developing methods for the analysis of 204 pesticide residues in baby food (Makni et al., 2022) and in bivalves (Diallo et al., 2022), as well as for the analysis of 694 and 850 contaminants in sugary products (Makni et al., 2023a) and seafood (Diallo et al., 2023), respectively.

A major effort was made to optimize sample preparation, which is the key step in an analysis to cover the largest possible spectrum of contaminants, especially in HRMS. For these optimizations, we used Taguchi fractional factorial experimental designs, which allow simultaneous evaluation of several parameters that influence method performances, while reducing the number of experiments required. This work also provided us with the opportunity to propose a new sample preparation method, QuEChUP, which is a sequential method consisting of an initial QuEChERS extraction, followed by a QuPPE extraction, and a common purification of the two combined extracts. This new method shows promise, as in the literature, QuEChERS extraction methods are the most commonly used for multi-residue analysis in food matrices. However, the extraction of polar compounds such as certain veterinary drugs generally requires complementary methods. The newly proposed QuEChUP method enables the analysis of polar chemicals such as certain drug residues, but also covers compounds with a more dynamic range of polarity, such as pesticide residues or certain industrial contaminants, classically extracted with a QuEChERS protocol. This represents a significant advance in the field of multi-residue analysis of contaminants in foodstuffs, because this method extends the chemical coverage and therefore covers a broader spectrum of contaminants. The multiresidue extraction methods developed and proposed as a result of this thesis project are in line with the logic of extended analyses in HRMS, to better characterize consumer exposure and improve the food safety system.

In addition to sample preparation, other aspects of HRMS analysis were evaluated in the course of this thesis, such as the criteria and algorithms used for HRMS detection and identification, and the MS/MS acquisition modes. Extensive optimizations were carried out, particularly on acquisition modes, which represent a significant challenge in HRMS. The IDA mode was preferred to the SWATH-MS mode, as it provided much higher-quality MS/MS spectra, facilitating compound identification. However, further optimization of the IDA mode was necessary to improve the overall performance of the method and reduce the possibility of non-fragmentation of certain analytes of interest. This enabled us to significantly improve the performances of the method obtained between the first two analytical development works (Diallo et al., 2022; Makni et al., 2022), and the next two (Diallo et al., 2023; Makni et al., 2023a).

Also, one of the main strengths and original features of the conducted works was to propose methodologies for the targeted semi-quantification of several hundred contaminants in food matrices. These semi-quantification methods were successfully published, which are easy to

implement, inexpensive and compatible with multiresidue contaminant and high-throughput sample analysis. Further studies are required to verify their accuracy and reliability over time. Nevertheless, these semi-quantification methods could be very useful for high-throughput analysis of samples using HRMS, as they would provide quantitative data for a wider spectrum of contaminants than just those prioritized and routinely analyzed by tandem mass spectrometry. If implemented, this would lead to a better characterization of the risk associated with dietary exposure to chemical substances.

Furthermore, the works conducted will have enabled us to implement robust and automated suspect screening approaches, for an extended search for emerging and little-researched chemicals, without the analytical standards being available in the laboratory. These approaches, exclusive to HRMS, represent a real asset for improving the scope of monitoring and better characterizing consumer food exposure. In particular, a number of industrial contaminants and emerging substances could have been annotated, notably in fish products and honeys, using automated and large-scale suspect analyses.

Finally, non-targeted and multivariate workflows could be implemented, in order to characterize honey samples according to their type, floral and geographical origins. This could prove very useful in the context of food authenticity and traceability, but also for food safety in the event that the markers responsible for separating food samples are contaminants or chemicals of concern.

Overall, this research has contributed within the agency to highlighting HRMS as a tool of choice for improving food safety, and better characterizing the contaminants and chemical mixtures to which consumers are exposed. HRMS is a system that could be well integrated into routine laboratories in complement to LC-MS/MS, as an "early warning" system. Indeed, HRMS could be used to broaden the lists of contaminants and chemicals searched for, beyond those that are prioritized or of interest to the laboratory. This could help to alert on possible emergences such as the controversial occurrence and almost ubiquitous of some PFAS in the environment and food chain. It could also help to alert on misuses, allowing to prevent health scandals such as in 2017, when Belgian eggs were contaminated with Fipronil, a prohibited substance.

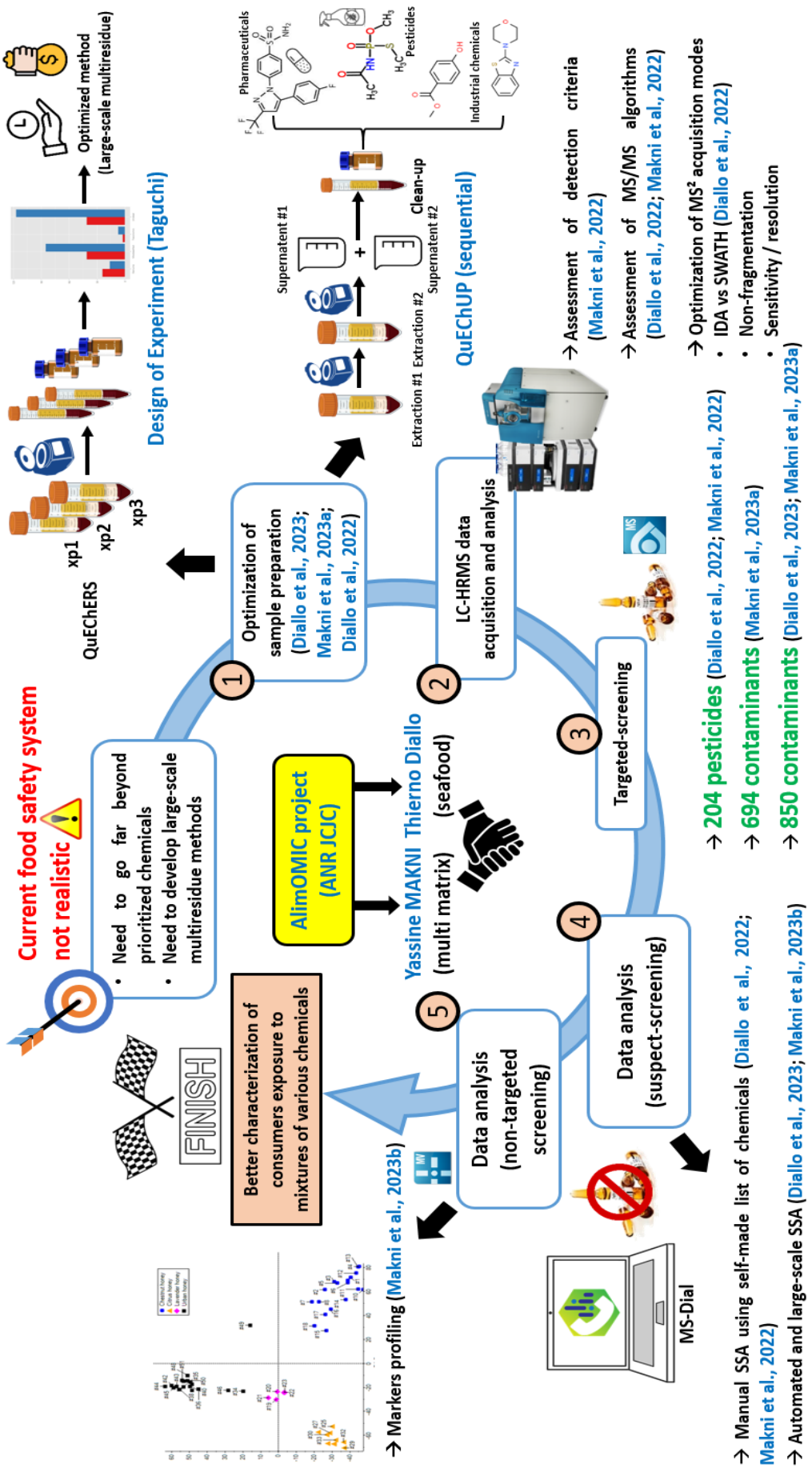

Fig.1. Summary of the work conducted and articles published within the framework of the AlimOMIC project and thesis

2. Limitations and outlook

a. Limitations and outlook of our works

In view of the work that was carried out, it would be necessary to include other families of contaminants and foodstuffs in future analytical developments. Indeed, for cost and practical reasons, pesticide and veterinary drug residues were the main families of chemical substances to used for method development and validation during this thesis. However, bearing in mind that we wish to use these methods to better characterize the actual state of consumer exposure, without being limited exclusively to pesticides and drugs, it is crucial to assess the methods on other types of chemicals frequently found in foodstuffs. In this sense, this is lacking in the conducted work, and therefore, represents a major limitation.

Moreover, analytical developments using GC-HRMS systems should be conducted. Indeed, the complementarity between LC and GC analysis is essential to cover polar to moderately polar contaminants, as well as non-polar substances. Unfortunately, this complementarity is a missing element in the works of this thesis, as the laboratory for food safety at Anses Maisons-Alfort is not yet equipped with a GC-HRMS system. This represents a major limitation to the research and method development that can be carried out internally, as part of the analytical chemical coverage is not taken into account.

Still from an instrumental, point of view the methods developed using HRMS were not compared with those available in LC-MS/MS within the laboratory. It would be important to demonstrate that the sensitivities obtained with the two types of instruments are not very far apart, in addition to the fact that HRMS systems enable to considerably increase the monitoring field, as was emphasized during this thesis. This would be a further convincing argument in favor of integrating HRMS into MCPs, as a complement to tandem mass spectrometry.

All the methods already developed, as well as those to be developed shortly (development in fruit, vegetables & meat), will be used for massive sample analysis as part of TDS carried out by Anses. These official studies are invaluable for assessing consumer exposure, with large-scale sampling representative of French dietary habits. HRMS analysis of these samples, in complement to LC/GC-MS/MS analysis, would enable the detection of newly emerging contaminants that are not targeted in this new TDS. In collaboration with the DER of Anses, these data could be used to warn of mixtures of chemical substances to which French consumers are exposed, in order to improve investigation and monitoring of their effects on human health.

b. Current limitations to integrate HRMS in routine

Although HRMS is a first-rate tool for improving the current food safety system, their acquisition implied high-cost instrumentation compared with tandem mass spectrometry. This represents a considerable limitation, as not all laboratories, or even some developing countries, possess the necessary budgets to integrate such instruments into their labs.

Another current limitation for integrating HRMS in routine is the lack of standardized protocols for analysis. Indeed, when methods are developed and validated in reference laboratories such as in laboratory for food safety of Anses, they are officially shared to the network of routine food control laboratories. However, this require prior evaluation of the performances achieved by the laboratories of the network during their participation in an interlaboratory proficiency test. Nevertheless, a lack of standardization in HRMS methods could make it difficult to compare results, as well as to apply methods to other high-resolution instruments. It appears crucial that the protocols and identification criteria used in HRMS be standardized, so that operators can rely on a common consensus making it possible to provide reliable and comparable results.

A final limitation would be the higher complexity of data processing in HRMS, particularly for suspect and non-targeted analysis. This requires additional skills over and above conventional targeted data processing. Considerable skills transfer is needed to adapt routine operators and analysts to these complex analyses. These approaches also require standardization of the tools and criteria to be used, as suspect and non-targeted analyses imply that analytical standards are not available in the laboratory

Annexes (Electronic Supplementary Materials)

CHAPTER 2: Development of analytical methods for the multiresidue and large-scale screening of contaminants in food samples

Article 1 (Makni et al., 2022): "Improving the monitoring of multi-class pesticides in baby foods using QuEChERS-UHPLC-Q-TOF with automated identification based on MS/MS similarity algorithms"

Table S1. List of the targeted pesticides with their corresponding formula, adduct or in-source fragment, theoretical *m/z* and retention time.

Pesticide	Mix number #	Formula [M]	Ion	Theoretical *m/z*	t_r (min)	LogP
Acephate	1	$C_4H_{10}NO_3PS$	$C_2H_8O_3PS^+$	142.99263	0.95	-0.85
Carbaryl	1	$C_{12}H_{11}NO_2$	$C_{10}H_9O^+$	145.06479	5.02	2.36
Dicrotophos	1	$C_8H_{16}NO_5P$	$[M+H]^+$	238.08389	2.58	0
Dimethoate	1	$C_5H_{12}NO_3PS_2$	$[M+H]^+$	230.0069	3.37	0.78
Dimethomorph	1	$C_{21}H_{22}ClNO_4$	$[M+H]^+$	388.13101	5.92	2.68
Isocarbophos	1	$C_{11}H_{16}NO_4PS$	$C_8H_8O_4PS^+$	230.98755	5.81	2.64
Methamidophos	1	$C_2H_8NO_2PS$	$[M+H]^+$	142.00862	0.96	-0.8
Mevinphos	1	$C_7H_{13}O_6P$	$C_6H_{10}O_5^+$	193.02604	3.63	0.13
Monocrotophos	1	$C_7H_{14}NO_5P$	$[M+H]^+$	224.06824	2.31	-0.2
Omethoate	1	$C_5H_{12}NO_4PS$	$[M+H]^+$	214.02974	0.96	-0.74
Temephos	1	$C_{16}H_{20}O_6P_2S_3$	$[M+H]^+$	466.99701	8.16	5.96
Trichlorfon	1	$C_4H_8Cl_3O_4P$	$[M+H]^+$	256.92986	2.93	0.51
Vamidothion	1	$C_8H_{18}NO_4PS_2$	$[M+H]^+$	288.04877	2.94	0.16
Alanycarb	2	$C_{17}H_{25}N_3O_4S_2$	$[M+H]^+$	400.13593	NA	3.43
Aldicarb sulfone / Butoxycarboxim (co-eluted)	2	$C_7H_{14}N_2O_4S$	$[M+H]^+$	223.07471	2.14	-0.57 / -0.72
Aldicarb sulfoxide	2	$C_7H_{14}N_2O_3S$	$[M+H]^+$	207.07979	1.8	/
Aldicarb	2	$C_7H_{14}N_2O_2S$	$[M+Na]^+$	213.06682	4.1	1.13
Benfuracarb	2	$C_{20}H_{30}N_2O_5S$	$[M+NH_4]^+$	428.22137	8.1	4.3
Butocarboxim	2	$C_7H_{14}N_2O_2$ S	$[M+Na]^+$	213.06682	3.9	1.1
Ethiofencarb	2	$C_{11}H_{15}NO_2S$	$[M+H]^+$	226.08963	5.19	2.04

Furathiocarb	2	$C_{18}H_{26}N_2O_5S$	$[M+H]^+$	383.16352	8.09	4.7
Methabenzthiazuron	2	$C_{10}H_{11}N_3OS$	$[M+H]^+$	222.06956	4.95	2.64
Methiocarb	2	$C_{11}H_{15}NO_2S$	$[M+H]^+$	226.08963	5.96	2.92
Methomyl	2	$C_5H_{10}N_2O_2S$	$[M+H]^+$	163.05358	2.41	0.6
Oxamyl	2	$C_7H_{13}N_3O_3S$	$[M+H]^+$	220.07504	2.28	-0.47
Tebuthiuron	2	$C_9H_{16}N_4OS$	$[M+H]^+$	229.11176	4.11	1.79
Thidiazuron	2	$C_9H_8N_4OS$	$[M+H]^+$	221.04916	4.15	1.77
Thiophanate-methyl	2	$C_{12}H_{14}N_4O_4S_2$	$[M+H]^+$	343.05293	4.54	1.4
3-Hydroxycarbofuran	3	$C_{12}H_{15}NO_4$	$C_{12}H_{14}NO_3^+$	220.09682	3.15	0.76
Bendiocarb	3	$C_{11}H_{13}NO_4$	$[M+H]^+$	224.09173	4.76	1.7
Bifenazate	3	$C_{17}H_{20}N_2O_3$	$C_{13}H_{12}NO^+$	198.09134	6.52	3.4
Carbofuran	3	$C_{12}H_{15}NO_3$	$[M+H]^+$	222.11247	4.83	2.32
Chlorfluazuron	3	$C_{20}H_9Cl_3F_5N_3O_3$	$[M+H]^+$	539.97024	8.41	5.8
Chlorotoluron	3	$C_{10}H_{13}ClN_2O$	$[M+H]^+$	213.07892	4.99	2.41
Chloroxuron	3	$C_{15}H_{15}ClN_2O_2$	$[M+H]^+$	291.08948	6.15	3.7
Cycluron	3	$C_{11}H_{22}N_2O$	$[M+H]^+$	199.18049	5.17	/
Diethofencarb	3	$C_{14}H_{21}NO_4$	$[M+H]^+$	268.15433	6.11	2.91
Diflubenzuron	3	$C_{14}H_9ClF_2N_2O_2$	$[M+H]^+$	311.03934	6.53	3.88
Dioxacarb	3	$C_{11}H_{13}NO_4$	$[M+H]^+$	224.09173	3.43	0.67
Diuron	3	$C_9H_{10}Cl_2N_2O$	$[M+H]^+$	233.02429	5.26	2.68
Fenobucarb	3	$C_{12}H_{17}NO_2$	$[M+H]^+$	208.13321	5.97	2.78
Fenoxycarb	3	$C_{17}H_{19}NO_4$	$[M+H]^+$	302.13868	6.72	4.3
Fenuron	3	$C_9H_{12}N_2O$	$[M+H]^+$	165.10224	3.24	0.98
Flufenoxuron	3	$C_{21}H_{11}ClF_6N_2O_3$	$[M+H]^+$	489.04352	8.19	6.16
Fluometuron	3	$C_{10}H_{11}F_3N_2O$	$[M+H]^+$	233.08962	5.06	2.42
Forchlorfenuron	3	$C_{12}H_{10}ClN_3O$	$[M+H]^+$	248.05852	5.01	3.2
Hexaflumuron	3	$C_{16}H_8Cl_2F_6N_2O_3$	$[M+H]^+$	460.98889	7.46	5.68
Indoxacarb	3	$C_{22}H_{17}ClF_3N_3O_7$	$[M+H]^+$	528.07799	7.63	4.65
Iprovalicarb	3	$C_{18}H_{28}N_2O_3$	$[M+H]^+$	321.21727	6.22	/
Isoprocarb	3	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.42	2.31
Isoproturon	3	$C_{12}H_{18}N_2O$	$[M+H]^+$	207.14919	5.25	2.87
Linuron	3	$C_9H_{10}Cl_2N_2O_2$	$[M+H]^+$	249.01921	6.06	3.2
Lufenuron	3	$C_{17}H_8Cl_2F_8N_2O_3$	$[M+H]^+$	510.9857	7.99	5.12
Metobromuron	3	$C_9H_{11}BrN_2O_2$	$[M+H]^+$	259.00767	5.43	2.38
Monolinuron	3	$C_9H_{11}ClN_2O_2$	$[M+H]^+$	215.05818	5.22	2.3

Neburon	3	$C_{12}H_{16}Cl_2N_2O$	$[M+H]^+$	275.07125	6.9	4.1
Novaluron	3	$C_{17}H_9ClF_8N_2O_4$	$[M+H]^+$	493.01959	7.63	5.27
Pirimicarb	3	$C_{11}H_{18}N_4O_2$	$[M+H]^+$	239.15025	3.9	1.7
Promecarb	3	$C_{12}H_{17}NO_2$	$[M+H]^+$	208.13321	6.15	3.1
Propham	3	$C_{10}H_{13}NO_2$	$C_7H_8NO_2^+$	138.05496	5.56	2.6
Propoxur	3	$C_{11}H_{15}NO_3$	$C_8H_{10}NO_3^+$	168.06552	4.78	1.52
Pyraclostrobin	3	$C_{19}H_{18}ClN_3O_4$	$[M+H]^+$	388.10586	7.4	3.99
Siduron	3	$C_{14}H_{20}N_2O$	$[M+H]^+$	233.16484	5.85	3.8
Teflubenzuron	3	$C_{14}H_6Cl_2F_4N_2O_2$	$[M+H]^+$	380.98152	7.56	4.56
Thiobencarb	3	$C_{12}H_{16}ClNOS$	$[M+H]^+$	258.07139	7.53	3.4
Triflumuron	3	$C_{15}H_{10}ClF_3N_2O_3$	$[M+H]^+$	359.04048	7.1	4.91
Acetamiprid	4	$C_{10}H_{11}ClN_4$	$[M+H]^+$	223.0745	3.5	0.8
Ametryn	4	$C_9H_{17}N_5S$	$[M+H]^+$	228.12774	5.14	2.98
Amitraz	4	$C_{19}H_{23}N_3$	$C_{10}H_{15}N_2^+$	163.12298	NA	5.5
Avermectin	4	$C_{48}H_{72}O_{14}$	$[M+Na]^+$	895.48143	8.99	4.4
Azoxystrobin	4	$C_{22}H_{17}N_3O_5$	$[M+H]^+$	404.1241	6.24	2.5
Benalaxyl	4	$C_{20}H_{23}NO_3$	$[M+H]^+$	326.17507	7.15	3.4
Benzoximate	4	$C_{18}H_{18}ClNO_5$	$C_9H_8ClO_3^+$	199.01565	7.71	3.73
Boscalid	4	$C_{18}H_{12}Cl_2N_2O$	$[M+H]^+$	343.03995	6.4	2.96
Butafenacil	4	$C_{20}H_{18}ClF_3N_2O_6$	$[M+NH_4]^+$	492.11437	6.89	3.2
Carbetamide	4	$C_{12}H_{16}N_2O_3$	$[M+H]^+$	237.12337	4.1	1,75
Carfentrazone-ethyl	4	$C_{15}H_{14}Cl_2F_3N_3O_3$	$[M+H]^+$	412.04371	7.03	3.36
Chlorantraniliprole	4	$C_{18}H_{14}BrCl_2N_5O_2$	$[M+H]^+$	481.97807	5.75	2.76
Clofentezine	4	$C_{14}H_8Cl_2N_4$	$[M+H]^+$	303.01988	7.49	3.1
Cymoxanil	4	$C_7H_{10}N_4O_3$	$C_4H_6N_3O_2^+$	128.04545	3.77	0.59
Cyprodinil	4	$C_{14}H_{15}N_3$	$[M+H]^+$	226.13387	6.57	4
Cyromazine	4	$C_6H_{10}N_6$	$[M+H]^+$	167.10397	0.86	-0.06
Dimoxystrobin	4	$C_{19}H_22N_2O_3$	$[M+H]^+$	327.17032	6.83	/
Dinotefuran	4	$C_7H_{14}N_4O_3$	$[M+H]^+$	203.11387	1.87	-0.55
Doramectin	4	$C_{50}H_{74}O_{14}$	$[M+Na]^+$	921.49708	9.39	4.4
Eprinomectin	4	$C_{50}H_{75}NO_{14}$	$[M+Na]^+$	936.50798	8.56	5.7
Famoxadone	4	$C_{22}H_{18}N_2O_4$	$[M+NH_4]^+$	392.16048	7.25	4.65
Fenazaquin	4	$C_{20}H_{22}N_2O$	$[M+H]^+$	307.18049	8.69	5.51
Fenhexamid	4	$C_{14}H_{17}Cl_2NO_2$	$[M+H]^+$	302.07091	6.39	3.51
Fenpyroximate	4	$C_{24}H_{27}N_3O_4$	$[M+H]^+$	422.20743	8.56	5.01

Flonicamid	4	$C_9H_6F_3N_3O$	$[M+H]^+$	230.05357	2.75	0.3
Fluazinam	4	$C_{13}H_4Cl_2F_6N_4O_4$	$[M+H]^+$	464.95866	8.01	4.01
Fludioxonil	4	$C_{12}H_6F_2N_2O_2$	$[M+H]^+$	249.04701	5.01	4.12
Fluoxastrobin	4	$C_{21}H_{16}ClFN_4O_5$	$[M+H]^+$	459.0866	6.78	2.86
Flutolanil	4	$C_{17}H_{16}F_3NO_2$	$[M+H]^+$	324.12059	6.66	3.7
Furalaxyl	4	$C_{17}H_{19}NO_4$	$[M+H]^+$	302.13868	6.03	2.61
Halofenozide	4	$C_{18}H_{19}ClN_2O_2$	$[M+H]^+$	331.12078	6.13	3.22
Imazalil	4	$C_{14}H_{14}Cl_2N_2O$	$[M+H]^+$	297.0556	3.95	3.82
Imidacloprid	4	$C_9H_{10}ClN_5O_2$	$[M+H]^+$	256.05958	3.24	0.57
Ivermectin	4	$C_{48}H_{74}O_{14}$	$[M+Na]^+$	897.49708	9.9	5.83
Kresoxim-methyl	4	$C_{18}H_{19}NO_4$	$[M+H]^+$	314.13868	7.09	3.4
Mandipropamid	4	$C_{23}H_{22}ClNO_4$	$[M+H]^+$	412.13101	6.31	3.2
Mepanipyrim	4	$C_{14}H_{13}N_3$	$[M+H]^+$	224.11822	6.55	3.28
Mepronil	4	$C_{17}H_{19}NO_2$	$[M+H]^+$	270.14886	6.6	3.66
Metaflumizone	4	$C_{24}H_{16}F_6N_4O_2$	$[M+H]^+$	507.12502	7.89	/
Metalaxyl	4	$C_{15}H_{21}NO_4$	$[M+H]^+$	280.15433	5.28	1.65
Methoxyfenozide	4	$C_{22}H_{28}N_2O_3$	$C_{18}H_{21}N_2O_3^+$	313.15467	6.58	3.7
Moxidectin	4	$C_{37}H_{53}NO_8$	$[M+H]^+$	640.38439	9.44	6
Myclobutanil	4	$C_{15}H_{17}ClN_4$	$[M+H]^+$	289.12145	6.22	2.94
Nitenpyram	4	$C_{11}H_{15}ClN_4O_2$	$[M+H]^+$	271.09563	2.17	-0.66
Oxadixyl	4	$C_{14}H_{18}N_2O_4$	$[M+H]^+$	279.13393	4.3	0.8
Picoxystrobin	4	$C_{18}H_{16}F_3NO_4$	$[M+H]^+$	368.11042	7.14	3.6
Piperonyl butoxide	4	$C_{19}H_{30}O_5$	$[M+NH_4]^+$	356.24315	8.1	4.75
Prochloraz	4	$C_{15}H_{16}Cl_3N_3O_2$	$[M+H]^+$	376.03809	6.66	4.1
Prometon / Secbumeton / Terbumeton (co-eluted)	4	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.28	2.99 / 3.1 / 3.1
Pymetrozine	4	$C_{10}H_{11}N_5O$	$[M+H]^+$	218.10364	0.96	-0.18
Pyracarbolid	4	$C_{13}H_{15}NO_2$	$[M+H]^+$	218.11756	4.95	/
Pyrimethanil	4	$C_{12}H_{13}N_3$	$[M+H]^+$	200.11822	5.61	2.84
Pyriproxyfen	4	$C_{20}H_{19}NO_3$	$[M+H]^+$	322.14377	8.23	5.37
Quinoxyfen	4	$C_{15}H_8Cl_2FNO$	$[M+H]^+$	308.00397	8.09	4.66
Rotenone	4	$C_{23}H_{22}O_6$	$[M+H]^+$	395.14892	6.81	4.1
Spiroxamine	4	$C_{18}H_{35}NO_2$	$[M+H]^+$	298.27406	4.59	/
Tebufenozide	4	$C_{22}H_{28}N_2O_2$	$C_{18}H_{21}N_2O_2^+$	297.15975	6.98	4.25
Tebufenpyrad	4	$C_{18}H_{24}ClN_3O$	$[M+H]^+$	334.16807	7.96	4.61

Triadimefon	4	$C_{14}H_{16}ClN_3O_2$	$[M+H]^+$	294.10038	6.36	2.77
Trifloxystrobin	4	$C_{20}H_{19}F_3N_2O_4$	$[M+H]^+$	409.13697	7.75	4.5
Zoxamide	4	$C_{14}H_{16}Cl_3NO_2$	$[M+H]^+$	336.03194	7.31	3.76
Acibenzolar-S-methyl	5	$C_8H_6N_2OS_2$	$[M+H]^+$	210.99943	6.17	3.1
Bupirimate	5	$C_{13}H_{24}N_4O_3S$	$[M+H]^+$	317.16419	6.6	2.7
Buprofezin	5	$C_{16}H_{23}N_3OS$	$[M+H]^+$	306.16346	8.07	4.3
Carboxin	5	$C_{12}H_{13}NO_2S$	$[M+H]^+$	236.07398	5.16	2.14
Clethodim	5	$C_{17}H_{26}ClNO_3S$	$[M+H]^+$	360.13947	7.98	4.21
Clothianidin	5	$C_6H_8ClN_5O_2S$	$[M+H]^+$	250.016	3.06	0.7
Cyazofamid	5	$C_{13}H_{13}ClN_4O_2S$	$[M+H]^+$	325.05205	7.02	3.2
Ethiprole	5	$C_{13}H_9Cl_2F_3N_4OS$	$[M+H]^+$	396.9899	5.92	2.9
Ethofumesate	5	$C_{13}H_{18}O_5S$	$[M+NH_4]^+$	304.12132	6.44	2.7
Fenamidone	5	$C_{17}H_{17}N_3OS$	$[M+H]^+$	312.11651	6.28	2.8
Fipronil	5	$C_{12}H_4Cl_2F_6N_4OS$	$[M+H]^+$	436.94598	6.97	4
Flubendiamide	5	$C_{23}H_{22}F_7IN_2O_4S$	$[M+H]^+$	683.03061	6.97	4.2
Flufenacet	5	$C_{14}H_{13}F_4N_3O_2S$	$[M+H]^+$	364.07374	6.79	3.2
Hexythiazox	5	$C_{17}H_{21}ClN_2O_2S$	$[M+H]^+$	353.1085	8.36	5.57
Mefenacet	5	$C_{16}H_{14}N_2O_2S$	$[M+H]^+$	299.08488	6.36	3.23
Mesotrione	5	$C_{14}H_{13}NO_7S$	$[M+H]^+$	340.04855	4.49	0.9
Methoprotryne	5	$C_{11}H_{21}N_5OS$	$[M+H]^+$	272.15396	5.1	2.82
Metribuzin	5	$C_8H_{14}N_4OS$	$[M+H]^+$	215.09611	NA	1.7
Prometryne / Terbutryn (co-eluted)	5	$C_{10}H_{19}N_5S$	$[M+H]^+$	189.15975	0.96	3.51 / 3.74
Propargite	5	$C_{19}H_{26}O_4S$	$[M+NH_4]^+$	368.18901	8.54	5
Prothioconazole	5	$C_{14}H_{15}Cl_2N_3OS$	$[M+H]^+$	344.03857	6.67	3.82
Pyridaben	5	$C_{19}H_{25}ClN_2OS$	$[M+H]^+$	365.14489	8.93	6.37
Simetryn	5	$C_8H_{15}N_5S$	$[M+H]^+$	214.11209	4.39	2.8
Sulfentrazone	5	$C_{11}H_{10}Cl_2F_2N_4O_3S$	$[M+H]^+$	386.98915	4.99	0.99
Thiabendazole	5	$C_{10}H_7N_3S$	$[M+H]^+$	202.04335	2.32	2.47
Thiacloprid	5	$C_{10}H_9ClN_4S$	$[M+H]^+$	253.03092	3.94	1.26
Thiamethoxam	5	$C_8H_{10}ClN_5O_3S$	$[M+H]^+$	292.02657	2.68	-0.13
Thiofanox	5	$C_9H_{18}N_2O_2S$	$[M+Na]^+$	241.09812	5.14	/
Tricyclazole	5	$C_9H_7N_3S$	$[M+H]^+$	190.04335	3.6	1.7

Bitertanol	6	$C_{20}H_{23}N_3O_2$	$[M+H]^+$	338.1863	6.73	4.16
Bromuconazole	6	$C_{13}H_{12}BrCl_2N_3O$	$[M+H]^+$	375.96136	6.25	3.24
Cyproconazole	6	$C_{15}H_{18}ClN_3O$	$[M+H]^+$	292.12112	6.04	2.9
Diclobutrazol	6	$C_{15}H_{19}Cl_2N_3O$	$[M+H]^+$	328.09779	6.57	3.8
Difenoconazole	6	$C_{19}H_{17}Cl_2N_3O_3$	$[M+H]^+$	406.07197	7.26	4.3
Diniconazole	6	$C_{15}H_{17}Cl_2N_3O$	$[M+H]^+$	326.08214	6.9	4.3
Epoxiconazole	6	$C_{17}H_{13}ClFN_3O$	$[M+H]^+$	330.08039	6.36	3.44
Etaconazole	6	$C_{14}H_{15}Cl_2N_3O_2$	$[M+H]^+$	328.06141	6.4	3.1
Ethirimol	6	$C_{11}H_{19}N_3O$	$[M+H]^+$	210.16009	2.83	2.22
Etoxazole	6	$C_{21}H_{23}F_2NO_2$	$[M+H]^+$	360.17696	8.55	5.59
Fenarimol	6	$C_{17}H_{12}Cl_2N_2O$	$[M+H]^+$	331.03995	6.25	3.6
Fenbuconazole	6	$C_{19}H_{17}ClN_4$	$[M+H]^+$	337.12145	6.58	3.23
Fluquinconazole	6	$C_{16}H_8Cl_2FN_5O$	$[M+H]^+$	376.01627	6.44	3.24
Flusilazole	6	$C_{16}H_{15}F_2N_3Si$	$[M+H]^+$	316.10761	6.58	3.7
Flutriafol	6	$C_{16}H_{13}F_2N_3O$	$[M+H]^+$	302.10995	5.04	2.29
Fuberidazole	6	$C_{11}H_8N_2O$	$[M+H]^+$	185.07094	2.44	2.67
Hexaconazole	6	$C_{14}H_{17}Cl_2N_3O$	$[M+H]^+$	314.08214	6.72	3.9
Ipconazole	6	$C_{18}H_{24}ClN_3O$	$[M+H]^+$	334.16807	7.28	4.21
Metconazole	6	$C_{17}H_{22}ClN_3O$	$[M+H]^+$	320.15242	6.82	3.85
Nuarimol	6	$C_{17}H_{12}ClFN_2O$	$[M+H]^+$	315.0695	5.69	3.18
Paclobutrazol	6	$C_{30}H_{40}Cl_2N_6O_2$	$[M+H]^+$	294.13677	5.9	3.2
Penconazole	6	$C_{13}H_{15}Cl_2N_3$	$[M+H]^+$	284.07158	6.77	3.72
Propiconazole	6	$C_{15}H_{17}Cl_2N_3O_2$	$[M+H]^+$	342.07706	6.95	3.72
Tebuconazole	6	$C_{16}H_{22}ClN_3O$	$[M+H]^+$	308.15242	6.57	3.7
Tetraconazole	6	$C_{13}H_{11}Cl_2F_4N_3O$	$[M+H]^+$	372.02881	6.41	3.56
Triadimenol	6	$C_{14}H_{18}ClN_3O_2$	$[M+H]^+$	296.11603	5.88	3.56
Triflumizole	6	$C_{15}H_{15}ClF_3N_3O$	$[M+H]^+$	346.09285	7.22	2.9
Triticonazole	6	$C_{17}H_{20}ClN_3O$	$[M+H]^+$	318.13677	6.09	3.29
Emamectin-benzoate	7	$C_{49}H_{75}NO_{13}$	$[M+H]^+$	886.53112	6.01	5.0
Fenpropimorph	7	$C_{20}H_{33}N_O$	$[M+H]^+$	304.26349	4.64	4.93
Spinetoram	7	$C_{42}H_{69}NO_{10}$	$[M+H]^+$	748.49942	5.88	/
Spinosad	7	$C_{41}H_{65}NO_{10}$	$[M+H]^+$	732.46812	5.47	2.8
Spirodiclofen	7	$C_{21}H_{24}Cl_2O_4$	$[M+H]^+$	411.11244	8.92	5.1

Spiromesifen	7	$C_{23}H_{30}O_4$	$[M+H]^+$	371.22169	8.81	4.55
Spirotetramat	7	$C_{21}H_{27}NO_5$	$[M+H]^+$	374.1962	6.11	/
Hydramethylnon	8	$C_{25}H_{24}F_6N_4$	$[M+H]^+$	495.19779	6.07	2.31
(Monceren) Pencycuron	9	$C_{19}H_{21}ClN_2O$	$[M+H]^+$	329.14152	7.53	4.82
Aminocarb	9	$C_{11}H_{16}N_2O_2$	$[M+H]^+$	209.12845	0.96	1.9
Desmedipham / Phenmedipham (co-eluted)	9	$C_{16}H_{16}N_2O_4$	$[M+H]^+$	318.14483	5.86	3.39 / 3.59
Formetanate HCl	9	$C_{11}H_{16}ClN_3O_2$	$[M+H]^+$	222.1237	0.96	0
Mexacarbate	9	$C_{12}H_{18}N_2O_2$	$[M+H]^+$	223.1441	3.5	2.56
Propamocarb	9	$C_9H_{20}N_2O_2$	$[M+H]^+$	242.14339	5.88	1.12
Carbendazim	10	$C_9H_9N_3O_2$	$[M+H]^+$	192.07675	2.1	1.52

Table S2. Composition of the supplied baby food samples.

Sample	Ingredients
Baby-food 1	Vegetables - Beef
Baby-food 2	Vegetables - Hake
Baby-food 3	Potatoes - Carrots - Beef
Baby-food 4	Tomatoes - Rice - Chicken
Baby-food 5	Apple - Pineapple
Baby-food 6	Apple - Pineapple
Baby-food 7	Apple - Blackcurrant
Baby-food 8	Apple - Blackcurrant
Baby-food 9	Carrots - Wheat semolina - Turkey meat - Onion
Baby-food 10	Carrots - Wheat semolina - Turkey meat - Onion
Baby-food 11	Carrots - Potatoes - Peas - Tomatoes - Ham - Turnips - Cauliflower
Baby-food 12	Carrots - Potatoes - Peas - Tomatoes - Ham - Turnips - Cauliflower
Baby-food 13	Peas - Green beans - Spinach - Salmon - Rice flour
Baby-food 14	Peas - Green beans - Spinach - Salmon - Rice flour

Table S3. Impact of different thresholds on the t_r and accurate mass measurement criteria regarding the false positives (%), in a set of 10 non-spiked baby food samples in triplicate.

	False positive (%) ± SD (%)		
	Reported criteria for detection		
Sample	**(t_r ± 0.1 min; ME ± 5-ppm)[1]**	**(t_r ± 0.5 min; ME ± 5-ppm)[2]**	**(t_r ± 0.25 min; ME ± 10-ppm)[3]**
Baby food 5	**6** ± 2	**8** ± 2	**13** ± 2
Baby food 6	**5** ± 1	**7** ± 1	**14** ± 3
Baby food 7	**5** ± 2	**7** ± 1	**11** ± 1
Baby food 8	**4** ± 0	**6** ± 1	**11** ± 3
Baby food 9	**3** ± 2	**5** ± 4	**9** ± 8
Baby food 10	**6** ± 1	**8** ± 2	**14** ± 3
Baby food 11	**3** ± 2	**5** ± 5	**9** ± 8
Baby food 12	**4** ± 4	**5** ± 5	**9** ± 8
Baby food 13	**6** ± 0	**8** ± 1	**15** ± 3
Baby food 14	**4** ± 4	**4** ± 4	**9** ± 8
Average (n = 30) ± SD (%)	**5 ± 2**	**6 ± 2**	**13 ± 5**

[1] SANTE/12682/2019; [2] FDA, 2015; Wang et al., 2019; [3] Pérez-Ortega et al., 2017

Table S4. Determination of SDL and LOI for each pesticide, regarding the 10 baby food samples in triplicate (n=30).

Pesticide	Number of detection out of 30 samples		SDL ($mg.kg^{-1}$)	Number of identification out of 30 samples		LOI ($mg.kg^{-1}$)
	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$		0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$	
(Monceren) Pencycuron	30	30	**0.01**	30	30	**0.01**
3-Hydroxycarbofuran	28	30	**0.1**	9	30	**0.1**
Acephate	9	30	**0.1**	0	4	**> 0.1**
Acetamiprid	0	30	**0.1**	0	30	**0.1**
Acibenzolar-S-methyl	30	30	**0.01**	19	30	**0.1**
Alanycarb	1	1	**> 0.1**	0	0	**> 0.1**
Aldicarb sulfone / Butoxycarboxim	28	30	**0.1**	0	14	**> 0.1**
Aldicarb sulfoxide	1	29	**0.1**	0	6	**> 0.1**
Aldicarb	18	30	**0.1**	1	18	**> 0.1**
Ametryn	30	30	**0.01**	30	30	**0.01**
Aminocarb	27	30	**0.1**	0	11	**> 0.1**
Amitraz	1	0	**> 0.1**	0	0	**> 0.1**
Avermectin	29	30	**0.01**	0	9	**> 0.1**
Azoxystrobin	30	30	**0.01**	29	30	**0.01**
Benalaxyl	30	30	**0.01**	30	30	**0.01**
Bendiocarb	28	30	**0.1**	26	30	**0.1**
Benfuracarb	29	30	**0.01**	0	1	**> 0.1**
Benzoximate	30	30	**0.01**	30	30	**0.01**
Bifenazate	30	30	**0.01**	1	28	**> 0.1**
Bitertanol	30	30	**0.01**	5	30	**0.1**
Boscalid	30	30	**0.01**	27	30	**0.1**
Bromuconazole	30	30	**0.01**	30	19	**0.01**
Bupirimate	30	30	**0.01**	30	30	**0.01**
Buprofezin	30	30	**0.01**	30	30	**0.01**
Butafenacil	30	30	**0.01**	30	30	**0.01**
Butocarboxim	19	30	**0.1**	5	27	**> 0.1**

Carbaryl	30	30	**0.01**	22	30	**0.1**
Carbendazim	20	30	**0.1**	12	25	**> 0.1**
Carbetamide	20	30	**0.1**	9	30	**0.1**
Carbofuran	30	30	**0.01**	30	30	**0.01**
Carboxin	8	20	**> 0.1**	7	20	**> 0.1**
Carfentrazone-ethyl	30	30	**0.01**	18	30	**0.1**
Chlorantraniliprole	30	30	**0.01**	25	30	**0.1**
Chlorfluazuron	26	30	**0.1**	23	30	**0.1**
Chlorotoluron	30	30	**0.01**	30	30	**0.01**
Chloroxuron	30	30	**0.01**	30	30	**0.01**
Clethodim	13	29	**0.1**	5	26	**> 0.1**
Clofentezine	30	30	**0.01**	17	30	**0.1**
Clothianidin	16	30	**0.1**	2	27	**> 0.1**
Cyazofamid	30	30	**0.01**	22	30	**0.1**
Cycluron	30	30	**0.01**	26	30	**0.1**
Cymoxanil	19	26	**> 0.1**	0	8	**> 0.1**
Cyproconazole	30	30	**0.01**	29	30	**0.01**
Cyprodinil	30	30	**0.01**	30	30	**0.01**
Cyromazine	30	30	**0.01**	9	30	**0.1**
Desmedipham / Phenmedipham	30	30	**0.01**	5	1	**> 0.1**
Diclobutrazol	30	30	**0.01**	28	27	**> 0.1**
Dicrotophos	29	30	**0.01**	24	30	**0.1**
Diethofencarb	30	30	**0.01**	28	30	**0.1**
Difenoconazole*	24	24	**0.01**	24	24	**0.01**
Diflubenzuron	30	30	**0.01**	18	10	**> 0.1**
Dimethoate	30	30	**0.01**	25	30	**0.1**
Dimethomorph	30	30	**0.01**	29	30	**0.01**
Dimoxystrobin	30	30	**0.01**	29	30	**0.01**
Diniconazole	30	30	**0.01**	9	26	**> 0.1**
Dinotefuran	10	30	**0.1**	1	2	**> 0.1**
Dioxacarb	26	30	**0.1**	22	30	**0.1**

Diuron	30	30	**0.01**	27	30	**0.1**
Doramectin	27	30	**0.1**	0	5	**> 0.1**
Emamectin-benzoate	30	30	**0.01**	29	30	**0.01**
Epoxiconazole	30	30	**0.01**	30	30	**0.01**
Eprinomectin	30	30	**0.01**	0	0	**> 0.1**
Etaconazole	30	30	**0.01**	30	30	**0.01**
Ethiofencarb	25	29	**0.1**	22	28	**> 0.1**
Ethiprole	30	30	**0.01**	26	30	**0.1**
Ethirimol	30	30	**0.01**	25	30	**0.1**
Ethofumesate	28	30	**0.1**	0	2	**> 0.1**
Etoxazole	30	30	**0.01**	30	30	**0.01**
Famoxadone	16	30	**0.1**	4	16	**> 0.1**
Fenamidone	30	30	**0.01**	30	30	**0.01**
Fenarimol	30	30	**0.01**	30	30	**0.01**
Fenazaquin	30	30	**0.01**	30	30	**0.01**
Fenbuconazole	30	30	**0.01**	14	0	**> 0.1**
Fenhexamid	30	30	**0.01**	15	12	**> 0.1**
Fenobucarb	23	29	**0.1**	21	29	**0.1**
Fenoxycarb	28	30	**0.1**	20	30	**0.1**
Fenpropimorph	30	30	**0.01**	30	30	**0.01**
Fenpyroximate	30	30	**0.01**	30	30	**0.01**
Fenuron	12	30	**0.1**	10	30	**0.1**
Fipronil	25	30	**0.1**	0	0	**> 0.1**
Flonicamid	29	30	**0.01**	5	30	**0.1**
Fluazinam	25	29	**0.1**	13	28	**> 0.1**
Flubendiamide	29	30	**0.01**	26	30	**0.1**
Fludioxonil	0	0	**> 0.1**	0	0	**> 0.1**
Flufenacet	30	30	**0.01**	29	27	**0.01**
Flufenoxuron	30	30	**0.01**	22	30	**0.1**
Fluometuron	30	30	**0.01**	30	30	**0.01**
Fluoxastrobin	30	30	**0.01**	30	30	**0.01**
Fluquinconazole	29	30	**0.01**	28	30	**0.1**

Flusilazole	30	30	**0.01**	30	30	**0.01**
Flutolanil	30	30	**0.01**	30	30	**0.01**
Flutriafol	30	30	**0.01**	30	30	**0.01**
Forchlorfenuron	29	30	**0.01**	29	30	**0.01**
Formetanate	30	30	**0.01**	21	30	**0.1**
Fuberidazole	24	30	**0.1**	16	29	**0.1**
Furalaxyl	30	30	**0.01**	30	30	**0.01**
Furathiocarb	30	30	**0.01**	30	30	**0.01**
Halofenozide	0	30	**0.1**	0	29	**0.1**
Hexaconazole	30	30	**0.01**	30	30	**0.01**
Hexaflumuron	30	30	**0.01**	10	30	**0.1**
Hexythiazox	30	30	**0.01**	12	30	**0.1**
Hydramethylnon	30	30	**0.01**	30	30	**0.01**
Imazalil	30	30	**0.01**	18	30	**0.1**
Imidacloprid	28	30	**0.1**	11	30	**0.1**
Indoxacarb	30	30	**0.01**	23	30	**0.1**
Ipconazole	30	30	**0.01**	30	30	**0.01**
Iprovalicarb	30	30	**0.01**	30	30	**0.01**
Isocarbophos	30	30	**0.01**	29	30	**0.01**
Isoprocarb	17	30	**0.1**	7	30	**0.1**
Isoproturon	30	30	**0.01**	30	30	**0.01**
Ivermectin	27	30	**0.1**	0	12	**> 0.1**
Kresoxim-methyl	29	30	**0.01**	6	30	**0.1**
Linuron	30	30	**0.01**	17	26	**> 0.1**
Lufenuron	15	29	**0.1**	1	27	**> 0.1**
Mandipropamid	30	30	**0.01**	26	30	**0.1**
Mefenacet	30	30	**0.01**	30	30	**0.01**
Mepanipyrim	30	30	**0.01**	30	30	**0.01**
Mepronil	30	30	**0.01**	28	30	**0.1**
Mesotrione	3	28	**> 0.1**	0	8	**> 0.1**
Metaflumizone	30	30	**0.01**	23	30	**0.1**
Metalaxyl	30	30	**0.01**	29	30	**0.01**

Metconazole	30	30	**0.01**	30	30	**0.01**
Methabenzthiazuron	30	30	**0.01**	29	30	**0.01**
Methamidophos	1	19	**0.1**	0	4	**> 0.1**
Methiocarb	30	30	**0.01**	30	26	**0.01**
Methomyl	1	1	**> 0.1**	0	0	**> 0.1**
Methoprotryne	30	30	**0.01**	30	30	**0.01**
Methoxyfenozide	30	30	**0.01**	28	1	**> 0.1**
Metobromuron	30	30	**0.01**	19	30	**0.1**
Metribuzin	1	10	**> 0.1**	0	10	**> 0.1**
Mevinphos	30	30	**0.01**	3	30	**0.1**
Mexacarbate	30	30	**0.01**	30	30	**0.01**
Monocrotophos	1	30	**0.1**	0	30	**0.1**
Monolinuron	29	30	**0.01**	17	29	**0.1**
Moxidectin	30	30	**0.01**	1	28	**> 0.1**
Myclobutanil	30	30	**0.01**	26	30	**0.1**
Neburon	30	30	**0.01**	20	30	**0.1**
Nitenpyram	28	30	**0.1**	0	20	**> 0.1**
Novaluron	27	30	**0.1**	11	30	**0.1**
Nuarimol	30	30	**0.01**	25	30	**0.1**
Omethoate	25	30	**0.1**	1	26	**> 0.1**
Oxadixyl	30	30	**0.01**	11	29	**0.1**
Oxamyl	25	30	**0.1**	0	4	**> 0.1**
Paclobutrazol	30	30	**0.01**	30	30	**0.01**
Penconazole	30	30	**0.01**	30	30	**0.01**
Picoxystrobin	30	30	**0.01**	30	30	**0.01**
Piperonyl butoxide	30	30	**0.01**	30	30	**0.01**
Pirimicarb	30	30	**0.01**	30	30	**0.01**
Prochloraz	30	30	**0.01**	27	30	**0.1**
Promecarb	29	30	**0.01**	26	30	**0.1**
Prometon / Secbumeton / Terbumeton	30	30	**0.01**	30	30	**0.01**

Prometryne / Terbutryn	30	30	**0.01**	30	30	**0.01**
Propamocarb	30	30	**0.01**	17	30	**0.1**
Propargite	30	30	**0.01**	0	29	**0.1**
Propham	26	30	**0.1**	10	30	**0.1**
Propiconazole	30	30	**0.01**	30	30	**0.01**
Propoxur	14	30	**0.1**	2	30	**0.1**
Prothioconazole	15	30	**0.1**	0	9	**> 0.1**
Pymetrozine	24	30	**0.1**	0	0	**> 0.1**
Pyracarbolid	30	30	**0.01**	30	30	**0.01**
Pyraclostrobin	30	30	**0.01**	30	30	**0.01**
Pyridaben	30	30	**0.01**	30	30	**0.01**
Pyrimethanil	30	30	**0.01**	30	30	**0.01**
Pyriproxyfen	30	30	**0.01**	30	30	**0.01**
Quinoxyfen	30	30	**0.01**	30	30	**0.01**
Rotenone	30	30	**0.01**	30	30	**0.01**
Siduron	30	30	**0.01**	28	30	**0.1**
Simetryn	26	30	**0.1**	2	30	**0.1**
Spinetoram	30	30	**0.01**	30	30	**0.01**
Spinosad (Spinosyn A)	30	30	**0.01**	28	30	**0.1**
Spirodiclofen	30	30	**0.01**	8	30	**0.1**
Spiromesifen	20	20	**0.1**	20	20	**> 0.1**
Spirotetramat	30	30	**0.01**	29	30	**0.01**
Spiroxamine	30	30	**0.01**	30	30	**0.01**
Sulfentrazone	26	30	**0.1**	6	11	**> 0.1**
Tebuconazole	30	30	**0.01**	30	30	**0.01**
Tebufenozide	30	30	**0.01**	30	30	**0.01**
Tebufenpyrad	28	30	**0.1**	28	30	**0.1**
Tebuthiuron	30	30	**0.01**	29	30	**0.01**
Teflubenzuron	29	30	**0.01**	3	30	**0.1**
Temephos	30	30	**0.01**	4	30	**0.1**

Tetraconazole	30	30	**0.01**	30	30	**0.01**
Thiabendazole	29	30	**0.01**	20	30	**0.1**
Thiacloprid	30	30	**0.01**	30	30	**0.01**
Thiamethoxam	28	30	**0.1**	0	21	**> 0.1**
Thidiazuron	30	30	**0.01**	17	30	**0.1**
Thiobencarb	30	30	**0.01**	30	30	**0.01**
Thiofanox	7	30	**0.1**	2	19	**> 0.1**
Thiophanate-methyl	25	30	**0.1**	21	30	**0.1**
Triadimefon	30	30	**0.01**	20	30	**0.1**
Triadimenol	10	30	**0.1**	8	1	**> 0.1**
Trichlorfon	28	30	**0.1**	0	18	**> 0.1**
Tricyclazole	30	30	**0.01**	26	30	**0.1**
Trifloxystrobin	30	30	**0.01**	30	30	**0.01**
Triflumizole	30	30	**0.01**	29	30	**0.01**
Triflumuron	30	30	**0.01**	20	30	**0.1**
Triticonazole	30	30	**0.01**	29	30	**0.01**
Vamidothion	30	30	**0.01**	14	30	**0.1**
Zoxamide	30	30	**0.01**	30	30	**0.01**

* The validation was performed on 24 samples because difenoconazole was found in 2 baby food samples (in triplicate).

Table S5. Expanded suspect-screening list of 531 organic contaminants with their corresponding formula and theoretical *m/z*.

Compound	Formula [M]	Ion	Theoretical m/z
1-(3,4-dichlorophenyl)-3-methyl urea	C8H8Cl2N2O	[M+H]+	219.00864
1-(4-nitrophenyl)-3-propylure	C10H13N3O3	[M+H]+	224.10297
1,2-benzisothiazol-3(2h)-one	C7H5NOS	[M+H]+	152.01646
1,3-diphenylurea	C13H12N2O	[M+H]+	213.10224
2,3,5-trimethacarb	C11H15NO2	[M+H]+	194.11756
2,4-dimethylaniline	C8H11N	[M+H]+	122.09643
2,6-dichlorobenzamide	C7H5Cl2NO	[M+H]+	189.9821
2,6-diethylaniline	C10H15N	[M+H]+	150.12773
2-ethylhexyl diphenyl phosphate	C20H27O4P	[M+H]+	363.17197
2-n-octyl-4-isothiazolin-3-one	C11H19NOS	[M+H]+	214.12601
3,4 dichloroaniline	C6H5Cl2N	[M+H]+	161.98718
3,4,5-trimethacarb	C11H15NO2	[M+H]+	194.11756
3-ketocarbofuran	C12H13NO4	[M+H]+	236.09173
4-bromo-3,5-dimethylphenyl-n-	C10H12BrNO2	[M+H]+	258.01242
Abate® (temephos)	C16H20O6P2S3	[M+H]+	466.99701
Aclonifen	C12H9ClN2O3	[M+H]+	265.03745
Aconitine	C34H47NO11	[M+H]+	646.32219
Akton	C12H14Cl3O3PS	[M+H]+	374.95396
Alachlor	C14H20ClNO2	[M+H]+	270.12553
Allethrin	C19H26O3	[M+H]+	303.19547
Allidochlor	C8H12ClNO	[M+H]+	174.06802
Alloxydim sodium	C17H24NNaO5	[M+H]+	346.16249
Ametoctradin	C15H25N5	[M+H]+	276.21827
Amicarbazone	C10H19N5O2	[M+H]+	242.16115
Amidosulfuron	C9H15N5O7S2	[M+H]+	370.04857
Anilazine	C9H5Cl3N4	[M+H]+	274.96526
Anilofos	C13H19ClNO3PS2	[M+H]+	368.03053
Aspon ™	C12H28O5P2S2	[M+H]+	379.09262
Asulam	C8H10N2O4S	[M+H]+	231.04341
Atraton	C9H17N5O	[M+H]+	212.15059
Atrazine desisopropyl	C5H8ClN5	[M+H]+	174.0541
Atrazine	C8H14ClN5	[M+H]+	216.10105
Azaconazole	C12H11Cl2N3O2	[M+H]+	300.03011
Azadirachtin (technical)	C35H44O16	[M+H]+	721.27021
Azamethiphos	C9H10ClN2O5PS	[M+H]+	324.98094

Azimsulfuron	C13H16N10O5S	[M+H]+	425.10986
Aziprotryne	C7H11N7S	[M+H]+	226.08694
Barban	C11H9Cl2NO2	[M+H]+	258.00831
Beflubutamid	C18H17F4NO2	[M+H]+	356.12682
Benazolin	C9H6ClNO3S	[M+H]+	243.98297
Benfluralin (benefin)	C13H16F3N3O4	[M+H]+	336.11657
Benfuresate	C12H16O4S	[M+H]+	257.08421
Benodanil	C13H10INO	[M+H]+	323.98799
Benomyl	C14H18N4O3	[M+H]+	291.14517
Benoxacor	C11H11Cl2NO2	[M+H]+	260.02396
Bensulfuron-methyl	C16H18N4O7S	[M+H]+	411.0969
Bensulide	C14H24NO4PS3	[M+H]+	398.06779
Bentazon	C10H12N2O3S	[M+H]+	241.06414
Benthiavalicarb-isopropyl	C18H24FN3O3S	[M+H]+	382.15952
Benzoylprop-ethyl	C18H17Cl2NO3	[M+H]+	366.06583
Benzthiazuron	C9H9N3OS	[M+H]+	208.05391
Bifenthrin	C23H22ClF3O2	[M+H]+	423.13332
Bioresmethrin	C22H26O3	[M+H]+	339.19547
Bixafen	C18H12Cl2F3N3O	[M+H]+	414.03823
Bladex	C9H13ClN6	[M+H]+	241.0963
Bromacil	C9H13BrN2O2	[M+H]+	261.02332
Bromofenvinphos-ethyl	C12H14BrCl2O4P	[M+H]+	402.92629
Bromophos-methyl	C8H8BrCl2O3PS	[M+H]+	364.8565
Bufencarb	C26H38N2O4	[M+H]+	443.29043
Butachlor	C17H26ClNO2	[M+H]+	312.17248
Butocarboxim-sulfoxide	C7H14N2O3S	[M+H]+	207.07979
Butroxydim	C24H33NO4	[M+H]+	400.24824
Buturon	C12H13ClN2O	[M+H]+	237.07892
Butylate	C11H23NOS	[M+H]+	218.15731
Cadusafos	C10H23O2PS2	[M+H]+	271.09499
Cafenstrole	C16H22N4O3S	[M+H]+	351.14854
Carbophenothion	C11H16ClO2PS3	[M+H]+	342.98114
Carpropamid	C15H18Cl3NO	[M+H]+	334.05267
Chinomethionate	C10H6N2OS2	[M+H]+	234.99943
Chlorbromuron	C9H10BrClN2O2	[M+H]+	292.96869
Chlorbufam	C11H10ClNO2	[M+H]+	224.04728
Chlordimeform	C10H13ClN2	[M+H]+	197.084
Chlorfenapyr	C15H11BrClF3N2O	[M+H]+	406.97681
Chloridazon	C10H8ClN3O	[M+H]+	222.04287
Chlorimuron-ethyl	C15H15ClN4O6S	[M+H]+	415.04736

Chlormephos	C5H12ClO2PS2	[M+H]+	234.97777
Chlormequat chloride	C5H13Cl2N	[M+H]+	158.04978
Chlorobenzuron	C14H10Cl2N2O2	[M+H]+	309.01921
Chlorosulfuron	C12H12ClN5O4S	[M+H]+	358.03713
Chlorotoluron	C10H13ClN2O	[M+H]+	213.07892
Chlorpyrifos	C9H11Cl3NO3PS	[M+H]+	349.93356
Chlorpyrifos-methyl	C7H7Cl3NO3PS	[M+H]+	321.90226
Chlorpyrifos-oxon	C9H11Cl3NO4P	[M+H]+	333.95641
Chlorthiamid	C7H5Cl2NS	[M+H]+	205.95925
Chlorthiophos	C11H15Cl2O3PS2	[M+H]+	360.96501
Chromafenozide	C24H30N2O3	[M+H]+	395.23292
Cinidon-ethyl	C19H17Cl2NO4	[M+H]+	394.06074
Cinmethylin	C18H26O2	[M+H]+	275.20056
Cinosulfuron	C15H19N5O7S	[M+H]+	414.1078
Clarithromycin	C38H69NO13	[M+H]+	748.48417
Climbazole	C15H17ClN2O2	[M+H]+	293.10513
Clodinafop (acid-free)	C14H11ClFNO4	[M+H]+	312.04334
Clodinafop-propargyl	C17H13ClFNO4	[M+H]+	350.05899
Clomeprop	C16H15Cl2NO2	[M+H]+	324.05526
Cloquintocet-mexyl	C18H22ClNO3	[M+H]+	336.1361
Cloransulam-methyl	C15H13ClFN5O5S	[M+H]+	430.03827
Command (clomazone)	C12H14ClNO2	[M+H]+	240.07858
Coumaphos-oxon	C14H16ClO6P	[M+H]+	347.04458
Coumaphos	C14H16ClO5PS	[M+H]+	363.02174
Crimidine	C7H10ClN3	[M+H]+	172.0636
Crotoxyphos	C14H19O6P	[M+H]+	315.0992
Crufomate	C12H19ClNO3P	[M+H]+	292.08639
Cumyluron	C17H19ClN2O	[M+H]+	303.12587
Cyanofenphos	C15H14NO2PS	[M+H]+	304.05557
Cyanophos	C9H10NO3PS	[M+H]+	244.01918
Cyantraniliprole	C19H14BrClN6O2	[M+H]+	473.01229
Cyclanilide	C11H9Cl2NO3	[M+H]+	274.00323
Cycloate	C11H21NOS	[M+H]+	216.14166
Cyclohexamide	C15H23NO4	[M+H]+	282.16998
Cycloprothrin	C26H21Cl2NO4	[M+H]+	482.09204
Cyclosulfamuron	C17H19N5O6S	[M+H]+	422.11288
Cyflufenamid	C20H17F5N2O2	[M+H]+	413.1283
Cyhalofop-butyl	C20H20FNO4	[M+H]+	358.14491
Cymiazole	C12H14N2S	[M+H]+	219.09505
Cypermethrin (mix Of Isomers)	C22H19Cl2NO3	[M+H]+	416.08148

Cyphenothrin	C24H25NO3	[M+H]+	376.19072
Cyprazine	C9H14ClN5	[M+H]+	228.10105
Cyprofuram	C14H14ClNO3	[M+H]+	280.0735
Cyprosulfamide	C18H18N2O5S	[M+H]+	375.10092
Cythioate	C8H12NO5PS2	[M+H]+	297.99673
Daimuron	C17H20N2O	[M+H]+	269.16484
Daminozide	C6H12N2O3	[M+H]+	161.09207
Danitol	C22H23NO3	[M+H]+	350.17507
Dazomet	C5H10N2S2	[M+H]+	163.03582
Dementon-s-methyl-sulfone	C6H15O5PS2	[M+H]+	263.01713
Demeton O	C8H19O3PS2	[M+H]+	259.0586
Demeton S	C8H19O3PS2	[M+H]+	259.0586
Demeton-s-methyl	C6H15O3PS2	[M+H]+	231.0273
Deoxynivalenol	C15H20O6	[M+H]+	297.13327
Desethyl atrazine	C6H10ClN5	[M+H]+	188.06975
Desmethyl norflurazon	C11H7ClF3N3O	[M+H]+	290.03025
Desmethyl-formamido-pirimicarb	C11H16N4O3	[M+H]+	253.12952
Desmetryn	C8H15N5S	[M+H]+	214.11209
Diafenthiuron	C23H32N2OS	[M+H]+	385.23081
Dialifos	C14H17ClNO4PS2	[M+H]+	394.00979
Diazinon	C12H21N2O3PS	[M+H]+	305.10833
Diazinon-o-analog	C12H21N2O4P	[M+H]+	289.13117
Dibrom	C4H7Br2Cl2O4P	[M+H]+	378.78985
Dichlofenthion	C10H13Cl2O3PS	[M+H]+	314.97729
Dichlormid	C8H11Cl2NO	[M+H]+	208.02905
Dichlorvos	C4H7Cl2O4P	[M+H]+	220.95318
Diclosulam	C13H10Cl2FN5O3S	[M+H]+	405.99382
Diethatyl-ethyl	C16H22ClNO3	[M+H]+	312.1361
Difenoxurone	C16H18N2O3	[M+H]+	287.13902
Diflufenicen	C19H11F5N2O2	[M+H]+	395.08135
Dimefox	C4H12FN2OP	[M+H]+	155.07441
Dimefuron	C15H19ClN4O3	[M+H]+	339.12184
Dimepiperate	C15H21NOS	[M+H]+	264.14166
Dimethachlor	C13H18ClNO2	[M+H]+	256.10988
Dimethametryn	C11H21N5S	[M+H]+	256.15904
Dimethenamid	C12H18ClNO2S	[M+H]+	276.08195
Dimethirimol	C11H19N3O	[M+H]+	210.16009
Dimethylvinphos	C10H10Cl3O4P	[M+H]+	330.94551
Dimetilan	C10H16N4O3	[M+H]+	241.12952
Dinitramine	C11H13F3N4O4	[M+H]+	323.09617

Dioxathion (mixture of isomers)	C12H26O6P2S4	[M+H]+	457.01603
Diphenamid	C16H17NO	[M+H]+	240.13829
Diphenylamine	C12H11N	[M+H]+	170.09643
Dipropetryn	C11H21N5S	[M+H]+	256.15904
Disosultap	C5H11NNa2O6S4	[M+H]+	355.93374
Disulfoton-sulfone	C8H19O4PS3	[M+H]+	307.02559
Disulfoton-sulfoxide	C8H19O3PS3	[M+H]+	291.03067
Ditalimfos	C12H14NO4PS	[M+H]+	300.04539
Dithianon	C14H4N2O2S2	[M+H]+	296.9787
Dithiopyr	C15H16F5NO2S2	[M+H]+	402.06154
Dmst	C9H14N2O2S	[M+H]+	215.08488
Dodemorph	C18H35NO	[M+H]+	282.27914
Dodine	C15H33N3O2	[M+H]+	288.26455
Dyfonate ™	C10H15OPS2	[M+H]+	247.03747
Edifenphos	C14H15O2PS2	[M+H]+	311.03239
Empenthrin	C18H26O2	[M+H]+	275.20056
Epn	C14H14NO4PS	[M+H]+	324.04539
Eptc (s-ethyl dipropylthiocarbamate)	C9H19NOS	[M+H]+	190.12601
Erythromycin	C37H67NO13	[M+H]+	734.46852
Esbiol	C19H26O3	[M+H]+	303.19547
Esprocarb	C15H23NOS	[M+H]+	266.15731
Ethaboxam	C14H16N4OS2	[M+H]+	321.08383
Ethametsulfuron-methyl	C15H18N6O6S	[M+H]+	411.10813
Ethephone	C2H6ClO3P	[M+H]+	144.98159
Ethidimuron	C7H12N4O3S2	[M+H]+	265.04236
Ethiofencarb-sulfone	C11H15NO4S	[M+H]+	258.07946
Ethiofencarb-sulfoxide	C11H15NO3S	[M+H]+	242.08454
Ethion	C9H22O4P2S4	[M+H]+	384.9949
Ethiozin	C9H16N4OS	[M+H]+	229.11176
Ethofenprox	C25H28O3	[M+H]+	377.21112
Ethoprophos (prophos)	C8H19O2PS2	[M+H]+	243.06369
Ethoxyquin	C14H19NO	[M+H]+	218.15394
Ethoxysulfuron	C15H18N4O7S	[M+H]+	399.0969
Ethyclozate	C11H11ClN2O2	[M+H]+	239.05818
Etobenzanid	C16H15Cl2NO3	[M+H]+	340.05018
Etrimfos	C10H17N2O4PS	[M+H]+	293.07194
Famphur	C10H16NO5PS2	[M+H]+	326.02803
Fenamiphos-sulfone	C13H22NO5PS	[M+H]+	336.10291
Fenamiphos-sulfoxide	C13H22NO4PS	[M+H]+	320.108

Fenamiphos	C13H22NO3PS	[M+H]+	304.11308
Fenazaflor	C15H7Cl2F3N2O2	[M+H]+	374.99094
Fenazox	C12H10N2O	[M+H]+	199.08659
Fenchlorazol-ethyl	C12H8Cl5N3O2	[M+H]+	401.91319
Fenchlorphos-oxon	C8H8Cl3O4P	[M+H]+	304.92986
Fenclorim	C10H6Cl2N2	[M+H]+	224.99808
Fenfuram	C12H11NO2	[M+H]+	202.08626
Fenitrothion	C9H12NO5PS	[M+H]+	278.02466
Fenothiocarb	C13H19NO2S	[M+H]+	254.12093
Fenoxanil	C15H18Cl2N2O2	[M+H]+	329.08181
Fenoxaprop	C16H12ClNO5	[M+H]+	334.04768
Fenoxaprop-p-ethyl	C18H16ClNO5	[M+H]+	362.07898
Fenoxycarb (same As Cmpd# 1871)	C17H19NO4	[M+H]+	302.13868
Fenpiclonil	C11H6Cl2N2	[M+H]+	236.99808
Fenpropathrin	C22H23NO3	[M+H]+	350.17507
Fenpropidin	C19H31N	[M+H]+	274.25293
Fensulfothion	C11H17O4PS2	[M+H]+	309.03787
Fensulfothion-oxon	C11H17O5PS	[M+H]+	293.06071
Fensulfothion-oxon-sulfone	C11H17O6PS	[M+H]+	309.05563
Fensulfothion-sulfone	C11H17O5PS2	[M+H]+	325.03278
Fenthion-oxon Sulfoxide	C10H15O5PS	[M+H]+	279.04506
Fenthion-oxon	C10H15O4PS	[M+H]+	263.05015
Fenthion-sulfoxide	C10H15O4PS2	[M+H]+	295.02222
Fenthion	C10H15O3PS2	[M+H]+	279.0273
Fenthion-ethyl	C12H19O3PS2	[M+H]+	307.0586
Fenthion-sulfone	C10H15O5PS2	[M+H]+	311.01713
Fenthoxon-sulfone	C10H15O6PS	[M+H]+	295.03998
Fentin acetate as fentin	C20H18O2Sn	[M+H]+	411.04016
Fipronil-sulfide	C12H4Cl2F6N4S	[M+H]+	420.95107
Fipronil-desulfinyl	C12H4Cl2F6N4	[M+H]+	388.979
Flamprop-isopropyl	C19H19ClFNO3	[M+H]+	364.11103
Flamprop-methyl (metavane)	C17H15ClFNO3	[M+H]+	336.07973
Flamprop-m-isopropyl	C19H19ClFNO3	[M+H]+	364.11103
Flazasulfuron	C13H12F3N5O5S	[M+H]+	408.0584
Florasulam	C12H8F3N5O3S	[M+H]+	360.03727
Fluacrypyrim	C20H21F3N2O5	[M+H]+	427.14753
Fluazifop	C15H12F3NO4	[M+H]+	328.07912
Fluazifop-butyl	C19H20F3NO4	[M+H]+	384.14172
Fluazifop-p-butyl	C19H20F3NO4	[M+H]+	384.14172
Fluazuron	C20H10Cl2F5N3O3	[M+H]+	506.00921

Flucarbazone-sodium	C12H10F3N4NaO6S	[M+H]+	419.02436
Fluchloralin	C12H13ClF3N3O4	[M+H]+	356.06195
Flucycloxuron	C25H20ClF2N3O3	[M+H]+	484.1234
Flucythrinate	C26H23F2NO4	[M+H]+	452.16679
Flumetralin	C16H12ClF4N3O4	[M+H]+	422.05252
Flumiclorac-pentyl	C21H23ClFNO5	[M+H]+	424.13216
Flumioxazin	C19H15FN2O4	[M+H]+	355.10886
Flumorph	C21H22FNO4	[M+H]+	372.16056
Fluoglycofene-ethyl	C18H13ClF3NO7	[M+H]+	448.04054
Fluopicolide	C14H8Cl3F3N2O	[M+H]+	382.97271
Fluopyram	C16H11ClF6N2O	[M+H]+	397.05369
Fluorodifen	C13H7F3N2O5	[M+H]+	329.03798
Fluotrimazol	C22H16F3N3	[M+H]+	380.13691
Flupyradifurone	C12H11ClF2N2O2	[M+H]+	289.05499
Flurenol-butyl	C18H18O3	[M+H]+	283.13287
Flurenol-methyl	C15H12O3	[M+H]+	241.08592
Fluridone	C19H14F3NO	[M+H]+	330.11003
Flurochloridon (iso)	C12H10Cl2F3NO	[M+H]+	312.01643
Fluroxypyr	C7H5Cl2FN2O3	[M+H]+	254.9734
Fluroxypyr-meptyl	C15H21Cl2FN2O3	[M+H]+	367.0986
Flurprimidol	C15H15F3N2O2	[M+H]+	313.11584
Flurtamone	C18H14F3NO2	[M+H]+	334.10494
Fluthiacet-methyl	C15H15ClFN3O3S2	[M+H]+	404.03002
Fomesafen	C15H10ClF3N2O6S	[M+H]+	438.9973
Foramsulfuron	C17H20N6O7S	[M+H]+	453.1187
Fosthiazate	C9H18NO3PS2	[M+H]+	284.05385
Furmecyclox	C14H21NO3	[M+H]+	252.15942
Guthion®	C10H12N3O3PS2	[M+H]+	318.01305
Halosulfuron-methyl	C13H15ClN6O7S	[M+H]+	435.04842
Haloxyfop	C15H11ClF3NO4	[M+H]+	362.04015
Haloxyfop-2-ethoxyethyl	C19H19ClF3NO5	[M+H]+	434.09766
Haloxyfop-methyl	C16H13ClF3NO4	[M+H]+	376.0558
Haloxyfop-p-methyl	C16H13ClF3NO4	[M+H]+	376.0558
Heptenophos	C9H12ClO4P	[M+H]+	251.02345
Hexazinon	C12H20N4O2	[M+H]+	253.1659
Hymexazole	C4H5NO2	[M+H]+	100.0393
Imazamethabenz-methyl	C16H20N2O3	[M+H]+	289.15467
Imazamox	C15H19N3O4	[M+H]+	306.14483
Imazapic	C14H17N3O3	[M+H]+	276.13427
Imazethapyr	C15H19N3O3	[M+H]+	290.14992

Imazosulfuron	C14H13ClN6O5S	[M+H]+	413.04294
Imidacloprid-olefin	C9H8ClN5O2	[M+H]+	254.04393
Imiprothrin (mix of isomers)	C17H22N2O4	[M+H]+	319.16523
Inabenfide	C19H15ClN2O2	[M+H]+	339.08948
Indanofan	C20H17ClO3	[M+H]+	341.0939
Indaziflam	C16H20FN5	[M+H]+	302.17755
Iodofenphos	C8H8Cl2IO3PS	[M+H]+	412.84264
Iodosulfuron-methyl-sodium	C14H13IN5NaO6S	[M+H]+	529.96018
Iprobenfos	C13H21O3PS	[M+H]+	289.10218
Iprodione	C13H13Cl2N3O3	[M+H]+	330.04067
Irgarol (cybutryne)	C11H19N5S	[M+H]+	254.14339
Isazophos	C9H17ClN3O3PS	[M+H]+	314.04896
Isocarbamide	C8H15N3O2	[M+H]+	186.1237
Isofenphos	C15H24NO4PS	[M+H]+	346.12365
Isofenphos-methyl	C14H22NO4PS	[M+H]+	332.108
Isofenphos-oxon	C15H24NO5P	[M+H]+	330.14649
Isomethiozin	C12H20N4OS	[M+H]+	269.14306
Isonoruron	C13H22N2O	[M+H]+	223.18049
Isopropalin	C15H23N3O4	[M+H]+	310.17613
Isoprothiolane	C12H18O4S2	[M+H]+	291.07193
Isouron	C10H17N3O2	[M+H]+	212.13935
Isoxaben	C18H24N2O4	[M+H]+	333.18088
Isoxadifen-ethyl	C18H17NO3	[M+H]+	296.12812
Isoxaflutole	C15H12F3NO4S	[M+H]+	360.05119
Isoxathion	C13H16NO4PS	[M+H]+	314.06104
Karbutilate	C14H21N3O3	[M+H]+	280.16557
Ketoprofen	C16H14O3	[M+H]+	255.10157
Lactofen	C19H15ClF3NO7	[M+H]+	462.05619
Lambda cyhalothrin	C23H19ClF3NO3	[M+H]+	450.10783
Lenacil	C13H18N2O2	[M+H]+	235.1441
Leptophos	C13H10BrCl2O2PS	[M+H]+	410.87723
Levofloxacin	C18H20FN3O4	[M+H]+	362.15106
Lontrel (clopyralid)	C6H3Cl2NO2	[M+H]+	191.96136
Malaoxon	C10H19O7PS	[M+H]+	315.06619
Malathion	C10H19O6PS2	[M+H]+	331.04335
Mecarbam	C10H20NO5PS2	[M+H]+	330.05933
Mefenpyr-diethyl	C16H18Cl2N2O4	[M+H]+	373.07164
Mefluidide	C11H13F3N2O3S	[M+H]+	311.06718
Mephosfolan	C8H16NO3PS2	[M+H]+	270.0382
Mepiquat chloride	C7H16ClN	[M+H]+	150.1044

Mesosulfuron-methyl	C17H21N5O9S2	[M+H]+	504.08535
Metazachlor	C14H16ClN3O	[M+H]+	278.10547
Methacrifos	C7H13O5PS	[M+H]+	241.02941
Methfuroxam	C14H15NO2	[M+H]+	230.11756
Methidathion	C6H11N2O4PS3	[M+H]+	302.96914
Methiocarb-sulfone	C11H15NO4S	[M+H]+	258.07946
Methiocarb-sulfoxide	C11H15NO3S	[M+H]+	242.08454
Methomyl-oxime	C3H7NOS	[M+H]+	106.03211
Methyl-paraoxon	C8H10NO6P	[M+H]+	248.03185
Methyl-parathion	C8H10NO5PS	[M+H]+	264.00901
Metolachlor	C15H22ClNO2	[M+H]+	284.14118
Metolcarb	C9H11NO2	[M+H]+	166.08626
Metominostrobin (e isomer)	C16H16N2O3	[M+H]+	285.12337
Metominostrobin (z-type)	C16H16N2O3	[M+H]+	285.12337
Metosulam	C14H13Cl2N5O4S	[M+H]+	418.01381
Metoxuron	C10H13ClN2O2	[M+H]+	229.07383
Metrafenone	C19H21BrO5	[M+H]+	409.06451
Metsulfuron-methyl	C14H15N5O6S	[M+H]+	382.08158
Mgk-264 (mixture of isomers)	C17H25NO2	[M+H]+	276.19581
Molinate	C9H17NOS	[M+H]+	188.11036
Morpholine	C4H9NO	[M+H]+	88.07569
N,n-diethyl-m-toluamide	C12H17NO	[M+H]+	192.13829
N,n'-ethylenethiourea	C3H6N2S	[M+H]+	103.03245
Naphthalophos (naftalofos)	C16H16NO6P	[M+H]+	350.0788
Napropamide	C17H21NO2	[M+H]+	272.16451
Naptalam	C18H13NO3	[M+H]+	292.09682
Nereistoxin-oxalate	C7H13NO4S2	[M+H]+	240.03588
Nicosulfuron	C15H18N6O6S	[M+H]+	411.10813
Nitenpyram(iso)	C11H15ClN4O2	[M+H]+	271.09563
Nitralin	C13H19N3O6S	[M+H]+	346.10673
Nitrapyrin (2-chloro-6-(trichloromethyl)	C6H3Cl4N	[M+H]+	229.90924
Nitroguanidine	CH4N4O2	[M+H]+	105.0407
Norflurazon	C12H9ClF3N3O	[M+H]+	304.0459
Noruron	C13H22N2O	[M+H]+	223.18049
Ofurace	C14H16ClNO3	[M+H]+	282.08915
Orbencarb	C12H16ClNOS	[M+H]+	258.07139
Orysastrobin	C18H25N5O5	[M+H]+	392.19285
Oryzalin	C12H18N4O6S	[M+H]+	347.10198
Oxadiargyl	C15H14Cl2N2O3	[M+H]+	341.04542

Oxadiazon	C15H18Cl2N2O3	[M+H]+	345.07672
Oxasulfuron	C17H18N4O6S	[M+H]+	407.10198
Oxaziclomefone	C20H19Cl2NO2	[M+H]+	376.08656
Oximino-oxamyl	C5H10N2O2S	[M+H]+	163.05358
Oxycarboxin	C12H13NO4S	[M+H]+	268.06381
Oxydemeton-methyl (demeton-s-	C6H15O4PS2	[M+H]+	247.02222
Oxyfluorfen	C15H11ClF3NO4	[M+H]+	362.04015
Paraoxon-ethyl	C10H14NO6P	[M+H]+	276.06315
Parathion	C10H14NO5PS	[M+H]+	292.04031
Pebulate	C10H21NOS	[M+H]+	204.14166
Penconazol	C13H15Cl2N3	[M+H]+	284.07158
Pendimethalin	C13H19N3O4	[M+H]+	282.14483
Penfluron	C15H9F5N2O2	[M+H]+	345.0657
Penoxsulam	C16H14F5N5O5S	[M+H]+	484.07086
Pentachlorocyanobenzene	C7Cl5N	[M+H]+	273.85461
Pentanochlor	C13H18ClNO	[M+H]+	240.11497
Penthiopyrad	C16H20F3N3OS	[M+H]+	360.1352
Pethoxamid	C16H22ClNO2	[M+H]+	296.14118
Phenothrin	C23H26O3	[M+H]+	351.19547
Phenthoate	C12H17O4PS2	[M+H]+	321.03787
Phenylurea	C7H8N2O	[M+H]+	137.07094
Phorate-oxon-sulfoxide	C7H17O4PS2	[M+H]+	261.03787
Phorate-sulfoxide	C7H17O3PS3	[M+H]+	277.01502
Phorate	C7H17O2PS3	[M+H]+	261.02011
Phorate-oxon-sulfone	C7H17O5PS2	[M+H]+	277.03278
Phorate-oxon	C7H17O3PS2	[M+H]+	245.04295
Phorat-sulfone	C7H17O4PS3	[M+H]+	293.00994
Phosalone	C12H15ClNO4PS2	[M+H]+	367.99414
Phosfolan	C7H14NO3PS2	[M+H]+	256.02255
Phosmet-oxon	C11H12NO5PS	[M+H]+	302.02466
Phosmet	C11H12NO4PS2	[M+H]+	318.00182
Phosphamidon	C10H19ClNO5P	[M+H]+	300.07622
Phoxim	C12H15N2O3PS	[M+H]+	299.06138
Picolinafen	C19H12F4N2O2	[M+H]+	377.09077
Piperalin	C16H21Cl2NO2	[M+H]+	330.10221
Piperophos	C14H28NO3PS2	[M+H]+	354.1321
Pirimicarb-desmethyl	C10H16N4O2	[M+H]+	225.1346
Pirimiphos-methyl	C11H20N3O3PS	[M+H]+	306.10358
Pirimiphos-ethyl	C13H24N3O3PS	[M+H]+	334.13488
Pirimiphos-methyl-n-desethyl	C9H16N3O3PS	[M+H]+	278.07228

Prallethrin	C19H24O3	[M+H]+	301.17982
Pretilachlor	C17H26ClNO2	[M+H]+	312.17248
Primisulfuron-methyl	C15H12F4N4O7S	[M+H]+	469.04356
Probenazole	C10H9NO3S	[M+H]+	224.03759
Procyazine	C10H13ClN6	[M+H]+	253.0963
Procymidone	C13H11Cl2NO2	[M+H]+	284.02396
Profenofos	C11H15BrClO3PS	[M+H]+	372.94242
Profoxydim lithium	C24H32ClNO4S	[M+H]+	466.18133
Prohydrojasmon	C15H26O3	[M+H]+	255.19547
Propachlor	C11H14ClNO	[M+H]+	212.08367
Propamocarb HCl	C9H21ClN2O2	[M+H]+	225.13643
Propanil	C9H9Cl2NO	[M+H]+	218.0134
Propaphos	C13H21O4PS	[M+H]+	305.0971
Propaquizafop	C22H22ClN3O5	[M+H]+	444.13208
Propazine	C9H16ClN5	[M+H]+	230.1167
Propazine-2-hydroxy	C9H17N5O	[M+H]+	212.15059
Propetamphos	C10H20NO4PS	[M+H]+	282.09235
Propisochlor	C15H22ClNO2	[M+H]+	284.14118
Propyzamide (pronamide)	C12H11Cl2NO	[M+H]+	256.02905
Proquinazid	C14H17IN2O2	[M+H]+	373.04076
Prosulfocarb	C14H21NOS	[M+H]+	252.14166
Prosulfuron	C15H16F3N5O4S	[M+H]+	420.09479
Prothioconazole-desthio	C14H15Cl2N3O	[M+H]+	312.06649
Pyraclofos	C14H18ClN2O3PS	[M+H]+	361.05371
Pyraflufen-ethyl	C15H13Cl2F3N2O4	[M+H]+	413.02772
Pyrazolynate	C19H16Cl2N2O4S	[M+H]+	439.02806
Pyrazophos	C14H20N3O5PS	[M+H]+	374.09341
Pyrazosulfuron-ethyl	C14H18N6O7S	[M+H]+	415.10305
Pyrazoxyfen	C20H16Cl2N2O3	[M+H]+	403.06107
Pyrethrin 1	C22H28O5	[M+H]+	373.20095
Pyrethrin 2	C21H28O3	[M+H]+	329.21112
Pyributicarb	C18H22N2O2S	[M+H]+	331.14748
Pyridalyl	C18H14Cl4F3NO3	[M+H]+	489.97527
Pyridaphenthion	C14H17N2O4PS	[M+H]+	341.07194
Pyridate	C19H23ClN2O2S	[M+H]+	379.12415
Pyrifenox (mixture of isomers))	C14H12Cl2N2O	[M+H]+	295.03995
Pyroquilon	C11H11NO	[M+H]+	174.09134
Pyroxsulam	C14H13F3N6O5S	[M+H]+	435.0693
Quinalphos	C12H15N2O3PS	[M+H]+	299.06138
Quinclorac	C10H5Cl2NO2	[M+H]+	241.97701

Quinine-sulfate (potentially -2H2O)	C40H54N4O10S	[M+H]+	783.36334
Quinmerac	C11H8ClNO2	[M+H]+	222.03163
Quinoclamine	C10H6ClNO2	[M+H]+	208.01598
Quinoline	C9H7N	[M+H]+	130.06513
Quizalofop	C17H13ClN2O4	[M+H]+	345.06366
Quizalofop-ethyl	C19H17ClN2O4	[M+H]+	373.09496
Quizalofop-p-ethyl	C19H17ClN2O4	[M+H]+	373.09496
Reserpine	C33H40N2O9	[M+H]+	609.28066
Resmethrin	C22H26O3	[M+H]+	339.19547
Rimsulfuron	C14H17N5O7S2	[M+H]+	432.06422
Roxithromycin	C41H76N2O15	[M+H]+	837.53185
Saflufenacil	C17H17ClF4N4O5S	[M+H]+	501.06171
Schradan (dmpa)	C8H24N4O3P2	[M+H]+	287.13964
Sebuthylazin	C9H16ClN5	[M+H]+	230.1167
Sebuthylazin-desethyl	C7H12ClN5	[M+H]+	202.0854
Selamectin Impurity B	C43H63NO11	[M+H]+	770.44739
Sethoxydim	C17H29NO3S	[M+H]+	328.19409
S-hydroprene	C17H30O2	[M+H]+	267.23186
Silthiofam	C13H21NOSSi	[M+H]+	268.11859
Simazine	C7H12ClN5	[M+H]+	202.0854
Simeconazole	C14H20FN3OSi	[M+H]+	294.14325
Simetone	C8H15N5O	[M+H]+	198.13494
S-metolachlor	C15H22ClNO2	[M+H]+	284.14118
Spirotetramat-enol	C18H23NO3	[M+H]+	302.17507
Spirotetramat-enol-glucoside	C24H33NO8	[M+H]+	464.22789
Spirotetramat-mono-hydroxy	C18H25NO3	[M+H]+	304.19072
Sulcotrione	C14H13ClO5S	[M+H]+	329.0245
Sulfallate	C8H14ClNS2	[M+H]+	224.0329
Sulfamerazine	C11H12N4O2S	[M+H]+	265.07537
Sulfamonomethoxine	C11H12N4O3S	[M+H]+	281.07029
Sulfometuron-methyl	C15H16N4O5S	[M+H]+	365.09142
Sulfosulfuron	C16H18N6O7S2	[M+H]+	471.07512
Sulfoxaflor	C10H10F3N3OS	[M+H]+	278.05695
Sulfuramid	C10H6F17NO2S	[M+H]+	527.99206
Sulprofos-sulfoxide	C12H19O3PS3	[M+H]+	339.03067
Systhane Tm	C15H17ClN4	[M+H]+	289.12145
Tau-fluvalinate	C26H22ClF3N2O3	[M+H]+	503.13438
Tdcpp	C9H15Cl6O4P	[M+H]+	428.89119
Tebupirimfos	C13H23N2O3PS	[M+H]+	319.12398

Tebutam	C15H23NO	[M+H]+	234.18524
Tembotrione	C17H16ClF3O6S	[M+H]+	441.0381
Tepraloxydim	C17H24ClNO4	[M+H]+	342.14666
Terbufos	C9H21O2PS3	[M+H]+	289.05141
Terbufos-sulfon	C9H21O4PS3	[M+H]+	321.04124
Terbufos-sulfoxide	C9H21O3PS3	[M+H]+	305.04633
Terbumeton-desethyl	C8H15N5O	[M+H]+	198.13494
Terbutaline-sulfate	C24H40N2O10S	[M+H]+	549.24764
Terbuthylazine	C9H16ClN5	[M+H]+	230.1167
Terbuthylazine-desethyl	C7H12ClN5	[M+H]+	202.0854
Terbutol (terbucarb)	C17H27NO2	[M+H]+	278.21146
Terbutylazine-2-hydroxy	C9H17N5O	[M+H]+	212.15059
Tetrachlorvinphos (iso))	C10H9Cl4O4P	[M+H]+	364.90653
Tetraethyl-dithiopyrophosphate	C8H20O5P2S2	[M+H]+	323.03002
Tetraethyl-pyrophosphate	C8H20O7P2	[M+H]+	291.07571
Tetramethrin	C19H25NO4	[M+H]+	332.18564
Thenylchlor	C16H18ClNO2S	[M+H]+	324.08195
Thiazafluron	C6H7F3N4OS	[M+H]+	241.03654
Thiazopyr	C16H17F5N2O2S	[M+H]+	397.10037
Thiencarbazone-methyl	C12H14N4O7S2	[M+H]+	391.03767
Thifensulfuron-methyl	C12H13N5O6S2	[M+H]+	388.038
Thifluzamide	C13H6Br2F6N2O2S	[M+H]+	526.84937
Thiocarbazyl	C16H25NOS	[M+H]+	280.17296
Thiocyclam Hydrogrnoxalate	C7H13NO4S3	[M+H]+	272.00795
Thiodicarb	C10H18N4O4S3	[M+H]+	355.0563
Thiofanox-sulfone	C9H18N2O4S	[M+H]+	251.10601
Thiofanox-sulfoxide	C9H18N2O3S	[M+H]+	235.11109
Thionazine (zinophos)	C8H13N2O3PS	[M+H]+	249.04573
Thiophanate-ethyl	C14H18N4O4S2	[M+H]+	371.08423
Tiadinil	C11H10ClN3OS	[M+H]+	268.03059
Tiamulin Fumarate	C32H51NO8S	[M+H]+	610.34082
Tokuthion®	C11H15Cl2O2PS2	[M+H]+	344.97009
Tolclofos-methyl	C9H11Cl2O3PS	[M+H]+	300.96164
Tolfenpyrade	C21H22ClN3O2	[M+H]+	384.14733
Tolylfluanid	C10H13Cl2FN2O2S2	[M+H]+	346.98523
Topramezone	C16H17N3O5S	[M+H]+	364.09617
Tralkoxydim	C20H27NO3	[M+H]+	330.20637
Triallate	C10H16Cl3NOS	[M+H]+	304.0091
Triasulfuron	C14H16ClN5O5S	[M+H]+	402.06334
Triazamate	C13H22N4O3S	[M+H]+	315.14854

Triaziflam	C17H24FN5O	[M+H]+	334.20377
Triazophos	C12H16N3O3PS	[M+H]+	314.07228
Triazoxid	C10H6ClN5O	[M+H]+	248.03336
Tribenuron-methyl	C15H17N5O6S	[M+H]+	396.09723
Tribufos (def)	C12H27OPS3	[M+H]+	315.10345
Trietazine	C9H16ClN5	[M+H]+	230.1167
Trifloxystrobin metabolite	C19H17F3N2O4	[M+H]+	395.12132
Trifloxysulfuron-sodium	C14H13F3N5NaO6S	[M+H]+	460.05091
Trifluralin	C13H16F3N3O4	[M+H]+	336.11657
Triflusulfuron-methyl	C17H19F3N6O6S	[M+H]+	493.11117
Triforine	C10H14Cl6N4O2	[M+H]+	432.93207
Trinexapac-ethyl	C13H16O5	[M+H]+	253.10705
Triphenyl-phosphorothionate	C18H15O3PS	[M+H]+	343.05523
Tris(2-chloroethyl)-phosphate	C6H12Cl3O4P	[M+H]+	284.96116
Tris(o-cresyl)-phosphate	C21H21O4P	[M+H]+	369.12502
Tritosulfuron	C13H9F6N5O4S	[M+H]+	446.03522
Uniconazole	C15H18ClN3O	[M+H]+	292.12112
Vernolate	C10H21NOS	[M+H]+	204.14166
Xmc (3,5-xylyl methylcarbamate)	C10H13NO2	[M+H]+	180.10191

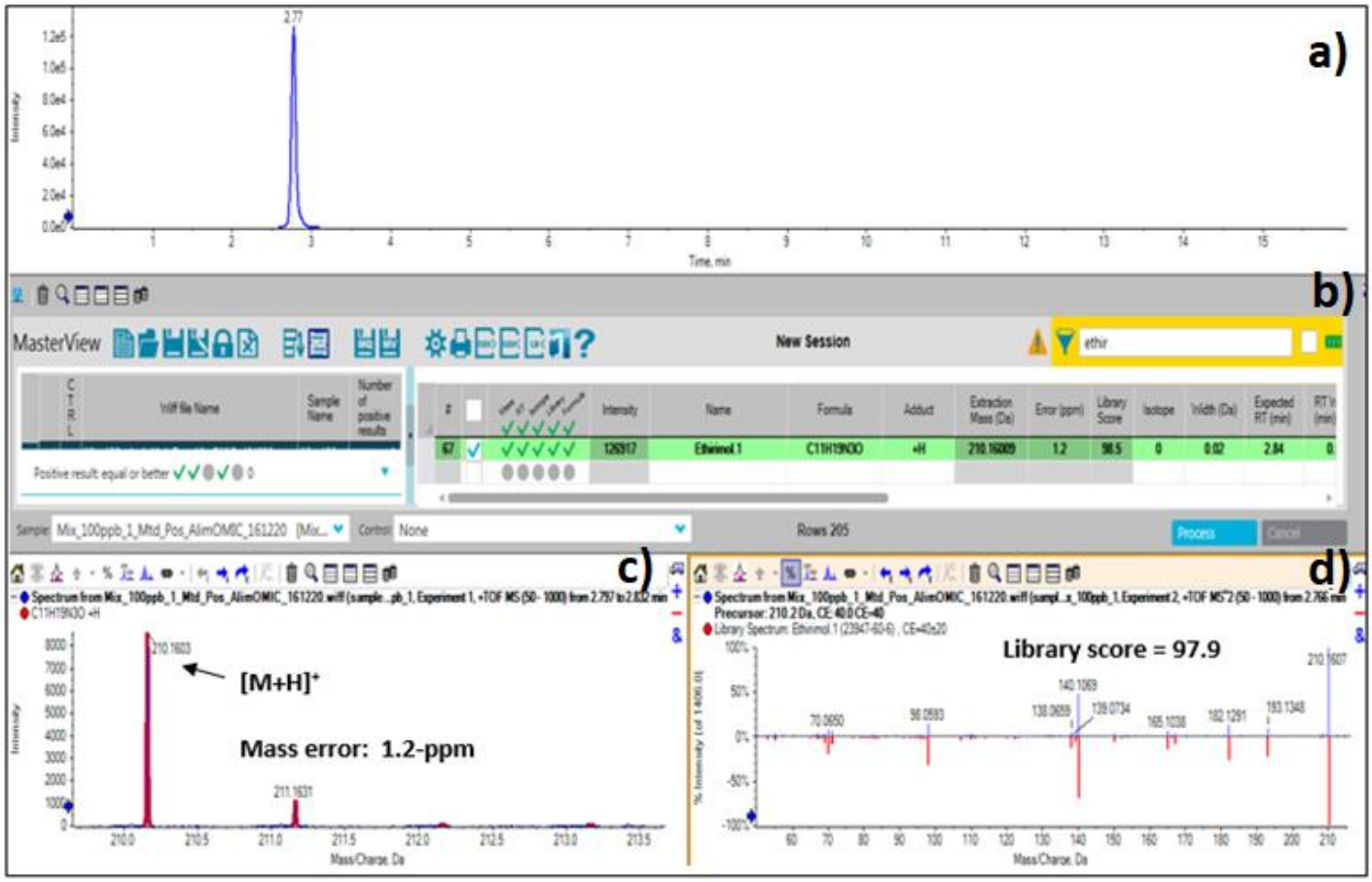

Fig. S1. Fast identification of 204 pesticides in solvent at 0.1 mg.L^{-1} using the user-friendly MasterView^{TM} software, based on accurate mass measurement, t_r and MS/MS information, with Ethirimol as the example $[M+H]^+$ (*m/z* = 210.16009; t_r = 2.77 min). (a) Extracted ion chromatogram of Ethrimol; (b) XIC list table with the corresponding related data; (c) Experimental isotopic pattern (in blue) against a theoretical pattern based on the elemental composition and adduct (in red); (d) Product ions spectrum (in blue) matching against an internal MS^2 spectral database made in solvent (in red).

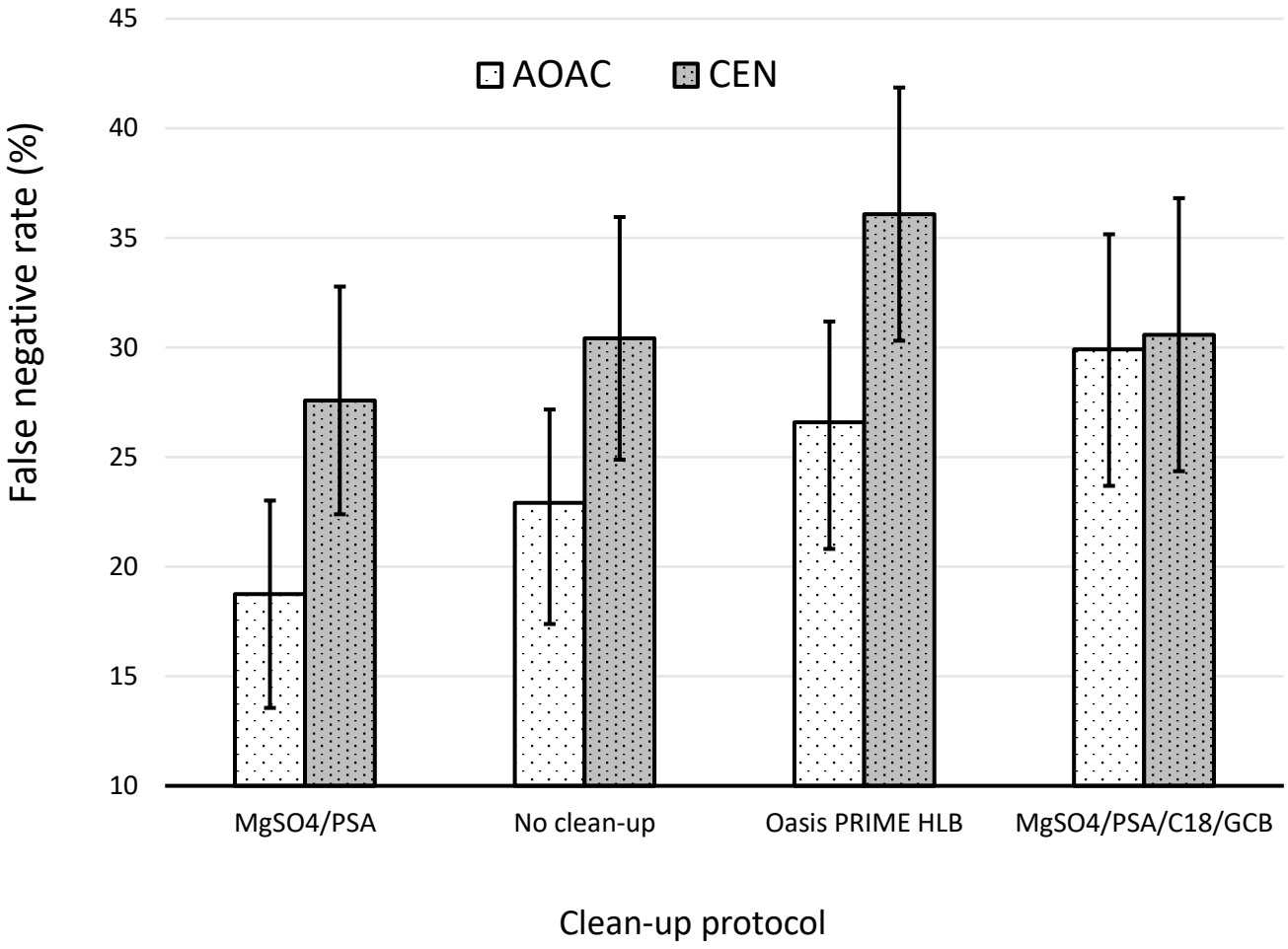

Fig.S2. Mean false negatives (%) obtained by grouping data from the 4 baby foods spiked at 0.01 mg.kg^{-1} using the 63 pesticides of mix #4. The error bars correspond to the relative standard deviation for the response measured (Mean ± SD, n=12).

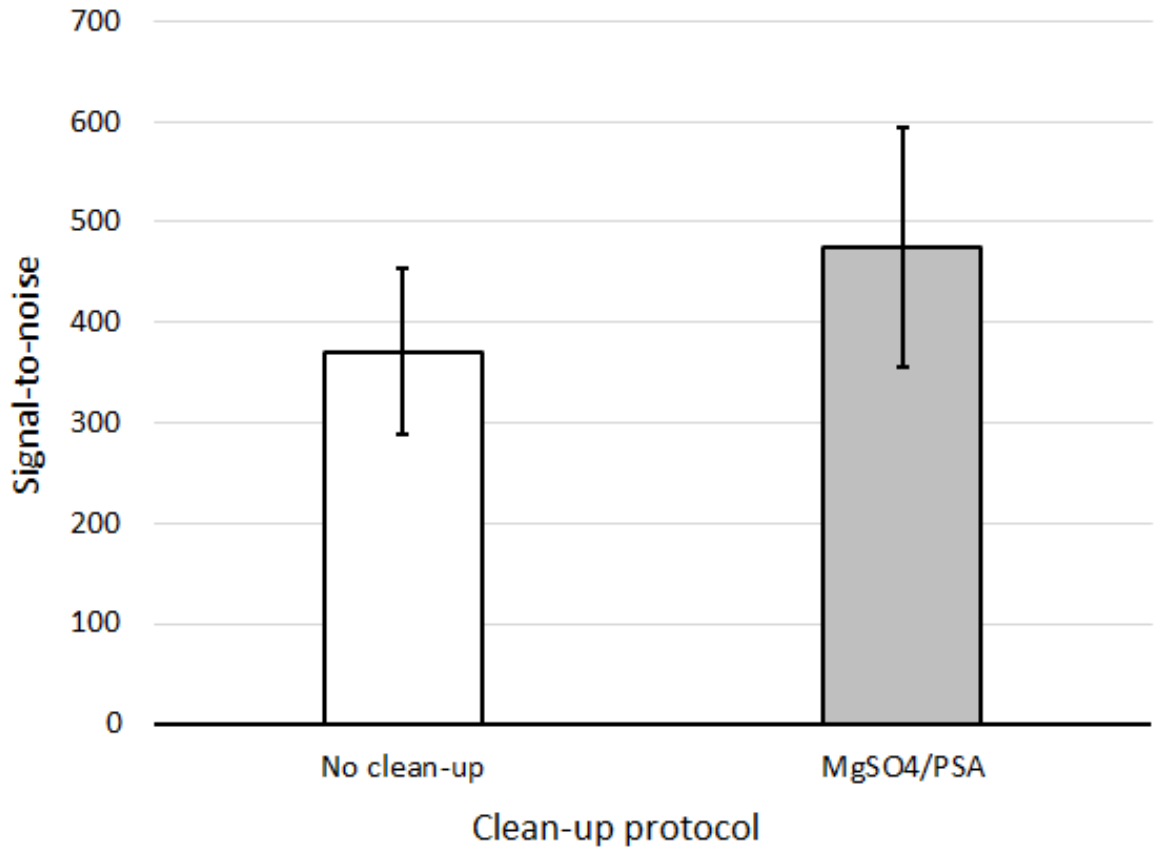

Fig.S3. Comparison of the mean S/N ratios of the pesticides extracted regarding both purification or no purification protocols, by grouping data for the 4 baby foods spiked at 0.01 $mg.kg^{-1}$ with the 63 pesticides of mix #4.

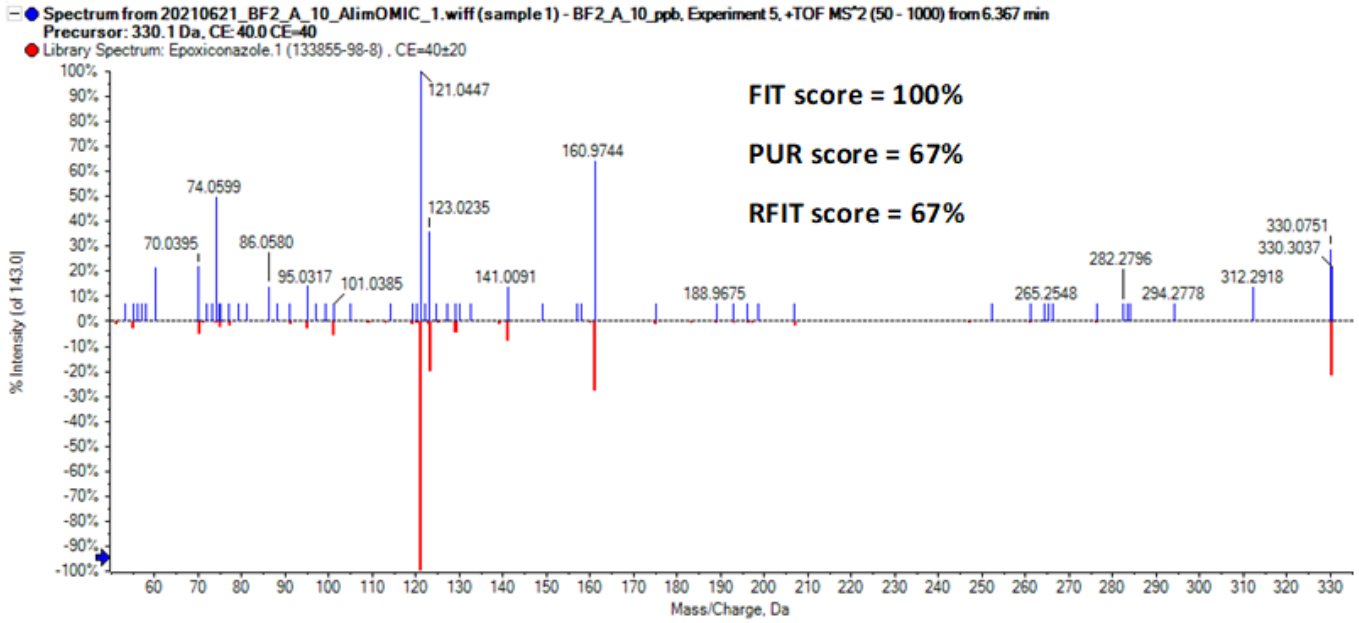

Fig.S4. Identification of pesticide epoxiconazole in a baby food sample spiked at 0.01 mg.kg^{-1}, with similarity score 100% using the FIT algorithm and similarity scores 67% using the PUR and RFIT algorithms. In blue, the experimental MS/MS spectrum of epoxiconazole; in red, the reference MS/MS spectrum of epoxiconazole.

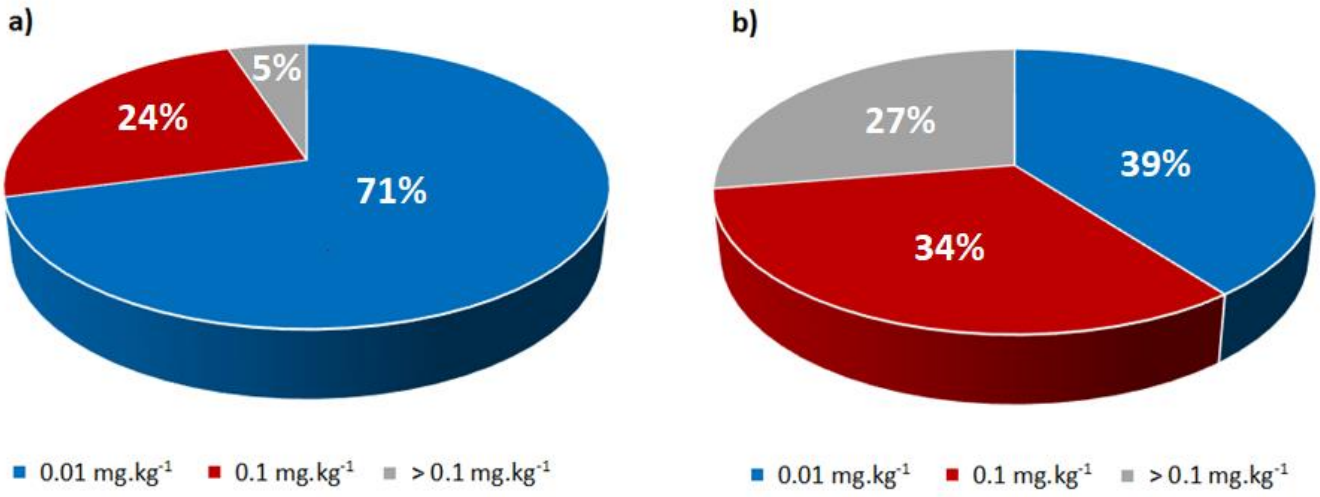

Fig.S5. Validation results of the targeted pesticides in all baby food samples (n=30) regarding **a)** the SDL; and **b)** the LOI. The percentages were calculated based on 199 compounds as some pesticides had identical formulas and were co-eluted: aldicarb sulfone/butoxycarboxim ($C_7H_{14}N_2O_4S$); desmedipham/phenmedipham ($C_{16}H_{16}N_2O_4$) prometon/secbumeton/terbumeton ($C_{10}H_{19}N_5O$) and prometryne/terbutryn ($C_{10}H_{19}N_5S$)

Article 2 (Diallo et al., 2022): "Development and validation according to the SANTE guidelines of a QuEChERS-UHPLC-QTOF-MS method for the screening of 204 pesticides in bivalves"

Table S1. List of the target pesticides with their corresponding formula, adduct or in-source fragment, theoretical *m/z* and retention time.

Name	Formula [M]	Adduct or in source fragment	Theoretical *m/z*	T_R (min)
3-Hydroxycarbofuran	$C_{12}H_{15}NO_4$	$C_{12}H_{14}NO_3^+$	220.09682	3.19
Acephate	$C_4H_{10}NO_3PS$	$C_2H_8O_3PS^+$	142.99263	1.00
Acetamiprid	$C_{10}H_{11}ClN_4$	$[M+H]^+$	223.0745	3.52
Acibenzolar-S-methyl	$C_8H_6N_2OS_2$	$[M+H]^+$	210.99943	6.23
Alanycarb	$C_{17}H_{25}N_3O_4S_2$	$[M+H]^+$	400.13593	N/A
Aldicarb sulfone	$C_7H_{14}N_2O_4S$	$[M+H]^+$	223.07471	2.13
Aldicarb sulfoxide	$C_7H_{14}N_2O_3S$	$[M+H]^+$	207.07979	1.82
Aldicarb	$C_7H_{14}N_2O_2S$	$[M+Na]^+$	213.06682	4.14
Ametryn	$C_9H_{17}N_5S$	$[M+H]^+$	228.12774	5.22
Aminocarb	$C_{11}H_{16}N_2O_2$	$[M+H]^+$	209.12845	1.67
Amitraz	$C_{19}H_{23}N_3$	$C_{10}H_{15}N_2^+$	163.12298	1.99
Avermectin	$C_{48}H_{72}O_{14}$	$[M+Na]^+$	895.48143	8.97
Azoxystrobin	$C_{22}H_{17}N_3O_5$	$[M+H]^+$	404.1241	6.28
Benalaxyl	$C_{20}H_{23}NO_3$	$[M+H]^+$	326.17507	7.21
Bendiocarb	$C_{11}H_{13}NO_4$	$[M+H]^+$	224.09173	4.82
Benfuracarb	$C_{20}H_{30}N_2O_5S$	$[M+NH_4]^+$	428.22137	8.13
Benzoximate	$C_{18}H_{18}ClNO_5$	$C_9H_8ClO_3^+$	199.01565	7.76
Bifenazate	$C_{17}H_{20}N_2O_3$	$C_{13}H_{12}NO^+$	198.09134	6.57
Bitertanol	$C_{20}H_{23}N_3O_2$	$[M+H]^+$	338.1863	6.78
Boscalid	$C_{18}H_{12}Cl_2N_2O$	$[M+H]^+$	343.03995	6.45
Bromuconazole	$C_{13}H_{12}BrCl_2N_3O$	$[M+H]^+$	375.96136	6.31
Bupirimate	$C_{13}H_{24}N_4O_3S$	$[M+H]^+$	317.16419	6.67
Buprofezin	$C_{16}H_{23}N_3OS$	$[M+H]^+$	306.16346	8.15
Butafenacil	$C_{20}H_{18}ClF_3N_2O_6$	$[M+NH_4]^+$	492.11437	6.94
Butocarboxim	$C_7H_{14}N_2O_2$ S	$[M+Na]^+$	213.06682	3.96
Butoxycarboxim	$C_7H_{14}N_2O_4S$	$[M+H]^+$	223.07471	2.26
Carbaryl	$C_{12}H_{11}NO_2$	$C_{10}H_9O^+$	145.06479	5.07
Carbendazim	$C_9H_9N_3O_2$	$[M+H]^+$	192.07675	2.12
Carbetamide	$C_{12}H_{16}N_2O_3$	$[M+H]^+$	237.12337	4.14
Carbofuran	$C_{12}H_{15}NO_3$	$[M+H]^+$	222.11247	4.88
Carboxin	$C_{12}H_{13}NO_2S$	$[M+H]^+$	236.07398	5.21
Carfentrazone-ethyl	$C_{15}H_{14}Cl_2F_3N_3O_3$	$[M+H]^+$	412.04371	7.08
Chlorantraniliprole	$C_{18}H_{14}BrCl_2N_5O_2$	$[M+H]^+$	481.97807	5.80
Chlorfluazuron	$C_{20}H_9Cl_3F_5N_3O_3$	$[M+H]^+$	539.97024	8.42
Chlorotoluron	$C_{10}H_{13}ClN_2O$	$[M+H]^+$	213.07892	5.05
Chloroxuron	$C_{15}H_{15}ClN_2O_2$	$[M+H]^+$	291.08948	6.20
Clethodim	$C_{17}H_{26}ClNO_3S$	$[M+H]^+$	360.13947	8.04

Clofentezine	$C_{14}H_8Cl_2N_4$	$[M+H]^+$	303.01988	7.55
Clothianidin	$C_6H_8ClN_5O_2S$	$[M+H]^+$	250.016	3.09
Cyazofamid	$C_{13}H_{13}ClN_4O_2S$	$[M+H]^+$	325.05205	7.06
Cycluron	$C_{11}H_{22}N_2O$	$[M+H]^+$	199.18049	5.24
Cymoxanil	$C_7H_{10}N_4O_3$	$C_4H_6N_3O_2^+$	128.04545	3.81
Cyproconazole	$C_{15}H_{18}ClN_3O$	$[M+H]^+$	292.12112	6.09
Cyprodinil	$C_{14}H_{15}N_3$	$[M+H]^+$	226.13387	6.65
Cyromazine	$C_6H_{10}N_6$	$[M+H]^+$	167.10397	0.85
Desmedipham	$C_{16}H_{16}N_2O_4$	$[M+H]^+$	318.14483	5.91
Diclobutrazol	$C_{15}H_{19}Cl_2N_3O$	$[M+H]^+$	328.09779	6.63
Dicrotophos	$C_8H_{16}NO_5P$	$[M+H]^+$	238.08389	2.61
Diethofencarb	$C_{14}H_{21}NO_4$	$[M+H]^+$	268.15433	6.17
Difenoconazole	$C_{19}H_{17}Cl_2N_3O_3$	$[M+H]^+$	406.07197	7.31
Diflubenzuron	$C_{14}H_9ClF_2N_2O_2$	$[M+H]^+$	311.03934	6.57
Dimethoate	$C_5H_{12}NO_3PS_2$	$[M+H]^+$	230.0069	3.41
Dimethomorph	$C_{21}H_{22}ClNO_4$	$[M+H]^+$	388.13101	5.80
Dimoxystrobin	$C_{19}H_2{}2N_2O_3$	$[M+H]^+$	327.17032	6.89
Diniconazole	$C_{15}H_{17}Cl_2N_3O$	$[M+H]^+$	326.08214	6.96
Dinotefuran	$C_7H_{14}N_4O_3$	$[M+H]^+$	203.11387	1.89
Dioxacarb	$C_{11}H_{13}NO_4$	$[M+H]^+$	224.09173	3.47
Diuron	$C_9H_{10}Cl_2N_2O$	$[M+H]^+$	233.02429	5.32
Doramectin	$C_{50}H_{74}O_{14}$	$[M+Na]^+$	921.49708	9.43
Emamectin-benzoate	$C_{49}H_{75}NO_{13}$	$[M+H]^+$	886.53112	6.02
Epoxiconazole	$C_{17}H_{13}ClFN_3O$	$[M+H]^+$	330.08039	6.41
Eprinomectin	$C_{50}H_{75}NO_{14}$	$[M+Na]^+$	936.50798	8.53
Etaconazole	$C_{14}H_{15}Cl_2N_3O_2$	$[M+H]^+$	328.06141	6.46
Ethiofencarb	$C_{11}H_{15}NO_2S$	$[M+H]^+$	226.08963	5.24
Ethiprole	$C_{13}H_9Cl_2F_3N_4OS$	$[M+H]^+$	396.9899	5.97
Ethirimol	$C_{11}H_{19}N_3O$	$[M+H]^+$	210.16009	2.84
Ethofumesate	$C_{13}H_{18}O_5S$	$[M+NH_4]^+$	304.12132	6.48
Etoxazole	$C_{21}H_{23}F_2NO_2$	$[M+H]^+$	360.17696	8.58
Famoxadone	$C_{22}H_{18}N_2O_4$	$[M+NH_4]^+$	392.16048	7.29
Fenamidone	$C_{17}H_{17}N_3OS$	$[M+H]^+$	312.11651	6.34
Fenarimol	$C_{17}H_{12}Cl_2N_2O$	$[M+H]^+$	331.03995	6.30
Fenazaquin	$C_{20}H_{22}N_2O$	$[M+H]^+$	307.18049	8.77
Fenbuconazole	$C_{19}H_{17}ClN_4$	$[M+H]^+$	337.12145	6.62
Fenhexamid	$C_{14}H_{17}Cl_2NO_2$	$[M+H]^+$	302.07091	6.45
Fenobucarb	$C_{12}H_{17}NO_2$	$[M+H]^+$	208.13321	6.02
Fenoxycarb	$C_{17}H_{19}NO_4$	$[M+H]^+$	302.13868	6.78
Fenpropimorph	$C_{20}H_{33}NO$	$[M+H]^+$	304.26349	4.62
Fenpyroximate	$C_{24}H_{27}N_3O_4$	$[M+H]^+$	422.20743	8.59
Fenuron	$C_9H_{12}N_2O$	$[M+H]^+$	165.10224	3.30
Fipronil	$C_{12}H_4Cl_2F_6N_4OS$	$[M+H]^+$	436.94598	7.03
Flonicamid	$C_9H_6F_3N_3O$	$[M+H]^+$	230.05357	2.80
Fluazinam	$C_{13}H_4Cl_2F_6N_4O_4$	$[M+H]^+$	464.95866	8.05
Flubendiamide	$C_{23}H_{22}F_7IN_2O_4S$	$[M+H]^+$	683.03061	7.02
Fludioxonil	$C_{12}H_6F_2N_2O_2$	$[M+H]^+$	249.04701	5.05
Flufenacet	$C_{14}H_{13}F_4N_3O_2S$	$[M+H]^+$	364.07374	6.84

Flufenoxuron	$C_{21}H_{11}ClF_6N_2O_3$	$[M+H]^+$	489.04352	8.21
Fluometuron	$C_{10}H_{11}F_3N_2O$	$[M+H]^+$	233.08962	5.11
Fluoxastrobin	$C_{21}H_{16}ClFN_4O_5$	$[M+H]^+$	459.0866	6.83
Fluquinconazole	$C_{16}H_8Cl_2FN_5O$	$[M+H]^+$	376.01627	6.49
Flusilazole	$C_{16}H_{15}F_2N_3Si$	$[M+H]^+$	316.10761	6.63
Flutolanil	$C_{17}H_{16}F_3NO_2$	$[M+H]^+$	324.12059	6.72
Flutriafol	$C_{16}H_{13}F_2N_3O$	$[M+H]^+$	302.10995	5.08
Forchlorfenuron	$C_{12}H_{10}ClN_3O$	$[M+H]^+$	248.05852	5.05
Formetanate-HCl	$C_{11}H_{16}ClN_3O_2$	$[M+H]^+$	222.1237	1.26
Fuberidazole	$C_{11}H_8N_2O$	$[M+H]^+$	185.07094	2.47
Furalaxyl	$C_{17}H_{19}NO_4$	$[M+H]^+$	302.13868	6.09
Furathiocarb	$C_{18}H_{26}N_2O_5S$	$[M+H]^+$	383.16352	8.14
Halofenozide	$C_{18}H_{19}ClN_2O_2$	$[M+H]^+$	331.12078	6.19
Hexaconazole	$C_{14}H_{17}Cl_2N_3O$	$[M+H]^+$	314.08214	6.78
Hexaflumuron	$C_{16}H_8Cl_2F_6N_2O_3$	$[M+H]^+$	460.98889	7.50
Hexythiazox	$C_{17}H_{21}ClN_2O_2S$	$[M+H]^+$	353.1085	8.39
Hydramethylnon	$C_{25}H_{24}F_6N_4$	$[M+H]^+$	495.19779	6.14
Imazalil	$C_{14}H_{14}Cl_2N_2O$	$[M+H]^+$	297.0556	3.92
Imidacloprid	$C_9H_{10}ClN_5O_2$	$[M+H]^+$	256.05958	3.28
Indoxacarb	$C_{22}H_{17}ClF_3N_3O_7$	$[M+H]^+$	528.07799	7.67
Ipconazole	$C_{18}H_{24}ClN_3O$	$[M+H]^+$	334.16807	7.33
Iprovalicarb	$C_{18}H_{28}N_2O_3$	$[M+H]^+$	321.21727	6.27
Isocarbophos	$C_{11}H_{16}NO_4PS$	$C_8H_8O_4PS^+$	230.98755	5.85
Isoprocarb	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.47
Isoproturon	$C_{12}H_{18}N_2O$	$[M+H]^+$	207.14919	5.31
Ivermectin	$C_{48}H_{74}O_{14}$	$[M+Na]^+$	897.49708	9.96
Kresoxim-methyl	$C_{18}H_{19}NO_4$	$[M+H]^+$	314.13868	7.15
Linuron	$C_9H_{10}Cl_2N_2O_2$	$[M+H]^+$	249.01921	6.11
Lufenuron	$C_{17}H_8Cl_2F_8N_2O_3$	$[M+H]^+$	510.9857	8.01
Mandipropamid	$C_{23}H_{22}ClNO_4$	$[M+H]^+$	412.13101	6.36
Mefenacet	$C_{16}H_{14}N_2O_2S$	$[M+H]^+$	299.08488	6.41
Mepanipyrim	$C_{14}H_{13}N_3$	$[M+H]^+$	224.11822	6.62
Mepronil	$C_{17}H_{19}NO_2$	$[M+H]^+$	270.14886	6.65
Mesotrione	$C_{14}H_{13}NO_7S$	$[M+H]^+$	340.04855	4.55
Metaflumizone	$C_{24}H_{16}F_6N_4O_2$	$[M+H]^+$	507.12502	7.92
Metalaxyl	$C_{15}H_{21}NO_4$	$[M+H]^+$	280.15433	5.33
Metconazole	$C_{17}H_{22}ClN_3O$	$[M+H]^+$	320.15242	6.87
Methabenzthiazuron	$C_{10}H_{11}N_3OS$	$[M+H]^+$	222.06956	5.01
Methamidophos	$C_2H_8NO_2PS$	$[M+H]^+$	142.00862	0.98
Methiocarb	$C_{11}H_{15}NO_2S$	$[M+H]^+$	226.08963	6.01
Methomyl	$C_5H_{10}N_2O_2S$	$[M+H]^+$	163.05358	2.50
Methoprotryne	$C_{11}H_{21}N_5OS$	$[M+H]^+$	272.15396	5.17
Methoxyfenozide	$C_{22}H_{28}N_2O_3$	$C_{18}H_{21}N_2O_3^+$	313.15467	6.64
Metobromuron	$C_9H_{11}BrN_2O_2$	$[M+H]^+$	259.00767	5.48
Metribuzin	$C_8H_{14}N_4OS$	$[M+H]^+$	215.09611	4.63
Mevinphos	$C_7H_{13}O_6P$	$C_6H_{10}O_5^+$	193.02604	3.18
Mexacarbate	$C_{12}H_{18}N_2O_2$	$[M+H]^+$	223.1441	3.58
Monocrotophos	$C_7H_{14}NO_5P$	$[M+H]^+$	224.06824	2.33

Monolinuron	$C_9H_{11}ClN_2O_2$	$[M+H]^+$	215.05818	5.27
Moxidectin	$C_{37}H_{53}NO_8$	$[M+H]^+$	640.38439	9.48
Myclobutanil	$C_{15}H_{17}ClN_4$	$[M+H]^+$	289.12145	6.27
Neburon	$C_{12}H_{16}Cl_2N_2O$	$[M+H]^+$	275.07125	6.96
Nitenpyram	$C_{11}H_{15}ClN_4O_2$	$[M+H]^+$	271.09563	2.19
Novaluron	$C_{17}H_9ClF_8N_2O_4$	$[M+H]^+$	493.01959	7.67
Nuarimol	$C_{17}H_{12}ClFN_2O$	$[M+H]^+$	315.0695	5.74
Omethoate	$C_5H_{12}NO_4PS$	$[M+H]^+$	214.02974	0.98
Oxadixyl	$C_{14}H_{18}N_2O_4$	$[M+H]^+$	279.13393	4.34
Oxamyl	$C_7H_{13}N_3O_3S$	$[M+H]^+$	220.07504	2.30
Paclobutrazol	$C_{30}H_{40}Cl_2N_6O_2$	$[M+H]^+$	294.13677	5.96
Penconazole	$C_{13}H_{15}Cl_2N_3$	$[M+H]^+$	284.07158	6.83
Pencycuron	$C_{19}H_{21}ClN_2O$	$[M+H]^+$	329.14152	7.58
Phenmedipham	$C_{16}H_{16}N_2O_4$	$[M+H]^+$	301.11828	5.91
Picoxystrobin	$C_{18}H_{16}F_3NO_4$	$[M+H]^+$	368.11042	7.19
Piperonyl butoxide	$C_{19}H_{30}O_5$	$[M+NH_4]^+$	356.24315	8.15
Pirimicarb	$C_{11}H_{18}N_4O_2$	$[M+H]^+$	239.15025	3.97
Prochloraz	$C_{15}H_{16}Cl_3N_3O_2$	$[M+H]^+$	376.03809	6.73
Promecarb	$C_{12}H_{17}NO_2$	$[M+H]^+$	208.13321	6.21
Prometon	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	0.00
Propamocarb	$C_9H_{20}N_2O_2$	$[M+H]^+$	242.14339	5.85
Prometryne	$C_{10}H_{19}N_5S$	$[M+H]^+$	189.15975	1.44
Propargite	$C_{19}H_{26}O_4S$	$[M+NH_4]^+$	368.18901	8.56
Propham	$C_{10}H_{13}NO_2$	$C_7H_8NO_2^+$	138.05496	5.63
Propiconazole	$C_{15}H_{17}Cl_2N_3O_2$	$[M+H]^+$	342.07706	7.01
Propoxur	$C_{11}H_{15}NO_3$	$C_8H_{10}NO_3^+$	168.06552	4.83
Prothioconazole	$C_{14}H_{15}Cl_2N_3OS$	$[M+H]^+$	344.03857	6.70
Pymetrozine	$C_{10}H_{11}N_5O$	$[M+H]^+$	218.10364	1.54
Pyracarbolid	$C_{13}H_{15}NO_2$	$[M+H]^+$	218.11756	5.01
Pyraclostrobin	$C_{19}H_{18}ClN_3O_4$	$[M+H]^+$	388.10586	7.46
Pyridaben	$C_{19}H_{25}ClN_2OS$	$[M+H]^+$	365.14489	8.99
Pyrimethanil	$C_{12}H_{13}N_3$	$[M+H]^+$	200.11822	5.70
Pyriproxyfen	$C_{20}H_{19}NO_3$	$[M+H]^+$	322.14377	8.26
Quinoxyfen	$C_{15}H_8Cl_2FNO$	$[M+H]^+$	308.00397	8.15
Rotenone	$C_{23}H_{22}O_6$	$[M+H]^+$	395.14892	6.87
Secbumeton	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.32
Siduron	$C_{14}H_{20}N_2O$	$[M+H]^+$	233.16484	5.91
Simetryn	$C_8H_{15}N_5S$	$[M+H]^+$	214.11209	4.46
Spinetoram	$C_{42}H_{69}NO_{10}$	$[M+H]^+$	748.49942	5.90
Spinosyn	$C_{41}H_{65}NO_{10}$	$[M+H]^+$	732.46812	5.47
Spirodiclofen	$C_{21}H_{24}Cl_2O_4$	$[M+H]^+$	411.11244	8.98
Spiromesifen	$C_{23}H_{30}O_4$	$[M+H]^+$	371.22169	8.86
Spirotetramat	$C_{21}H_{27}NO_5$	$[M+H]^+$	374.1962	6.16
Spiroxamine	$C_{18}H_{35}NO_2$	$[M+H]^+$	298.27406	4.56
Sulfentrazone	$C_{11}H_{10}Cl_2F_2N_4O_3S$	$[M+H]^+$	386.98915	5.02
Tebuconazole	$C_{16}H_{22}ClN_3O$	$[M+H]^+$	308.15242	6.63
Tebufenozide	$C_{22}H_{28}N_2O_2$	$C_{18}H_{21}N_2O_2^+$	297.15975	7.03
Tebufenpyrad	$C_{18}H_{24}ClN_3O$	$[M+H]^+$	334.16807	8.02

Tebuthiuron	$C_9H_{16}N_4OS$	$[M+H]^+$	229.11176	4.16
Teflubenzuron	$C_{14}H_6Cl_2F_4N_2O_2$	$[M+H]^+$	380.98152	7.60
Temephos	$C_{16}H_{20}O_6P_2S_3$	$[M+H]^+$	466.99701	8.17
Terbumeton	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.45
Terbutryn	$C_{10}H_{19}N_5S$	$[M+H]^+$	242.14339	5.97
Tetraconazole	$C_{13}H_{11}Cl_2F_4N_3O$	$[M+H]^+$	372.02881	6.45
Thiabendazole	$C_{10}H_7N_3S$	$[M+H]^+$	202.04335	2.35
Thiacloprid	$C_{10}H_9ClN_4S$	$[M+H]^+$	253.03092	3.99
Thiamethoxam	$C_8H_{10}ClN_5O_3S$	$[M+H]^+$	292.02657	2.70
Thidiazuron	$C_9H_8N_4OS$	$[M+H]^+$	221.04916	4.18
Thiobencarb	$C_{12}H_{16}ClNOS$	$[M+H]^+$	258.07139	7.60
Thiofanox	$C_9H_{18}N_2O_2S$	$[M+Na]^+$	241.09812	5.20
Thiophanate-methyl	$C_{12}H_{14}N_4O_4S_2$	$[M+H]^+$	343.05293	4.58
Triadimefon	$C_{14}H_{16}ClN_3O_2$	$[M+H]^+$	294.10038	6.41
Triadimenol	$C_{14}H_{18}ClN_3O_2$	$[M+H]^+$	296.11603	5.93
Trichlorfon	$C_4H_8Cl_3O_4P$	$[M+H]^+$	256.92986	2.96
Tricyclazole	$C_9H_7N_3S$	$[M+H]^+$	190.04335	3.65
Trifloxystrobin	$C_{20}H_{19}F_3N_2O_4$	$[M+H]^+$	409.13697	7.80
Triflumizole	$C_{15}H_{15}ClF_3N_3O$	$[M+H]^+$	346.09285	7.30
Triflumuron	$C_{15}H_{10}ClF_3N_2O_3$	$[M+H]^+$	359.04048	7.15
Triticonazole	$C_{17}H_{20}ClN_3O$	$[M+H]^+$	318.13677	6.14
Vamidothion	$C_8H_{18}NO_4PS_2$	$[M+H]^+$	288.04877	2.98
Zoxamide	$C_{14}H_{16}Cl_3NO_2$	$[M+H]^+$	336.03194	7.36

Table S2. L9 TOA for factor optimisation.

Experiment	Factor			
	Solvent acidification	**Salt**	**dSPE**	**Dilution**
1	1	1	1	1
2	1	2	2	2
3	1	3	3	3
4	2	2	1	3
5	2	3	2	1
6	2	1	3	2
7	3	3	1	2
8	3	1	2	3
9	3	2	3	1

Table S3. SWATH acquisition MS settings for fixed windows and variable windows size.

SWATH® acquisition	**F-SWATH® Windows**				**V-SWATH® Windows**			
No. SWATH® Windows	20	30	40	50	20	30	40	50
Window size (Da)	48	33	25	20	V	V	V	V
MS accumulation time (ms)	100	100	100	100	100	100	100	100
MS/MS accumulation time (ms)	50	50	50	50	50	50	50	50
Cycle time (ms)	1150	1650	2150	2650	1150	1650	2150	2650
No. of cycles	834	581	446	362	834	581	446	362

Table S4. Validation results for 204 pesticides across 28 samples mainly spiked at 0.01, 0.05 and 0.1 mg.kg-1 with corresponding SDL and LOI.

Compounds	No. detections			SDL ($mg.kg^{-1}$)	No. identifications			LOI ($mg.kg^{-1}$)
	0.01 $mg.kg^{-1}$	0.05 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$		0.01 $mg.kg^{-1}$	0.05 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$	
3-Hydroxycarbofuran	28	28	28	0.01	12	26	28	0.1
Acephate	24	28	28	0.5	0	0	0	> 0.1
Acetamiprid	0	13	28	0.1	0	12	25	> 0.1
Acibenzolar-S-methyl	28	28	28	0.01	17	27	28	0.05
Alanycarb	0	0	0	> 0.1	0	0	0	> 0.1
Aldicarb sulfone	18	26	28	0.1	0	2	0	> 0.1
Aldicarb sulfoxide	0	0	0	> 0.1	0	0	4	> 0.1
Aldicarb	2	8	19	0.1	0	3	3	> 0.1
Ametryn	28	28	28	0.01	28	28	28	0.01
Aminocarb	26	28	28	0.5	19	27	28	0.05
Amitraz	0	0	19	> 0.1	0	0	4	> 0.1
Avermectin	12	26	28	0.1	0	0	0	> 0.1
Azoxystrobin	28	28	28	0.01	17	28	28	0.05
Benalaxyl	28	28	28	0.01	28	28	28	0.01
Bendiocarb	28	28	28	0.01	15	28	28	0.05
Benfuracarb	1	7	16	> 0.1	0	0	0	> 0.1
Benzoximate	28	28	28	0.01	25	28	28	0.1
Bifenazate	13	18	23	> 0.1	0	2	4	> 0.1
Bitertanol	28	28	28	0.01	7	20	28	0.1
Boscalid	28	28	28	0.01	21	28	28	0.05
Bromuconazole	8	8	9	> 0.1	8	7	4	> 0.1
Bupirimate	28	28	28	0.01	28	28	28	0.01
Buprofezin	25	28	28	0.5	25	28	28	0.05
Butafenacil	28	28	28	0.01	28	28	28	0.01
Butocarboxim	8	7	5	> 0.1	0	2	3	> 0.1
Butoxycarboxim	0	0	0	> 0.1	0	0	0	> 0.1
Carbaryl	28	28	28	0.01	15	23	27	0.1
Carbendazim	28	28	28	0.01	28	28	28	0.01
Carbetamide	15	28	28	0.5	6	25	27	0.1
Carbofuran	28	28	28	0.01	28	28	28	0.01
Carboxin	6	16	28	0.1	4	15	28	0.1
Carfentrazone-ethyl	8	17	20	> 0.1	2	3	9	> 0.1
Chlorantraniliprole	25	28	28	0.5	5	13	20	> 0.1
Chlorfluazuron	28	28	28	0.01	17	22	28	0.1
Chlorotoluron	28	28	28	0.01	26	28	28	0.05
Chloroxuron	28	28	28	0.01	28	28	28	0.01
Clethodim	28	28	28	0.01	7	14	23	> 0.1
Clofentezine	21	25	28	0.1	7	11	19	> 0.1
Clothianidin	14	26	28	0.1	7	15	24	> 0.1
Cyazofamid	28	28	28	0.01	6	19	27	0.1
Cycluron	28	28	28	0.01	28	28	28	0.01
Cymoxanil	15	27	28	0.5	0	1	2	> 0.1
Cyproconazole	28	28	28	0.01	27	28	28	0.01
Cyprodinil	0	0	2	> 0.1	0	0	2	> 0.1
Cyromazine	28	28	28	0.01	1	0	6	> 0.1
Desmedipham	0	0	0	> 0.1	0	0	0	> 0.1
Diclobutrazol	28	28	28	0.01	19	9	12	> 0.1

Dicrotophos	28	28	28	0.01	23	28	28	0.05
Diethofencarb	28	28	28	0.01	26	28	28	0.05
Difenoconazole	28	28	28	0.01	22	28	28	0.05
Diflubenzuron	28	28	28	0.01	17	19	13	> 0.1
Dimethoate	28	28	28	0.01	19	25	28	0.1
Dimethomorph	25	27	28	0.5	20	23	28	0.1
Dimoxystrobin	28	28	28	0.01	28	28	28	0.01
Diniconazole	28	28	28	0.01	28	28	28	0.01
Dinotefuran	14	28	28	0.5	0	2	6	> 0.1
Dioxacarb	28	28	28	0.01	12	20	20	> 0.1
Diuron	28	28	28	0.01	25	27	28	0.05
Doramectin	1	15	23	> 0.1	0	5	18	> 0.1
Emamectin-benzoate	28	28	28	0.01	27	28	28	0.01
Epoxiconazole	28	28	28	0.01	28	28	28	0.01
Eprinomectin	11	22	26	> 0.1	2	12	21	> 0.1
Etaconazole	28	28	28	0.01	18	24	27	0.1
Ethiofencarb	28	28	28	0.01	19	28	28	0.05
Ethiprole	28	28	28	0.01	21	27	28	0.05
Ethirimol	28	28	28	0.01	28	28	28	0.01
Ethofumesate	28	28	28	0.01	2	1	0	> 0.1
Etoxazole	28	28	28	0.01	28	28	28	0.01
Famoxadone	12	26	28	0.1	0	0	0	> 0.1
Fenamidone	28	28	28	0.01	28	28	28	0.01
Fenarimol	28	28	28	0.01	23	28	28	0.05
Fenazaquin	28	28	28	0.01	28	28	28	0.01
Fenbuconazole	28	28	28	0.01	14	3	1	> 0.1
Fenhexamid	28	28	28	0.01	12	19	19	> 0.1
Fenobucarb	22	22	25	> 0.1	18	21	25	> 0.1
Fenoxycarb	28	28	28	0.01	4	7	15	> 0.1
Fenpropimorph	28	28	28	0.01	28	28	28	0.01
Fenpyroximate	28	28	28	0.01	28	28	28	0.01
Fenuron	28	28	28	0.01	19	27	28	0.05
Fipronil	15	28	28	0.5	0	0	0	> 0.1
Flonicamid	28	28	28	0.01	13	24	27	0.1
Fluazinam	17	28	28	0.5	3	20	24	> 0.1
Flubendiamide	28	28	28	0.01	0	0	0	> 0.1
Fludioxonil	0	0	0	> 0.1	0	0	0	> 0.1
Flufenacet	28	28	28	0.01	28	28	28	0.01
Flufenoxuron	27	28	28	0.01	2	18	27	0.1
Fluometuron	28	28	28	0.01	27	28	28	0.01
Fluoxastrobin	28	28	28	0.01	28	28	28	0.01
Fluquinconazole	28	28	28	0.01	22	28	28	0.05
Flusilazole	28	28	28	0.01	28	28	28	0.01
Flutolanil	28	28	28	0.01	28	28	28	0.01
Flutriafol	28	28	28	0.01	27	28	28	0.01
Forchlorfenuron	28	28	28	0.01	28	28	28	0.01
Formetanate-HCl	0	3	27	0.1	0	0	23	> 0.1
Fuberidazole	25	28	28	0.5	25	28	28	0.05
Furalaxyl	28	28	28	0.01	28	28	28	0.01
Furathiocarb	26	28	28	0.5	19	20	22	> 0.1
Halofenozide	5	28	28	0.05	2	23	28	0.1
Hexaconazole	28	28	28	0.01	28	28	28	0.01
Hexaflumuron	22	28	28	0.05	2	13	24	> 0.1
Hexythiazox	28	28	28	0.01	3	12	27	0.1

Hydramethylnon	21	20	21	> 0.1	21	20	21	> 0.1
Imazalil	28	28	28	0.01	27	28	28	0.01
Imidacloprid	28	28	28	0.01	11	26	28	0.1
Indoxacarb	28	28	28	0.01	8	24	28	0.1
Ipconazole	28	28	28	0.01	28	28	28	0.01
Iprovalicarb	28	28	28	0.01	28	28	28	0.01
Isocarbophos	25	28	28	0.05	2	14	28	0.1
Isoprocarb	17	28	28	0.05	3	20	28	0.1
Isoproturon	28	28	28	0.01	27	27	28	0.01
Ivermectin	0	2	12	> 0.1	0	0	0	> 0.1
Kresoxim-methyl	28	28	28	0.01	11	23	27	0.1
Linuron	28	28	28	0.01	10	25	27	0.1
Lufenuron	19	28	28	0.05	2	12	20	> 0.1
Mandipropamid	28	28	28	0.01	26	28	28	0.05
Mefenacet	28	28	28	0.01	27	28	28	0.01
Mepanipyrim	28	28	28	0.01	28	28	28	0.01
Mepronil	28	28	28	0.01	27	27	28	0.01
Mesotrione	0	3	9	> 0.1	0	0	1	> 0.1
Metaflumizone	28	28	28	0.01	11	23	28	0.1
Metalaxyl	28	28	28	0.01	28	28	28	0.01
Metconazole	28	28	28	0.01	27	28	28	0.01
Methabenzthiazuron	28	28	28	0.01	28	28	28	0.01
Methamidophos	0	3	27	0.1	0	0	0	> 0.1
Methiocarb	28	28	28	0.01	21	26	27	0.1
Methomyl	2	27	28	0.05	0	2	3	> 0.1
Methoprotryne	28	28	28	0.01	28	28	28	0.01
Methoxyfenozide	28	28	28	0.01	0	0	3	> 0.1
Metobromuron	28	28	28	0.01	19	27	28	0.05
Metribuzin	0	4	28	0.1	0	4	28	0.1
Mevinphos	23	28	28	0.05	3	8	21	> 0.1
Mexacarbate	14	15	13	> 0.1	14	15	13	0.01
Monocrotophos	0	11	28	0.1	0	0	15	> 0.1
Monolinuron	28	28	28	0.01	1	15	27	0.1
Moxidectin	24	28	28	0.05	1	3	18	> 0.1
Myclobutanil	28	28	28	0.01	25	28	28	0.05
Neburon	28	28	28	0.01	14	26	28	0.1
Nitenpyram	28	28	28	0.01	2	7	11	> 0.1
Novaluron	28	28	28	0.01	10	21	27	0.1
Nuarimol	28	28	28	0.01	25	27	27	0.05
Omethoate	28	28	28	0.01	8	9	21	> 0.1
Oxadixyl	28	28	28	0.01	1	8	25	> 0.1
Oxamyl	0	0	5	> 0.1	0	0	0	> 0.1
Paclobutrazol	28	28	28	0.01	28	28	28	0.01
Penconazole	28	28	28	0.01	20	28	28	0.05
Pencycuron	28	28	28	0.01	28	28	28	0.01
Phenmedipham	28	28	28	0.01	19	27	28	0.05
Picoxystrobin	28	28	28	0.01	28	28	28	0.01
Piperonyl butoxide	28	28	28	0.01	28	28	28	0.01
Pirimicarb	28	28	28	0.01	26	27	27	0.05
Prochloraz	28	28	28	0.01	23	28	28	0.05
Promecarb	4	5	6	> 0.1	3	3	6	> 0.1
Prometon	14	28	28	0.05	13	18	23	> 0.1
Propamocarb	13	26	28	0.1	0	6	24	> 0.1
Prometryne	28	28	28	0.01	24	25	16	> 0.1

Propargite	27	28	28	0.01	1	0	0	> 0.1
Propham	12	27	28	0.05	3	10	17	> 0.1
Propiconazole	28	28	28	0.01	24	28	28	0.05
Propoxur	28	28	28	0.01	11	18	28	0.1
Prothioconazole	15	27	28	0.05	0	0	2	> 0.1
Pymetrozine	14	28	28	0.05	5	14	27	0.1
Pyracarbolid	28	28	28	0.01	27	28	28	0.01
Pyraclostrobin	28	28	28	0.01	27	28	28	0.01
Pyridaben	28	28	28	0.01	28	28	28	0.01
Pyrimethanil	0	0	0	> 0.1	0	0	0	> 0.1
Pyriproxyfen	28	28	28	0.01	28	28	28	0.01
Quinoxyfen	28	28	28	0.01	28	28	28	0.01
Rotenone	28	28	28	0.01	24	28	28	0.05
Secbumeton	28	28	28	0.01	28	28	28	0.01
Siduron	28	28	28	0.01	24	26	27	0.1
Simetryn	14	28	28	0.05	2	3	22	> 0.1
Spinetoram	28	28	28	0.01	28	28	28	0.01
Spinosyn	28	28	28	0.01	28	28	28	0.01
Spirodiclofen	28	28	28	0.01	0	2	9	> 0.1
Spiromesifen	28	28	28	0.01	0	0	0	> 0.1
Spirotetramat	24	24	27	0.1	0	2	8	> 0.1
Spiroxamine	28	28	28	0.01	28	28	28	0.01
Sulfentrazone	26	28	28	0.05	0	8	8	> 0.1
Tebuconazole	28	28	28	0.01	27	28	28	0.01
Tebufenozide	28	28	28	0.01	27	28	28	0.01
Tebufenpyrad	28	28	28	0.01	27	27	28	0.01
Tebuthiuron	28	28	28	0.01	28	28	28	0.01
Teflubenzuron	25	28	28	0.05	3	13	24	> 0.1
Temephos	28	28	28	0.01	1	11	24	> 0.1
Terbumeton	4	1	1	> 0.1	4	1	1	> 0.1
Terbutryn	18	28	27	0.05	18	28	28	0.05
Tetraconazole	28	28	28	0.01	25	28	28	0.05
Thiabendazole	26	28	28	0.05	25	28	28	0.05
Thiacloprid	28	28	28	0.01	27	28	28	0.01
Thiamethoxam	26	28	28	0.05	10	12	24	> 0.1
Thidiazuron	28	28	28	0.01	11	28	28	0.05
Thiobencarb	28	28	28	0.01	22	28	28	0.05
Thiofanox	26	28	28	0.05	0	3	6	> 0.1
Thiophanate-methyl	28	28	28	0.01	20	28	28	0.05
Triadimefon	28	28	28	0.01	26	27	28	0.05
Triadimenol	5	8	11	> 0.1	3	6	8	> 0.1
Trichlorfon	27	28	28	0.01	1	4	17	> 0.1
Tricyclazole	28	28	28	0.01	28	28	28	0.01
Trifloxystrobin	28	28	28	0.01	28	28	28	0.01
Triflumizole	28	28	28	0.01	24	28	28	0.05
Triflumuron	28	28	28	0.01	10	20	27	0.1
Triticonazole	28	28	28	0.01	26	28	28	0.05
Vamidothion	28	28	28	0.01	26	27	28	0.05
Zoxamide	28	28	28	0.01	27	27	28	0.01

Table S5. Pesticide detected and identified by target screening analysis in mussel and oyster samples collected in the Pertuis Charentais littoral area.

Species	Site	Sampling Date	Pesticides detected[a] and identified[b]
Mussels	/	May-19	Diuron
	Ile de Ré	Sept-19	/
		Jan-20	Diuron
	Sèvre Niortaise	Sept-19	/
		Jan-20	Fenpropimorph
	Charente	Sept-19	Diuron
		Jan-20	/
Oysters	/	May-19	Diuron
	Ile de Ré	Sept-19	Diuron
		Jan-20	/
	Sèvre Niortaise	Sept-19	Diuron
		Jan-20	/
	Charente	Sept-19	Diuron
		Jan-20	Diuron

[a] T_R ± 0,1min, accuracy and mass ± 5 ppm compared with home-made database
[b] T_R ± 0,1min, accuracy mass, ± 5 ppm, and purity > 70% for MS/MS matching compared with home-made database

Table S6. Pesticide detected and identified by suspect screening analysis in mussel and oyster samples collected in the Pertuis Charentais littoral area.

Species	Site	Sampling Date	Compounds Confirmed with reference standard (level 1)
Mussels	/	May-19	1-(3,4-Dichlorophenyl)-3-methylurea; EHDPP
	Ile de Ré	Sept-19	EHDPP
		Jan-20	1-(3,4-Dichlorophenyl)-3-methylurea; EHDPP; Diphenylamine
	Sèvre Niortaise	Sept-19	1-(3,4-Dichlorophenyl)-3-methylurea; DEET
		Jan-20	EHDPP
	Charente	Sept-19	1-(3,4-Dichlorophenyl)-3-methylurea; EHDPP
		Jan-20	1-(3,4-Dichlorophenyl)-3-methylurea; EHDPP; Diphenylamine
Oysters	/	May-19	1-(3,4-Dichlorophenyl)-3-methylurea; EHDPP
	Ile de Ré	Sept-19	1-(3,4-Dichlorophenyl)-3-methylurea; EHDPP
		Jan-20	EHDPP; TCEP
	Sèvre Niortaise	Sept-19	1-(3,4-Dichlorophenyl)-3-methylurea; EHDPP
		Jan-20	EHDPP; TCEP
	Charente	Sept-19	1-(3,4-Dichlorophenyl)-3-methylurea; EHDPP; TCEP
		Jan-20	1-(3,4-Dichlorophenyl)-3-methylurea; EHDPP; TCEP

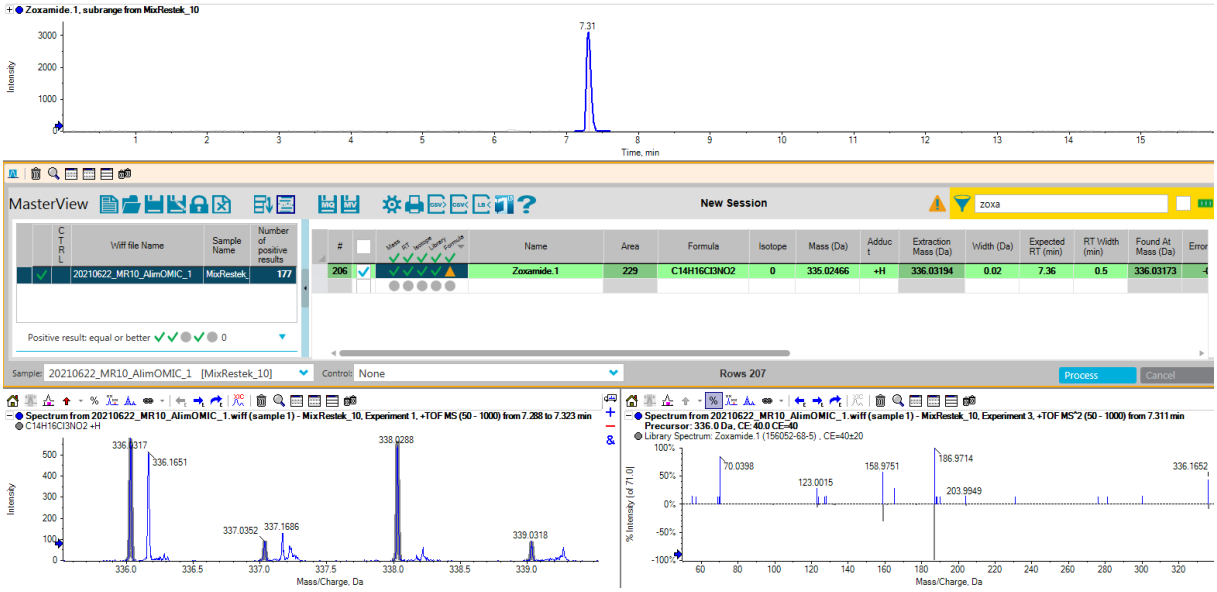

Fig. S1. Extracted Ion Chromatogram (top), MS spectra (bottom left) and MS/MS (bottom right) observed in the MasterViewTM software interface.

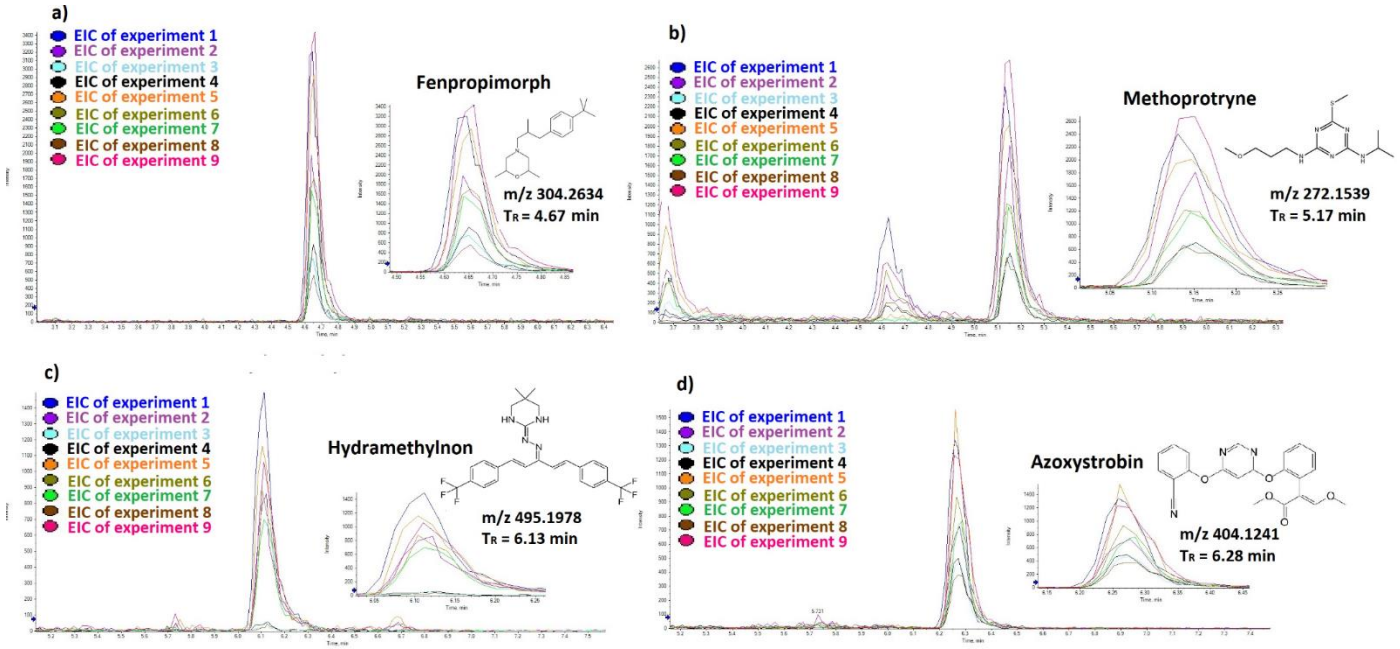

Fig. S2. Chromatograms of fenpropimorph (a), methoprotryne (b), hydramethylnon (c) and azoxystrobin (d) in oyster samples spiked at 0.01 mg.kg-1.

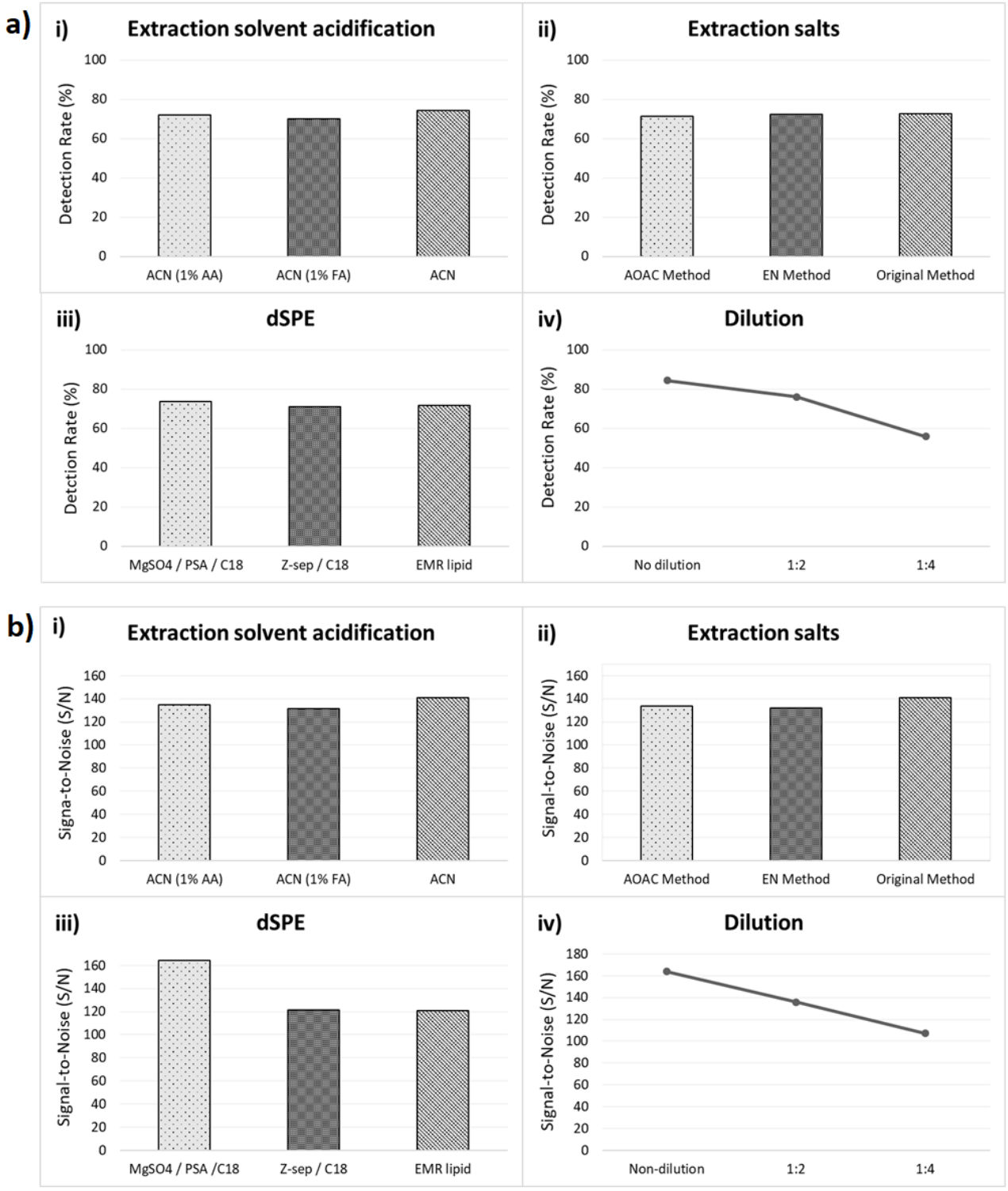

Fig. S3. Effects of extraction solvent acidification (i), extraction salts (ii), dSPE (iii) and dilution (iv) on pesticide detection rates (a) and pesticide S/N (b).

Article 3 (Makni et al., 2023a): "Optimisation and implementation of QuEChERS-based sample preparation for identification and semi-quantification of 694 targeted contaminants in honey, jam, jelly, and syrup by UHPLC-Q/ToF high-resolution mass spectrometry"

Table S1. List of the 694 targeted contaminants with their corresponding formula, adduct or in-source fragment, theoretical *m/z*, retention time and LogP

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
1-(3,4-dichlorophenyl)-3-methyl Urea	TP**	$C_8H_8Cl_2N_2O$	$[M-H]^-$	216.99409	4.78	2.94
1-(4-nitrophenyl)-3-propylure	Industrial contaminant	$C_{10}H_{13}N_3O_3$	$[M-H]^-$	222.08842	4.69	2.4***
1,2-benzisothiazol-3(2h)-one	Fungicide	C_7H_5NOS	$[M+H]^+$	152.01646	2.78	1.95
1,3-diphenylurea	Plant hormone	$C_{13}H_{12}N_2O$	$[M+H]^+$	213.10224	5.19	3.00
2,3,5-trimethacarb	Insecticide	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.35	2.50
2,4-dimethylaniline	TP**	$C_8H_{11}N$	$[M+H]^+$	122.09643	2.47	1.68
2,6-dichlorobenzamide	TP**	$C_7H_5Cl_2NO$	$[M+H]^+$	189.98210	2.71	0.77
2,6-diethylaniline	TP**	$C_{10}H_{15}N$	$[M+H]^+$	150.12773	5.75	2.70
2-ethylhexyl Diphenyl Phosphate	Industrial contaminant	$C_{20}H_{27}O_4P$	$[M+H]^+$	363.17197	8.64	6.30
2-n-octyl-4-isothiazolin-3-one	Antimicrobial agent	$C_{11}H_{19}NOS$	$[M+H]^+$	214.12601	6.29	2.45
3,4 Dichloroaniline	Industrial contaminant	$C_6H_5Cl_2N$	$[M+H]^+$	161.98718	5.32	2.70
3,4,5-trimethacarb	Insecticide	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.28	2.70
3-hydroxycarbofuran*	TP**	$C_{12}H_{15}NO_4$	$C_{12}H_{14}NO_3^+$	220.09682	3.08	0.76
3-ketocarbofuran	TP**	$C_{12}H_{13}NO_4$	$[M+H]^+$	236.09173	4.03	1.80
4-bromo-3,5-dimethylphenyl-n-	Insecticide	$C_{10}H_{12}BrNO_2$	$[M+H]^+$	258.01242	5.91	3.10
Abamectin	Acaricide / Insecticide	$C_{48}H_{72}O_{14}$	$[M+Na]^+$	895.48143	8.78	3.80
Abate® (temephos)*	Insecticide	$C_{16}H_{20}O_6P_2S_3$	$[M+H]^+$	466.99701	8.03	6.00
Acephate*	Insecticide	$C_4H_{10}NO_3PS$	$C_2H_8O_3PS^+$	142.99263	0.96	-0.80
Acetamiprid*	Insecticide	$C_{10}H_{11}ClN_4$	$[M+H]^+$	223.07450	3.44	0.80
Acibenzolar-s-methyl*	Fungicide	$C_8H_6N_2OS_2$	$[M+H]^+$	210.99943	6.07	3.10
Aclonifen	Herbicide	$C_{12}H_9ClN_2O_3$	$[M+H]^+$	265.03745	6.93	4.04
Aconitine	Plant toxin	$C_{34}H_{47}NO_{11}$	$[M+H]^+$	646.32219	4.71	0.3***
Akton	Insecticide	$C_{12}H_{14}Cl_3O_3PS$	$[M+H]^+$	374.95396	8.30	4.8***
Alachlor	Herbicide	$C_{14}H_{20}ClNO_2$	$[M+H]^+$	270.12553	6.68	3.50
Aldicarb*	Insecticide	$C_7H_{14}N_2O_2S$	$[M+Na]^+$	213.06682	3.80	1.13
Aldicarb Sulphone*	TP**	$C_7H_{14}N_2O_4S$	$[M+H]^+$	223.07471	3.44	0.79
Aldicarb Sulphoxide*	TP**	$C_7H_{14}N_2O_3S$	$[M+H]^+$	207.07979	0.94	-0.20

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Allethrin	Insecticide	$C_{19}H_{26}O_3$	$[M+H]^+$	303.19547	8.08	4.78
Allidochlor	Herbicide	$C_8H_{12}ClNO$	$[M+H]^+$	174.06802	4.23	1.83
Alloxydim Sodium	Herbicide	$C_{17}H_{24}NNaO_5$	$[M+H]^+$	346.16249	7.12	/
Ametoctradin	Fungicide	$C_{15}H_{25}N_5$	$[M-H]^-$	274.20372	6.57	4.6***
Ametryn*	Herbicide	$C_9H_{17}N_5S$	$[M+H]^+$	228.12774	5.03	2.98
Amicarbazone	Herbicide	$C_{10}H_{19}N_5O_2$	$[M+H]^+$	242.16115	4.06	1.23
Amidosulfuron	Herbicide	$C_9H_{15}N_5O_7S_2$	$[M+H]^+$	370.04857	4.77	1.63
Aminocarb	Insecticide	$C_{11}H_{16}N_2O_2$	$[M+H]^+$	209.12845	1.71	1.90
Ancymidol	Rodenticide	$C_{15}H_{16}N_2O_2$	$[M+H]^+$	257.12845	4.26	1..91
Anilazine	Fungicide	$C_9H_5Cl_3N_4$	$[M+H]^+$	274.96526	6.26	3.88
Anilofos	Herbicide	$C_{13}H_{19}ClNO_3PS_2$	$[M+H]^+$	368.03053	7.12	3.81
Aspon ™	Insecticide	$C_{12}H_{28}O_5P_2S_2$	$[M+H]^+$	379.09262	8.73	6.00
Asulam	Herbicide	$C_8H_{10}N_2O_4S$	$[M+H]^+$	231.04341	2.25	-0.27
Atraton	Herbicide	$C_9H_{17}N_5O$	$[M+H]^+$	212.15059	3.75	2.70
Atrazine	Herbicide	$C_8H_{14}ClN_5$	$[M+H]^+$	216.10105	5.12	2.60
Atrazine Desisopropyl	TP**	$C_5H_8ClN_5$	$[M+H]^+$	174.05410	2.51	1.1***
Azaconazole	Fungicide	$C_{12}H_{11}Cl_2N_3O_2$	$[M+H]^+$	300.03011	5.21	2.32
Azadirachtin	Insecticide	$C_{35}H_{44}O_{16}$	$[M+H]^+$	721.27021	5.01	1.09
Azamethiphos	Insecticide	$C_9H_{10}ClN_2O_5PS$	$[M+H]^+$	324.98094	4.44	1.05
Azimsulfuron	Herbicide	$C_{13}H_{16}N_{10}O_5S$	$[M+H]^+$	425.10986	5.03	0.65
Aziprotryne	Herbicide	$C_7H_{11}N_7S$	$[M+H]^+$	226.08694	6.15	3.00
Azoxystrobin*	Fungicide	$C_{22}H_{17}N_3O_5$	$[M+H]^+$	404.12410	6.16	2.50
Beflubutamid	Herbicide	$C_{18}H_{17}F_4NO_2$	$[M+H]^+$	356.12682	6.96	4.70
Benalaxyl*	Fungicide	$C_{20}H_{23}NO_3$	$[M+H]^+$	326.17507	7.04	3.40
Benazolin	Herbicide	$C_9H_6ClNO_3S$	$[M+H]^+$	243.98297	3.88	2.50
Benodanil	Fungicide	$C_{13}H_{10}INO$	$[M+H]^+$	323.98799	5.67	2.85
Benomyl	Fungicide	$C_{14}H_{18}N_4O_3$	$[M+H]^+$	291.14517	6.10	2.12
Benoxacor	Herbicide	$C_{11}H_{11}Cl_2NO_2$	$[M+H]^+$	260.02396	6.06	2.70
Bensulfuron-methyl	Herbicide	$C_{16}H_{18}N_4O_7S$	$[M+H]^+$	411.09690	5.44	2.18
Bensulide	Herbicide	$C_{14}H_{24}NO_4PS_3$	$[M+H]^+$	398.06779	7.09	4.20
Bentazon	Herbicide	$C_{10}H_{12}N_2O_3S$	$[M+H]^+$	241.06414	4.48	2.34
Benthiavalicarb-isopropyl	Fungicide	$C_{18}H_{24}FN_3O_3S$	$[M+H]^+$	382.15952	5.93	2.52
Benzoximate*	Acaricide	$C_{18}H_{18}ClNO_5$	$C_9H_8ClO_3^+$	199.01565	7.53	3.73
Benzoylprop Ethyl	Herbicide	$C_{18}H_{17}Cl_2NO_3$	$[M+H]^+$	366.06583	7.28	4.1***
Benzthiazuron	Herbicide	$C_9H_9N_3OS$	$[M-H]^-$	206.03936	3.88	1.6***
Bioresmethrin	Insecticide	$C_{22}H_{26}O_3$	$[M+H]^+$	339.19547	8.89	4.70
Bitertanole* (mixture of isomers)	Fungicide	$C_{20}H_{23}N_3O_2$	$[M+H]^+$	338.18630	6.65	4.16
Bixafen	Fungicide	$C_{18}H_{12}Cl_2F_3N_3O$	$[M-H]^-$	412.02368	6.69	4.7***
Bladex	Herbicide	$C_9H_{13}ClN_6$	$[M+H]^+$	241.09630	4.40	2.22
Boscalid*	Fungicide	$C_{18}H_{12}Cl_2N_2O$	$[M+H]^+$	343.03995	6.32	2.96

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Bromacil	Herbicide	$C_9H_{13}BrN_2O_2$	$[M-H]^-$	259.00876	4.18	2.11
Bromofenvinphos-ethyl	Insecticide	$C_{12}H_{14}BrCl_2O_4P$	$[M+H]^+$	404.92397	7.03	3.2***
Bromophos Methyl	Insecticide	$C_8H_8BrCl_2O_3PS$	$[M+H]^+$	366.85409	8.06	5.21
Bromuconazole* (mixture of isomers)	Fungicide	$C_{13}H_{12}BrCl_2N_3O$	$[M+H]^+$	377.95902	6.12	3.24
Bupirimate*	Fungicide	$C_{13}H_{24}N_4O_3S$	$[M+H]^+$	317.16419	6.49	2.70
Buprofezin*	Insecticide	$C_{16}H_{23}N_3OS$	$[M+H]^+$	306.16346	7.96	4.30
Butachlor	Herbicide	$C_{17}H_{26}ClNO_2$	$[M+H]^+$	312.17248	8.11	4.50
Butafenacil*	Herbicide	$C_{20}H_{18}ClF_3N_2O_6$	$[M+NH_4]^+$	492.11437	6.72	3.20
Butocarboxim Sulphoxide	TP**	$C_7H_{14}N_2O_3S$	$[M+Na]^+$	229.06174	0.96	-1.02
Butoxycarboxim*	Insecticide	$C_7H_{14}N_2O_4S$	$[M+H]^+$	223.07471	3.44	-0.10
Butroxydim	Herbicide	$C_{24}H_{33}NO_4$	$[M+H]^+$	400.24824	8.14	1.90
Buturon	Herbicide	$C_{12}H_{13}ClN_2O$	$[M+H]^+$	237.07892	5.57	3***
Butylate	Herbicide	$C_{11}H_{23}NOS$	$[M+H]^+$	218.15731	7.97	4.15
Cadusafos	Insecticide	$C_{10}H_{23}O_2PS_2$	$[M+H]^+$	271.09499	7.33	3.90
Cafenstrole	Herbicide	$C_{16}H_{22}N_4O_3S$	$[M+H]^+$	351.14854	6.62	3.21
Carbaryl*	Insecticide	$C_{12}H_{11}NO_2$	$C_{10}H_9O^+$	145.06479	4.89	2.36
Carbendazim*	Fungicide	$C_9H_9N_3O_2$	$[M+H]^+$	192.07675	2.19	1.52
Carbetamide*	Herbicide	$C_{12}H_{16}N_2O_3$	$[M+H]^+$	237.12337	4.04	1,75
Carbofuran*	Insecticide	$C_{12}H_{15}NO_3$	$[M+H]^+$	222.11247	4.75	2.32
Carbophenothion	Insecticide	$C_{11}H_{16}ClO_2PS_3$	$[M+H]^+$	342.98114	8.39	5.33
Carboxin*	Fungicide	$C_{12}H_{13}NO_2S$	$[M+H]^+$	236.07398	5.07	2.14
Carfentrazone-ethyl*	Herbicide	$C_{15}H_{14}Cl_2F_3N_3O_3$	$[M+H]^+$	412.04371	6.93	3.36
Carpropamid	Fungicide	$C_{15}H_{18}Cl_3NO$	$[M+H]^+$	334.05267	7.10	4.23
Chinomethionate	Acaricide / Fungicide	$C_{10}H_6N_2OS_2$	$[M+H]^+$	234.99943	7.38	3.78
Chlorantraniliprole*	Acaricide / Insecticide	$C_{18}H_{14}BrCl_2N_5O_2$	$[M+H]^+$	483.97579	5.68	2.76
Chlorbromuron	Herbicide	$C_9H_{10}BrClN_2O_2$	$[M+H]^+$	294.96648	6.10	3.09
Chlordimeform	Insecticide	$C_{10}H_{13}ClN_2$	$[M+H]^+$	197.08400	2.64	2.89
Chlorfenapyr	Insecticide	$C_{15}H_{11}BrClF_3N_2O$	$[M+H]^+$	408.97465	7.93	4.83
Chlorfenvinphos (mixture Of Z and E)	Insecticide	$C_{12}H_{14}Cl_3O_4P$	$[M+H]^+$	358.97681	6.93	3.81
Chlorfluazuron*	Insecticide	$C_{20}H_9Cl_3F_5N_3O_3$	$[M-H]^-$	537.95569	8.30	5.80
Chloridazon	Herbicide	$C_{10}H_8ClN_3O$	$[M+H]^+$	222.04287	3.19	1.14
Chlorimuron Ethyl	Herbicide	$C_{15}H_{15}ClN_4O_6S$	$[M+H]^+$	415.04736	6.06	2.50
Chlorobenzuron	Insecticide	$C_{14}H_{10}Cl_2N_2O_2$	$[M+H]^+$	309.01921	6.64	5***
Chlorosulfuron	Herbicide	$C_{12}H_{12}ClN_5O_4S$	$[M+H]^+$	358.03713	4.80	/
Chlorotoluron*	Herbicide	$C_{10}H_{13}ClN_2O$	$[M+H]^+$	213.07892	4.93	2.41
Chloroxuron*	Herbicide	$C_{15}H_{15}ClN_2O_2$	$[M+H]^+$	291.08948	6.07	3.70
Chlorpyrifos	Insecticide	$C_9H_{11}Cl_3NO_3PS$	$[M+H]^+$	349.93356	8.21	4.96

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Chlorpyrifos-methyl	Insecticide	$C_7H_7Cl_3NO_3PS$	$[M+H]^+$	321.90226	7.49	4.31
Chlorpyrifos-oxon	TP**	$C_9H_{11}Cl_3NO_4P$	$[M+H]^+$	333.95641	6.48	3.5***
Chlorthiophos	Insecticide	$C_{11}H_{15}Cl_2O_3PS_2$	$[M+H]^+$	360.96501	8.36	6***
Chromafenozide	Insecticide	$C_{24}H_{30}N_2O_3$	$[M-H]^-$	393.21837	6.65	5***
Cinidon-ethyl	Herbicide	$C_{19}H_{17}Cl_2NO_4$	$[M+H]^+$	394.06074	7.85	4.51
Cinmethylin	Herbicide	$C_{18}H_{26}O_2$	$[M+NH_4]^+$	292.22711	8.08	4.62
Cinosulfuron	Herbicide	$C_{15}H_{19}N_5O_7S$	$[M+H]^+$	414.10780	4.57	2.04
Clarithromycin	Antibiotic	$C_{38}H_{69}NO_{13}$	$[M+H]^+$	748.48417	4.89	3.16
Clethodim*	Herbicide	$C_{17}H_{26}ClNO_3S$	$[M+H]^+$	360.13947	7.86	4.21
Climbazol	Antifungal	$C_{15}H_{17}ClN_2O_2$	$[M+H]^+$	293.10513	5.02	3.76
Clodinafop (acid Free)	Herbicide	$C_{14}H_{11}ClFNO_4$	$[M+H]^+$	312.04334	5.76	3.4***
Clodinafop-propargyl	Herbicide	$C_{17}H_{13}ClFNO_4$	$[M+H]^+$	350.05899	7.11	3.90
Clofentezine*	Acaricide	$C_{14}H_8Cl_2N_4$	$[M+H]^+$	303.01988	7.39	3.10
Clomeprop	Herbicide	$C_{16}H_{15}Cl_2NO_2$	$[M-H]^-$	322.04071	7.76	4.80
Cloquintocet-mexyl	Herbicide	$C_{18}H_{22}ClNO_3$	$[M+H]^+$	336.13610	7.90	5.03
Cloransulam-methyl	Herbicide	$C_{15}H_{13}ClFN_5O_5S$	$[M+H]^+$	430.03827	5.41	-0.37
Clothianidin*	Insecticide	$C_6H_8ClN_5O_2S$	$[M+H]^+$	250.01600	3.03	0.70
Command (clomazone)	Herbicide	$C_{12}H_{14}ClNO_2$	$[M+H]^+$	240.07858	5.69	2.50
Coumaphos	Insecticide	$C_{14}H_{16}ClO_5PS$	$[M+H]^+$	363.02174	7.33	4.13
Coumaphos Oxon	Insecticide	$C_{14}H_{16}ClO_6P$	$[M+H]^+$	347.04458	5.69	2.78
Crimidine	Rodenticide	$C_7H_{10}ClN_3$	$[M+H]^+$	172.06360	3.73	1.31
Crotoxyphos	Insecticide	$C_{14}H_{19}O_6P$	$[M+NH_4]^+$	332.12575	5.89	3.30
Crufomate	Insecticide	$C_{12}H_{19}ClNO_3P$	$[M+H]^+$	292.08639	6.23	3.42
Cumyluron	Herbicide	$C_{17}H_{19}ClN_2O$	$[M+H]^+$	303.12587	6.15	3.70
Cyanofenphos	Insecticide	$C_{15}H_{14}NO_2PS$	$[M+H]^+$	304.05557	7.17	4.29
Cyanophos	Insecticide	$C_9H_{10}NO_3PS$	$[M+H]^+$	244.01918	5.85	2.71
Cyantraniliprole	Insecticide	$C_{19}H_{14}BrClN_6O_2$	$[M+H]^+$	475.01020	5.17	3.9***
Cyazofamid*	Fungicide	$C_{13}H_{13}ClN_4O_2S$	$[M+H]^+$	325.05205	6.92	3.20
Cyclanilide	Plant growth regulator	$C_{11}H_9Cl_2NO_3$	$[M+H]^+$	274.00323	5.71	3.25
Cycloate	Herbicide	$C_{11}H_{21}NOS$	$[M+H]^+$	216.14166	7.62	3.88
Cyclohexamide	Antifungal	$C_{15}H_{23}NO_4$	$[M+H]^+$	282.16998	3.79	0.55
Cycloprothrin	Insecticide	$C_{26}H_{21}Cl_2NO_4$	$[M+H]^+$	482.09204	8.52	6.2***
Cyclosulfamuron	Herbicide	$C_{17}H_{19}N_5O_6S$	$[M+H]^+$	422.11288	6.36	2.05
Cycloxidim	Herbicide	$C_{17}H_{27}NO_3S$	$[M+H]^+$	326.17844	7.78	3.23
Cycluron*	Herbicide	$C_{11}H_{22}N_2O$	$[M+H]^+$	199.18049	5.12	2.4***
Cyflufenamid	Fungicide	$C_{20}H_{17}F_5N_2O_2$	$[M+H]^+$	413.12830	7.55	4.70
Cyhalofop-butyl	Herbicide	$C_{20}H_{20}FNO_4$	$[M+H]^+$	358.14491	7.75	3.31
Cymiazole	Veterinary drug	$C_{12}H_{14}N_2S$	$[M+H]^+$	219.09505	3.19	3***
Cymoxanil*	Fungicide	$C_7H_{10}N_4O_3$	$C_4H_6N_3O_2^+$	128.04545	3.66	0.59
Cyphenothrin	Insecticide	$C_{24}H_{25}NO_3$	$[M+H]^+$	376.19072	8.89	6.29

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Cyprazine	Herbicide	$C_9H_{14}ClN_5$	$[M+H]^+$	228.10105	5.13	3.06
Cyproconazole* (mixture of isomers)	Fungicide	$C_{15}H_{18}ClN_3O$	$[M+H]^+$	292.12112	6.17	2.90
Cyprodinil*	Fungicide	$C_{14}H_{15}N_3$	$[M+H]^+$	226.13387	6.48	4.00
Cyprofuram	Fungicide	$C_{14}H_{14}ClNO_3$	$[M+H]^+$	280.07350	5.23	2.5***
Cyprosulphamide	Herbicide	$C_{18}H_{18}N_2O_5S$	$[M+H]^+$	375.10092	4.73	2.1***
Cyromazine*	Insecticide	$C_6H_{10}N_6$	$[M+H]^+$	167.10397	0.94	-0.06
Cythioate	Insecticide	$C_8H_{12}NO_5PS_2$	$[M+H]^+$	297.99673	4.41	1.6***
Daimuron	Herbicide	$C_{17}H_{20}N_2O$	$[M+H]^+$	269.16484	6.22	2.70
Daminozide	Plant growth regulator	$C_6H_{12}N_2O_3$	$[M+H]^+$	161.0921	0.90	-1.50
Danitol	Acaricide	$C_{22}H_{23}NO_3$	$[M+H]^+$	350.17507	8.59	5.70
Dazomet	Fungicide / Herbicide	$C_5H_{10}N_2S_2$	$[M+H]^+$	163.03582	2.51	0.63
Dementon-s-methyl-sulphone	TP**	$C_6H_{15}O_5PS_2$	$[M+H]^+$	263.01713	2.55	-0.30
Demeton O	Insecticide	$C_8H_{19}O_3PS_2$	$[M+H]^+$	259.05860	7.05	3.21
Demeton S	Insecticide	$C_8H_{19}O_3PS_2$	$[M+H]^+$	259.05860	5.51	2.09
Demeton-s-methyl	TP**	$C_6H_{15}O_3PS_2$	$[M+H]^+$	231.02730	4.48	1.02
Deoxynivalenol	Mycotoxin	$C_{15}H_{20}O_6$	$[M+H]^+$	297.13327	0.93	-0.71
Desethyl Atrazine	TP**	$C_6H_{10}ClN_5$	$[M+H]^+$	188.06975	3.28	1.51
Desmedipham	Herbicide	$C_{16}H_{16}N_2O_4$	$[M+H]^+$	301.11828	5.78	3.39
Desmethyl Norflurazon	TP**	$C_{11}H_7ClF_3N_3O$	$[M-H]^-$	288.01570	4.82	1.6***
Desmethyl-formamido-pirimicarb	TP**	$C_{11}H_{16}N_4O_3$	$[M+H]^+$	253.12952	4.36	0.9***
Desmetryn	Herbicide	$C_8H_{15}N_5S$	$[M+H]^+$	214.11209	4.36	2.38
Dialifos	Insecticide	$C_{14}H_{17}ClNO_4PS_2$	$[M+H]^+$	394.00979	7.60	4.69
Diazinon	Insecticide	$C_{12}H_{21}N_2O_3PS$	$[M+H]^+$	305.10833	7.39	3.81
Diazinon-o-analog	TP**	$C_{12}H_{21}N_2O_4P$	$[M+H]^+$	289.13117	5.37	2.07
Dibrom	Acaricide / Insecticide	$C_4H_7Br_2Cl_2O_4P$	$[M+H]^+$	380.78760	5.46	1.38
Dichlofenthion	Nematicide	$C_{10}H_{13}Cl_2O_3PS$	$[M+H]^+$	314.97729	8.17	5.14
Dichlormid	Herbicide	$C_8H_{11}Cl_2NO$	$[M+H]^+$	208.02905	5.21	1.84
Dichlorvos	Acaricide / Insecticide	$C_4H_7Cl_2O_4P$	$[M+H]^+$	220.95318	4.40	1.43
Diclobutrazol* (mixture of stereo isomers)	Fungicide	$C_{15}H_{19}Cl_2N_3O$	$[M+H]^+$	328.09779	6.49	3.80
Diclocymet	Insecticide	$C_{15}H_{18}Cl_2N_2O$	$[M+H]^+$	313.08690	6.74	4.3***
Diclosulam	Herbicide	$C_{13}H_{10}Cl_2FN_5O_3S$	$[M+H]^+$	405.99382	5.50	0.85
Dicrotophos*	Insecticide	$C_8H_{16}NO_5P$	$[M+H]^+$	238.08389	2.57	0.00
Diethatyl Ethyl	Herbicide	$C_{16}H_{22}ClNO_3$	$[M+H]^+$	312.13610	6.96	3.60
Diethofencarb*	Fungicide	$C_{14}H_{21}NO_4$	$[M+H]^+$	268.15433	6.01	2.91
Difenoconazole* (mixture of isomers)	Fungicide	$C_{19}H_{17}Cl_2N_3O_3$	$[M+H]^+$	406.07197	7.18	4.30

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Difenoxurone	Herbicide	$C_{16}H_{18}N_2O_3$	$[M+H]^+$	287.13902	5.28	2.54
Diflubenzuron*	Insecticide	$C_{14}H_9ClF_2N_2O_2$	$[M+H]^+$	311.03934	6.43	3.88
Diflufenicen	Herbicide	$C_{19}H_{11}F_5N_2O_2$	$[M-H]^-$	393.06679	7.56	4.6***
Dimefox	Acaricide / Insecticide	$C_4H_{12}FN_2OP$	$[M+H]^+$	155.07441	2.66	-0.43
Dimefuron	Herbicide	$C_{15}H_{19}ClN_4O_3$	$[M+H]^+$	339.12184	5.64	2.51
Dimepiperate	Herbicide	$C_{15}H_{21}NOS$	$[M+H]^+$	264.14166	7.70	4.02
Dimethachlor	Herbicide	$C_{13}H_{18}ClNO_2$	$[M+H]^+$	256.10988	5.58	2.17
Dimethametryn	Herbicide	$C_{11}H_{21}N_5S$	$[M+H]^+$	256.15904	6.36	3.90
Dimethenamid	Herbicide	$C_{12}H_{18}ClNO_2S$	$[M+H]^+$	276.08195	6.11	2.15
Dimethirimol	Fungicide	$C_{11}H_{19}N_3O$	$[M+H]^+$	210.16009	3.01	1.5***
Dimethoate*	Acaricide / Insecticide	$C_5H_{12}NO_3PS_2$	$[M+H]^+$	230.00690	3.33	0.78
Dimethomorph*	Fungicide	$C_{21}H_{22}ClNO_4$	$[M+H]^+$	388.13101	5.85	2.68
Dimethylvinphos	Insecticide	$C_{10}H_{10}Cl_3O_4P$	$[M+H]^+$	330.94551	6.19	3.13
Dimetilan	Insecticide	$C_{10}H_{16}N_4O_3$	$[M+H]^+$	241.12952	3.41	0.27
Dimoxystrobin*	Fungicide	$C_{19}H_{22}N_2O_3$	$[M+H]^+$	327.17032	6.75	3.9***
Diniconazole* (e isomer)	Fungicide	$C_{15}H_{17}Cl_2N_3O$	$[M+H]^+$	326.08214	6.82	4.30
Diniconazole* (z isomer)	Fungicide	$C_{15}H_{17}Cl_2N_3O$	$[M+H]^+$	326.08214	6.82	4.30
Dinitramine	Herbicide	$C_{11}H_{13}F_3N_4O_4$	$[M-H]^-$	321.08161	7.18	4.30
Dinotefuran*	Insecticide	$C_7H_{14}N_4O_3$	$[M+H]^+$	203.11387	1.83	-0.55
Dioxacarb*	Insecticide	$C_{11}H_{13}NO_4$	$[M+H]^+$	224.09173	3.37	0.67
Diphenamid	Herbicide	$C_{16}H_{17}NO$	$[M+H]^+$	240.13829	5.62	2.17
Diphenylamine	Fungicide	$C_{12}H_{11}N$	$[M+H]^+$	170.09643	6.57	3.50
Dipropetryn	Herbicide	$C_{11}H_{21}N_5S$	$[M+H]^+$	256.15904	6.37	3.81
Disulfoton Sulphone	TP**	$C_8H_{19}O_4PS_3$	$[M+H]^+$	307.02559	5.65	1.87
Disulfoton Sulphoxide	TP**	$C_8H_{19}O_3PS_3$	$[M+H]^+$	291.03067	5.00	1.73
Ditalimfos	Fungicide	$C_{12}H_{14}NO_4PS$	$[M+H]^+$	300.04539	6.63	3.48
Dithianon	Fungicide	$C_{14}H_4N_2O_2S_2$	$[M+H]^+$	296.9787	6.45	2.84
Dithiopyr	Herbicide	$C_{15}H_{16}F_5NO_2S_2$	$[M+H]^+$	402.06154	7.82	4.75
Diuron*	Herbicide	$C_9H_{10}Cl_2N_2O$	$[M-H]^-$	231.00974	5.20	2.68
Dodemorph	Fungicide	$C_{18}H_{35}NO$	$[M+H]^+$	282.27914	5.10	5.8***
Doramectin*	Veterinary drug	$C_{50}H_{74}O_{14}$	$[M+Na]^+$	921.49708	9.18	4.40
Dyfonate ™	Insecticide	$C_{10}H_{15}OPS_2$	$[M+H]^+$	247.03747	7.39	3.94
Edifenphos	Fungicide	$C_{14}H_{15}O_2PS_2$	$[M+H]^+$	311.03239	6.91	3.48
Emamectin*	Insecticide	$C_{49}H_{75}NO_{13}$	$[M+H]^+$	886.53112	6.92	5.00
Empenthrin	Insecticide	$C_{18}H_{26}O_2$	$[M+H]^+$	275.20056	8.82	/
Epn	Insecticide	$C_{14}H_{14}NO_4PS$	$[M+H]^+$	324.04539	7.56	4.78
Epoxiconazole* (iso)	Fungicide	$C_{17}H_{13}ClFN_3O$	$[M+H]^+$	330.08039	6.29	3.44
Eprinomectin*	Veterinary drug	$C_{50}H_{75}NO_{14}$	$[M+H]^+$	914.52603	8.46	5.70

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Eptc (s-ethyl Dipropylthiocarbamate)	Herbicide	$C_9H_{19}NOS$	$[M+H]^+$	190.12601	6.91	3.21
Erythromycin	Antibiotic	$C_{37}H_{67}NO_{13}$	$[M+H]^+$	734.46852	4.15	3.06
Esbiol	Insecticide	$C_{19}H_{26}O_3$	$[M+H]^+$	303.19547	8.07	/
Esprocarb	Herbicide	$C_{15}H_{23}NOS$	$[M+H]^+$	266.15731	8.06	4.60
Etaconazole*	Fungicide	$C_{14}H_{15}Cl_2N_3O_2$	$[M+H]^+$	328.06141	6.34	3.10
Ethaboxam	Fungicide	$C_{14}H_{16}N_4OS_2$	$[M+H]^+$	321.08383	5.10	/
Ethametsulfuron-methyl	Herbicide	$C_{15}H_{18}N_6O_6S$	$[M+H]^+$	411.10813	4.93	1.59
Ethidimuron	Herbicide	$C_7H_{12}N_4O_3S_2$	$[M+H]^+$	265.04236	3.07	/
Ethiofencarb*	Insecticide	$C_{11}H_{15}NO_2S$	$[M+H]^+$	226.08963	5.05	2.04
Ethiofencarb-sulphone	TP**	$C_{11}H_{15}NO_4S$	$[M+H]^+$	258.07946	3.03	/
Ethiofencarb-sulphoxide	TP**	$C_{11}H_{15}NO_3S$	$[M+H]^+$	242.08454	2.95	/
Ethion	Acaricide / Insecticide	$C_9H_{22}O_4P_2S_4$	$[M+H]^+$	384.9949	8.22	5.07
Ethiozin	Herbicide	$C_9H_{16}N_4OS$	$[M+H]^+$	229.11176	5.19	2.08
Ethiprole*	Insecticide	$C_{13}H_9Cl_2F_3N_4OS$	$[M-H]^-$	394.97535	5.85	2.90
Ethirimol*	Fungicide	$C_{11}H_{19}N_3O$	$[M+H]^+$	210.16009	3.07	2.22
Ethofumesate*	Herbicide	$C_{13}H_{18}O_5S$	$[M+H]^+$	287.09477	6.28	2.70
Ethoprophos (prophos)	Nematicide	$C_8H_{19}O_2PS_2$	$[M+H]^+$	243.06369	6.38	3.59
Ethoxyquin	Industrial contaminant	$C_{14}H_{19}NO$	$[M+H]^+$	218.15394	6.19	4.05
Ethoxysulfuron	Herbicide	$C_{15}H_{18}N_4O_7S$	$[M+H]^+$	399.09690	6.07	/
Ethyclozate	Plant hormone	$C_{11}H_{11}ClN_2O_2$	$[M+H]^+$	239.05818	5.28	/
Etobenzanid	Herbicide	$C_{16}H_{15}Cl_2NO_3$	$[M+H]^+$	340.05018	7.25	/
Etoxazole*	Acaricide	$C_{21}H_{23}F_2NO_2$	$[M+H]^+$	360.17696	8.46	5.59
Etrimfos	Insecticide	$C_{10}H_{17}N_2O_4PS$	$[M+H]^+$	293.07194	7.21	/
Famphur	Insecticide	$C_{10}H_{16}NO_5PS_2$	$[M+H]^+$	326.02803	5.80	2.20
Fenamidone*	Fungicide	$C_{17}H_{17}N_3OS$	$[M+H]^+$	312.11651	6.19	2.80
Fenamiphos	Insecticide	$C_{13}H_{22}NO_3PS$	$[M+H]^+$	304.11308	6.17	3.23
Fenamiphos Sulphone	TP**	$C_{13}H_{22}NO_5PS$	$[M+H]^+$	336.10291	4.58	/
Fenamiphos Sulphoxide	TP**	$C_{13}H_{22}NO_4PS$	$[M+H]^+$	320.10800	4.04	/
Fenarimol*	Fungicide	$C_{17}H_{12}Cl_2N_2O$	$[M+H]^+$	331.03995	6.17	3.60
Fenazaquin*	Acaricide	$C_{20}H_{22}N_2O$	$[M+H]^+$	307.18049	8.51	5.51
Fenazox	Insecticide	$C_{12}H_{10}N_2O$	$[M+H]^+$	199.08659	7.02	#N/A
Fenbuconazole*	Fungicide	$C_{19}H_{17}ClN_4$	$[M+H]^+$	337.12145	6.50	3.23
Fenchlorazol-ethyl	Herbicide	$C_{12}H_8Cl_5N_3O_2$	$[M+H]^+$	403.91031	7.51	/
Fenchlorphos-oxon	TP**	$C_8H_8Cl_3O_4P$	$[M+H]^+$	304.92986	6.17	/
Fenfuram	Fungicide	$C_{12}H_{11}NO_2$	$[M+H]^+$	202.08626	5.14	2.2***
Fenhexamid*	Fungicide	$C_{14}H_{17}Cl_2NO_2$	$[M+H]^+$	302.07091	6.31	3.51
Fenitrothion	Insecticide	$C_9H_{12}NO_5PS$	$[M+H]^+$	278.02466	6.58	3.30
Fenobucarb*	Insecticide	$C_{12}H_{17}NO_2$	$[M+H]^+$	208.13321	5.87	2.78
Fenothiocarb	Acaricide	$C_{13}H_{19}NO_2S$	$[M+H]^+$	254.12093	6.76	3.30

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Fenoxanil	Fungicide	$C_{15}H_{18}Cl_2N_2O_2$	$[M+H]^+$	329.08181	6.89	4.50
Fenoxaprop	Herbicide	$C_{16}H_{12}ClNO_5$	$[M+H]^+$	334.04768	6.22	3.4***
Fenoxaprop-p-ethyl	Herbicide	$C_{18}H_{16}ClNO_5$	$[M+H]^+$	362.07898	7.70	4.1***
Fenoxycarb*	Insecticide	$C_{17}H_{19}NO_4$	$[M+H]^+$	302.13868	5.94	4.30
Fenpiclonil	Fungicide	$C_{11}H_6Cl_2N_2$	$[M+H]^+$	236.99808	5.72	4.3***
Fenpropathrin	Acaricide	$C_{22}H_{23}NO_3$	$[M+H]^+$	350.17507	8.60	6.00
Fenpropidin	Fungicide	$C_{19}H_{31}N$	$[M+H]^+$	274.25293	5.25	5.50
Fenpropimorph*	Fungicide	$C_{20}H_{33}NO$	$[M+H]^+$	304.26349	5.34	4.93
Fenpyroximate*	Acaricide / Insecticide	$C_{24}H_{27}N_3O_4$	$[M+H]^+$	422.20743	8.46	5.01
Fensulfothion	Insecticide / Nematicide	$C_{11}H_{17}O_4PS_2$	$[M+H]^+$	309.03787	5.37	2.23
Fensulfothion-oxon	TP**	$C_{11}H_{17}O_5PS$	$[M+H]^+$	293.06071	3.56	1.4***
Fensulfothion-oxon-sulphone	TP**	$C_{11}H_{17}O_6PS$	$[M+H]^+$	309.05563	4.11	1.5***
Fensulfothion-sulphone	TP**	$C_{11}H_{17}O_5PS_2$	$[M+H]^+$	325.03278	5.94	2.6***
Fenthion	Insecticide	$C_{10}H_{15}O_3PS_2$	$[M+H]^+$	279.02730	7.14	4.10
Fenthion Oxon	TP**	$C_{10}H_{15}O_4PS$	$[M+H]^+$	263.05015	5.37	2.4***
Fenthion Oxon Sulphoxide	TP**	$C_{10}H_{15}O_5PS$	$[M+H]^+$	279.04506	3.03	1***
Fenthion Sulphoxide	TP**	$C_{10}H_{15}O_4PS_2$	$[M+H]^+$	295.02222	4.76	2.7***
Fenthion-ethyl	Insecticide	$C_{12}H_{19}O_3PS_2$	$[M+H]^+$	307.05860	7.86	5***
Fenthion-sulphone	TP**	$C_{10}H_{15}O_5PS_2$	$[M+H]^+$	311.01713	5.41	2.8***
Fenthoxon Sulphone	TP**	$C_{10}H_{15}O_6PS$	$[M+H]^+$	295.03998	3.57	1.1***
Fenuron*	Herbicide	$C_9H_{12}N_2O$	$[M+H]^+$	165.10224	3.19	0.98
Ferimzone	Fungicide	$C_{15}H_{18}N_4$	$[M+H]^+$	255.16042	4.37	3.5***
Fipronil*	Acaricide / Insecticide	$C_{12}H_4Cl_2F_6N_4OS$	$[M-H]^-$	434.93143	6.87	4.00
Fipronil Sulfide	TP**	$C_{12}H_4Cl_2F_6N_4S$	$[M-H]^-$	418.93652	7.30	5.5***
Fipronil-desulfinyl	TP**	$C_{12}H_4Cl_2F_6N_4$	$[M-H]^-$	386.96444	7.05	4.6***
Flamprop Isopropyl	Herbicide	$C_{19}H_{19}ClFNO_3$	$[M+H]^+$	364.11103	7.25	4***
Flamprop-methyl (metavane)	TP**	$C_{17}H_{15}ClFNO_3$	$[M+H]^+$	336.07973	6.47	3.2***
Flamprop-m-isopropyl	Herbicide	$C_{19}H_{19}ClFNO_3$	$[M+H]^+$	364.11103	7.25	4***
Flazasulfuron	Herbicide	$C_{13}H_{12}F_3N_5O_5S$	$[M+H]^+$	408.05840	5.48	1.08
Flonicamid*	Insecticide	$C_9H_6F_3N_3O$	$[M+H]^+$	230.05357	2.71	0.30
Florasulam	Herbicide	$C_{12}H_8F_3N_5O_3S$	$[M+H]^+$	360.03727	4.63	1.22
Fluacrypyrim	Acaricide	$C_{20}H_{21}F_3N_2O_5$	$[M+H]^+$	427.14753	7.64	4.1***
Fluazifop	Herbicide	$C_{15}H_{12}F_3NO_4$	$[M+H]^+$	328.07912	5.77	2.9***
Fluazifop-butyl	Herbicide	$C_{19}H_{20}F_3NO_4$	$[M+H]^+$	384.14172	8.04	4.50
Fluazifop-p-butyl	Herbicide	$C_{19}H_{20}F_3NO_4$	$[M+H]^+$	384.14172	8.03	4.5***
Fluazinam*	Fungicide	$C_{13}H_4Cl_2F_6N_4O_4$	$[M-H]^-$	462.94410	7.90	4.01
Fluazuron	Acaricide	$C_{20}H_{10}Cl_2F_5N_3O_3$	$[M+H]^+$	506.00921	7.89	6.1***

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Flubendiamide*	Insecticide	$C_{23}H_{22}F_7IN_2O_4S$	$[M-H]^-$	681.01605	6.88	4.20
Flucarbazone-sodium	Herbicide	$C_{12}H_{10}F_3N_4NaO_6S$	$[M+H]^+$	419.02436	4.21	-1.85
Fluchloralin	Herbicide	$C_{12}H_{13}ClF_3N_3O_4$	$[M+H]^+$	356.06195	7.69	5.07
Flucycloxuron	Acaricide / Insecticide	$C_{25}H_{20}ClF_2N_3O_3$	$[M+H]^+$	484.12340	8.11	6.1***
Fludioxonil*	Fungicide	$C_{12}H_6F_2N_2O_2$	$[M-H]^-$	248.03973	8.21	4.12
Flufenacet*	Herbicide	$C_{14}H_{13}F_4N_3O_2S$	$[M+H]^+$	364.07374	6.70	3.20
Flufenoxuron*	Insecticide	$C_{21}H_{11}ClF_6N_2O_3$	$[M+H]^+$	489.04352	8.09	6.16
Flumestulam	Herbicide	$C_{12}H_9F_2N_5O_2S$	$[M-H]^-$	324.03723	7.76	0.21
Flumetralin	Herbicide	$C_{16}H_{12}ClF_4N_3O_4$	$[M+H]^+$	422.05252	8.23	5.2***
Flumiclorac-pentyl	Herbicide	$C_{21}H_{23}ClFNO_5$	$[M+NH_4]^+$	441.15870	7.88	4.8***
Flumioxazin	Herbicide	$C_{19}H_{15}FN_2O_4$	$[M+H]^+$	355.10886	5.84	2.55
Flumorph	Fungicide	$C_{21}H_{22}FNO_4$	$[M+H]^+$	372.16056	5.30	3.4***
Fluoglycofene-ethyl	Herbicide	$C_{18}H_{13}ClF_3NO_7$	$[M+NH_4]^+$	465.06709	7.69	3.6***
Fluometuron*	Herbicide	$C_{10}H_{11}F_3N_2O$	$[M-H]^-$	231.07507	5.00	2.42
Fluopicolide	Fungicide	$C_{14}H_8Cl_3F_3N_2O$	$[M+H]^+$	382.97271	6.41	3.26
Fluopyram	Fungicide	$C_{16}H_{11}ClF_6N_2O$	$[M+H]^+$	397.05369	6.46	4.5***
Fluoxastrobin*	Fungicide	$C_{21}H_{16}ClFN_4O_5$	$[M+H]^+$	459.08660	6.69	2.86
Flupyradifurone	Insecticide	$C_{12}H_{11}ClF_2N_2O_2$	$[M+H]^+$	289.05499	3.72	2.3***
Flupyrsulfuron-methyl-sodium	Herbicide	$C_{15}H_{13}F_3N_5NaO_7S$	$[M+H]^+$	488.04583	5.79	/
Fluquinconazole*	Fungicide	$C_{16}H_8Cl_2FN_5O$	$[M+H]^+$	376.01627	6.34	3.24
Fluridone	Herbicide	$C_{19}H_{14}F_3NO$	$[M+H]^+$	330.11003	5.86	1.87
Flurilazole	Herbicide	$C_{11}H_{13}Cl_2NO_3$	$[M+H]^+$	278.03453	3.66	2***
Flurochloridon (iso)	Herbicide	$C_{12}H_{10}Cl_2F_3NO$	$[M+H]^+$	312.01643	6.56	3.4***
Fluroxypyr	Herbicide	$C_7H_5Cl_2FN_2O_3$	$[M+H]^+$	254.97340	4.03	2.20
Fluroxypyr-meptyl	Herbicide	$C_{15}H_{21}Cl_2FN_2O_3$	$[M+H]^+$	367.09860	8.43	5.4***
Flurprimidol	Plant growth regulator	$C_{15}H_{15}F_3N_2O_2$	$[M+H]^+$	313.11584	5.92	3.3***
Flurtamone	Herbicide	$C_{18}H_{14}F_3NO_2$	$[M-H]^-$	332.09039	5.95	4.5***
Flusilazole*	Fungicide	$C_{16}H_{15}F_2N_3Si$	$[M+H]^+$	316.10761	6.51	3.70
Fluthiacet-methyl	Herbicide	$C_{15}H_{15}ClFN_3O_3S_2$	$[M+H]^+$	404.03002	6.92	3.77
Flutolanil*	Fungicide	$C_{17}H_{16}F_3NO_2$	$[M-H]^-$	322.10604	6.56	3.70
Flutriafol*	Fungicide	$C_{16}H_{13}F_2N_3O$	$[M+H]^+$	302.10995	4.98	2.29
Fomesafen	Herbicide	$C_{15}H_{10}ClF_3N_2O_6S$	$[M-H]^-$	436.98274	6.13	2.4***
Foramsulfuron	Herbicide	$C_{17}H_{20}N_6O_7S$	$[M+H]^+$	453.11870	4.20	0.17
Forchlorfenuron*	Plant growth regulator	$C_{12}H_{10}ClN_3O$	$[M-H]^-$	246.04396	4.95	3.20
Formetanate*	Acaricide / Insecticide	$C_{11}H_{15}N_3O_2$	$[M+H]^+$	222.12370	0.95	/
Fosthiazate	Nematicide	$C_9H_{18}NO_3PS_2$	$[M+H]^+$	284.05385	5.05	1.68

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Fuberidazole*	Fungicide	$C_{11}H_8N_2O$	$[M+H]^+$	185.07094	2.55	2.67
Furalaxyl*	Fungicide	$C_{17}H_{19}NO_4$	$[M+H]^+$	302.13868	5.94	2.61
Furathiocarb*	Insecticide	$C_{18}H_{26}N_2O_5S$	$[M+H]^+$	383.16352	7.97	4.70
Furmecyclox	Fungicide	$C_{14}H_{21}NO_3$	$[M+H]^+$	252.15942	6.94	3.1***
Guthion Ethyl	Insecticide	$C_{12}H_{16}N_3O_3PS_2$	$[M+H]^+$	346.04435	6.67	3.4***
Halofenozide*	Insecticide	$C_{18}H_{19}ClN_2O_2$	$[M+H]^+$	331.12078	5.99	3.22
Halosulfuron-methyl	Insecticide	$C_{13}H_{15}ClN_6O_7S$	$[M+H]^+$	435.04842	6.05	1.3***
Haloxyfop	Herbicide	$C_{15}H_{11}ClF_3NO_4$	$[M+H]^+$	362.04015	6.47	4.2***
Haloxyfop-2-ethoxyethyl	Herbicide	$C_{19}H_{19}ClF_3NO_5$	$[M+H]^+$	434.09766	7.81	4.7***
Haloxyfop-methyl	TP**	$C_{16}H_{13}ClF_3NO_4$	$[M+H]^+$	376.05580	7.51	4.5***
Haloxyfop-p Methyl	TP**	$C_{16}H_{13}ClF_3NO_4$	$[M+H]^+$	376.05580	7.52	4.5***
Heptenophos	Insecticide	$C_9H_{12}ClO_4P$	$[M+H]^+$	251.02345	5.31	2.32
Hexaconazole*	Fungicide	$C_{14}H_{17}Cl_2N_3O$	$[M+H]^+$	314.08214	6.52	3.90
Hexaflumuron*	Acaricide / Insecticide	$C_{16}H_8Cl_2F_6N_2O_3$	$[M-H]^-$	458.97434	7.37	5.68
Hexazinon	Herbicide	$C_{12}H_{20}N_4O_2$	$[M+H]^+$	253.16590	4.13	1.85
Hexythiazox*	Acaricide	$C_{17}H_{21}ClN_2O_2S$	$[M+H]^+$	353.10850	8.23	5.57
Hymexazole	Fungicide	$C_4H_5NO_2$	$[M+H]^+$	100.03930	1.73	0.1***
Imazalil*	Fungicide	$C_{14}H_{14}Cl_2N_2O$	$[M+H]^+$	297.05560	4.47	3.82
Imazamethabenz-methyl	Herbicide	$C_{16}H_{20}N_2O_3$	$[M+H]^+$	289.15467	4.14	2.6***
Imazamox	Herbicide	$C_{15}H_{19}N_3O_4$	$[M+H]^+$	306.14483	3.19	0.73
Imazapic	Herbicide	$C_{14}H_{17}N_3O_3$	$[M+H]^+$	276.13427	3.30	0.39
Imazaquin	Herbicide	$C_{17}H_{17}N_3O_3$	$[M+H]^+$	312.13427	4.45	2.5***
Imazethapyr	Herbicide	$C_{15}H_{19}N_3O_3$	$[M+H]^+$	290.14992	3.95	1.00
Imazosulfuron	Herbicide	$C_{14}H_{13}ClN_6O_5S$	$[M+H]^+$	413.04294	5.53	1.49
Imibenconazole	Fungicide	$C_{17}H_{13}Cl_3N_4S$	$[M-H]^-$	408.98538	7.69	5.8***
Imidacloprid*	Insecticide	$C_9H_{10}ClN_5O_2$	$[M+H]^+$	256.05958	3.19	0.57
Imidacloprid-olefin	TP**	$C_9H_8ClN_5O_2$	$[M+H]^+$	254.04393	2.60	2***
Imiprothrin (mixture of isomers)	Insecticide	$C_{17}H_{22}N_2O_4$	$[M+H]^+$	319.16523	6.51	2.90
Inabenfide	Insecticide	$C_{19}H_{15}ClN_2O_2$	$[M+H]^+$	339.08948	5.55	3.7***
Indaziflam	Herbicide	$C_{16}H_{20}FN_5$	$[M+H]^+$	302.17755	5.78	3.2***
Indoxacarb*	Insecticide	$C_{22}H_{17}ClF_3N_3O_7$	$[M+H]^+$	528.07799	7.52	4.65
Iodofenphos	Acaricide / Insecticide	$C_8H_8Cl_2IO_3PS$	$[M+H]^+$	412.84264	8.14	5.51
Iodosulfuron-methyl-sodium	Herbicide	$C_{14}H_{13}IN_5NaO_6S$	$[M+H]^+$	529.96018	5.57	/
Ipconazole*	Fungicide	$C_{18}H_{28}N_2O_3$	$[M+H]^+$	321.21727	6.08	4.1***
Iprobenfos	Fungicide	$C_{13}H_{21}O_3PS$	$[M+H]^+$	289.10218	6.61	3.00
Iprodione	Fungicide	$C_{13}H_{13}Cl_2N_3O_3$	$[M+H]^+$	330.04067	6.49	3.34
Iprovalicarb*	Fungicide	$C_{18}H_{28}N_2O_3$	$[M+H]^+$	321.21727	6.14	3.37***
Irgarol (cybutryne)	Algaecide	$C_{11}H_{19}N_5S$	$[M+H]^+$	254.14339	5.99	3.95

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Isazophos	Insecticide	$C_9H_{17}ClN_3O_3PS$	$[M+H]^+$	314.04896	6.89	3.82
Isocarbamide	Herbicide	$C_8H_{15}N_3O_2$	$[M+H]^+$	186.12370	3.14	0.8***
Isofenphos	Insecticide	$C_{15}H_{24}NO_4PS$	$[M+H]^+$	346.12365	7.64	4.12
Isofenphos-methyl	TP**	$C_{14}H_{22}NO_4PS$	$[M+H]^+$	332.10800	7.27	3.8***
Isofenphos-oxon	TP**	$C_{15}H_{24}NO_5P$	$[M+H]^+$	330.14649	6.02	2.4***
Isomethiozin	Herbicide	$C_{12}H_{20}N_4OS$	$[M+H]^+$	269.14306	6.20	3.5***
Isonoruron	Herbicide	$C_{13}H_{22}N_2O$	$[M+H]^+$	223.18049	5.46	2.3***
Isoprocarb*	Insecticide	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.34	2.31
Isopropalin	Herbicide	$C_{15}H_{23}N_3O_4$	$[M+H]^+$	310.17613	8.73	5.6***
Isoprothiolane	Fungicide	$C_{12}H_{18}O_4S_2$	$[M+H]^+$	291.07193	6.59	2.88
Isoproturon*	Herbicide	$C_{12}H_{18}N_2O$	$[M+H]^+$	207.14919	5.19	2.87
Isouron	Herbicide	$C_{10}H_{17}N_3O_2$	$[M+H]^+$	212.13935	4.34	1.6***
Isoxaben	Herbicide	$C_{18}H_{24}N_2O_4$	$[M+H]^+$	333.18088	6.40	3.94
Isoxadifen-ethyl	Herbicide	$C_{18}H_{17}NO_3$	$[M+H]^+$	296.12812	7.03	3.50
Isoxaflutole	Herbicide	$C_{15}H_{12}F_3NO_4S$	$[M+H]^+$	360.05119	6.00	2.32
Isoxathion	Insecticide	$C_{13}H_{16}NO_4PS$	$[M+H]^+$	314.06104	7.53	3.73
Ivermectin*	Veterinary drug	$C_{48}H_{74}O_{14}$	$[M+Na]^+$	897.49708	9.69	5.83
Karbutilate	Insecticide	$C_{14}H_{21}N_3O_3$	$[M+H]^+$	280.16557	4.62	1.7***
Ketoprofen	Anti-inflammatory drug	$C_{16}H_{14}O_3$	$[M+H]^+$	255.10157	5.26	3.12
Kresoxim Methyl*	Fungicide	$C_{18}H_{19}NO_4$	$[M+H]^+$	314.13868	6.86	3.40
Lactofen	Fungicide / Herbicide	$C_{19}H_{15}ClF_3NO_7$	$[M+NH_4]^+$	479.08274	7.97	4.81
Lambda Cyhalothrin	Insecticide	$C_{23}H_{19}ClF_3NO_3$	$[M+H]^+$	450.10783	8.71	7.00
Lenacil	Herbicide	$C_{13}H_{18}N_2O_2$	$[M-H]^-$	233.12955	4.59	1.7***
Leptophos	Fungicide	$C_{13}H_{10}BrCl_2O_2PS$	$[M+H]^+$	412.87485	8.86	6.3***
Levofloxacin	Antibiotic	$C_{18}H_{20}FN_3O_4$	$[M+H]^+$	362.15106	2.32	-0.39
Linuron*	Herbicide	$C_9H_{10}Cl_2N_2O_2$	$[M+H]^+$	249.01921	5.96	3.20
Lontrel (clopyralid)	Herbicide	$C_6H_3Cl_2NO_2$	$[M+H]^+$	191.96136	1.72	1.06
Lufenuron*	Fungicide / Insecticide	$C_{17}H_8Cl_2F_8N_2O_3$	$[M+H]^+$	510.98570	7.89	5.12
Malaoxon	TP**	$C_{10}H_{19}O_7PS$	$[M+H]^+$	315.06619	4.68	0.6***
Malathion	Insecticide	$C_{10}H_{19}O_6PS_2$	$[M+H]^+$	331.04335	6.53	2.36
Mandipropamid*	Fungicide	$C_{23}H_{22}ClNO_4$	$[M+H]^+$	412.13101	6.23	3.20
Mecarbam	Acaricide / Insecticide	$C_{10}H_{20}NO_5PS_2$	$[M+H]^+$	330.05933	6.84	2.29
Mefenacet*	Herbicide	$C_{16}H_{14}N_2O_2S$	$[M+H]^+$	299.08488	6.26	3.23
Mefenpyr-diethyl	Plant protection agent	$C_{16}H_{18}Cl_2N_2O_4$	$[M+H]^+$	373.07164	7.41	3.9***
Mefluidide	Plant growth regulator	$C_{11}H_{13}F_3N_2O_3S$	$[M+H]^+$	311.06718	4.61	2.02
Mepanipyrim*	Fungicide	$C_{14}H_{13}N_3$	$[M+H]^+$	224.11822	6.46	3.28
Mephosfolan	Acaricide / Insecticide	$C_8H_{16}NO_3PS_2$	$[M+H]^+$	270.03820	4.27	1***

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Mepronil*	Fungicide	$C_{17}H_{19}NO_2$	$[M+H]^+$	270.14886	6.49	3.66
Mesosulfuron-methyl	Herbicide	$C_{17}H_{21}N_5O_9S_2$	$[M+H]^+$	504.08535	4.96	-0.48
Mesotrione*	Herbicide	$C_{14}H_{13}NO_7S$	$[M+H]^+$	340.04855	4.34	0.90
Metaflumizone*	Insecticide	$C_{24}H_{16}F_6N_4O_2$	$[M-H]^-$	505.11047	7.80	6.2***
Metalaxyl*	Fungicide	$C_{15}H_{21}NO_4$	$[M+H]^+$	280.15433	5.21	1.65
Metalaxyl-m	Fungicide	$C_{15}H_{21}NO_4$	$[M+H]^+$	280.15433	5.21	1.6***
Metamitron	Herbicide	$C_{10}H_{10}N_4O$	$[M+H]^+$	203.09274	3.03	0.83
Metazachlor	Herbicide	$C_{14}H_{16}ClN_3O$	$[M+H]^+$	278.10547	5.48	2.7***
Metconazole*	Fungicide	$C_{17}H_{22}ClN_3O$	$[M+H]^+$	320.15242	6.75	3.85
Methabenzthiazuron*	Herbicide	$C_{10}H_{11}N_3OS$	$[M+H]^+$	222.06956	4.89	2.64
Methacrifos	Insecticide	$C_7H_{13}O_5PS$	$[M+H]^+$	241.02941	5.91	1.9***
Methamidophos*	Insecticide	$C_2H_8NO_2PS$	$[M+H]^+$	142.00862	0.92	-0.80
Methfuroxam	Fungicide	$C_{14}H_{15}NO_2$	$[M+H]^+$	230.11756	5.91	3***
Methidathion	Insecticide	$C_6H_{11}N_2O_4PS_3$	$[M+H]^+$	302.96914	5.87	2.20
Methiocarb*	Acaricide / Insecticide	$C_{11}H_{15}NO_2S$	$C_9H_{13}OS^+$	169.06816	5.82	2.92
Methiocarb Sulphone	TP**	$C_{11}H_{15}NO_4S$	$[M+H]^+$	258.07946	3.67	1.6***
Methiocarb Sulphoxide	TP**	$C_{11}H_{15}NO_3S$	$[M+H]^+$	242.08454	2.96	1.5***
Methomyl*	Insecticide	$C_5H_{10}N_2O_2S$	$[M+H]^+$	163.05358	2.40	0.60
Methomyl-oxime	TP**	C_3H_7NOS	$[M+H]^+$	106.03211	1.81	0.2***
Methoprotryne*	Herbicide	$C_{11}H_{21}N_5OS$	$[M+H]^+$	272.15396	5.09	2.82
Methoxyfenozide*	Insecticide	$C_{22}H_{28}N_2O_3$	$[M-H]^-$	367.20272	6.43	3.70
Methyl Paraoxon	TP**	$C_8H_{10}NO_6P$	$[M+H]^+$	248.03185	4.27	1.3***
Methyl Parathion	TP**	$C_8H_{10}NO_5PS$	$[M+H]^+$	264.00901	6.25	2.86
Metobromuron*	Herbicide	$C_9H_{11}BrN_2O_2$	$[M+H]^+$	259.00767	5.34	2.38
Metolachlor	Herbicide	$C_{15}H_{22}ClNO_2$	$[M+H]^+$	284.14118	6.71	3.13
Metolcarb	Acaricide / Insecticide	$C_9H_{11}NO_2$	$[M+H]^+$	166.08626	4.32	1.70
Metominostrobin (e isomer)	Fungicide	$C_{16}H_{16}N_2O_3$	$[M+H]^+$	285.12337	5.52	3.2***
Metominostrobin (z-type)	Fungicide	$C_{16}H_{16}N_2O_3$	$[M+H]^+$	285.12337	5.58	3.2***
Metosulam	Herbicide	$C_{14}H_{13}Cl_2N_5O_4S$	$[M+H]^+$	418.01381	5.02	3.08
Metoxuron	Herbicide	$C_{10}H_{13}ClN_2O_2$	$[M+H]^+$	229.07383	3.99	1.6***
Metrafenone	Fungicide	$C_{19}H_{21}BrO_5$	$[M+H]^+$	409.06451	7.65	4.6***
Metribuzin*	Herbicide	$C_8H_{14}N_4OS$	$[M+H]^+$	215.09611	4.49	1.70
Metsulfuron-methyl	Herbicide	$C_{14}H_{15}N_5O_6S$	$[M+H]^+$	382.08158	4.55	2.20
Mevinphos*	Insecticide	$C_7H_{13}O_6P$	$C_6H_{10}O_5P^+$	193.02604	3.54	0.13
Mexacarbate*	Insecticide	$C_{12}H_{18}N_2O_2$	$[M+H]^+$	223.14410	3.48	2.56
Mgk-264 (mixture of isomers)	Synergist	$C_{17}H_{25}NO_2$	$[M+H]^+$	276.19581	7.42	3.70
Molinate	Herbicide	$C_9H_{17}NOS$	$[M+H]^+$	188.11036	6.31	3.21
Monocrotophos*	Insecticide	$C_7H_{14}NO_5P$	$[M+H]^+$	224.06824	2.29	-0.20

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Monolinuron*	Algaecide	$C_9H_{11}ClN_2O_2$	$[M+H]^+$	215.05818	5.14	2.30
Monuron	Herbicide	$C_9H_{11}ClN_2O$	$[M+H]^+$	199.06327	4.31	1.94
Moxidectin*	Veterinary drug	$C_{37}H_{53}NO_8$	$[M+H]^+$	640.38439	9.33	6.00
N,n-diethyl-m-toluamide	Insect repellent	$C_{12}H_{17}NO$	$[M+H]^+$	192.13829	5.23	2.02
N,n'-ethylenethiourea	Industrial contaminant	$C_3H_6N_2S$	$[M+H]^+$	103.03245	0.90	-0.50
Naphthalophos (naftalofos)	Veterinary drug	$C_{16}H_{16}NO_6P$	$[M+H]^+$	350.07880	5.76	2.4***
Napropamide	Herbicide	$C_{17}H_{21}NO_2$	$[M+H]^+$	272.16451	6.49	3.36
Naptalam	Herbicide	$C_{18}H_{13}NO_3$	$[M+H]^+$	292.09682	4.49	3.5***
Neburon*	Herbicide	$C_{12}H_{16}Cl_2N_2O$	$[M+H]^+$	275.07125	6.80	4.10
Nicosulfuron	Herbicide	$C_{15}H_{18}N_6O_6S$	$[M+H]^+$	411.10813	4.05	/
Nitenpyram(iso)*	Insecticide / Veterinary drug	$C_{11}H_{15}ClN_4O_2$	$[M+H]^+$	271.09563	2.25	-0.66
Nitralin	Herbicide	$C_{13}H_{19}N_3O_6S$	$[M+H]^+$	346.10673	6.84	3.7***
Norflurazon	Herbicide	$C_{12}H_9ClF_3N_3O$	$[M+H]^+$	304.04590	5.34	2.30
Noruron	Pesticide	$C_{13}H_{22}N_2O$	$[M+H]^+$	223.18049	5.52	2.3***
Novaluron*	Insecticide	$C_{17}H_9ClF_8N_2O_4$	$[M-H]^-$	491.00503	7.54	5.27
Nuarimol*	Fungicide	$C_{17}H_{12}ClFN_2O$	$[M+H]^+$	315.06950	5.62	3.18
Ofurace	Fungicide	$C_{14}H_{16}ClNO_3$	$[M+H]^+$	282.08915	5.09	2.7***
Omethoate*	Insecticide	$C_5H_{12}NO_4PS$	$[M+H]^+$	214.02974	0.92	-0.74
Orbencarb	Herbicide	$C_{12}H_{16}ClNOS$	$[M+H]^+$	258.07139	7.36	3.4***
Orysastrobin	Fungicide	$C_{18}H_{25}N_5O_5$	$[M+H]^+$	392.19285	6.23	2.5***
Oryzalin	Herbicide	$C_{12}H_{18}N_4O_6S$	$[M-H]^-$	345.08743	6.47	3.73
Oxadiargyl	Herbicide	$C_{15}H_{14}Cl_2N_2O_3$	$[M+H]^+$	341.04542	7.35	4.1***
Oxadiazon	Herbicide	$C_{15}H_{18}Cl_2N_2O_3$	$[M+H]^+$	345.07672	8.15	4.80
Oxadixyl*	Fungicide	$C_{14}H_{18}N_2O_4$	$[M+H]^+$	279.13393	4.24	0.80
Oxasulfuron	Herbicide	$C_{17}H_{18}N_4O_6S$	$[M+H]^+$	407.10198	4.40	1.6***
Oxaziclomefone	Herbicide	$C_{20}H_{19}Cl_2NO_2$	$[M+H]^+$	376.08656	7.98	5.2***
Oximino Oxamyl	Nematicide	$C_5H_{10}N_2O_2S$	$[M+H]^+$	163.05358	1.77	1.2***
Oxycarboxin	Fungicide	$C_{12}H_{13}NO_4S$	$[M+H]^+$	268.06381	3.84	0.77
Oxydemeton-methyl	Acaricide / Insecticide	$C_6H_{15}O_4PS_2$	$[M+H]^+$	247.02222	2.14	-0.74
Oxyfluorfen	Herbicide	$C_{15}H_{11}ClF_3NO_4$	$[M+H]^+$	362.04015	7.98	4.73
Paclobutrazol* (mixture of stereoisomers)	Fungicide	$C_{15}H_{20}ClN_3O$	$[M+H]^+$	294.13677	5.83	3.20
Paraoxon Ethyl	Insecticide	$C_{10}H_{14}NO_6P$	$[M+H]^+$	276.06315	5.28	1.98
Parathion	Insecticide	$C_{10}H_{14}NO_5PS$	$[M+H]^+$	292.04031	7.10	3.83
Pebulate	Herbicide	$C_{10}H_{21}NOS$	$[M+H]^+$	204.14166	7.57	3.83
Penconazol	Fungicide	$C_{13}H_{15}Cl_2N_3$	$[M+H]^+$	284.07158	6.70	3.72
Pencycuron	Fungicide	$C_{19}H_{21}ClN_2O$	$[M-H]^-$	327.12696	7.42	4.8***
Pendimethalin	Herbicide	$C_{13}H_{19}N_3O_4$	$[M+H]^+$	282.14483	8.22	5.20

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Penfluron	Insecticide	$C_{15}H_9F_5N_2O_2$	$[M-H]^-$	343.05114	6.73	4***
Penoxsulam	Herbicide	$C_{16}H_{14}F_5N_5O_5S$	$[M-H]^-$	482.05631	5.37	-0.35
Pentanochlor	Herbicide	$C_{13}H_{18}ClNO$	$[M+H]^+$	240.11497	6.89	4.3***
Penthiopyrad	Fungicide	$C_{16}H_{20}F_3N_3OS$	$[M-H]^-$	358.12064	7.03	4***
Pethoxamid	Herbicide	$C_{16}H_{22}ClNO_2$	$[M+H]^+$	296.14118	6.66	3.5***
Phenmedipham	Herbicide	$C_{16}H_{16}N_2O_4$	$[M+H]^+$	301.11828	5.78	3.6***
Phenothrin	Insecticide	$C_{23}H_{26}O_3$	$[M+H]^+$	351.19547	9.11	7.54
Phenthoate	Insecticide	$C_{12}H_{17}O_4PS_2$	$[M+H]^+$	321.03787	7.15	3.7***
Phenylurea	Herbicide	$C_7H_8N_2O$	$[M+H]^+$	137.07094	2.34	0.8***
Phorate Oxon Sulphoxide	TP**	$C_7H_{17}O_4PS_2$	$[M+H]^+$	261.03787	3.03	1.8***
Phorate Sulphoxide	TP**	$C_7H_{17}O_3PS_3$	$[M+H]^+$	277.01502	5.00	3.5***
Phorate-oxon Sulphone	TP**	$C_7H_{17}O_5PS_2$	$[M+H]^+$	277.03278	3.66	2***
Phorat-sulphone	TP**	$C_7H_{17}O_4PS_3$	$[M+H]^+$	293.00994	5.71	3.7***
Phosalone	Acaricide / Insecticide	$C_{12}H_{15}ClNO_4PS_2$	$[M+H]^+$	367.99414	7.45	4.38
Phosfolan	Insecticide	$C_7H_{14}NO_3PS_2$	$[M+H]^+$	256.02255	3.72	0.6***
Phosmet	Insecticide	$C_{11}H_{12}NO_4PS_2$	$[M+H]^+$	318.00182	6.03	2.95
Phosmet Oxon	TP**	$C_{11}H_{12}NO_5PS$	$[M+H]^+$	302.02466	4.07	1.1***
Phosphamidon	Insecticide	$C_{10}H_{19}ClNO_5P$	$[M+H]^+$	300.07622	4.11	0.80
Phospholan-methyl	TP**	$C_5H_{10}NO_3PS_2$	$[M+H]^+$	227.99125	2.58	1.1***
Phoxim	Insecticide	$C_{12}H_{15}N_2O_3PS$	$[M+H]^+$	299.06138	7.04	4.4***
Picolinafen	Herbicide	$C_{19}H_{12}F_4N_2O_2$	$[M+H]^+$	377.09077	7.85	4.9***
Picoxystrobin*	Fungicide	$C_{18}H_{16}F_3NO_4$	$[M+H]^+$	368.11042	7.03	3.60
Piperalin	Fungicide	$C_{16}H_{21}Cl_2NO_2$	$[M+H]^+$	330.10221	4.56	4.31
Piperonyl Butoxide*	Synergise	$C_{19}H_{30}O_5$	$[M+NH_4]^+$	356.24315	7.92	4.75
Piperophos	Herbicide	$C_{14}H_{28}NO_3PS_2$	$[M+H]^+$	354.13210	7.59	4.2***
Pirimicarb*	Insecticide	$C_{11}H_{18}N_4O_2$	$[M+H]^+$	239.15025	3.91	1.70
Pirimicarb-desmethyl	TP**	$C_{10}H_{16}N_4O_2$	$[M+H]^+$	225.13460	2.68	1.6***
Pirimiphos Methyl	TP**	$C_{11}H_{20}N_3O_3PS$	$[M+H]^+$	306.10358	7.47	4.12
Pirimiphos-ethyl	TP**	$C_{13}H_{24}N_3O_3PS$	$[M+H]^+$	334.13488	8.17	5.00
Pirimiphos-methyl-n-desethyl	TP**	$C_9H_{16}N_3O_3PS$	$[M+H]^+$	278.07228	5.36	3.7***
Prallethrin	Insecticide	$C_{19}H_{24}O_3$	$[M+H]^+$	301.17982	7.58	4.49
Pretilachlor	Herbicide	$C_{17}H_{26}ClNO_2$	$[M+H]^+$	312.17248	7.69	4.1***
Primisulfuron-methyl	TP**	$C_{15}H_{12}F_4N_4O_7S$	$[M-H]^-$	467.02901	6.19	/
Probenazole	Fungicide	$C_{10}H_9NO_3S$	$[M+H]^+$	224.03759	4.96	1.4***
Prochloraz*	Fungicide	$C_{15}H_{16}Cl_3N_3O_2$	$[M+H]^+$	376.03809	6.62	4.10
Procyazine	Herbicide	$C_{10}H_{13}ClN_6$	$[M+H]^+$	253.09630	4.55	2.4***
Procymidone	Fungicide	$C_{13}H_{11}Cl_2NO_2$	$[M+H]^+$	284.02396	6.64	3***
Profenofos	Insecticide	$C_{11}H_{15}BrClO_3PS$	$[M+H]^+$	374.94017	7.68	4.68
Profoxydim Lithium	Herbicide	$C_{24}H_{32}ClNO_4S$	$[M+H]^+$	466.18133	8.88	/

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Prohydrojasmon	Plant growth retardant	$C_{15}H_{26}O_3$	$[M+H]^+$	255.19547	7.50	3.6***
Promecarb*	Insecticide	$C_{12}H_{17}NO_2$	$[M+H]^+$	208.13321	5.87	3.10
Prometon*	Herbicide	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.41	2.99
Prometryn*	Herbicide	$C_{10}H_{19}N_5S$	$[M+H]^+$	242.14339	5.88	3.51
Propachlor	Herbicide	$C_{11}H_{14}ClNO$	$[M+H]^+$	212.08367	5.49	2.18
Propamocarb*	Fungicide	$C_9H_{20}N_2O_2$	$[M+H]^+$	189.15975	0.96	1.12
Propanil	Herbicide	$C_9H_9Cl_2NO$	$[M-H]^-$	215.99884	5.69	3.07
Propaphos	Insecticide	$C_{13}H_{21}O_4PS$	$[M+H]^+$	305.09710	6.75	3.67
Propaquizafop	Herbicide	$C_{22}H_{22}ClN_3O_5$	$[M+H]^+$	444.13208	7.84	4.60
Propargite*	Insecticide	$C_{19}H_{26}O_4S$	$[M+NH_4]^+$	368.18901	8.36	5.00
Propazine	Herbicide	$C_9H_{16}ClN_5$	$[M+H]^+$	230.11670	6.53	2.93
Propazine-2-hydroxy	TP**	$C_9H_{17}N_5O$	$[M+H]^+$	212.15059	3.71	0.6***
Propetamphos	Insecticide	$C_{10}H_{20}NO_4PS$	$[M+H]^+$	282.09235	6.50	3.82
Propham*	Herbicide	$C_{10}H_{13}NO_2$	$C_7H_8NO_2^+$	138.05496	5.41	2.60
Propiconazol* (mixture of isomers)	Fungicide	$C_{15}H_{17}Cl_2N_3O_2$	$[M+H]^+$	342.07706	6.87	3.72
Propisochlor	Herbicide	$C_{15}H_{22}ClNO_2$	$[M+H]^+$	284.14118	6.71	3.9***
Propoxur*	Insecticide	$C_{11}H_{15}NO_3$	$C_8H_{10}NO_3^+$	168.06552	4.65	1.52
Propyzamide (pronamide)	Herbicide	$C_{12}H_{11}Cl_2NO$	$[M+H]^+$	256.02905	6.31	3.43
Proquinazid	Fungicide	$C_{14}H_{17}IN_2O_2$	$[M+H]^+$	373.04076	8.68	3.7***
Prosulfocarb	Herbicide	$C_{14}H_{21}NOS$	$[M+H]^+$	252.14166	7.80	3.9***
Prosulfuron	Herbicide	$C_{15}H_{16}F_3N_5O_4S$	$[M+H]^+$	420.09479	5.87	-0.21
Prothioconazole-desthio	TP**	$C_{14}H_{15}Cl_2N_3O$	$[M+H]^+$	312.06649	6.24	2.7***
Pymetrozine*	Insecticide	$C_{10}H_{11}N_5O$	$[M+H]^+$	218.10364	1.62	-0.18
Pyracarbolid*	Fungicide	$C_{13}H_{15}NO_2$	$[M+H]^+$	218.11756	4.88	2.1***
Pyraclofos	Insecticide	$C_{14}H_{18}ClN_2O_3PS$	$[M+H]^+$	361.05371	7.16	3.8***
Pyraclostrobin*	Fungicide	$C_{19}H_{18}ClN_3O_4$	$[M+H]^+$	388.10586	7.30	3.99
Pyraflufen-ethyl	TP**	$C_{15}H_{13}Cl_2F_3N_2O_4$	$[M+H]^+$	413.02772	7.12	3.49
Pyrazolynate	Herbicide	$C_{19}H_{16}Cl_2N_2O_4S$	$[M+H]^+$	439.02806	7.48	3.8***
Pyrazophos	Fungicide	$C_{14}H_{20}N_3O_5PS$	$[M+H]^+$	374.09341	7.27	3.1***
Pyrazosulfuron-ethyl	TP**	$C_{14}H_{18}N_6O_7S$	$[M+H]^+$	415.10305	5.93	0.7***
Pyrazoxyfen	Herbicide	$C_{20}H_{16}Cl_2N_2O_3$	$[M+H]^+$	403.06107	6.96	3.7***
Pyrethrin (mixture of isomers)	Insecticide	$C_{22}H_{28}O_5$	$[M+H]^+$	373.20095	7.57	4.30
Pyributicarb	Insecticide	$C_{18}H_{22}N_2O_2S$	$[M+H]^+$	331.14748	8.21	5.2***
Pyridaben*	Insecticide	$C_{19}H_{25}ClN_2OS$	$[M+H]^+$	365.14489	8.82	6.37
Pyridafol	Herbicide	$C_{10}H_7ClN_2O$	$[M+H]^+$	207.03197	3.48	2.4***
Pyridalyl	Insecticide	$C_{18}H_{14}Cl_4F_3NO_3$	$[M+H]^+$	491.97250	9.59	7.59
Pyridaphenthion	Insecticide	$C_{14}H_{17}N_2O_4PS$	$[M+H]^+$	341.07194	6.32	3.3***
Pyridate	Herbicide	$C_{19}H_{23}ClN_2O_2S$	$[M+H]^+$	379.12415	9.25	6.6***

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Pyrifenox (mixture of isomers))	Fungicide	$C_{14}H_{12}Cl_2N_2O$	$[M+H]^+$	295.03995	5.56	2.5***
Pyrimethanil*	Fungicide	$C_{12}H_{13}N_3$	$[M+H]^+$	200.11822	5.49	2.84
Pyriproxyfen*	Insecticide	$C_{20}H_{19}NO_3$	$[M+H]^+$	322.14377	8.11	5.37
Pyroquilon	Fungicide	$C_{11}H_{11}NO$	$[M+H]^+$	174.09134	4.07	1.57
Pyroxsulam	Herbicide	$C_{14}H_{13}F_3N_6O_5S$	$[M+H]^+$	435.06930	4.66	1.7***
Quinalphos	Insecticide	$C_{12}H_{15}N_2O_3PS$	$[M+H]^+$	299.06138	7.04	4.4***
Quinclorac	Herbicide	$C_{10}H_5Cl_2NO_2$	$[M+H]^+$	241.97701	3.81	2.97
Quinmerac	Herbicide	$C_{11}H_8ClNO_2$	$[M+H]^+$	222.03163	3.21	2.7***
Quinoclamine	Herbicide	$C_{10}H_6ClNO_2$	$[M+H]^+$	208.01598	4.36	2.1***
Quinoline	Antimicrobial agent	C_9H_7N	$[M+H]^+$	130.06513	2.10	2.03
Quinoxyfen*	Fungicide	$C_{15}H_8Cl_2FNO$	$[M+H]^+$	308.00397	8.00	4.66
Quizalofop	Herbicide	$C_{17}H_{13}ClN_2O_4$	$[M+H]^+$	345.06366	6.27	3.6***
Quizalofop-ethyl	TP**	$C_{19}H_{17}ClN_2O_4$	$[M+H]^+$	373.09496	7.75	4.28
Quizalofop-p-ethyl	TP**	$C_{19}H_{17}ClN_2O_4$	$[M+H]^+$	373.09496	7.74	4.30
Reserpine	Antihypertensive	$C_{33}H_{40}N_2O_9$	$[M+H]^+$	609.28066	4.84	3.20
Resmethrin	Insecticide	$C_{22}H_{26}O_3$	$[M+H]^+$	339.19547	8.89	5.43
Rimsulfuron	Herbicide	$C_{14}H_{17}N_5O_7S_2$	$[M+H]^+$	432.06422	4.77	-1.47
Rotenone*	Insecticide	$C_{23}H_{22}O_6$	$[M+H]^+$	395.14892	6.72	4.10
Roxithromycin	Antibiotic	$C_{41}H_{76}N_2O_{15}$	$[M+H]^+$	837.53185	4.99	1.70
Saflufenacil	Herbicide	$C_{17}H_{17}ClF_4N_4O_5S$	$[M+H]^+$	501.06171	5.99	2.1***
Schradan (dmpa)	Herbicide	$C_8H_{24}N_4O_3P_2$	$[M+H]^+$	287.13964	3.05	-0.30
Sebuthylazin	Herbicide	$C_9H_{16}ClN_5$	$[M+H]^+$	230.11670	5.90	3.1***
Sebuthylazin-desethyl	TP**	$C_7H_{12}ClN_5$	$[M+H]^+$	202.08540	3.98	2.2***
Secbumeton*	Herbicide	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.45	3.2***
Selamectin Impurity B	Veterinary drug	$C_{43}H_{63}NO_{11}$	$[M+H]^+$	770.44739	9.65	5.4***
Sethoxydim	Herbicide	$C_{17}H_{29}NO_3S$	$[M+H]^+$	328.19409	8.09	/
S-hydroprene	Insecticide	$C_{17}H_{30}O_2$	$[M+H]^+$	267.23186	10.05	6.50
Siduron*	Herbicide	$C_{14}H_{20}N_2O$	$[M+H]^+$	233.16484	5.77	3.80
Silthiofam	Fungicide	$C_{13}H_{21}NOSSi$	$[M+H]^+$	268.11859	0.00	/
Simazine	Herbicide	$C_7H_{12}ClN_5$	$[M+H]^+$	202.08540	4.40	2.18
Simeconazole	Fungicide	$C_{14}H_{20}FN_3OSi$	$[M+H]^+$	294.14325	6.16	/
Simetone	Herbicide	$C_8H_{15}N_5O$	$[M+H]^+$	198.13494	3.36	1.80
Simetryn*	Herbicide	$C_8H_{15}N_5S$	$[M+H]^+$	214.11209	4.41	2.80
S-metolachlor	Herbicide	$C_{15}H_{22}ClNO_2$	$[M+H]^+$	284.14118	6.72	3.10
Spinetoram* (mixture of isomers)	Insecticide	$C_{42}H_{69}NO_{10}$	$[M+H]^+$	748.49942	6.94	5.9***
Spinosad* (mixure of Spinosyn A And D)	Insecticide	$C_{41}H_{65}NO_{10}$	$[M+H]^+$	732.46812	6.34	4.9***
Spirodiclofen*	Insecticide	$C_{21}H_{24}Cl_2O_4$	$[M+H]^+$	411.11244	8.81	5.10
Spiromesifen*	Insecticide	$C_{23}H_{30}O_4$	$[M+H]^+$	371.22169	8.70	4.55

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Spirotetramat*	Insecticide	$C_{21}H_{27}NO_5$	$[M+H]^+$	374.19620	6.04	3.2***
Spirotetramat-enol	TP**	$C_{18}H_{23}NO_3$	$[M+H]^+$	302.17507	4.45	2.4***
Spirotetramat-enol-glucoside	TP**	$C_{24}H_{33}NO_8$	$[M+H]^+$	464.22789	2.38	0.5***
Spirotetramat-mono-hydroxy	TP**	$C_{21}H_{27}NO_5$	$[M+H]^+$	374.19620	6.04	2.1***
Spiroxamine (mixture of isomers)*	Fungicide	$C_{18}H_{35}NO_2$	$[M+H]^+$	298.27406	5.39	4.2***
Sulcotrione	Herbicide	$C_{14}H_{13}ClO_5S$	$[M+H]^+$	329.02450	4.61	1.5***
Sulfallate	Herbicide	$C_8H_{14}ClNS_2$	$[M+H]^+$	224.03290	7.25	3.15
Sulfamerazine	Antibacterial agent	$C_{11}H_{12}N_4O_2S$	$[M+H]^+$	265.07537	2.46	0.14
Sulfamonomethoxine	Antibacterial agent	$C_{11}H_{12}N_4O_3S$	$[M+H]^+$	281.07029	3.00	0.80
Sulfentrazone*	Herbicide	$C_{11}H_{10}Cl_2F_2N_4O_3S$	$[M+H]^+$	386.98915	4.91	0.99
Sulfometuron Methyl	Herbicide	$C_{15}H_{16}N_4O_5S$	$[M+H]^+$	365.09142	4.73	1.20
Sulfosulfuron	Herbicide	$C_{16}H_{18}N_6O_7S_2$	$[M+H]^+$	471.07512	5.30	-0.77
Sulfoxaflor	Insecticide	$C_{10}H_{10}F_3N_3OS$	$[M+H]^+$	278.05695	3.91	0.80
Sulfuramid	Insecticide	$C_{10}H_6F_{17}NO_2S$	$[M-H]^-$	525.97750	8.32	5.6***
Sulprofos Sulphoxide	TP**	$C_{12}H_{19}O_3PS_3$	$[M+H]^+$	339.03067	6.37	3.5***
Systhane Tm	Fungicide	$C_{15}H_{17}ClN_4$	$[M+H]^+$	289.12145	6.16	2.94
Tau-fluvalinate	Insecticide	$C_{26}H_{22}ClF_3N_2O_3$	$[M+H]^+$	503.13438	9.02	7.7***
Tdcpp	Industrial contaminant	$C_9H_{15}Cl_6O_4P$	$[M+H]^+$	430.88829	6.89	3.65
Tebuconazol* (folicur)	Fungicide	$C_{16}H_{22}ClN_3O$	$[M+H]^+$	308.15242	6.49	3.70
Tebufenozide*	Insecticide	$C_{22}H_{28}N_2O_2$	$C_{18}H_{21}N_2O_2^+$	297.15975	6.82	4.25
Tebufenpyrad*	Acaricide	$C_{18}H_{24}ClN_3O$	$[M+H]^+$	334.16807	7.86	4.61
Tebupirimfos	Insecticide	$C_{13}H_{23}N_2O_3PS$	$[M+H]^+$	319.12398	8.21	4.20
Tebutam	Herbicide	$C_{15}H_{23}NO$	$[M+H]^+$	234.18524	6.72	3.4***
Tebuthiuron*	Herbicide	$C_9H_{16}N_4OS$	$[M+H]^+$	229.11176	4.06	1.79
Teflubenzuron*	Insecticide	$C_{14}H_6Cl_2F_4N_2O_2$	$[M+H]^+$	380.98152	7.46	4.56
Tembotrione	Herbicide	$C_{17}H_{16}ClF_3O_6S$	$[M+NH_4]^+$	458.06465	5.97	-1.09
Tepraloxydim	Herbicide	$C_{17}H_{24}ClNO_4$	$[M-H]^-$	340.13211	6.44	2.6***
Terbufos-sulphone	TP**	$C_9H_{21}O_4PS_3$	$[M+H]^+$	321.04124	6.33	2.5***
Terbufos-sulphoxide	TP**	$C_9H_{21}O_3PS_3$	$[M+H]^+$	305.04633	5.74	2.2***
Terbumeton*	Herbicide	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.41	3.1***
Terbumeton-desethyl	TP**	$C_8H_{15}N_5O$	$[M+H]^+$	198.13494	3.27	2.1***
Terbuthylazine	Herbicide	$C_9H_{16}ClN_5$	$[M+H]^+$	230.11670	5.96	3.40
Terbuthylazine-desethyl	TP**	$C_7H_{12}ClN_5$	$[M+H]^+$	202.08540	4.40	2***
Terbutol (terbucarb)	Insecticide	$C_{17}H_{27}NO_2$	$[M+H]^+$	278.21146	7.52	5.2***
Terbutryne*	Herbicide	$C_{10}H_{19}N_5S$	$[M+H]^+$	242.14339	5.88	3.74
Terbutylazine-2-hydroxy	TP**	$C_9H_{17}N_5O$	$[M+H]^+$	212.15059	2.69	0.3***
Tetrachlorvinphos (iso))	Insecticide	$C_{10}H_9C_{l4}O_4P$	$[M+H]^+$	366.90367	6.65	3.53
Tetraconazole*	Fungicide	$C_{13}H_{11}Cl_2F_4N_3O$	$[M+H]^+$	372.02881	6.33	3.56

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Tetraethyl Dithiopyrophosphate	Insecticide	$C_8H_{20}O_5P_2S_2$	$[M+H]^+$	323.03002	7.36	3.99
Tetraethyl Pyrophosphate	Insecticide	$C_8H_{20}O_7P_2$	$[M+H]^+$	291.07571	4.04	/
Tetramethrin	Insecticide	$C_{19}H_{25}NO_4$	$[M+H]^+$	332.18564	7.96	4.73
Thenylchlor	Herbicide	$C_{16}H_{18}ClNO_2S$	$[M+H]^+$	324.08195	6.69	3.8***
Thiabendazole*	Anthelmintic / Fungicide	$C_{10}H_7N_3S$	$[M+H]^+$	202.04335	2.43	2.47
Thiacloprid*	Insecticide	$C_{10}H_9ClN_4S$	$[M+H]^+$	253.03092	3.90	1.26
Thiamethoxam*	Insecticide	$C_8H_{10}ClN_5O_3S$	$[M+H]^+$	292.02657	2.63	-0.13
Thiazafluron	Herbicide	$C_6H_7F_3N_4OS$	$[M+H]^+$	241.03654	4.41	0.8***
Thiazopyr	Herbicide	$C_{16}H_{17}F_5N_2O_2S$	$[M+H]^+$	397.10037	7.30	3.89
Thidiazuron*	Herbicide	$C_9H_8N_4OS$	$[M-H]^-$	219.03461	4.09	1.77
Thiencarbazone-methyl	Herbicide	$C_{12}H_{14}N_4O_7S_2$	$[M+H]^+$	391.03767	4.54	1.2***
Thifensulfuron-methyl	Herbicide	$C_{12}H_{13}N_5O_6S_2$	$[M+H]^+$	388.03800	4.41	/
Thifluzamide	Fungicide	$C_{13}H_6Br_2F_6N_2O_2S$	$[M+H]^+$	528.84733	6.91	6***
Thiobencarb*	Herbicide	$C_{12}H_{16}ClNOS$	$[M+H]^+$	258.07139	7.36	3.40
Thiocarbazyl	Herbicide	$C_{16}H_{25}NOS$	$[M+H]^+$	280.17296	8.55	/
Thiodicarb	Insecticide	$C_{10}H_{18}N_4O_4S_3$	$[M+H]^+$	355.05630	4.71	1.62
Thiofanox*	Insecticide	$C_9H_{18}N_2O_2S$	$[M+Na]^+$	241.09812	5.02	2.2***
Thiofanox-sulfone	TP**	$C_9H_{18}N_2O_4S$	$[M+H]^+$	251.10601	3.38	0.9***
Thiofanox-sulfoxide	TP**	$C_9H_{18}N_2O_3S$	$[M+H]^+$	235.11109	2.80	0.8***
Thionazine (zinophos)	Insecticide	$C_8H_{13}N_2O_3PS$	$[M+H]^+$	249.04573	5.66	2***
Thiophanate Methyl*	Fungicide	$C_{12}H_{14}N_4O_4S_2$	$[M+H]^+$	343.05293	4.48	2.6***
Thiophanate-ethyl	Fungicide	$C_{14}H_{18}N_4O_4S_2$	$[M+H]^+$	371.08423	5.49	3.3***
Tiadinil	Fungicide	$C_{11}H_{10}ClN_3OS$	$[M-H]^-$	266.01604	6.13	3***
Tokuthion®	Insecticide	$C_{11}H_{15}Cl_2O_2PS_2$	$[M+H]^+$	344.97009	8.96	4.9***
Tolclofos-methyl	Fungicide	$C_9H_{11}Cl_2O_3PS$	$[M+H]^+$	300.96164	7.47	4.56
Tolfenpyrade	Herbicide	$C_{21}H_{22}ClN_3O_2$	$[M+H]^+$	384.14733	7.84	4.7***
Tolylfluanid	Fungicide	$C_{10}H_{13}Cl_2FN_2O_2S_2$	$[M+H]^+$	346.98523	7.35	3.90
Topramezone	Herbicide	$C_{16}H_{17}N_3O_5S$	$[M+H]^+$	364.09617	3.57	1.44
Tralkoxydim	Herbicide	$C_{20}H_{27}NO_3$	$[M+H]^+$	330.20637	8.24	4.1***
Triadimefon*	Fungicide	$C_{14}H_{16}ClN_3O_2$	$[M+H]^+$	294.10038	6.27	2.77
Triallate	Herbicide	$C_{10}H_{16}Cl_3NOS$	$[M+H]^+$	304.00910	8.50	4.60
Triasulfuron	Herbicide	$C_{14}H_{16}ClN_5O_5S$	$[M+H]^+$	402.06334	4.75	-0.59
Triazamate	Insecticide	$C_{13}H_{22}N_4O_3S$	$[M+H]^+$	315.14854	6.69	2.7***
Triaziflam	Herbicide	$C_{17}H_{24}FN_5O$	$[M+H]^+$	334.20377	6.12	3.5***
Triazophos	Insecticide	$C_{12}H_{16}N_3O_3PS$	$[M+H]^+$	314.07228	6.58	3.34
Triazoxid	Fungicide	$C_{10}H_6ClN_5O$	$[M+H]^+$	248.03336	4.56	0.9***
Tribenuron-methyl	Herbicide	$C_{15}H_{17}N_5O_6S$	$[M+H]^+$	396.09723	5.55	0.78
Tribufos (def)	Herbicide	$C_{12}H_{27}OPS_3$	$[M+H]^+$	315.10345	8.89	3.2***
Trichlorfon*	Insecticide	$C_4H_8Cl_3O_4P$	$[M+H]^+$	256.92986	2.90	0.51

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)	LogP
Tricyclazole*	Fungicide	$C_9H_7N_3S$	$[M+H]^+$	190.04335	3.57	1.70
Tridemorph (mixture of isomers)	Fungicide	$C_{19}H_{39}NO$	$[M+H]^+$	298.31044	6.43	6.9***
Trietazine	Herbicide	$C_9H_{16}ClN_5$	$[M+H]^+$	230.11670	6.58	3.34
Trifloxystrobin*	Fungicide	$C_{20}H_{19}F_3N_2O_4$	$[M+H]^+$	409.13697	7.64	4.50
Trifloxystrobin Metabolite	TP**	$C_{19}H_{17}F_3N_2O_4$	$[M+H]^+$	395.12132	6.71	4.3***
Trifloxysulfuron-sodium	Herbicide	$C_{14}H_{13}F_3N_5NaO_6S$	$[M+H]^+$	460.05091	5.07	/
Triflumizole*	Fungicide	$C_{15}H_{15}ClF_3N_3O$	$[M+H]^+$	346.09285	7.12	2.90
Triflumuron*	Insecticide	$C_{15}H_{10}ClF_3N_2O_3$	$[M+H]^+$	359.04048	7.00	4.91
Triflusulfuron-methyl	Herbicide	$C_{17}H_{19}F_3N_6O_6S$	$[M+H]^+$	493.11117	6.22	3.1***
Triforine	Fungicide	$C_{10}H_{14}Cl_6N_4O_2$	$[M+H]^+$	434.92917	5.30	2.20
Trinexapac-ethyl	Plant growth regulator	$C_{13}H_{16}O_5$	$[M+H]^+$	253.10705	5.52	0.9***
Triphenyl Phosphorothionate	Industrial contaminant	$C_{18}H_{15}O_3PS$	$[M+H]^+$	343.05523	8.21	6.3***
Tris(2-chloroethyl) Phosphate	Industrial contaminant	$C_6H_{12}Cl_3O_4P$	$[M+H]^+$	284.96116	4.71	1.78
Tris(o-cresyl) Phosphate	Industrial contaminant	$C_{21}H_{21}O_4P$	$[M+H]^+$	369.12502	8.28	6.34
Triticonazole*	Fungicide	$C_{17}H_{20}ClN_3O$	$[M+H]^+$	318.13677	6.03	3.29
Tritosulfuron	Herbicide	$C_{13}H_9F_6N_5O_4S$	$[M-H]^-$	444.02067	5.93	3.1***
Uniconazole	Plant growth regulator	$C_{15}H_{18}ClN_3O$	$[M+H]^+$	292.12112	6.22	3.6***
Vamidothion*	Insecticide	$C_8H_{18}NO_4PS_2$	$[M+H]^+$	288.04877	2.92	0.16
Vamidothion Sulfoxide	Insecticide	$C_8H_{18}NO_5PS_2$	$[M+H]^+$	304.04368	0.93	-1.10
Vernolate	Herbicide	$C_{10}H_{21}NOS$	$[M+H]^+$	204.14166	7.57	3.84
Xmc (3,5-xylyl Methylcarbamate)	Insecticide	$C_{10}H_{13}NO_2$	$[M+H]^+$	180.10191	4.97	2.23
Z-mevinphos	Insecticide	$C_7H_{13}O_6P$	$[M+H]^+$	193.02604	3.06	1.2***
Zoxamide*	Fungicide	$C_{14}H_{16}Cl_3NO_2$	$[M+H]^+$	336.03194	7.20	3.76

*Compound also used during sample preparation optimisation
**Transformation product
***XLogP3-AA indicated since no experimental LogP is available

Table S2: List of the samples used in this study and their associated metadata

Sample	ID	Used for	Type	Origin	Organic	Sugar content*	Water content*
Honey	**#1**	(i) method optimisation	Acacia	France	No	~ 80%	~ 18%
	#2	(i) method optimisation	Mountain	France	No	~ 80%	~ 18%
	#3	(i) method optimisation	Mulberry tree	France	No	~ 80%	~ 18%
	#4	(i) method optimisation	Multi-flower	France	No	~ 80%	~ 18%
	#5	(i) method optimisation & (ii) method validation	Chestnut	France	No	~ 80%	~ 18%
	#6	(i) method optimisation & (iii) application of the method	Eucalyptus	Mexico	Yes	~ 80%	~ 18%
	#7	(ii) method validation & (iii) application of the method	Acacia	France	No	~ 80%	~ 18%
	#8	(ii) method validation & (iii) application of the method	Alfalfa	France	No	~ 80%	~ 18%
	#9	(ii) method validation & (iii) application of the method	Buckwheat	France	No	~ 80%	~ 18%
	#10	(ii) method validation & (iii) application of the method	Clover	France	No	~ 80%	~ 18%
	#11	(ii) method validation & (iii) application of the method	Fir	France	No	~ 80%	~ 18%
	#12	(ii) method validation & (iii) application of the method	Forest	France	No	~ 80%	~ 18%
	#13	(ii) method validation & (iii) application of the method	Lavender	France	Yes	~ 80%	~ 18%
	#14	(ii) method validation & (iii) application of the method	Lemon tree	Spain	No	~ 80%	~ 18%
	#15	(ii) method validation & (iii) application of the method	Lime	France	No	~ 80%	~ 18%
	#16	(ii) method validation & (iii) application of the method	Multi-flowes	France	No	~ 80%	~ 18%
	#17	(ii) method validation & (iii) application of the method	Multi-flower	France	No	~ 80%	~ 18%
	#18	(ii) method validation & (iii) application of the method	Rapeseed	France	Yes	~ 80%	~ 18%
	#19	(iii) application of the method	Cactus	Morocco	Yes	~ 80%	~ 18%
	#20	(iii) application of the method	Chestnut	Spain	Yes	~ 80%	~ 18%

Sample	ID	Used for	Type	Origin	Organic	Sugar content*	Water content*
	#21	(iii) application of the method	Eucalyptus	Madagascar	No	~ 80%	~ 18%
	#22	(iii) application of the method	Forest	France	No	~ 80%	~ 18%
	#23	(iii) application of the method	Forest	Chile	Yes	~ 80%	~ 18%
	#24	(iii) application of the method	Lavender	France	No	~ 80%	~ 18%
	#25	(iii) application of the method	Mountain	Chile / Spain	Yes	~ 80%	~ 18%
	#26	(iii) application of the method	Multi-flowes	France	No	~ 80%	~ 18%
	#27	(iii) application of the method	Multi-flower	Madagascar	No	~ 80%	~ 18%
	#28	(iii) application of the method	Multi-flower	Kyrgyzstan	No	~ 80%	~ 18%
	#29	(iii) application of the method	Niaouli	Madagascar	No	~ 80%	~ 18%
	#30	(iii) application of the method	Orange tree	Spain	No	~ 80%	~ 18%
	#31	(iii) application of the method	Rapeseed	France	No	~ 80%	~ 18%
	#32	(iii) application of the method	Rapeseed	France	No	~ 80%	~ 18%
	#33	(iii) application of the method	Sunflower	France	No	~ 80%	~ 18%
	#34	(iii) application of the method	Unspecified	France	No	~ 80%	~ 18%
	#35	(iii) application of the method	Unspecified	France	No	~ 80%	~ 18%
	#36	(iii) application of the method	Unspecified	France	No	~ 80%	~ 18%
	#37	(iii) application of the method	Unspecified	Ukraine	No	~ 80%	~ 18%
Jam	**#38**	(ii) method validation & (iii) application of the method	Apricot	France	Yes	~ 60%	~ 39%
	#39	(ii) method validation & (iii) application of the method	Blueberry	France	Yes	~ 59%	~ 39%
	#40	(ii) method validation & (iii) application of the method	Fig	France	Yes	~ 59%	~ 38%
	#41	(ii) method validation & (iii) application of the method	Orange	France	Yes	~ 60%	~ 39%
	#42	(ii) method validation & (iii) application of the method	Strawberry	France	Yes	~ 60%	~ 38%
	#43	(iii) application of the method	Apricot	France	No	~ 59%	~ 38%
	#44	(iii) application of the method	Cherry	France	No	~ 59%	~ 38%

Sample	ID	Used for	Type	Origin	Organic	Sugar content*	Water content*
	#45	(iii) application of the method	Orange	France	No	~ 59%	~ 38%
	#46	(iii) application of the method	Raspberry	France	No	~ 59%	~ 38%
	#47	(iii) application of the method	Strawberry	France	No	~ 60%	~ 38%
	#48	(iii) application of the method	Strawberry	France	No	~ 60%	~ 38%
	#49	(iii) application of the method	Strawberry	France	No	~ 60%	~ 38%
Jelly	**#50**	(iii) application of the method	Currant	France	No	~ 59%	~ 38%
	#51	(iii) application of the method	Currant / Raspberry	France	No	~ 59%	~ 38%
Syrup	**#52**	(ii) method validation & (iii) application of the method	Agave	Non-UE	Yes	~ 62%	~ 32%
	#53	(ii) method validation & (iii) application of the method	Maple	Canada	Yes	~ 75%	~ 22%
	#54	(iii) application of the method	Maple	Canada	No	~ 75%	~ 22%

*Information available in Ciqual Table of nutritional composition of foods (anses.fr)

Table S3: List of experiments provided by the L18 TOA and the associated detection rates.

Experiment	Volume of water added (mL)	Solvent acidification	Extraction salts	Clean-up	Dilution / Concentration ratio	Detection rates (%)			
						Replicate A	Replicate B	Replicate C	Average
1	2	0	AOAC 2007.01[a]	No purification	No dilution or concentration	81	83	80	**81**
2	2	0	EN 15667[b]	$MgSO_4$/PSA	Concentration 10:1	90	92	91	**91**
3	2	0.1	AOAC 2007.01[a]	$MgSO_4$/PSA/C18	Concentration 10:1	90	91	91	**90**
4	5	0.1	EN 15667[b]	$MgSO_4$/PSA	Dilution 1:2	81	75	79	**78**
5	5	0.1	Original[c]	$MgSO_4$/PSA/C18	No dilution or concentration	82	80	80	**81**
6	5	1	EN 15667[b]	No purification	No dilution or concentration	79	78	77	**78**
7	8	0	Original[c]	$MgSO_4$/PSA	Dilution 1:2	75	81	78	**78**
8	8	1	AOAC 2007.01[a]	No purification	Dilution 1:2	77	75	80	**77**
9	8	1	Original[c]	$MgSO_4$/PSA/C18	Concentration 10:1	84	89	88	**87**
10	2	0.1	Original[c]	No purification	Dilution 1:2	72	75	73	**73**
11	2	1	EN 15667[b]	$MgSO_4$/PSA/C18	Dilution 1:2	76	75	77	**76**
12	2	1	Original[c]	$MgSO_4$/PSA	No dilution or concentration	82	83	76	**80**
13	5	0	AOAC 2007.01[a]	$MgSO_4$/PSA/C18	Dilution 1:2	74	78	81	**78**
14	5	0	Original[c]	No purification	Concentration 10:1	86	86	87	**86**
15	5	1	AOAC 2007.01[a]	$MgSO_4$/PSA	Concentration 10:1	89	89	89	**89**
16	8	0	EN 15667[b]	$MgSO_4$/PSA/C18	No dilution or concentration	82	83	81	**82**
17	8	0.1	AOAC 2007.01[a]	$MgSO_4$/PSA	No dilution or concentration	84	82	85	**84**
18	8	0.1	EN 15667[b]	No purification	Concentration 10:1	84	84	88	**85**
R*	0	2	2	3	11				

[a] 4.0 g $MgSO_4$ / 1.0 g NaOAc

[b] 4.0 g $MgSO_4$ / 1.0 g NaCl / 1.0 g of sodium citrate / 0.5 g of sodium citrate sesquihydrate

[c] 4.0 g $MgSO_4$ / 1.0 g NaCl

* The range of detection rates for different factors. It is used to rank the factors by their impact on the detection rate. The higher this value, the greater the impact of the given parameter on the detection rate.

Table S4: List of experiments provided by the L18 TOA and the associated mean signal-to-noise ratio.

Experiment	Volume of water added (mL)	Solvent acidification	Extraction salts	Clean-up	Dilution / Concentration ratio	Mean S/N			
						Replicate A	Replicate B	Replicate C	Average
1	2	0	AOAC 2007.01[a]	No purification	No dilution or concentration	252	353	326	**310**
2	2	0	EN 15667[b]	$MgSO_4$/PSA	Concentration 10:1	713	712	805	**743**
3	2	0.1	AOAC 2007.01[a]	$MgSO_4$/PSA/C18	Concentration 10:1	780	1033	750	**855**
4	5	0.1	EN 15667[b]	$MgSO_4$/PSA	Dilution 1:2	261	159	230	**217**
5	5	0.1	Original[c]	$MgSO_4$/PSA/C18	No dilution or concentration	336	232	254	**274**
6	5	1	EN 15667[b]	No purification	No dilution or concentration	289	328	228	**282**
7	8	0	Original[c]	$MgSO_4$/PSA	Dilution 1:2	161	305	156	**207**
8	8	1	AOAC 2007.01[a]	No purification	Dilution 1:2	227	233	269	**243**
9	8	1	Original[c]	$MgSO_4$/PSA/C18	Concentration 10:1	598	666	652	**639**
10	2	0.1	Original[c]	No purification	Dilution 1:2	139	155	170	**155**
11	2	1	EN 15667[b]	$MgSO_4$/PSA/C18	Dilution 1:2	130	147	157	**145**
12	2	1	Original[c]	$MgSO_4$/PSA	No dilution or concentration	289	283	150	**241**
13	5	0	AOAC 2007.01[a]	$MgSO_4$/PSA/C18	Dilution 1:2	163	202	216	**193**
14	5	0	Original[c]	No purification	Concentration 10:1	657	554	589	**600**
15	5	1	AOAC 2007.01[a]	$MgSO_4$/PSA	Concentration 10:1	678	801	824	**768**
16	8	0	EN 15667[b]	$MgSO_4$/PSA/C18	No dilution or concentration	245	282	275	**268**
17	8	0.1	AOAC 2007.01[a]	$MgSO_4$/PSA	No dilution or concentration	288	250	303	**280**
18	8	0.1	EN 15667[b]	No purification	Concentration 10:1	655	577	717	**650**
R*	27	19	89	36	516				

[a] 4.0 g $MgSO_4$ / 1.0 g NaOAc
[b] 4.0 g $MgSO_4$ / 1.0 g NaCl / 1.0 g of sodium citrate / 0.5 g of sodium citrate sesquihydrate
[c] 4.0 g $MgSO_4$ / 1.0 g NaCl
* The range of S/N for different factors. It is used to rank the factors by their impact on the S/N. The higher this value, the greater the impact of the given parameter on the S/N.

Table S5: Determination of SDL and LOI for each contaminants, regarding the 20 samples used for method validation

Compound	Number of detections out of 20 samples			**SDL (mg.kg^{-1})**	Number of identifications out of 20 samples			**LOI (mg.kg^{-1})**
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
1-(3,4-dichlorophenyl)-3-methyl Urea	20	20	20	**0.001**	14	20	20	**0.01**
1-(4-nitrophenyl)-3-propylure	20	20	20	**0.001**	19	20	20	**0.001**
1,2-benzisothiazol-3(2h)-one	17	20	20	**0.01**	11	18	20	**0.05**
1,3-diphenylurea	20	20	20	**0.001**	16	20	20	**0.01**
2,3,5-trimethacarb	18	20	20	**0.01**	9	18	19	**0.05**
2,4-dimethylaniline	17	20	20	**0.01**	7	20	20	**0.01**
2,6-dichlorobenzamide	19	20	20	**0.001**	3	13	20	**0.05**
2,6-diethylaniline	15	20	20	**0.01**	0	19	20	**0.01**
2-ethylhexyl Diphenyl Phosphate	18	19	20	**0.01**	17	18	20	**0.05**
2-n-octyl-4-isothiazolin-3-one	19	20	20	**0.001**	0	19	20	**0.01**
3,4 Dichloroaniline	5	19	20	**0.01**	1	15	19	**0.05**
3,4,5-trimethacarb	18	20	20	**0.01**	9	18	19	**0.05**
3-hydroxycarbofuran	3	0	16	**> 0.05**	0	0	3	**> 0.05**
3-ketocarbofuran	13	19	20	**0.01**	2	18	20	**0.05**
4-bromo-3,5-dimethylphenyl-n-	8	20	20	**0.01**	1	16	19	**0.05**
Abamectin	2	13	16	**> 0.05**	0	0	0	**> 0.05**
Abate® (temephos)	20	20	20	**0.001**	1	19	20	**0.01**
Acephate	4	20	20	**0.01**	0	6	19	**0.05**
Acetamiprid*	/	/	/	**/**	**/**	**/**	**/**	**/**
Acibenzolar-s-methyl	18	20	20	**0.01**	5	19	20	**0.01**
Aclonifen	18	20	20	**0.01**	0	0	0	**> 0.05**
Aconitine	20	20	20	**0.001**	20	20	20	**0.001**
Akton	1	15	17	**> 0.05**	0	7	16	**> 0.05**
Alachlor	19	20	20	**0.001**	0	0	0	**> 0.05**
Aldicarb	0	3	7	**> 0.05**	0	2	4	**> 0.05**
Aldicarb Sulfone	15	20	20	**0.01**	15	20	20	**0.01**
Aldicarb Sulfoxide	2	6	15	**> 0.05**	1	3	12	**> 0.05**
Allethrin	18	20	20	**0.01**	0	17	20	**0.05**
Allidochlor	19	20	20	**0.001**	1	9	19	**0.05**
Alloxydim Sodium	4	14	19	**0.05**	0	4	11	**> 0.05**
Ametoctradin	20	20	20	**0.001**	20	20	20	**0.001**
Ametryne	20	20	20	**0.001**	20	20	20	**0.001**
Amicarbazone	3	18	20	**0.05**	3	18	20	**0.05**
Amidosulfuron	7	19	20	**0.01**	0	15	20	**0.05**
Aminocarb	1	19	20	**0.01**	0	19	20	**0.01**
Ancymidol	16	20	20	**0.01**	12	19	20	**0.01**
Anilazine	0	5	14	**> 0.05**	0	0	5	**> 0.05**
Anilofos	20	20	20	**0.001**	17	20	20	**0.01**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Aspon ™	16	20	20	**0.01**	6	19	20	**0.01**
Asulam	0	1	18	**> 0.05**	0	0	6	**> 0.05**
Atraton	20	20	20	**0.001**	20	20	20	**0.001**
Atrazine	0	20	20	**0.01**	0	20	20	**0.01**
Atrazine Desisopropyl	18	20	20	**0.01**	0	16	20	**0.05**
Azaconazole	20	20	20	**0.001**	20	20	20	**0.001**
Azadirachtin (technical)	17	19	20	**0.01**	0	0	0	**> 0.05**
Azamethiphos	20	20	20	**0.001**	18	20	20	**0.01**
Azimsulfuron	6	20	20	**0.01**	0	19	20	**0.01**
Aziprotryne	19	20	20	**0.001**	14	20	20	**0.01**
Azoxystrobin*	/	/	/	**0.001**	/	/	/	**/**
Beflubutamid	20	20	20	**0.001**	20	20	20	**0.001**
Benalaxyl	20	20	20	**0.001**	20	20	20	**0.001**
Benazolin	0	0	0	**> 0.05**	0	0	0	**> 0.05**
Benodanil	20	20	20	**0.001**	19	20	20	**0.001**
Benomyl	1	10	11	**> 0.05**	0	6	1	**> 0.05**
Benoxacor	17	20	20	**0.01**	0	15	19	**0.05**
Bensulfuron-methyl	20	20	20	**0.001**	16	20	20	**0.01**
Bensulide	20	20	20	**0.001**	13	20	20	**0.01**
Bentazon	10	18	20	**0.05**	4	17	20	**0.05**
Benthiavalicarb-isopropyl	20	20	20	**0.001**	20	20	20	**0.001**
Benzoximate	20	20	20	**0.001**	9	20	20	**0.01**
Benzoylprop Ethyl	20	20	20	**0.001**	19	20	20	**0.001**
Benzthiazuron	20	20	20	**0.001**	19	20	20	**0.001**
Bioresmethrin	10	20	20	**0.01**	3	18	18	**> 0.05**
Bitertanole (mixture of isomers)	19	20	20	**0.001**	1	20	20	**0.01**
Bixafen	20	20	20	**0.001**	18	20	20	**0.01**
Bladex	19	20	20	**0.001**	17	20	20	**0.01**
Boscalid	20	20	20	**0.001**	19	20	20	**0.001**
Bromacil	20	20	20	**0.001**	16	20	20	**0.01**
Bromofenvinphos-ethyl	20	20	20	**0.001**	17	20	20	**0.01**
Bromophos Methyl	0	13	17	**> 0.05**	0	0	0	**> 0.05**
Bromuconazole (mixture of isomers)	19	20	20	**0.001**	14	20	19	**0.01**
Bupirimate	20	20	20	**0.001**	18	20	20	**0.01**
Buprofezin	19	20	20	**0.001**	19	20	20	**0.001**
Butachlor	18	20	20	**0.01**	1	19	18	**0.01**
Butafenacil	20	20	17	**0.001**	17	19	17	**0.01**
Butocarboxim Sulfoxide	0	0	1	**> 0.05**	0	0	0	**> 0.05**
Butoxycarboxim	15	20	20	**0.01**	15	20	20	**0.01**
Butroxydim	20	20	20	**0.001**	14	20	20	**0.01**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Buturon	17	20	20	**0.01**	0	20	20	**0.01**
Butylate	6	20	20	**0.01**	0	14	20	**0.05**
Cadusafos	15	20	20	**0.01**	12	20	20	**0.01**
Cafenstrole	18	20	20	**0.01**	3	12	18	**> 0.05**
Carbaryl	14	12	20	**0.05**	2	12	20	**0.05**
Carbendazim	16	20	20	**0.01**	14	20	20	**0.01**
Carbetamide	7	20	20	**0.01**	2	20	20	**0.01**
Carbofuran	20	20	20	**0.001**	19	20	20	**0.001**
Carbophenothion	1	15	16	**> 0.05**	0	6	16	**> 0.05**
Carboxin	13	20	20	**0.01**	10	19	20	**0.01**
Carfentrazone-ethyl	17	20	20	**0.01**	8	20	20	**0.01**
Carpropamid	20	20	20	**0.001**	17	20	20	**0.01**
Chinomethionate	1	17	19	**0.05**	0	14	19	**0.05**
Chlorantraniliprole	20	20	20	**0.001**	9	20	19	**0.01**
Chlorbromuron	19	20	20	**0.001**	3	19	20	**0.01**
Chlordimeform	15	20	20	**0.01**	7	19	20	**0.01**
Chlorfenapyr	0	18	18	**> 0.05**	0	0	0	**> 0.05**
Chlorfenvinphos (mixture Of Z and E)	20	20	20	**0.001**	18	20	20	**0.01**
Chlorfluazuron	20	20	19	**0.001**	19	20	19	**0.001**
Chloridazon	20	20	20	**0.001**	15	20	20	**0.01**
Chlorimuron Ethyl	10	20	19	**0.01**	0	20	19	**0.01**
Chlorobenzuron	20	20	20	**0.001**	11	20	20	**0.01**
Chlorosulfuron	3	18	20	**0.05**	0	10	20	**0.05**
Chlorotoluron	20	20	20	**0.001**	17	20	20	**0.01**
Chloroxuron	20	20	20	**0.001**	19	20	20	**0.001**
Chlorpyrifos	5	17	20	**0.05**	1	16	20	**0.05**
Chlorpyrifos-methyl	1	14	20	**0.05**	0	4	15	**> 0.05**
Chlorpyrifos-oxon	20	20	20	**0.001**	17	20	20	**0.01**
Chlorthiophos	1	17	20	**0.05**	0	0	0	**> 0.05**
Chromafenozide	20	20	20	**0.001**	19	20	20	**0.001**
Cinidon-ethyl	6	20	20	**0.01**	2	17	7	**> 0.05**
Cinmethylin	1	3	19	**0.05**	0	1	17	**> 0.05**
Cinosulfuron	16	20	20	**0.01**	5	20	20	**0.01**
Clarithromycin	20	20	19	**0.001**	18	20	19	**0.01**
Clethodim	19	20	20	**0.001**	3	17	16	**> 0.05**
Climbazol	20	20	20	**0.001**	7	20	20	**0.01**
Clodinafop (acid Free)	11	11	19	**0.05**	0	1	2	**> 0.05**
Clodinafop-propargyl	20	20	20	**0.001**	11	20	20	**0.01**
Clofentezine	18	20	20	**0.01**	7	18	19	**0.05**
Clomeprop	20	20	20	**0.001**	18	20	20	**0.01**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Cloquintocet-mexyl	20	20	20	**0.001**	19	20	20	**0.001**
Cloransulam-methyl	5	20	19	**0.01**	0	20	16	**0.01**
Clothianidin	20	20	20	**0.001**	2	19	20	**0.01**
Command (clomazone)	20	20	20	**0.001**	18	16	19	**0.05**
Coumaphos*	/	/	/	**/**	/	/	/	**/**
Coumaphos Oxon	20	20	20	**0.001**	10	18	20	**0.05**
Crimidine	18	20	20	**0.01**	17	20	20	**0.01**
Crotoxyphos	15	20	20	**0.01**	4	9	1	**> 0.05**
Crufomate	20	20	20	**0.001**	20	18	20	**0.001**
Cumyluron	19	20	20	**0.001**	14	20	20	**0.01**
Cyanofenphos	7	20	17	**0.01**	6	3	8	**> 0.05**
Cyanophos	6	19	20	**0.01**	0	0	0	**> 0.05**
Cyantraniliprole	20	20	20	**0.001**	9	17	16	**> 0.05**
Cyazofamid	19	20	20	**0.001**	6	16	20	**0.05**
Cyclanilide	0	14	18	**> 0.05**	0	5	12	**> 0.05**
Cycloate	19	20	20	**0.001**	0	11	20	**0.05**
Cyclohexamide	17	20	20	**0.01**	1	4	13	**> 0.05**
Cycloprothrin	2	2	4	**> 0.05**	0	0	0	**> 0.05**
Cyclosulfamuron	20	20	20	**0.001**	8	20	20	**0.01**
Cycloxidim	8	20	20	**0.01**	2	7	20	**0.05**
Cycluron	18	20	20	**0.01**	10	20	20	**0.01**
Cyflufenamid	20	20	20	**0.001**	15	20	20	**0.01**
Cyhalofop-butyl	4	13	15	**> 0.05**	0	2	4	**> 0.05**
Cymiazole	11	20	20	**0.01**	10	20	20	**0.01**
Cymoxanil	2	18	20	**0.05**	0	2	16	**> 0.05**
Cyphenothrin	0	8	14	**> 0.05**	0	0	4	**> 0.05**
Cyprazine	16	20	20	**0.01**	16	20	20	**0.01**
Cyproconazole (mixture of isomers)	20	20	20	**0.001**	17	18	20	**0.05**
Cyprodinil*	/	/	/	**/**	/	/	/	**/**
Cyprofuram	19	20	20	**0.001**	18	20	20	**0.01**
Cyprosulfamide	11	20	20	**0.01**	2	13	17	**> 0.05**
Cyromazine	4	15	20	**0.05**	2	8	18	**> 0.05**
Cythioate	20	20	20	**0.001**	0	3	1	**> 0.05**
Daimuron	20	20	20	**0.001**	17	20	20	**0.01**
Daminozide	0	0	2	**> 0.05**	0	0	0	**> 0.05**
Danitol	0	11	11	**> 0.05**	0	1	10	**> 0.05**
Dazomet	0	0	12	**> 0.05**	0	0	0	**> 0.05**
Dementon-s-methyl-sulfone	20	20	20	**0.001**	6	20	20	**0.01**
Demeton O	0	15	20	**0.05**	0	12	18	**> 0.05**
Demeton S	3	19	20	**0.01**	0	14	18	**> 0.05**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Demeton-s-methyl	1	15	19	**0.05**	0	2	0	**> 0.05**
Deoxynivalenol	4	5	7	**> 0.05**	1	0	1	**> 0.05**
Desethyl Atrazine	20	20	20	**0.001**	10	20	20	**0.01**
Desmedipham	19	20	20	**0.001**	7	12	20	**0.05**
Desmethyl Norflurazon	20	20	20	**0.001**	20	20	20	**0.001**
Desmethyl-formamido-pirimicarb	20	20	20	**0.001**	20	20	20	**0.001**
Desmetryn	7	20	20	**0.01**	0	20	20	**0.01**
Dialifos	2	18	20	**0.05**	0	17	19	**0.05**
Diazinon	20	20	20	**0.001**	20	20	20	**0.001**
Diazinon-o-analog	15	16	18	**> 0.05**	14	16	16	**> 0.05**
Dibrom	2	18	19	**0.05**	0	0	0	**> 0.05**
Dichlofenthion	1	14	19	**0.05**	0	0	13	**> 0.05**
Dichlormid	19	20	20	**0.001**	0	4	19	**0.05**
Dichlorvos	20	20	20	**0.001**	5	13	19	**0.05**
Diclobutrazol (mixture of isomers)	20	20	20	**0.001**	15	20	20	**0.01**
Diclocymet	20	20	20	**0.001**	20	20	20	**0.001**
Diclosulam	7	19	20	**0.01**	0	15	17	**> 0.05**
Dicrotophos	19	20	20	**0.001**	8	20	20	**0.01**
Diethatyl Ethyl	20	20	20	**0.001**	19	20	20	**0.001**
Diethofencarb	19	20	20	**0.001**	0	12	8	**> 0.05**
Difenoconazole* (mixture of isomers)	/	/	/	**/**	/	/	/	**/**
Difenoxurone	20	20	20	**0.001**	11	20	20	**0.01**
Diflubenzuron	20	20	20	**0.001**	15	20	20	**0.01**
Diflufenicen	20	20	20	**0.001**	19	20	20	**0.001**
Dimefox	0	18	20	**0.05**	0	9	20	**0.05**
Dimefuron	19	20	20	**0.001**	12	20	20	**0.01**
Dimepiperate	6	19	20	**0.01**	2	19	18	**0.01**
Dimethachlor	17	20	20	**0.01**	12	19	20	**0.01**
Dimethametryn	20	20	20	**0.001**	20	20	20	**0.001**
Dimethenamid	20	20	20	**0.001**	18	20	20	**0.01**
Dimethirimol	20	20	20	**0.001**	15	20	20	**0.01**
Dimethoate	19	20	20	**0.001**	13	20	20	**0.01**
Dimethomorph	19	20	20	**0.001**	15	20	20	**0.01**
Dimethylvinphos	19	20	20	**0.001**	12	20	20	**0.01**
Dimetilan	7	12	17	**> 0.05**	6	12	17	**> 0.05**
Dimoxystrobin	19	20	20	**0.001**	17	20	20	**0.01**
Diniconazole (e isomer)	20	20	20	**0.001**	20	20	20	**0.001**
Diniconazole (z isomer)	20	20	20	**0.001**	20	20	20	**0.001**
Dinitramine	20	20	20	**0.001**	16	20	20	**0.01**
Dinotefuran	5	19	20	**0.01**	0	4	9	**> 0.05**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Dioxacarb	4	15	16	**> 0.05**	0	13	15	**> 0.05**
Diphenamid	19	20	20	**0.001**	18	20	20	**0.01**
Diphenylamine	20	20	20	**0.001**	9	20	20	**0.01**
Dipropetryn	20	19	17	**0.001**	20	19	17	**0.001**
Disulfoton Sulfone	17	20	20	**0.01**	0	14	20	**0.05**
Disulfoton Sulfoxide	20	20	20	**0.001**	9	20	20	**0.01**
Ditalimfos	19	20	20	**0.001**	7	13	14	**> 0.05**
Dithianon	0	1	0	**> 0.05**	0	0	0	**> 0.05**
Dithiopyr	16	20	20	**0.01**	1	18	20	**0.05**
Diuron	20	20	20	**0.001**	19	20	20	**0.001**
Dodemorph	20	20	20	**0.001**	19	20	20	**0.001**
Doramectin	4	15	19	**0.05**	0	0	6	**> 0.05**
Dyfonate ™	13	20	20	**0.01**	2	19	20	**0.01**
Edifenphos	20	20	20	**0.001**	19	20	20	**0.001**
Emamectin	20	19	10	**0.001**	20	19	10	**0.001**
Empenthrin	8	12	19	**0.05**	0	0	1	**> 0.05**
Epn	9	20	18	**0.01**	0	9	15	**> 0.05**
Epoxiconazole (iso)	20	20	20	**0.001**	19	20	20	**0.001**
Eprinomectin	9	18	19	**0.05**	0	9	16	**> 0.05**
Eptc (s-ethyl Dipropylthiocarbamate)	15	19	20	**0.01**	0	3	2	**> 0.05**
Erythromycin	15	19	19	**0.01**	10	17	17	**> 0.05**
Esbiol	18	20	20	**0.01**	0	17	20	**0.05**
Esprocarb	20	20	20	**0.001**	15	20	20	**0.01**
Etaconazole	20	20	20	**0.001**	20	20	20	**0.001**
Ethaboxam	20	20	20	**0.001**	18	20	20	**0.01**
Ethametsulfuron-methyl	18	20	20	**0.01**	6	20	20	**0.01**
Ethidimuron	18	20	20	**0.01**	1	20	19	**0.01**
Ethiofencarb	4	13	20	**0.05**	2	12	19	**0.05**
Ethiofencarb-sulfone	13	20	20	**0.01**	6	19	20	**0.01**
Ethiofencarb-sulfoxide	10	16	17	**> 0.05**	7	15	16	**> 0.05**
Ethion	17	19	20	**0.01**	8	17	19	**0.05**
Ethiozin	13	19	19	**0.01**	10	18	19	**0.05**
Ethiprole	20	20	20	**0.001**	16	20	20	**0.01**
Ethirimol	20	20	20	**0.001**	16	20	20	**0.01**
Ethofumesate	7	10	15	**> 0.05**	0	0	0	**> 0.05**
Ethoprophos (prophos)	20	20	20	**0.001**	10	20	20	**0.01**
Ethoxyquin	11	20	20	**0.01**	0	20	17	**0.01**
Ethoxysulfuron	3	19	20	**0.01**	0	5	17	**> 0.05**
Ethyclozate	19	20	20	**0.001**	18	20	20	**0.01**
Etobenzanid	20	20	20	**0.001**	8	20	20	**0.01**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Etoxazole	20	20	20	**0.001**	19	20	20	**0.001**
Etrimfos	20	20	20	**0.001**	14	20	20	**0.01**
Famphur	19	20	20	**0.001**	1	18	20	**0.05**
Fenamidone	20	20	20	**0.001**	20	20	20	**0.001**
Fenamiphos	18	20	20	**0.01**	17	20	20	**0.01**
Fenamiphos Sulfone	20	20	20	**0.001**	11	20	20	**0.01**
Fenamiphos Sulfoxide	20	20	20	**0.001**	1	8	2	**> 0.05**
Fenarimol	20	20	20	**0.001**	12	20	20	**0.01**
Fenazaquin	19	20	20	**0.001**	15	20	20	**0.01**
Fenazox	1	16	20	**0.05**	0	11	19	**0.05**
Fenbuconazole	20	20	20	**0.001**	19	20	20	**0.001**
Fenchlorazol-ethyl	15	10	20	**0.05**	3	7	19	**0.05**
Fenchlorphos-oxon	19	20	20	**0.001**	10	14	18	**> 0.05**
Fenfuram	18	20	20	**0.01**	15	20	19	**0.01**
Fenhexamid	15	20	20	**0.01**	9	20	20	**0.01**
Fenitrothion	6	20	20	**0.01**	0	6	7	**> 0.05**
Fenobucarb	15	20	20	**0.01**	8	20	20	**0.01**
Fenothiocarb	18	20	20	**0.01**	14	19	20	**0.01**
Fenoxanil	20	20	20	**0.001**	16	20	20	**0.01**
Fenoxaprop	0	1	3	**> 0.05**	0	1	1	**> 0.05**
Fenoxaprop-p-ethyl	20	20	20	**0.001**	19	20	20	**0.001**
Fenoxycarb (same As Cmpd# 1871)	20	20	20	**0.001**	20	20	20	**0.001**
Fenpiclonil	20	20	20	**0.001**	9	20	20	**0.01**
Fenpropathrin	0	11	11	**> 0.05**	0	1	10	**> 0.05**
Fenpropidin	0	20	20	**0.01**	0	20	20	**0.01**
Fenpropimorph 2	20	20	20	**0.001**	20	20	20	**0.001**
Fenpyroximate	19	20	20	**0.001**	19	20	20	**0.001**
Fensulfothion	19	20	20	**0.001**	9	19	20	**0.01**
Fensulfothion-oxon	20	20	20	**0.001**	19	20	20	**0.001**
Fensulfothion-oxon-sulfone	6	16	20	**0.05**	6	16	20	**0.05**
Fensulfothion-sulfone	20	20	20	**0.001**	4	20	20	**0.01**
Fenthion	12	20	20	**0.01**	0	5	17	**> 0.05**
Fenthion Oxon	20	20	20	**0.001**	17	20	20	**0.01**
Fenthion Oxon Sulfoxide	19	20	20	**0.001**	18	19	20	**0.01**
Fenthion Sulfoxide	20	20	20	**0.001**	15	20	19	**0.01**
Fenthion-ethyl	16	20	20	**0.01**	0	19	20	**0.01**
Fenthion-sulfone	14	19	20	**0.01**	0	12	19	**0.05**
Fenthoxon Sulfone	20	20	20	**0.001**	13	20	20	**0.01**
Fenuron	0	14	19	**0.05**	0	14	19	**0.05**
Ferimzone	16	20	20	**0.01**	13	20	20	**0.01**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Fipronil	20	20	20	**0.001**	20	20	18	**0.001**
Fipronil Sulfide	20	20	20	**0.001**	20	20	20	**0.001**
Fipronil-desulfinyl	20	20	20	**0.001**	20	20	20	**0.001**
Flamprop Isopropyl	20	20	20	**0.001**	19	20	20	**0.001**
Flamprop-methyl (metavane)	20	20	20	**0.001**	9	20	11	**0.01**
Flamprop-m-isopropyl	20	20	20	**0.001**	19	20	20	**0.001**
Flazasulfuron	0	20	19	**0.01**	0	12	8	**> 0.05**
Flonicamid*	/	/	/	**/**	/	/	/	**/**
Florasulam	5	20	20	**0.01**	1	18	20	**0.05**
Fluacrypyrim	19	20	20	**0.001**	19	18	20	**0.001**
Fluazifop	4	18	20	**0.05**	0	4	10	**> 0.05**
Fluazifop-butyl	20	20	20	**0.001**	20	20	20	**0.001**
Fluazifop-p-butyl	20	20	20	**0.001**	20	20	20	**0.001**
Fluazinam	20	20	20	**0.001**	20	20	19	**0.001**
Fluazuron	20	20	20	**0.001**	16	19	20	**0.01**
Flubendiamide	20	20	19	**0.001**	18	20	17	**0.01**
Flucarbazone-sodium	0	1	1	**> 0.05**	0	0	0	**> 0.05**
Fluchloralin	0	0	17	**> 0.05**	0	0	0	**> 0.05**
Flucycloxuron	20	20	20	**0.001**	20	20	20	**0.001**
Fludioxonil	20	20	20	**0.001**	20	20	20	**0.001**
Flufenacet	20	20	20	**0.001**	15	20	20	**0.01**
Flufenoxuron	20	20	20	**0.001**	16	20	20	**0.01**
Flumestulam	20	20	20	**0.001**	14	20	19	**0.01**
Flumetralin	0	8	12	**> 0.05**	0	0	0	**> 0.05**
Flumiclorac-pentyl	18	20	20	**0.01**	17	20	19	**0.01**
Flumioxazin	13	19	19	**0.01**	11	18	19	**0.05**
Flumorph	19	20	20	**0.001**	14	20	20	**0.01**
Fluoglycofene-ethyl	1	18	18	**> 0.05**	0	14	15	**> 0.05**
Fluometuron	20	20	20	**0.001**	20	20	20	**0.001**
Fluopicolide	20	20	20	**0.001**	19	20	20	**0.001**
Fluopyram*	/	/	/	**/**	/	/	/	**/**
Fluoxastrobin	20	20	20	**0.001**	20	20	20	**0.001**
Flupyradifurone	15	20	20	**0.01**	11	20	20	**0.01**
Flupyrsulfuron-methyl-sodium	0	5	9	**> 0.05**	0	0	0	**> 0.05**
Fluquinconazole	12	19	20	**0.01**	5	19	20	**0.01**
Fluridone	20	20	20	**0.001**	20	20	20	**0.001**
Flurilazole	14	14	19	**0.05**	0	6	14	**> 0.05**
Flurochloridon (iso)	20	20	20	**0.001**	9	18	20	**0.05**
Fluroxypyr	1	1	4	**> 0.05**	0	0	0	**> 0.05**
Fluroxypyr-meptyl	7	16	20	**0.05**	1	15	20	**0.05**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Flurprimidol	19	20	20	**0.001**	19	20	20	**0.001**
Flurtamone	20	20	20	**0.001**	20	20	20	**0.001**
Flusilazole	20	20	20	**0.001**	20	20	20	**0.001**
Fluthiacet-methyl	20	20	20	**0.001**	19	20	20	**0.001**
Flutolanil	20	20	20	**0.001**	19	20	20	**0.001**
Flutriafol	18	20	20	**0.01**	12	20	20	**0.01**
Fomesafen	17	20	19	**0.01**	4	19	18	**0.01**
Foramsulfuron	5	20	19	**0.01**	1	10	19	**0.05**
Forchlorfenuron	20	20	20	**0.001**	20	20	20	**0.001**
Formetanate HCl	5	18	20	**0.05**	0	16	20	**0.05**
Fosthiazate	20	20	20	**0.001**	19	20	20	**0.001**
Fuberidazole*	/	/	/	**/**	/	/	/	**/**
Furalaxyl	20	20	20	**0.001**	20	20	20	**0.001**
Furathiocarb	19	20	20	**0.001**	19	20	20	**0.001**
Furmecyclox	18	20	20	**0.01**	4	19	18	**0.01**
Guthion Ethyl	8	17	20	**0.05**	0	2	8	**> 0.05**
Halofenozide	20	20	20	**0.001**	18	20	20	**0.01**
Halosulfuron-methyl	14	20	20	**0.01**	0	16	18	**> 0.05**
Haloxyfop	0	9	6	**> 0.05**	0	0	0	**> 0.05**
Haloxyfop-2-ethoxyethyl	20	20	20	**0.001**	19	20	20	**0.001**
Haloxyfop-methyl	20	20	20	**0.001**	19	20	20	**0.001**
Haloxyfop-p Methyl	20	20	20	**0.001**	19	20	20	**0.001**
Heptenophos	18	20	20	**0.01**	7	17	20	**0.05**
Hexaconazole	9	20	20	**0.01**	9	20	20	**0.01**
Hexaflumuron	20	20	20	**0.001**	17	20	20	**0.01**
Hexazinon	11	20	20	**0.01**	10	20	20	**0.01**
Hexythiazox	17	20	20	**0.01**	3	19	20	**0.01**
Hymexazole	2	4	11	**> 0.05**	0	0	0	**> 0.05**
Imazalil	20	20	20	**0.001**	18	20	20	**0.01**
Imazamethabenz-methyl	19	20	20	**0.001**	18	20	20	**0.01**
Imazamox	3	7	8	**> 0.05**	0	0	2	**> 0.05**
Imazapic	2	6	13	**> 0.05**	0	0	8	**> 0.05**
Imazaquin	5	14	19	**0.05**	0	4	14	**> 0.05**
Imazethapyr	2	1	1	**> 0.05**	0	1	1	**> 0.05**
Imazosulfuron	9	20	20	**0.01**	0	17	18	**> 0.05**
Imibenconazole	20	20	20	**0.001**	20	20	20	**0.001**
Imidacloprid	19	20	20	**0.001**	11	19	20	**0.01**
Imidacloprid-olefin	19	20	20	**0.001**	0	19	20	**0.01**
Imiprothrin (mix of isomers)	3	0	3	**> 0.05**	1	0	2	**> 0.05**
Inabenfide	20	20	20	**0.001**	17	20	20	**0.01**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Indaziflam	20	20	20	**0.001**	19	20	20	**0.001**
Indoxacarb	20	20	19	**0.001**	12	18	19	**0.05**
Iodofenphos	0	12	18	**> 0.05**	0	0	3	**> 0.05**
Iodosulfuron-methyl-sodium	1	1	7	**> 0.05**	0	0	0	**> 0.05**
Ipconazole	20	20	20	**0.001**	20	20	20	**0.001**
Iprobenfos	20	20	20	**0.001**	17	20	20	**0.01**
Iprodione	18	20	20	**0.01**	6	2	10	**> 0.05**
Iprovalicarb	20	20	20	**0.001**	20	20	20	**0.001**
Irgarol (cybutryne)	20	20	20	**0.001**	20	20	20	**0.001**
Isazophos	20	20	20	**0.001**	18	20	20	**0.01**
Isocarbamide	11	19	20	**0.01**	1	13	19	**0.05**
Isofenphos	0	19	19	**0.01**	0	18	16	**> 0.05**
Isofenphos-methyl	1	19	20	**0.01**	0	17	17	**> 0.05**
Isofenphos-oxon	20	20	20	**0.001**	19	20	20	**0.001**
Isomethiozin	16	20	20	**0.01**	15	19	20	**0.01**
Isonoruron	19	20	20	**0.001**	18	20	20	**0.01**
Isoprocarb	18	20	20	**0.01**	9	18	19	**0.05**
Isopropalin	15	20	20	**0.01**	0	6	18	**> 0.05**
Isoprothiolane	20	20	20	**0.001**	20	20	20	**0.001**
Isoproturon	15	20	20	**0.01**	13	20	20	**0.01**
Isouron	20	20	20	**0.001**	19	19	20	**0.001**
Isoxaben	20	20	20	**0.001**	20	20	20	**0.001**
Isoxadifen-ethyl	20	20	20	**0.001**	8	20	20	**0.01**
Isoxaflutole	16	19	20	**0.01**	5	18	20	**0.05**
Isoxathion	19	20	20	**0.001**	5	20	20	**0.01**
Ivermectin	1	17	18	**> 0.05**	0	0	0	**> 0.05**
Karbutilate	20	20	20	**0.001**	8	20	20	**0.01**
Ketoprofen	16	17	19	**0.05**	1	3	17	**> 0.05**
Kresoxim Methyl	0	1	3	**> 0.05**	0	1	2	**> 0.05**
Lactofen	4	20	18	**0.01**	0	18	18	**> 0.05**
Lambda Cyhalothrin	0	0	0	**> 0.05**	0	0	0	**> 0.05**
Lenacil	16	20	20	**0.01**	14	20	20	**0.01**
Leptophos	0	10	16	**> 0.05**	0	1	8	**> 0.05**
Levofloxacin	3	2	2	**> 0.05**	0	0	0	**> 0.05**
Linuron	20	20	20	**0.001**	8	19	20	**0.01**
Lontrel (clopyralid)	0	0	0	**> 0.05**	0	0	0	**> 0.05**
Lufenuron	20	20	20	**0.001**	10	20	19	**0.01**
Malaoxon	18	20	20	**0.01**	17	20	20	**0.01**
Malathion	19	20	20	**0.001**	8	10	17	**> 0.05**
Mandipropamid	19	20	20	**0.001**	15	19	20	**0.01**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Mecarbam	1	0	0	**> 0.05**	1	0	0	**> 0.05**
Mefenacet	20	20	20	**0.001**	15	20	20	**0.01**
Mefenpyr-diethyl	20	20	20	**0.001**	19	20	20	**0.001**
Mefluidide	17	20	20	**0.01**	10	20	20	**0.01**
Mepanipyrim	20	20	20	**0.001**	20	20	20	**0.001**
Mephosfolan	20	20	20	**0.001**	20	20	20	**0.001**
Mepronil	20	20	20	**0.001**	19	20	20	**0.001**
Mesosulfuron-methyl	18	20	19	**0.01**	6	20	19	**0.01**
Mesotrione	6	8	17	**> 0.05**	0	0	0	**> 0.05**
Metaflumizone	20	20	20	**0.001**	20	20	20	**0.001**
Metalaxyl	20	20	20	**0.001**	20	20	20	**0.001**
Metalaxyl-m	20	20	20	**0.001**	20	20	20	**0.001**
Metamitron	17	20	20	**0.01**	3	20	20	**0.01**
Metazachlor	18	20	20	**0.01**	18	20	20	**0.01**
Metconazole	20	20	20	**0.001**	17	20	20	**0.01**
Methabenzthiazuron	20	20	20	**0.001**	20	20	20	**0.001**
Methacrifos	0	7	20	**0.05**	0	0	0	**> 0.05**
Methamidophos	0	10	14	**> 0.05**	0	0	1	**> 0.05**
Methfuroxam	18	20	20	**0.01**	17	19	20	**0.01**
Methidathion	14	19	20	**0.01**	0	10	7	**> 0.05**
Methiocarb	19	20	20	**0.001**	0	17	20	**0.05**
Methiocarb Sulfone	15	19	20	**0.01**	7	19	20	**0.01**
Methiocarb Sulfoxide	10	16	17	**> 0.05**	7	16	15	**> 0.05**
Methomyl	0	0	1	**> 0.05**	0	0	0	**> 0.05**
Methomyl-oxime	0	0	17	**> 0.05**	0	0	0	**> 0.05**
Methoprotryne	20	20	20	**0.001**	20	20	20	**0.001**
Methoxyfenozide	20	20	20	**0.001**	20	20	20	**0.001**
Methyl Paraoxon	18	20	20	**0.01**	4	20	20	**0.01**
Methyl Parathion	0	12	17	**> 0.05**	0	0	0	**> 0.05**
Metobromuron	19	20	20	**0.001**	8	19	20	**0.01**
Metolachlor	20	20	20	**0.001**	20	20	20	**0.001**
Metolcarb	1	19	19	**0.01**	0	4	6	**> 0.05**
Metominostrobin (e isomer)	15	20	20	**0.01**	5	15	18	**> 0.05**
Metominostrobin (z-type)	14	20	20	**0.01**	5	15	18	**> 0.05**
Metosulam	4	20	20	**0.01**	0	20	20	**0.01**
Metoxuron	18	20	20	**0.01**	18	20	20	**0.01**
Metrafenone	19	20	20	**0.001**	19	20	20	**0.001**
Metribuzin	0	20	20	**0.01**	0	20	20	**0.01**
Metsulfuron-methyl	6	20	20	**0.01**	1	18	20	**0.05**
Mevinphos	19	20	20	**0.001**	6	20	20	**0.01**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Mexacarbate	7	18	3	**> 0.05**	7	18	3	**> 0.05**
Mgk-264 (mixture of isomers)	1	20	20	**0.01**	0	18	20	**0.05**
Molinate	10	20	20	**0.01**	0	12	16	**> 0.05**
Monocrotophos	12	20	20	**0.01**	5	20	20	**0.01**
Monolinuron	19	20	20	**0.001**	3	18	20	**0.05**
Monuron	14	20	20	**0.01**	7	20	20	**0.01**
Moxidectin	14	19	20	**0.01**	0	4	13	**> 0.05**
N,n-diethyl-m-toluamide	20	20	20	**0.001**	18	20	20	**0.01**
N,n'-ethylenethiourea	0	0	1	**> 0.05**	0	0	0	**> 0.05**
Naphthalophos (naftalofos)	19	20	20	**0.001**	19	20	20	**0.001**
Napropamide	20	20	20	**0.001**	18	20	20	**0.01**
Naptalam	3	2	1	**> 0.05**	0	0	0	**> 0.05**
Neburon	20	20	20	**0.001**	19	20	20	**0.001**
Nicosulfuron	5	16	20	**0.05**	1	7	14	**> 0.05**
Nitenpyram(iso)	5	18	20	**0.05**	0	10	19	**0.05**
Nitralin	16	19	20	**0.01**	0	0	0	**> 0.05**
Norflurazon	20	20	20	**0.001**	20	20	20	**0.001**
Noruron	19	20	20	**0.001**	18	20	20	**0.01**
Novaluron	20	20	20	**0.001**	17	20	20	**0.01**
Nuarimol	13	20	20	**0.01**	7	18	19	**0.05**
Ofurace	20	20	20	**0.001**	16	20	20	**0.01**
Omethoate	11	16	20	**0.05**	0	8	14	**> 0.05**
Orbencarb	20	20	20	**0.001**	19	20	20	**0.001**
Orysastrobin	20	20	20	**0.001**	20	19	20	**0.001**
Oryzalin	20	20	20	**0.001**	19	20	20	**0.001**
Oxadiargyl	18	20	20	**0.01**	1	20	16	**0.01**
Oxadiazon	17	20	20	**0.01**	0	20	20	**0.01**
Oxadixyl	15	19	20	**0.01**	6	19	20	**0.01**
Oxasulfuron	11	20	20	**0.01**	6	20	20	**0.01**
Oxaziclomefone	20	20	20	**0.001**	20	20	19	**0.001**
Oximino Oxamyl	0	0	1	**> 0.05**	0	0	0	**> 0.05**
Oxycarboxin	19	20	20	**0.001**	14	20	20	**0.01**
Oxydemeton-methyl	15	19	20	**0.01**	0	6	12	**> 0.05**
Oxyfluorfen	1	19	20	**0.01**	0	12	14	**> 0.05**
Paclobutrazol (mixture Of Stereo)	20	20	20	**0.001**	19	20	20	**0.001**
Paraoxon Ethyl	19	20	20	**0.001**	12	20	20	**0.01**
Parathion	1	19	20	**0.01**	0	3	12	**> 0.05**
Pebulate	19	20	20	**0.001**	0	4	18	**> 0.05**
Penconazol	20	20	20	**0.001**	20	20	20	**0.001**
Pencycuron	20	20	20	**0.001**	20	20	20	**0.001**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Pendimethalin	8	14	20	**0.05**	0	5	18	**> 0.05**
Penfluron	20	20	20	**0.001**	19	20	20	**0.001**
Penoxsulam	19	20	20	**0.001**	12	20	20	**0.01**
Pentanochlor	20	20	20	**0.001**	14	20	20	**0.01**
Penthiopyrad	20	20	20	**0.001**	20	20	20	**0.001**
Pethoxamid	20	20	20	**0.001**	19	20	20	**0.001**
Phenmedipham	19	20	20	**0.001**	7	12	20	**0.05**
Phenothrin	1	16	20	**0.05**	0	9	17	**> 0.05**
Phenthoate	9	20	20	**0.01**	0	19	16	**0.01**
Phenylurea	0	5	19	**0.05**	0	5	19	**0.05**
Phorate Oxon Sulfoxide	19	20	20	**0.001**	0	10	14	**> 0.05**
Phorate Sulfoxide	20	20	20	**0.001**	10	19	20	**0.01**
Phorate-oxon Sulfone	20	20	20	**0.001**	6	20	20	**0.01**
Phorat-sulfone	10	15	20	**0.05**	0	11	20	**0.05**
Phosalone	18	20	20	**0.01**	8	19	20	**0.01**
Phosfolan	20	20	20	**0.001**	17	20	20	**0.01**
Phosmet	14	19	20	**0.01**	11	19	19	**0.01**
Phosmet Oxon	19	19	20	**0.001**	18	19	19	**0.01**
Phosphamidon	20	20	20	**0.001**	19	20	20	**0.001**
Phospholan-methyl	19	20	20	**0.001**	7	20	20	**0.01**
Phoxim	19	20	20	**0.001**	14	20	20	**0.01**
Picolinafen	20	20	20	**0.001**	8	5	9	**> 0.05**
Picoxystrobin	19	20	20	**0.001**	19	20	20	**0.001**
Piperalin	19	20	20	**0.001**	18	20	20	**0.01**
Piperonyl Butoxide	19	20	20	**0.001**	15	20	20	**0.01**
Piperophos	20	20	20	**0.001**	20	20	20	**0.001**
Pirimicarb	20	20	20	**0.001**	19	20	20	**0.001**
Pirimicarb-desmethyl	6	10	20	**0.05**	6	10	19	**0.05**
Pirimiphos Methyl	20	20	20	**0.001**	20	20	20	**0.001**
Pirimiphos-ethyl	20	20	20	**0.001**	20	20	20	**0.001**
Pirimiphos-methyl-n-desethyl	20	20	20	**0.001**	19	20	20	**0.001**
Prallethrin	8	20	20	**0.01**	0	16	20	**0.05**
Pretilachlor	20	20	20	**0.001**	20	20	20	**0.001**
Primisulfuron-methyl	19	20	19	**0.001**	8	20	18	**0.01**
Probenazole	14	19	20	**0.01**	2	7	1	**> 0.05**
Prochloraz	20	20	20	**0.001**	8	20	20	**0.01**
Procyazine	18	20	20	**0.01**	14	20	20	**0.01**
Procymidone	4	20	20	**0.01**	4	20	20	**0.01**
Profenofos	20	20	20	**0.001**	11	20	19	**0.01**
Profoxydim Lithium	15	20	20	**0.01**	5	20	20	**0.01**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Prohydrojasmon	3	13	20	**0.05**	0	3	16	**> 0.05**
Promecarb	15	20	20	**0.01**	8	20	20	**0.01**
Prometon	20	20	20	**0.001**	20	20	20	**0.001**
Prometryn	20	20	20	**0.001**	20	20	20	**0.001**
Propachlor	6	20	20	**0.01**	6	20	20	**0.01**
Propamocarb	4	19	20	**0.01**	0	14	18	**> 0.05**
Propanil	20	20	20	**0.001**	15	20	20	**0.01**
Propaphos	20	20	20	**0.001**	16	20	20	**0.01**
Propaquizafop	20	20	20	**0.001**	6	20	20	**0.01**
Propargite	12	18	20	**0.05**	0	17	18	**> 0.05**
Propazine	20	20	20	**0.001**	20	20	20	**0.001**
Propazine-2-hydroxy	20	20	20	**0.001**	20	20	20	**0.001**
Propetamphos	0	20	20	**0.01**	0	0	1	**> 0.05**
Propham	7	20	20	**0.01**	1	19	18	**0.01**
Propiconazol (mixture of isomers)	20	20	20	**0.001**	20	20	20	**0.001**
Propisochlor	20	20	20	**0.001**	20	20	20	**0.001**
Propoxur	18	20	20	**0.01**	0	15	19	**0.05**
Propyzamide (pronamide)	20	20	20	**0.001**	16	20	20	**0.01**
Proquinazid	20	20	20	**0.001**	19	20	20	**0.001**
Prosulfocarb	20	20	20	**0.001**	15	20	20	**0.01**
Prosulfuron	12	20	20	**0.01**	4	19	18	**0.01**
Prothioconazole-desthio*	/	/	/	**/**	/	/	/	**/**
Pymetrozine	5	16	20	**0.05**	0	9	20	**0.05**
Pyracarbolid	20	20	20	**0.001**	18	20	20	**0.01**
Pyraclofos	20	20	20	**0.001**	8	19	18	**0.01**
Pyraclostrobin	20	20	20	**0.001**	18	20	20	**0.01**
Pyraflufen-ethyl	20	20	20	**0.001**	12	20	20	**0.01**
Pyrazolynate	17	20	20	**0.01**	15	20	20	**0.01**
Pyrazophos	20	20	20	**0.001**	17	20	20	**0.01**
Pyrazosulfuron-ethyl	12	20	20	**0.01**	0	14	16	**> 0.05**
Pyrazoxyfen	20	20	20	**0.001**	12	19	18	**0.01**
Pyrethrin (mixture of isomers)	3	15	18	**> 0.05**	2	2	10	**> 0.05**
Pyributicarb	20	20	20	**0.001**	15	20	20	**0.01**
Pyridaben	19	20	20	**0.001**	18	20	20	**0.01**
Pyridafol	15	20	20	**0.01**	3	20	20	**0.01**
Pyridalyl	18	20	19	**0.01**	3	18	19	**0.05**
Pyridaphenthion	20	20	20	**0.001**	20	20	20	**0.001**
Pyridate	11	17	17	**> 0.05**	9	11	16	**> 0.05**
Pyrifenox (mixture of isomers))	12	20	19	**0.01**	7	19	19	**0.01**
Pyrimethanil	20	20	20	**0.001**	17	20	20	**0.01**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Pyriproxyfen	20	20	20	**0.001**	20	20	20	**0.001**
Pyroquilon	19	20	20	**0.001**	15	20	20	**0.01**
Pyroxsulam	12	20	20	**0.01**	3	19	19	**0.01**
Quinalphos	19	20	20	**0.001**	14	20	20	**0.01**
Quinclorac	0	0	0	**> 0.05**	0	0	0	**> 0.05**
Quinmerac	0	0	0	**> 0.05**	0	0	0	**> 0.05**
Quinoclamine	19	20	20	**0.001**	8	19	20	**0.01**
Quinoline	20	20	20	**0.001**	20	20	20	**0.001**
Quinoxyfen	20	20	20	**0.001**	19	20	20	**0.001**
Quizalofop	8	7	1	**> 0.05**	1	3	0	**> 0.05**
Quizalofop-ethyl	20	20	20	**0.001**	20	20	20	**0.001**
Quizalofop-p-ethyl	20	20	20	**0.001**	20	20	20	**0.001**
Reserpine	19	20	19	**0.001**	19	20	19	**0.001**
Resmethrin	10	20	20	**0.01**	3	18	18	**> 0.05**
Rimsulfuron	0	16	19	**0.05**	0	3	11	**> 0.05**
Rotenone	19	20	20	**0.001**	17	20	20	**0.01**
Roxithromycin	20	20	19	**0.001**	20	20	19	**0.001**
Saflufenacil	17	20	20	**0.01**	1	15	17	**> 0.05**
Schradan (dmpa)	8	18	20	**0.05**	8	18	20	**0.05**
Sebuthylazin	18	19	18	**0.01**	17	18	18	**> 0.05**
Sebuthylazin-desethyl	20	20	20	**0.001**	16	19	20	**0.01**
Secbumeton	17	17	18	**> 0.05**	16	16	18	**> 0.05**
Selamectin Impurity B	16	20	19	**0.01**	8	18	19	**0.05**
Sethoxydim	19	20	20	**0.001**	1	19	20	**0.01**
S-hydroprene	0	0	0	**> 0.05**	0	0	0	**> 0.05**
Siduron	20	20	20	**0.001**	16	20	20	**0.01**
Silthiofam	1	13	20	**0.05**	0	0	0	**> 0.05**
Simazine	20	20	20	**0.001**	13	20	20	**0.01**
Simeconazole	20	20	20	**0.001**	15	20	20	**0.01**
Simetone	14	20	20	**0.01**	14	20	19	**0.01**
Simetryn	7	20	20	**0.01**	0	20	20	**0.01**
S-metolachlor	20	20	20	**0.001**	20	20	20	**0.001**
Spinetoram (mixture of Isomers)	20	20	14	**0.001**	19	19	14	**0.001**
Spinosad* (mixure Of Spinosyn A And D)	/	/	/	**/**	/	/	/	**/**
Spirodiclofen	17	20	20	**0.01**	5	14	20	**0.05**
Spiromesifen	12	18	20	**0.05**	3	17	20	**0.05**
Spirotetramat	20	20	20	**0.001**	18	19	20	**0.01**
Spirotetramat-enol	13	20	20	**0.01**	5	20	20	**0.01**
Spirotetramat-enol-glucoside	0	11	17	**> 0.05**	0	6	15	**> 0.05**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Spirotetramat-mono-hydroxy	20	20	20	**0.001**	18	19	20	**0.01**
Spiroxamine (mix of isomers)	20	20	20	**0.001**	20	20	20	**0.001**
Sulcotrione	0	4	10	**> 0.05**	0	1	2	**> 0.05**
Sulfallate	1	18	20	**0.05**	0	7	17	**> 0.05**
Sulfamerazine	2	15	20	**0.05**	0	0	17	**> 0.05**
Sulfamonomethoxine	4	16	19	**0.05**	0	7	18	**> 0.05**
Sulfentrazone	20	20	20	**0.001**	16	20	20	**0.01**
Sulfometuron Methyl	18	20	20	**0.01**	9	20	20	**0.01**
Sulfosulfuron	7	20	20	**0.01**	0	14	19	**0.05**
Sulfoxaflor	19	20	20	**0.001**	10	20	20	**0.01**
Sulfuramid	20	20	18	**0.001**	20	20	18	**0.001**
Sulprofos Sulfoxide	20	20	20	**0.001**	16	19	20	**0.01**
Systhane Tm	19	20	20	**0.001**	12	20	20	**0.01**
Tau-fluvalinate	5	17	18	**> 0.05**	0	7	13	**> 0.05**
Tdcpp	20	20	20	**0.001**	3	11	5	**> 0.05**
Tebuconazol (folicur)	20	20	20	**0.001**	20	20	20	**0.001**
Tebufenozide	20	20	20	**0.001**	20	20	20	**0.001**
Tebufenpyrad	20	20	20	**0.001**	20	20	20	**0.001**
Tebupirimfos	20	20	20	**0.001**	19	20	20	**0.001**
Tebutam	20	20	20	**0.001**	20	20	20	**0.001**
Tebuthiuron	14	20	20	**0.01**	14	20	20	**0.01**
Teflubenzuron	20	20	20	**0.001**	13	20	20	**0.01**
Tembotrione	2	8	5	**> 0.05**	0	0	0	**> 0.05**
Tepraloxydim	19	20	20	**0.001**	6	20	19	**0.01**
Terbufos-sulfon	20	20	20	**0.001**	5	20	20	**0.01**
Terbufos-sulfoxide	19	20	20	**0.001**	7	19	20	**0.01**
Terbumeton	20	20	20	**0.001**	20	20	20	**0.001**
Terbumeton-desethyl	14	20	20	**0.01**	14	20	19	**0.01**
Terbuthylazine	18	19	17	**0.01**	17	18	15	**> 0.05**
Terbuthylazine-desethyl	20	20	20	**0.001**	13	20	20	**0.01**
Terbutol (terbucarb)	9	18	20	**0.05**	5	18	20	**0.05**
Terbutryne	20	20	20	**0.001**	20	20	20	**0.001**
Terbutylazine-2-hydroxy	12	20	20	**0.01**	2	18	19	**0.05**
Tetrachlorvinphos (iso))	20	20	20	**0.001**	0	0	0	**> 0.05**
Tetraconazole	20	20	20	**0.001**	20	20	20	**0.001**
Tetraethyl Dithiopyrophosphate	20	20	20	**0.001**	7	20	20	**0.01**
Tetraethyl Pyrophosphate	18	20	20	**0.01**	15	20	20	**0.01**
Tetramethrin	19	20	20	**0.001**	14	20	20	**0.01**
Thenylchlor	20	20	20	**0.001**	17	20	20	**0.01**
Thiabendazole	11	17	19	**0.05**	11	17	19	**0.05**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Thiacloprid*	/	/	/	/	/	/	/	/
Thiamethoxam	10	20	20	**0.01**	0	8	20	**0.05**
Thiazafluron	20	20	20	**0.001**	16	20	20	**0.01**
Thiazopyr	20	20	20	**0.001**	20	20	20	**0.001**
Thidiazuron	19	20	20	**0.001**	5	20	20	**0.01**
Thiencarbazone-methyl	0	14	20	**0.05**	0	0	3	> **0.05**
Thifensulfuron-methyl	3	20	19	**0.01**	0	17	19	**0.05**
Thifluzamide	20	20	19	**0.001**	0	0	0	> **0.05**
Thiobencarb	20	20	20	**0.001**	19	20	20	**0.001**
Thiocarbazyl	5	20	20	**0.01**	4	20	20	**0.01**
Thiodicarb	15	17	18	> **0.05**	10	17	18	> **0.05**
Thiofanox	2	12	19	**0.05**	0	1	3	> **0.05**
Thiofanox-sulfone	1	13	19	**0.05**	0	0	14	> **0.05**
Thiofanox-sulfoxide	0	12	20	**0.05**	0	1	2	> **0.05**
Thionazine (zinophos)	14	20	20	**0.01**	3	20	20	**0.01**
Thiophanate Methyl	0	20	20	**0.01**	0	8	20	**0.05**
Thiophanate-ethyl	5	20	20	**0.01**	0	18	19	**0.05**
Tiadinil	20	20	20	**0.001**	19	20	20	**0.001**
Tokuthion®	0	14	17	> **0.05**	0	0	0	> **0.05**
Tolclofos-methyl	2	18	20	**0.05**	0	16	20	**0.05**
Tolfenpyrade	15	20	19	**0.01**	12	20	17	**0.01**
Tolylfluanid	0	2	12	> **0.05**	0	0	1	> **0.05**
Topramezone	3	0	3	> **0.05**	0	0	0	> **0.05**
Tralkoxydim	20	20	20	**0.001**	5	20	20	**0.01**
Triadimefon	20	20	20	**0.001**	12	20	20	**0.01**
Triallate	5	15	20	**0.05**	0	8	16	> **0.05**
Triasulfuron	16	20	20	**0.01**	4	20	20	**0.01**
Triazamate	20	20	20	**0.001**	20	20	20	**0.001**
Triaziflam	20	20	20	**0.001**	19	20	20	**0.001**
Triazophos	20	20	20	**0.001**	20	20	20	**0.001**
Triazoxid	20	20	20	**0.001**	18	20	20	**0.01**
Tribenuron-methyl	2	20	20	**0.01**	0	0	0	> **0.05**
Tribufos (def)	20	20	20	**0.001**	15	20	20	**0.01**
Trichlorfon	9	18	20	**0.05**	1	3	11	> **0.05**
Tricyclazole	19	20	20	**0.001**	13	20	20	**0.01**
Tridemorph (mixture of isomers)	20	20	17	**0.001**	15	20	17	**0.01**
Trietazine	20	20	20	**0.001**	20	20	20	**0.001**
Trifloxystrobin	20	20	20	**0.001**	20	20	20	**0.001**
Trifloxystrobin Metabolite	1	1	2	> **0.05**	0	1	2	> **0.05**
Trifloxysulfuron-sodium	2	17	16	> **0.05**	0	0	0	> **0.05**

Compound	Number of detections out of 20 samples			SDL (mg.kg^{-1})	Number of identifications out of 20 samples			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.05 mg.kg^{-1}	
Triflumizole	20	20	20	**0.001**	16	20	20	**0.01**
Triflumuron	20	20	20	**0.001**	17	20	20	**0.01**
Triflusulfuron-methyl	20	20	20	**0.001**	11	19	20	**0.01**
Triforine	14	20	20	**0.01**	1	12	18	**> 0.05**
Trinexapac-ethyl	3	6	17	**> 0.05**	0	0	6	**> 0.05**
Triphenyl Phosphorothionate	14	19	20	**0.01**	5	19	19	**0.01**
Tris(2-chloroethyl) Phosphate	19	20	20	**0.001**	1	8	8	**> 0.05**
Tris(o-cresyl)phosphate	17	20	20	**0.01**	15	20	20	**0.01**
Triticonazole	19	20	20	**0.001**	18	20	20	**0.01**
Tritosulfuron	17	20	20	**0.01**	9	20	19	**0.01**
Uniconazole	20	20	20	**0.001**	17	18	20	**0.05**
Vamidothion	20	20	20	**0.001**	9	20	20	**0.01**
Vamidothion Sulfoxide	11	19	20	**0.01**	0	16	19	**0.05**
Vernolate	19	20	20	**0.001**	0	4	18	**> 0.05**
Xmc (3,5-xylyl Methylcarbamate)	8	20	20	**0.01**	0	11	19	**0.05**
Z-mevinphos	16	20	20	**0.01**	4	17	20	**0.05**
Zoxamide	20	20	20	**0.001**	19	20	20	**0.001**

***Compound discarded from method validation since it was found in non-spiked samples**

Table S6: Comparison of analytical performances using LODs provided by (Gómez-Pérez et al., 2012) and the SDLs of the present study, for each mutual compound

Compound*	LOD ($mg.kg^{-1}$) **	SDL ($mg.kg^{-1}$)
2,6-dichlorobenzamide	0.005	0.001
Alachlor	0.001	0.001
Aldicarb sulfone	0.001	0.01
Aldicarb sulfoxide	0.001	> 0.05
Ametryn	0.001	0.001
Atrazine	0.001	0.01
Atrazine desisopropyl	0.001	0.01
Azaconazole	0.001	0.001
Benalaxyl	0.001	0.001
Benthiavalicarb-Isopropyl	0.001	0.001
Bitertanol	0.01	0.001
Boscalid	0.05	0.001
Bromuconazole	0.005	0.001
Bupirimate	0.001	0.001
Buprofezin	0.001	0.001
Butocarboxim sulfoxide	0.001	> 0.05
Butoxycarboxim	0.005	0.01
Cadusafos	0.001	0.01
Carbaryl	0.005	0.05
Carbendazim	0.001	0.01
Carbofuran	0.001	0.001
Chloridazon	0.001	0.001
Chlorpyrifos	0.05	0.05
Cinosulfuron	0.001	0.01
Clethodim	0.025	0.001
Clodinafop-propargyl	0.01	0.001
Clofentezine	0.01	0.01
Clothianidin	0.005	0.001
Cyazofamid	0.001	0.001
Cycloate	0.01	0.001
Cyproconazole	0.001	0.001
Demeton-S-methyl	0.001	0.05
Desethyl atrazine	0.005	0.001
Desmedipham	0.001	0.001
Desmetryn	0.001	0.01
Diazinon	0.001	0.001
Dichlorvos	0.005	0.001
Diclobutrazole	0.001	0.001
Diethofencarb	0.001	0.001

Compound*	LOD (mg.kg^{-1}) **	SDL (mg.kg^{-1})
Diflubenzuron	0.005	0.001
Dimethoate	0.001	0.001
Dimethomorph	0.001	0.001
Diphenylamine	0.025	0.001
Disulfoton Sulfone	0.001	0.01
Disulfoton Sulfoxide	0.001	0.001
Diuron	0.001	0.001
EPN	0.001	0.01
Erythromycin	0.01	0.01
Ethiofencarb	0.01	0.05
Ethion	0.001	0.01
Ethiprole	0.005	0.001
Ethoprophos	0.001	0.001
Etoxazole	0.001	0.001
Etrimfos	0.001	0.001
Fenamiphos sulfone	0.05	0.001
Fenamiphos sulfoxide	0.01	0.001
Fenarimol	0.005	0.001
Fenazaquin	0.001	0.001
Fenbuconazole	0.005	0.001
Fenhexamid	0.005	0.01
Fenoxaprop-P-ethyl	0.001	0.001
Fenoxycarb	0.005	0.001
Fenpropathrin	0.05	> 0.05
Fenpropidin	0.001	0.01
Fenpyroximate	0.001	0.001
Fensulfothion	0.001	0.001
Fenthion	0.01	0.01
Fenthion sulfoxide	0.01	0.001
Fipronil	0.001	0.001
Fluazifop	0.01	0.05
Fluazinam	0.001	0.001
Fludioxonil	0.001	0.001
Fluquinconazole	0.005	0.01
Flusilazole	0.001	0.001
Flutolanil	0.001	0.001
Flutriafol	0.001	0.01
Forchlorfenuron	0.001	0.001
Furalaxyl	0.005	0.001
Furathiocarb	0.001	0.001
Furmecyclox	0.001	0.01
Haloxyfop	0.005	> 0.05

Compound*	LOD (mg.kg^{-1}) **	SDL (mg.kg^{-1})
Heptenophos	0.001	0.01
Hexaconazole	0.005	0.01
Hexythiazox	0.005	0.01
Imazalil	0.001	0.001
Imidacloprid	0.001	0.001
Indoxacarb	0.005	0.001
Iprovalicarb	0.001	0.001
Isofenphos	0.005	0.01
Isoproturon	0.001	0.01
Isoxaflutole	0.001	0.01
Ketoprofen	0.005	0.05
Lenacil	0.001	0.01
Linuron	0.005	0.001
Lufenuron	0.005	0.001
Malaoxon	0.05	0.01
Malathion	0.005	0.001
Mecarbam	0.001	> 0.05
Mepanipyrim	0.001	0.001
Metaflumizone	0.005	0.001
Metalaxyl	0.001	0.001
Metamitron	0.005	0.01
Metazachlor	0.001	0.01
Methidathion	0.005	0.01
Methiocarb	0.01	0.001
Methiocarb sulfone	0.005	0.01
Methiocarb sulfoxide	0.001	> 0.05
Methomyl	0.001	> 0.05
Metobromuron	0.001	0.001
Metolachlor	0.001	0.001
Metoxuron	0.001	0.01
Metsulfuron-methyl	0.01	0.01
Mevinphos	0.001	0.001
Monocrotophos	0.001	0.01
Monolinuron	0.001	0.001
Norflurazon	0.001	0.001
Nuarimol	0.001	0.01
Ofurace	0.005	0.001
Omethoate	0.005	0.05
Oxadixyl	0.005	0.01
Oxyfluorfen	0.005	0.01
Paclobutrazole	0.005	0.001
Phenmedipham	0.001	0.001
Phenthoate	0.001	0.01

Compound*	LOD (mg.kg^{-1}) **	SDL (mg.kg^{-1})
Phosalone	0.001	0.01
Phosmet	0.001	0.01
Phosphamidon	0.001	0.001
Prochloraz	0.001	0.001
Profenofos	0.005	0.001
Promecarb	0.001	0.01
Prometryn	0.001	0.001
Propachlor	0.001	0.01
Propamocarb	0.005	0.01
Propaquizafop	0.001	0.001
Propargite	0.005	0.05
Propazine	0.001	0.001
Propiconazole	0.001	0.001
Propoxur	0.001	0.01
Propyzamide	0.005	0.001
Proquinazid	0.001	0.001
Prosulfocarb	0.005	0.001
Prosulfuron	0.05	0.01
Pyraclostrobin	0.001	0.001
Pyrazophos	0.001	0.001
Pyridaben	0.001	0.001
Pyridaphenthion	0.001	0.001
Pyrifenox	0.001	0.01
Pyrimethanil	0.001	0.001
Pyriproxyfen	0.001	0.001
Quinalphos	0.001	0.001
Quinmerac	0.001	> 0.05
Quinoxyfen	0.001	0.001
Rotenone	0.001	0.001
Roxithromycin	0.001	0.001
Sethoxydim	0.01	0.001
Simazine	0.001	0.001
Simetryn	0.001	0.01
Spirodiclofen	0.001	0.01
Spiromesifen	0.001	0.05
Spiroxamine	0.005	0.001
Sulfamerazine	0.001	0.05
Tebuconazole	0.001	0.001
Tebufenozide	0.005	0.001
Tebutam	0.001	0.001
Teflubenzuron	0.001	0.001
Tepraloxydim	0.01	0.001
Terbumeton	0.001	0.001

Compound*	LOD (mg.kg^{-1}) **	SDL (mg.kg^{-1})
Terbuthylazine	0.001	0.01
Tetrachlorvinphos	0.01	0.001
Tetraconazole	0.001	0.001
Tetramethrin	0.001	0.001
Thiabendazole	0.001	0.05
Thiamethoxam	0.005	0.01
Thiazopyr	0.001	0.001
Thiodicarb	0.001	> 0.05
Thiophanate methyl	0.001	0.01
Triadimefon	0.001	0.001
Triallate	0.001	0.05
Triasulfuron	0.005	0.01
Triazophos	0.001	0.001
Trichlorfon	0.005	0.05
Trietazine	0.001	0.001
Trifloxystrobin	0.001	0.001
Triflumizole	0.001	0.001
Triflumuron	0.005	0.001
Vamidothion	0.001	0.001
Zoxamide	0.001	0.001

*Mutual pesticide residues analysed in the present work and in the study published by Gómez-Pérez et al. (2012)

**LODs provided in the study of Gómez-Pérez et al. (2012)

Table S7: Estimated concentrations in positive samples by using three methods of semi-quantification

				Estimated concentration (mg.kg^{-1})		
Compound	**MRL in honey (mg.kg^{-1})**	**Positive sample**	**Type**	**Method A**	**Method B**	**Method C**
acetamiprid	0.05	honey	lemon tree	**< SDL***	**< SDL***	**< SDL***
			mountain	**< SDL***	**< SDL***	**< SDL***
			orange tree	**< SDL***	**< SDL***	**< SDL***
azoxystrobin	0.05	honey	clover	**< SDL***	**< SDL***	**< SDL***
			multi-flower	**< SDL***	**< SDL***	**0.001**
			multi-flower	**0.038**	**0.041**	**0.030**
			rapeseed	**0.002**	**0.002**	**< SDL***
		jam	raspberry	**< SDL***	**0.002**	**0.002**
			strawberry	**< SDL***	**0.002**	**0.002**
boscalid	0.15	jam	raspberry	**0.002**	**0.002**	**0.002**
		jelly	currant	**0.002**	**0.002**	**0.002**
carbendazim	1	jam	cherry	**< SDL***	**< SDL***	**< SDL***
			strawberry	**< SDL***	**< SDL***	**< SDL***
			strawberry	**< SDL***	**< SDL***	**< SDL***
			strawberry	**< SDL***	**< SDL***	**< SDL***
		jelly	currant	**< SDL***	**< SDL***	**< SDL***
			currant / raspberry	**< SDL***	**< SDL***	**< SDL***
coumaphos	0.1	honey	chestnut	**0.004**	**0.004**	**0.007**
			lemon tree	**0.006**	**0.006**	**undetermined****
			orange tree	**0.002**	**0.001**	**undetermined****
cyproconazole	0.05	honey	multi-flower	**0.033**	**0.036**	**0.027**
cyprodinil	0.05	jam	apricot	**0.001**	**0.001**	**0.002**
			raspberry	**0.002**	**0.002**	**0.002**
			strawberry	**0.001**	**0.001**	**0.001**
			strawberry	**0.001**	**0.001**	**0.001**
			strawberry	**0.003**	**0.003**	**0.003**
		jelly	currant	**0.001**	**0.001**	**0.002**
		jelly	currant / raspberry	**0.002**	**0.002**	**0.002**
difenoconazole	0.05	honey	multi-flower	**0.001**	**0.001**	**0.002**
		jam	apricot	**0.001**	**0.002**	**0.002**
			cherry	**0.003**	**0.003**	**0.003**
			raspberry	**0.008**	**0.007**	**0.006**
			strawberry	**0.004**	**0.004**	**0.004**
			strawberry	**0.002**	**0.002**	**0.003**
		jelly	currant	**0.001**	**0.002**	**0.002**
dimoxystrobin	0.05	honey	unspecified	**< SDL***	**< SDL***	**< SDL***
fenbuconazole	0.05	jam	cherry	**0.001**	**0.002**	**0.002**
fenhexamid	0.05	jam	raspberry	**0.066**	**0.056**	**0.040**
flonicamid	0.05	honey	clover	**0.001**	**0.001**	**undetermined****
			lemon tree	**0.001**	**0.001**	**undetermined****
			multi-flower	**< SDL***	**< SDL***	**< SDL***

fludioxinil	0.05	honey	mountain	**< SDL***	**< SDL***	**< SDL***
		jam	apricot	**< SDL***	**< SDL***	**< SDL***
			raspberry	**< SDL***	**< SDL***	**< SDL***
			strawberry	**0.009**	**0.009**	**0.009**
			strawberry	**< SDL***	**< SDL***	**< SDL***
			strawberry	**0.001**	**0.001**	**0.001**
		jelly	currant	**< SDL***	**< SDL***	**< SDL***
			currant / raspberry	**< SDL***	**< SDL***	**< SDL***
fluopyram	0.05	honey	alfalfa	**< SDL***	**< SDL***	**< SDL***
			buckwheat	**< SDL***	**< SDL***	**< SDL***
			clover	**< SDL***	**< SDL***	**< SDL***
			lemon tree	**< SDL***	**< SDL***	**< SDL***
			multi-flower	**0.001**	**< SDL***	**0.002**
			rapeseed	**0.005**	**< SDL***	**< SDL***
			unspecified	**< SDL***	**< SDL***	**0.001**
			unspecified	**< SDL***	**< SDL***	**0.001**
		jam	cherry	**0.023**	**0.020**	**0.015**
			strawberry	**0.004**	**0.005**	**0.004**
			strawberry	**0.002**	**0.003**	**0.003**
			strawberry	**0.004**	**0.004**	**0.004**
		jelly	currant	**< SDL***	**0.001**	**0.002**
fuberidazole	0.05	honey	forest	**< SDL***	**< SDL***	**0.002**
imazalil	0.05	jam	apricot	**0.001**	**0.001**	**0.002**
			strawberry	**0.005**	**0.005**	**0.005**
metconazole	0.05	honey	multi-flower	**0.001**	**0.001**	**0.002**
			unspecified	**0.001**	**< SDL***	**0.002**
penconazole	0.05	jam	strawberry	**0.001**	**0.001**	**0.002**
pyrimethanil	0.05	honey	mountain	**< SDL***	**< SDL***	**0.003**
		jam	strawberry	**0.002**	**0.002**	**0.003**
			strawberry	**0.015**	**0.013**	**0.011**
			strawberry	**0.002**	**0.002**	**0.003**
		jelly	currant	**0.001**	**0.002**	**0.002**
			currant / raspberry	**0.003**	**0.004**	**0.004**
spinosyn A	0.05	jam	raspberry	**0.003**	**0.003**	**0.003**
			strawberry	**0.003**	**0.003**	**0.003**
			strawberry	**0.003**	**0.003**	**0.003**
			strawberry	**0.001**	**0.002**	**0.002**
			strawberry	**0.001**	**0.001**	**0.002**
tebuconazole	0.05	honey	rapeseed	**0.002**	**0.002**	**0.002**
		jam	cherry	**0.011**	**0.010**	**0.008**
		jelly	currant / raspberry	**0.002**	**0.002**	**0.002**
tetraconazole	0.02	jam	strawberry	**0.002**	**0.002**	**0.003**
		jelly	currant	**0.001**	**0.002**	**0.002**
thiacloprid	0.2	honey	lemon tree	**0.001**	**< SDL***	**0.001**
		jam	cherry	**0.001**	**0.002**	**0.002**
		jelly	currant	**0.001**	**0.002**	**0.002**

trifloxystrobin	0.05	jam	raspberry	**0.004**	**0.004**	**0.004**
			strawberry	**0.004**	**0.004**	**0.004**
Transformation product						
prothioconazole-desthio	0.05	honey	multi-flower	**0.002**	**0.001**	**0.002**
prothioconazole-desthio			rapeseed	**0.002**	**0.002**	**0.002**
prothioconazole-desthio			rapeseed	**0.004**	**0.004**	**0.003**

*****Concentration below the SDL established during method validation

******Concentration was not estimated because the coefficient of determination of the slope was < 0.99

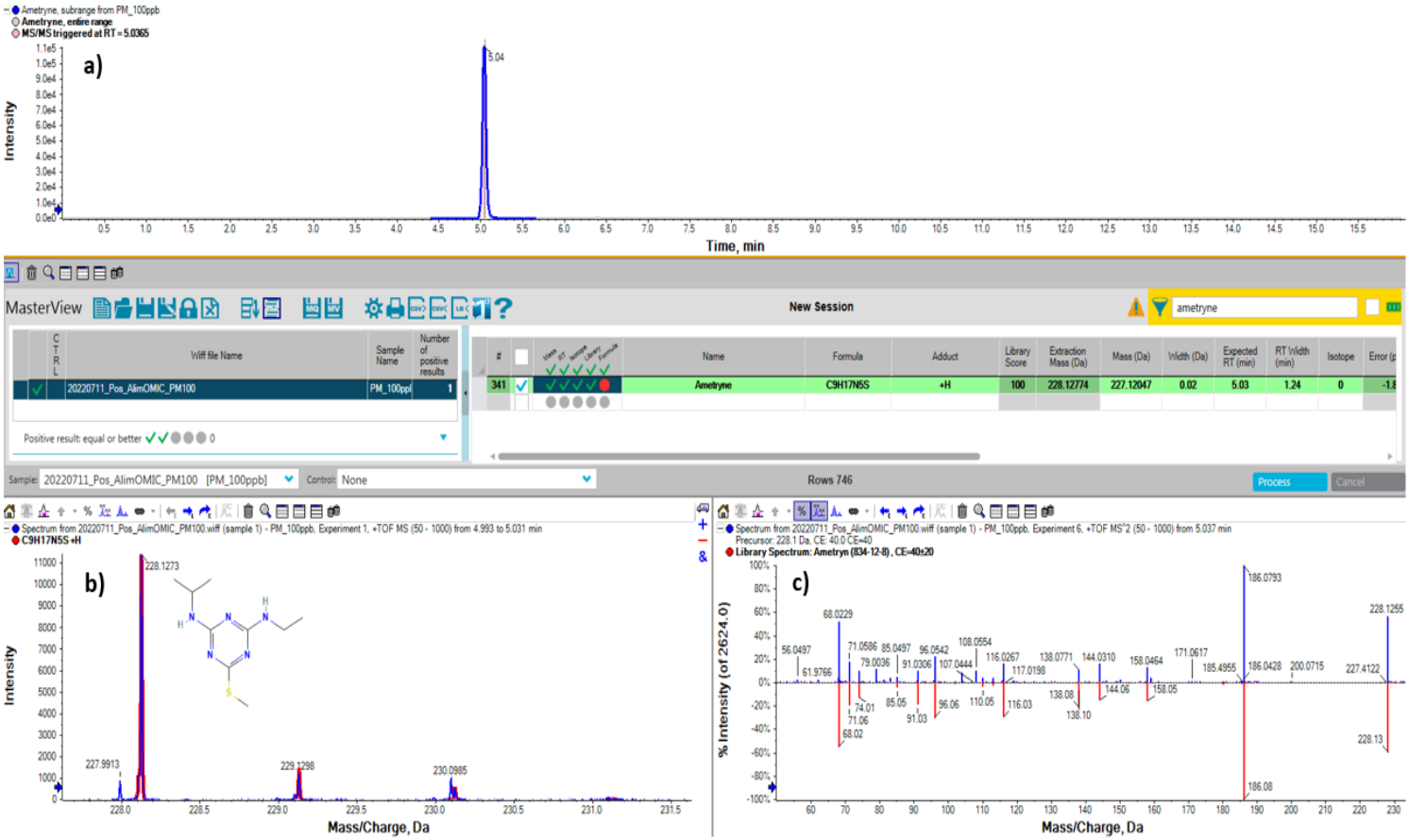

Fig. S1. Example of fast identification of Ametryn $[M+H]^+$ (*m/z* 228.12774; t_R = 5.03 min) in solvent at 0.1 mg.L^{-1} using MasterView™ software. The identification was based on t_R variation, accurate mass measurement, and library score. **(a)** Extracted ion chromatogram of Ametryn; **(b)** Experimental isotopic pattern (in blue) against a theoretical pattern based on the elemental composition and adduct (in red); **(c)** Product ion spectrum (in blue) matched against the HCDB using solvent (in red)

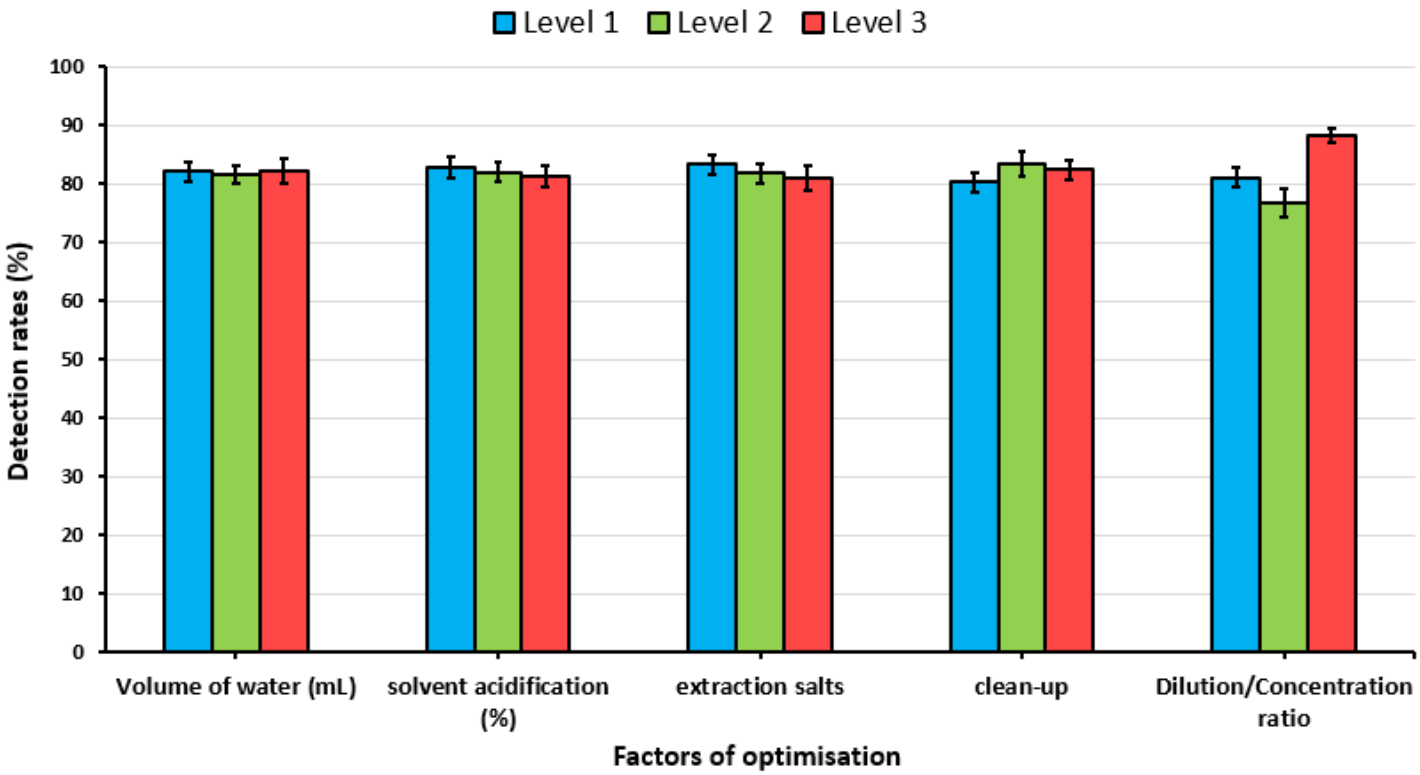

Fig. S2. Detection performances obtained for each of the five factors of optimisation (L18 TOA), as well as their different levels. The error bars correspond to the standard deviation for the response measured (Mean ± SD, n=18).

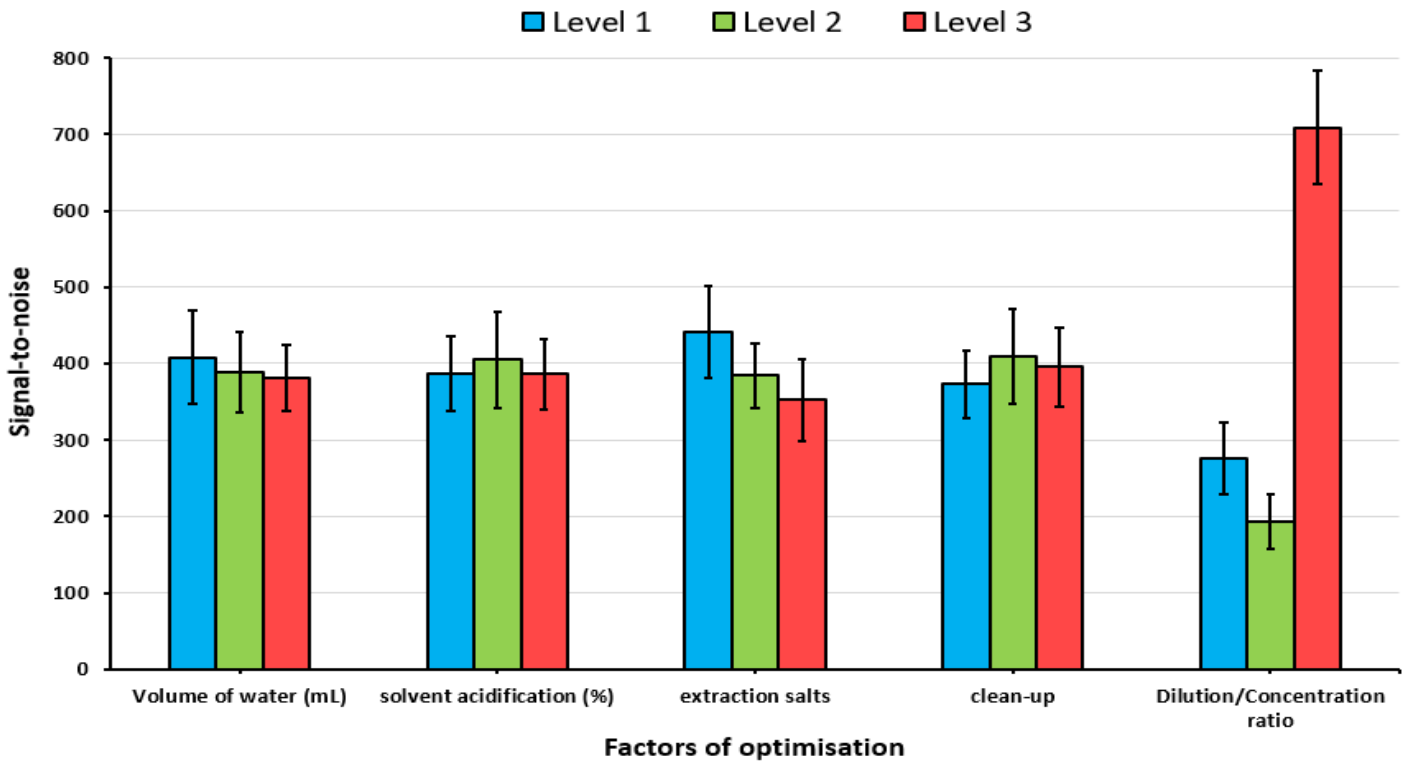

Fig. S3. Signal-to-noise value obtained for each of the five factors of optimisation (L18 TOA), as well as their different levels. The error bars correspond to the standard deviation for the response measured (Mean ± SD, n=18).

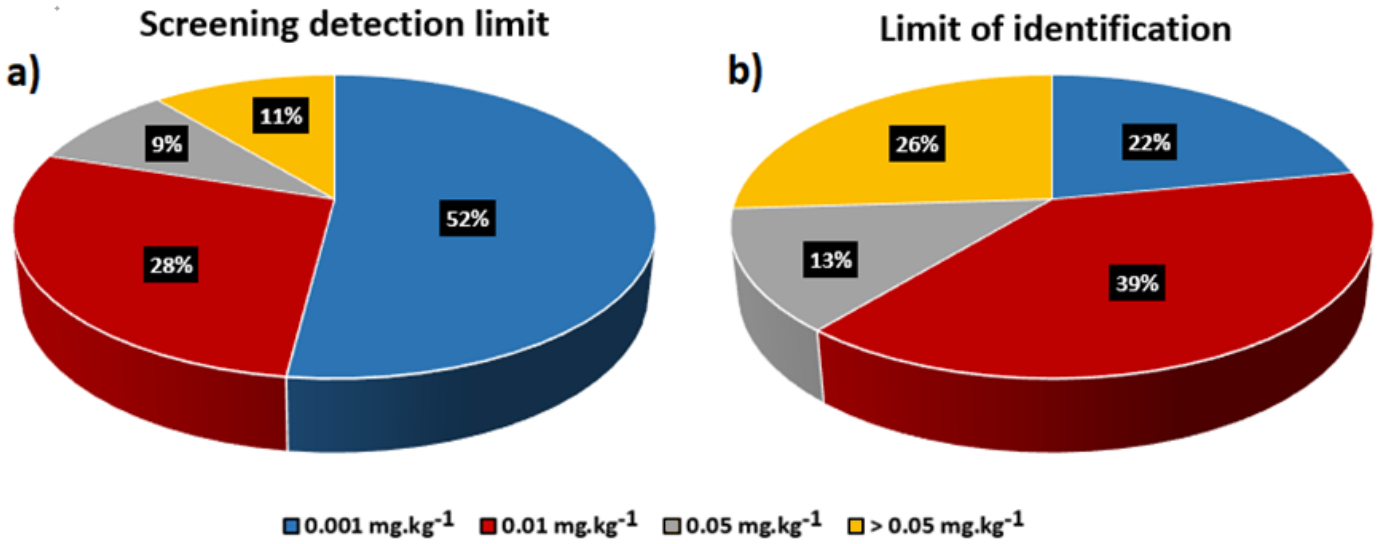

Fig. S4. Validation results of the 683 contaminants included in method validation using sweet samples (n=20) with (**a)** the screening detection limits (SDLs); and (**b)** the limits of identification (LOIs).

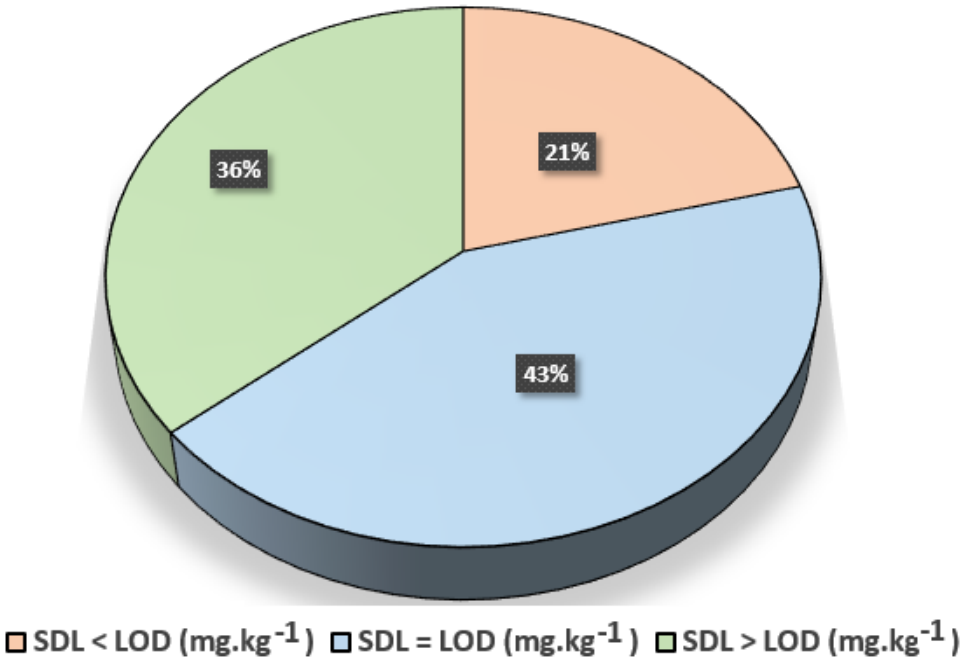

Fig. S5. Comparison of the aforementioned screening detection limits (SDLs) with the limits of detection (LODs) provided by Gómez-Pérez et al., (2012), for the same group of pesticides. The percentages were calculated based on 194 mutual compounds.

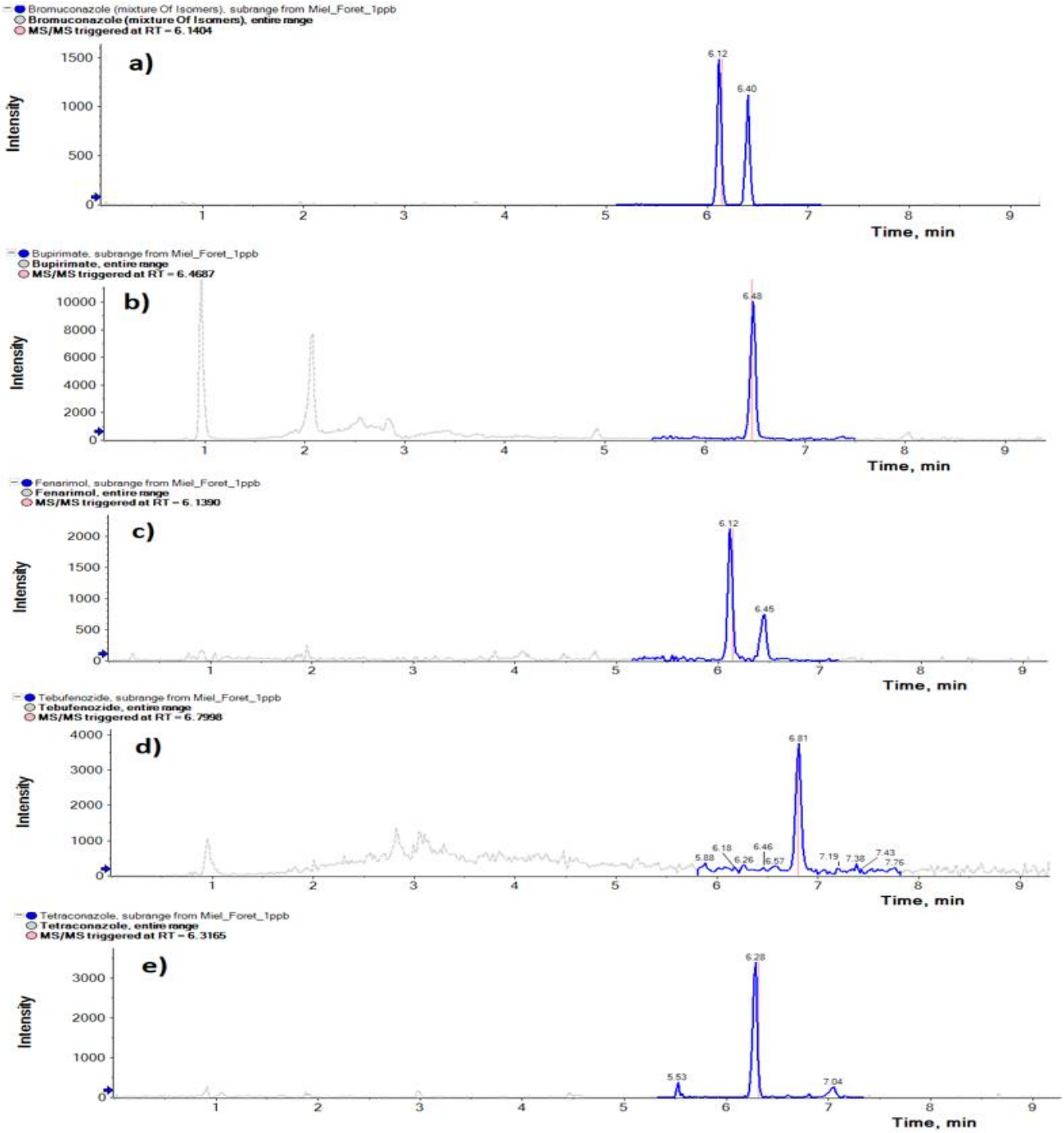

Fig. S6. Extracted Ion Chromatograms of **(a)** bromuconazole; **(b)** bupirimate; **(c)** fenarimol; **(d)** tebufenozide; **(e)** tetraconazole, in a forest honey sample spiked at 0.001 mg.kg^{-1}.

Article 4 (Diallo et al., 2023): "Wide-scope screening of multi-class contaminants in seafood using a novel sample preparation (QuEChUP) procedure coupled with UHPLC-Q-TOF-MS: Application for semi-quantitation of real seafood samples"

Table S1. List of the target contaminants with their corresponding formulae, adduct or in-source fragments, theoretical m/z, retention times (T_R) and LogP values.

Compound	MRL (mg.kg^{-1})*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
1-(3,4-Dichlorophenyl)-3-methylurea	0.01	$C_8H_8Cl_2N_2O$	$[M-H]^-$	219.00864	4.78	2.94
1-(4-Nitrophenyl)-3-propylure	0.01	$C_{10}H_{13}N_3O_3$	$[M-H]^-$	224.10297	4.69	2.4**
1,2-Benzisothiazol-3(*2H*)-one	0.01	C_7H_5NOS	$[M+H]^+$	152.01646	2.78	1.95
1,3-Diphenylurea	0.01	$C_{13}H_{12}N_2O$	$[M+H]^+$	213.10224	5.19	3
2,3,5-Trimethacarb	0.01	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.35	2.5
2,4-Dimethylaniline	0.01	$C_8H_{11}N$	$[M+H]^+$	122.09643	2.47	1.68
2,6-Dichlorobenzamide	0.01	$C_7H_5Cl_2NO$	$[M+H]^+$	189.9821	2.71	0.77
2,6-Diethylaniline	0.01	$C_{10}H_{15}N$	$[M+H]^+$	150.12773	5.75	2.7
2-Ethylhexyl diphenyl phosphate	0.01	$C_{20}H_{27}O_4P$	$[M+H]^+$	363.17197	8.64	6.3
2-N-Octyl-4-isothiazolin-3-one	0.01	$C_{11}H_{19}NOS$	$[M+H]^+$	214.12601	6.29	2.45
3,4-Dichloroaniline	0.01	$C_6H_5Cl_2N$	$[M+H]^+$	161.98718	5.32	2.7
3,4,5-Trimethacarb	0.01	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.28	2.7
3-Hydroxycarbofuran	0.01	$C_{12}H_{15}NO_4$	$C_{12}H_{14}NO_3^+$	220.09682	3.08	0.76
3-Ketocarbofuran	0.01	$C_{12}H_{13}NO_4$	$[M+H]^+$	236.09173	4.03	1.8
4-Acethylaminoantipyrine	0.01	$C_{13}H_{15}N_3O_2$	$[M+Na]^+$	246.12370	2.27	0
4-Aminoantipyrine	0.01	$C_{11}H_{13}N_3O$	$[M+H]^+$	204.11314	2.24	0.1
4-Bromo-3,5-dimethylphenyl-N-methylcarbamate	0.01	$C_{10}H_{12}BrNO_2$	$[M+H]^+$	258.01242	5.91	3.1
4-Dimethylaminoantipyrine	0.01	$C_{13}H_{17}N_3O$	$[M+H]^+$	232.14444	1.98	1
4-Formylaminoantipyrine	0.01	$C_{12}H_{13}N_3O_2$	$[M+H]^+$	232.10805	2.24	0
4-Methylaminoantipyrine	0.01	$C_{12}H_{15}N_3O$	$[M+H]^+$	218.12879	1.86	0
5-Hydroxy-flunixin	0.01	$C_{14}H_{11}F_3N_2O_3$	$[M+H]^+$	313.07945	5.10	3.7
8-Hydroxy-mutilin	0.01	$C_{20}H_{32}O_4$	$[M+H]^+$	337.23734	3.61	/
Abamectin	0.01	$C_{48}H_{72}O_{14}$	$[M+Na]^+$	895.48143	8.78	3.8
Abamectin B1a	0.01	$C_{48}H_{72}O_{14}$	$[M+Na]^+$	873.49948	8.86	3.8
Abamectin B1b	0.01	$C_{47}H_{70}O_{14}$	$[M+CH_3COO]^-$	876.51038	/	3.5
Abate® (temephos)	0.01	$C_{16}H_{20}O_6P_2S_3$	$[M+H]^+$	466.99701	8.03	6

Compound	MRL (mg.kg^{-1})*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Acephate	0.01	$C_4H_{10}NO_3PS$	$C_2H_8O_3PS^+$	142.99263	0.96	-0.8
Acetamiprid	0.01	$C_{10}H_{11}ClN_4$	$[M+H]^+$	223.0745	3.44	0.8
Acibenzolar-*S*-methyl	0.01	$C_8H_6N_2OS_2$	$[M+H]^+$	210.99943	6.07	3.1
Aclonifen	0.01	$C_{12}H_9ClN_2O_3$	$[M+H]^+$	265.03745	6.93	4.04
Aconitine	0.01	$C_{34}H_{47}NO_{11}$	$[M+H]^+$	646.32219	4.71	0.3**
Akton	0.01	$C_{12}H_{14}Cl_3O_3PS$	$[M+H]^+$	374.95396	8.3	4.8**
Alachlor	0.01	$C_{14}H_{20}ClNO_2$	$[M+H]^+$	270.12553	6.68	3.5
Albendazole	0.01	$C_{12}H_{15}N_3O_2S$	$[M+H]^+$	266.09578	4.80	2.7
Albendazole amino sulfone	0.01	$C_{10}H_{13}N_3O_2S$	$[M+H]^+$	240.08013	1.96	1.4
Albendazole sulfone	0.01	$C_{12}H_{15}N_3O_4S$	$[M+H]^+$	298.08560	3.44	1.6
Albendazole sulfoxide	0.01	$C_{12}H_{15}N_3O_3S$	$[M+H]^+$	282.09069	2.93	1.3
Aldicarb	0.01	$C_7H_{14}N_2O_2S$	$[M+Na]^+$	213.06682	3.8	1.13
Aldicarb sulfone	0.01	$C_7H_{14}N_2O_4S$	$[M+H]^+$	223.07471	3.44	0.79
Aldicarb sulfoxide	0.01	$C_7H_{14}N_2O_3S$	$[M+H]^+$	207.07979	0.94	-0.2
Allethrin	0.01	$C_{19}H_{26}O_3$	$[M+H]^+$	303.19547	8.08	4.78
Allidochlor	0.01	$C_8H_{12}ClNO$	$[M+H]^+$	174.06802	4.23	1.83
Alloxydim sodium	0.01	$C_{17}H_{24}NNaO_5$	$[M+H]^+$	346.16249	7.12	/
Alpha-cypermethrin	0.01	$C_{22}H_{19}Cl_2NO_3$	$[M+H]^+$	433.10802	8.74	6.6
Ametoctradin	0.01	$C_{15}H_{25}N_5$	$[M+H]^-$	276.21827	6.57	4.6**
Ametryne	0.01	$C_9H_{17}N_5S$	$[M+H]^+$	228.12774	5.03	2.98
Amicarbazone	0.01	$C_{10}H_{19}N_5O_2$	$[M+H]^+$	242.16115	4.06	1.23
Amidosulfuron	0.01	$C_9H_{15}N_5O_7S_2$	$[M+H]^+$	370.04857	4.77	1.63
Amino flubendazole	0.01	$C_{14}H_{10}FN_3O$	$[M+H]^+$	256.08807	3.21	1.6
Amino mebendazole	0.01	$C_{14}H_{11}N_3O$	$[M+H]^+$	238.09749	3.02	2.6
Aminocarb	0.01	$C_{11}H_{16}N_2O_2$	$[M+H]^+$	209.12845	1.71	1.9
Amitraze	0.01	$C_{19}H_{23}N_3$	$[M+H]^+$	294.19647	8.58	5.5
Amoxicillin	0.01	$C_{16}H_{19}N_3O_5S$	$[M+H]^+$	366.11182	0.92	-2
Ampicillin +4	0.01	$C_{16}H_{19}N_3O_4S$	$[M+H]^+$	350.11690	0.95	-1.1
Ancymidol	0.01	$C_{15}H_{16}N_2O_2$	$[M+H]^+$	257.12845	4.26	1..91
Anilazine	0.01	$C_9H_5Cl_3N_4$	$[M+H]^+$	274.96526	6.26	3.88
Anilofos	0.01	$C_{13}H_{19}ClNO_3PS_2$	$[M+H]^+$	368.03053	7.12	3.81
Antipyrine phenazone	0.01	$C_{11}H_{12}N_2O$	$[M+H]^+$	189.10224	2.88	0.4
Aspon ™	0.01	$C_{12}H_{28}O_5P_2S_2$	$[M+H]^+$	379.09262	8.73	6
Asulam	0.01	$C_8H_{10}N_2O_4S$	$[M+H]^+$	231.04341	2.25	-0.27
Atraton	0.01	$C_9H_{17}N_5O$	$[M+H]^+$	212.15059	3.75	2.7
Atrazine	0.01	$C_8H_{14}ClN_5$	$[M+H]^+$	216.10105	5.12	2.6
Atrazine desisopropyl	0.01	$C_5H_8ClN_5$	$[M+H]^+$	174.0541	2.51	1.1**

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Avilamycin	0.01	$C_{61}H_{88}Cl_2O_{32}$	$[M+H]^+$	1403.47085	/	/
Azaconazole	0.01	$C_{12}H_{11}Cl_2N_3O_2$	$[M+H]^+$	300.03011	5.21	2.32
Azadirachtin	0.01	$C_{35}H_{44}O_{16}$	$[M+H]^+$	721.27021	5.01	1.09
Azamethiphos	0.01	$C_9H_{10}ClN_2O_5PS$	$[M+H]^+$	324.98094	4.44	1.05
Azimsulfuron	0.01	$C_{13}H_{16}N_{10}O_5S$	$[M+H]^+$	425.10986	5.03	0.65
Aziprotryne	0.01	$C_7H_{11}N_7S$	$[M+H]^+$	226.08694	6.15	3
Azoxystrobin	0.01	$C_{22}H_{17}N_3O_5$	$[M+H]^+$	404.1241	6.16	2.5
Bacitracin A	0.01	$C_{66}H_{103}N_{17}O_{16}S$	$[M+H]^+$	1422.75622	/	/
Baquiloprim	0.01	$C_{17}H_{20}N_6$	$[M+NH_4]^+$	326.20877	/	/
Barban	0.01	$C_{11}H_9Cl_2NO_2$	$[M+H]^+$	258.00831	6.25	3.47
Beflubutamid	0.01	$C_{18}H_{17}F_4NO_2$	$[M+H]^+$	356.12682	6.96	4.7
Benalaxyl	0.01	$C_{20}H_{23}NO_3$	$[M+H]^+$	326.17507	7.04	3.4
Benazolin	0.01	$C_9H_6ClNO_3S$	$[M+H]^+$	243.98297	3.88	2.5
Bendiocarb	0.01	$C_{11}H_{13}NO_4$	$[M+H]^+$	224.09173	4.7	1.7
Benfluralin (benefin)	0.01	$C_{13}H_{16}F_3N_3O_4$	$[M+H]^+$	336.11657	8.17	5.29
Benfuresate	0.01	$C_{12}H_{16}O_4S$	$[M+H]^+$	257.08421	6	2.41
Benodanil	0.01	$C_{13}H_{10}INO$	$[M+H]^+$	323.98799	5.67	2.85
Benomyl	0.01	$C_{14}H_{18}N_4O_3$	$[M+H]^+$	291.14517	6.1	2.12
Benoxacor	0.01	$C_{11}H_{11}Cl_2NO_2$	$[M+H]^+$	260.02396	6.06	2.7
Bensulfuron-methyl	0.01	$C_{16}H_{18}N_4O_7S$	$[M+H]^+$	411.0969	5.44	2.18
Bensulide	0.01	$C_{14}H_{24}NO_4PS_3$	$[M+H]^+$	398.06779	7.09	4.2
Bentazon	0.01	$C_{10}H_{12}N_2O_3S$	$[M+H]^+$	241.06414	4.48	2.34
Bentazon-methyl	0.01	$C_{11}H_{14}N_2O_3S$	$[M+H]^+$	255.07979	5.32	2.31
Benthiavalicarb-isopropyl	0.01	$C_{18}H_{24}FN_3O_3S$	$[M+H]^+$	382.15952	5.93	2.52
Benzoximate	0.01	$C_{18}H_{18}ClNO_5$	$C_9H_8ClO_3^+$	199.01565	7.53	3.73
Benzoylprop ethyl	0.01	$C_{18}H_{17}Cl_2NO_3$	$[M+H]^+$	366.06583	7.28	4.1**
Benzthiazuron	0.01	$C_9H_9N_3OS$	$[M+H]^-$	208.05391	3.88	1.6**
Bifenthrin	0.01	$C_{23}H_{22}ClF_3O_2$	$[M+H]^+$	423.13332	/	6
Bioresmethrin	0.01	$C_{22}H_{26}O_3$	$[M+H]^+$	339.19547	8.89	4.7
Bitertanole (mixture of isomers)	0.01	$C_{20}H_{23}N_3O_2$	$[M+H]^+$	338.1863	6.65	4.16
Bixafen	0.01	$C_{18}H_{12}Cl_2F_3N_3O$	$[M+H]^-$	414.03823	6.69	4.7**
Bladex	0.01	$C_9H_{13}ClN_6$	$[M+H]^+$	241.0963	4.4	2.22
Boscalid	0.01	$C_{18}H_{12}Cl_2N_2O$	$[M+H]^+$	343.03995	6.32	2.96
Bromacil	0.01	$C_9H_{13}BrN_2O_2$	$[M+H]^-$	261.02332	4.18	2.11
Bromofenvinphos-ethyl	0.01	$C_{12}H_{14}BrCl_2O_4P$	$[M+H]^+$	404.92397	7.03	3.2**
Bromophos-methyl	0.01	$C_8H_8BrCl_2O_3PS$	$[M+H]^+$	366.85409	8.06	5.21

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Bromuconazole (mixture of isomers)	0.01	$C_{13}H_{12}BrCl_2N_3O$	$[M+H]^+$	377.95902	6.12	3.24
Bufencarb	0.01	$C_{26}H_{38}N_2O_4$	$[M+H]^+$	443.29043	/	/
Bupirimate	0.01	$C_{13}H_{24}N_4O_3S$	$[M+H]^+$	317.16419	6.49	2.7
Buprofezin	0.01	$C_{16}H_{23}N_3OS$	$[M+H]^+$	306.16346	7.96	4.3
Butachlor	0.01	$C_{17}H_{26}ClNO_2$	$[M+H]^+$	312.17248	8.11	4.5
Butafenacil	0.01	$C_{20}H_{18}ClF_3N_2O_6$	$[M+NH_4]^+$	492.11437	6.72	3.2
Butocarboxim	0.01	$C_7H_{14}N_2O_2S$	$[M+H]^+$	191.08488	4	1.1
Butocarboxim sulfoxide	0.01	$C_7H_{14}N_2O_3S$	$[M+Na]^+$	229.06174	0.96	-1.02
Butoxycarboxim	0.01	$C_7H_{14}N_2O_4S$	$[M+H]^+$	223.07471	3.44	-0.1
Butroxydim	0.01	$C_{24}H_{33}NO_4$	$[M+H]^+$	400.24824	8.14	1.9
Buturon	0.01	$C_{12}H_{13}ClN_2O$	$[M+H]^+$	237.07892	5.57	3**
Butylate	0.01	$C_{11}H_{23}NOS$	$[M+H]^+$	218.15731	7.97	4.15
Cadusafos	0.01	$C_{10}H_{23}O_2PS_2$	$[M+H]^+$	271.09499	7.33	3.9
Cafenstrole	0.01	$C_{16}H_{22}N_4O_3S$	$[M+H]^+$	351.14854	6.62	3.21
Carbaryl	0.01	$C_{12}H_{11}NO_2$	$C_{10}H_9O^+$	145.06479	4.89	2.36
Carbendazim	0.01	$C_9H_9N_3O_2$	$[M+H]^+$	192.07675	2.19	1.52
Carbetamide	0.01	$C_{12}H_{16}N_2O_3$	$[M+H]^+$	237.12337	4.04	1,75
Carbofuran	0.01	$C_{12}H_{15}NO_3$	$[M+H]^+$	222.11247	4.75	2.32
Carbophenothion	0.01	$C_{11}H_{16}ClO_2PS_3$	$[M+H]^+$	342.98114	8.39	5.33
Carboxine	0.01	$C_{12}H_{13}NO_2S$	$[M+H]^+$	236.07398	5.07	2.14
Carfentrazone-ethyl	0.01	$C_{15}H_{14}Cl_2F_3N_3O_3$	$[M+H]^+$	412.04371	6.93	3.36
Carprofen	0.01	$C_{15}H_{12}ClNO_2$	$[M+H]^+$	274.06293	6.01	4
Carpropamid	0.01	$C_{15}H_{18}Cl_3NO$	$[M+H]^+$	334.05267	7.1	4.23
Cefacetrile	0.01	$C_{13}H_{13}N_3O_6S$	$[M+H]^+$	357.08633	/	/
Cefalexine	0.01	$C_{16}H_{17}N_3O_4S$	$[M+H]^+$	348.10125	0.95	0.6
Cefapirine	0.01	$C_{17}H_{17}N_3O_6S_2$	$[M-H]^+$	424.06316	0.95	-1.1
Cefazolin	0.01	$C_{14}H_{14}N_8O_4S_3$	$[M+H]^+$	455.03729	2.41	-0.6
Cefoperazone	0.01	$C_{25}H_{27}N_9O_8S_2$	$[M+H]^+$	646.14968	2.90	-0.7
Ceftiofur +4	0.01	$C_{19}H_{17}N_5O_7S_3$	$[M+H]^+$	524.03629	3.58	0.2
Ceftriaxone (CAS)	0.01	$C_{18}H_{18}N_8O_7S_3$	$[M+H]^+$	555.05334	/	/
Cefuroxim	0.01	$C_{16}H_{16}N_4O_8S$	$[M-H]^-$	442.10271	2.58	-0.2
Cephradine	0.01	$C_{16}H_{19}N_3O_4S$	$[M+H]^+$	350.11690	0.95	/
Chinomethionate	0.01	$C_{10}H_6N_2OS_2$	$[M+H]^+$	234.99943	7.38	3.78
Chlorantraniliprole	0.01	$C_{18}H_{14}BrCl_2N_5O_2$	$[M+H]^+$	483.97579	5.68	2.76
Chlorbromuron	0.01	$C_9H_{10}BrClN_2O_2$	$[M+H]^+$	294.96648	6.1	3.09
Chlorbufam	0.01	$C_{11}H_{10}ClNO_2$	$[M+H]^+$	224.04728	4.95	3.59

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Chlordimeform	0.01	$C_{10}H_{13}ClN_2$	$[M+H]^+$	197.084	2.64	2.89
Chlorfenapyr	0.01	$C_{15}H_{11}BrClF_3N_2O$	$[M+H]^+$	408.97465	7.93	4.83
Chlorfenvinphos (mixture of Z and E)	0.01	$C_{12}H_{14}Cl_3O_4P$	$[M+H]^+$	358.97681	6.93	3.81
Chlorfluazuron	0.01	$C_{20}H_9Cl_3F_5N_3O_3$	$[M-H]^-$	539.97024	8.3	5.8
Chloridazon	0.01	$C_{10}H_8ClN_3O$	$[M+H]^+$	222.04287	3.19	1.14
Chlorimuron-ethyl	0.01	$C_{15}H_{15}ClN_4O_6S$	$[M+H]^+$	415.04736	6.06	2.5
Chlormephos	0.01	$C_5H_{12}ClO_2PS_2$	$[M+H]^+$	234.97777	/	3
Chlormequat chloride	0.01	$C_5H_{13}Cl_2N$	$[M+H]^+$	158.04978	/	/
Chlorobenzuron	0.01	$C_{14}H_{10}Cl_2N_2O_2$	$[M+H]^+$	309.01921	6.64	5**
Chlorosulfuron	0.01	$C_{12}H_{12}ClN_5O_4S$	$[M+H]^+$	358.03713	4.8	/
Chlorotoluron	0.01	$C_{10}H_{13}ClN_2O$	$[M+H]^+$	213.07892	4.93	2.41
Chloroxuron	0.01	$C_{15}H_{15}ClN_2O_2$	$[M+H]^+$	291.08948	6.07	3.7
Chlorpyrifos	0.01	$C_9H_{11}Cl_3NO_3PS$	$[M+H]^+$	349.93356	8.21	4.96
Chlorpyrifos-methyl	0.01	$C_7H_7Cl_3NO_3PS$	$[M+H]^+$	321.90226	7.49	4.31
Chlorpyrifos-oxon	0.01	$C_9H_{11}Cl_3NO_4P$	$[M+H]^+$	333.95641	6.48	3.5**
Chlortetracycline	0.01	$C_{22}H_{23}ClN_2O_8$	$[M+H]^+$	479.12157	/	/
Chlorthiamid	0.01	$C_7H_5Cl_2NS$	$[M+H]^+$	205.95925	4.16	1.4**
Chlorthiophos	0.01	$C_{11}H_{15}Cl_2O_3PS_2$	$[M+H]^+$	360.96501	8.36	6**
Chromafenozide	0.01	$C_{24}H_{30}N_2O_3$	$[M-H]^-$	395.23292	6.65	5**
Cinidon-ethyl	0.01	$C_{19}H_{17}Cl_2NO_4$	$[M+H]^+$	394.06074	7.85	4.51
Cinmethylin	0.01	$C_{18}H_{26}O_2$	$[M+NH_4]^+$	292.22711	8.08	4.62
Cinosulfuron	0.01	$C_{15}H_{19}N_5O_7S$	$[M+H]^+$	414.1078	4.57	2.04
Cinoxacin	0.01	$C_{12}H_{10}N_2O_5$	$[M+H]^+$	263.06625	3.58	1.5
Ciprofloxacin	0.01	$C_{17}H_{18}FN_3O_3$	$[M+H]^+$	332.14050	2.46	-1.1
Clarithromycin	0.01	$C_{38}H_{69}NO_{13}$	$[M+H]^+$	748.48417	4.89	3.16
Clarithromycin	0.01	$C_{38}H_{69}NO_{13}$	$[M+H]^+$	748.48417	5.17	3.2
Clethodim	0.01	$C_{17}H_{26}ClNO_3S$	$[M+H]^+$	360.13947	7.86	4.21
Climbazol	0.01	$C_{15}H_{17}ClN_2O_2$	$[M+H]^+$	293.10513	5.02	3.76
Clindamycin	0.01	$C_{18}H_{33}ClN_2O_5S$	$[M+H]^+$	425.18715	3.30	2.2
Clodinafop (acid-free)	0.01	$C_{14}H_{11}ClFNO_4$	$[M+H]^+$	312.04334	5.76	3.4**
Clodinafop-propargyl	0.01	$C_{17}H_{13}ClFNO_4$	$[M+H]^+$	350.05899	7.11	3.9
Clofentezine	0.01	$C_{14}H_8Cl_2N_4$	$[M+H]^+$	303.01988	7.39	3.1
Clomeprop	0.01	$C_{16}H_{15}Cl_2NO_2$	$[M-H]^-$	324.05526	7.76	4.8
Cloquintocet-mexyl	0.01	$C_{18}H_{22}ClNO_3$	$[M+H]^+$	336.1361	7.9	5.03
Cloransulam-methyl	0.01	$C_{15}H_{13}ClFN_5O_5S$	$[M+H]^+$	430.03827	5.41	-0.365
Clorsulon	0.01	$C_8H_8Cl_3N_3O_4S_2$	$[M-H]^-$	401.89140	/	1.2

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Closantel	0.01	$C_{22}H_{14}Cl_2I_2N_2O_2$	$[M+H]^+$	662.85946	9.00	7.2
Clothianidin	0.01	$C_6H_8ClN_5O_2S$	$[M+H]^+$	250.016	3.03	0.7
Cloxacillin	0.01	$C_{12}H_{10}N_2O_5$	$[M+H]^+$	263.06625	3.58	2.4
Command (clomazone)	0.01	$C_{12}H_{14}ClNO_2$	$[M+H]^+$	240.07858	5.69	2.5
Coumaphos	0.01	$C_{14}H_{16}ClO_5PS$	$[M+H]^+$	363.02174	7.33	4.13
Coumaphos-oxon	0.01	$C_{14}H_{16}ClO_6P$	$[M+H]^+$	347.04458	5.69	2.78
Crimidine	0.01	$C_7H_{10}ClN_3$	$[M+H]^+$	172.0636	3.73	1.31
Crotoxyphos	0.01	$C_{14}H_{19}O_6P$	$[M+NH_4]^+$	332.12575	5.89	3.3
Crufomate	0.01	$C_{12}H_{19}ClNO_3P$	$[M+H]^+$	292.08639	6.23	3.42
Cumyluron	0.01	$C_{17}H_{19}ClN_2O$	$[M+H]^+$	303.12587	6.15	3.7
Cyanofenphos	0.01	$C_{15}H_{14}NO_2PS$	$[M+H]^+$	304.05557	7.17	4.29
Cyanophos	0.01	$C_9H_{10}NO_3PS$	$[M+H]^+$	244.01918	5.85	2.71
Cyantraniliprole	0.01	$C_{19}H_{14}BrClN_6O_2$	$[M+H]^+$	475.0102	5.17	3.9**
Cyazofamid	0.01	$C_{13}H_{13}ClN_4O_2S$	$[M+H]^+$	325.05205	6.92	3.2
Cyclanilide	0.01	$C_{11}H_9Cl_2NO_3$	$[M+H]^+$	274.00323	5.71	3.25
Cycloate	0.01	$C_{11}H_{21}NOS$	$[M+H]^+$	216.14166	7.62	3.88
Cyclohexamide	0.01	$C_{15}H_{23}NO_4$	$[M+H]^+$	282.16998	3.79	0.55
Cycloprothrin	0.01	$C_{26}H_{21}Cl_2NO_4$	$[M+H]^+$	482.09204	8.52	6.2**
Cyclosulfamuron	0.01	$C_{17}H_{19}N_5O_6S$	$[M+H]^+$	422.11288	6.36	2.05
Cycloxidim	0.01	$C_{17}H_{27}NO_3S$	$[M+H]^+$	326.17844	7.78	3.23
Cycluron	0.01	$C_{11}H_{22}N_2O$	$[M+H]^+$	199.18049	5.12	2.4**
Cyflufenamid	0.01	$C_{20}H_{17}F_5N_2O_2$	$[M+H]^+$	413.1283	7.55	4.7
Cyhalofop-butyl	0.01	$C_{20}H_{20}FNO_4$	$[M+H]^+$	358.14491	7.75	3.31
Cymiazole	0.01	$C_{12}H_{14}N_2S$	$[M+H]^+$	219.09505	3.19	3**
Cymoxanil	0.01	$C_7H_{10}N_4O_3$	$C_4H_6N_3O_2^+$	128.04545	3.66	0.59
Cypermethrin (mixture of isomers)	0.01	$C_{22}H_{19}Cl_2NO_3$	$[M+H]^+$	416.08148	8.78	6.6
Cyphenothrin	0.01	$C_{24}H_{25}NO_3$	$[M+H]^+$	376.19072	8.89	6.29
Cyprazine	0.01	$C_9H_{14}ClN_5$	$[M+H]^+$	228.10105	5.13	3.06
Cyproconazole (mixture of isomers)	0.01	$C_{15}H_{18}ClN_3O$	$[M+H]^+$	292.12112	6.17	2.9
Cyprodinil	0.01	$C_{14}H_{15}N_3$	$[M+H]^+$	226.13387	6.48	4
Cyprofuram	0.01	$C_{14}H_{14}ClNO_3$	$[M+H]^+$	280.0735	5.23	2.5**
Cyprosulfamide	0.01	$C_{18}H_{18}N_2O_5S$	$[M+H]^+$	375.10092	4.73	2.1**
Cyromazine	0.01	$C_6H_{10}N_6$	$[M+H]^+$	167.10397	0.94	-0.06
Cythioate	0.01	$C_8H_{12}NO_5PS_2$	$[M+H]^+$	297.99673	4.41	1.6**
Daimuron	0.01	$C_{17}H_{20}N_2O$	$[M+H]^+$	269.16484	6.22	2.7
Daminozide	0.01	$C_6H_{12}N_2O_3$	$[M+H]^+$	161.09207	0.9	-1.5

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Danitol	0.01	$C_{22}H_{23}NO_3$	$[M+H]^+$	350.17507	8.59	5.7
Danofloxacin	0.01	$C_{19}H_{20}FN_3O_3$	$[M+H]^+$	358.15615	2.60	-0.3
Dapsone	0.01	$C_{12}H_{12}N_2O_2S$	$[M+H]^+$	249.06923	3.02	1
Dazomet	0.01	$C_5H_{10}N_2S_2$	$[M+H]^+$	163.03582	2.51	0.63
Dementon-*S*-methyl sulfone	0.01	$C_6H_{15}O_5PS_2$	$[M+H]^+$	263.01713	2.55	-0.3
Demeton O	0.01	$C_8H_{19}O_3PS_2$	$[M+H]^+$	259.0586	/	3.21
Demeton S	0.01	$C_8H_{19}O_3PS_2$	$[M+H]^+$	259.0586	5.51	2.09
Demeton-*S*-methyl	0.01	$C_6H_{15}O_3PS_2$	$[M+H]^+$	231.0273	4.48	1.02
Deoxynivalenol	0.01	$C_{15}H_{20}O_6$	$[M+H]^+$	297.13327	0.93	-0.71
Desethyl atrazine	0.01	$C_6H_{10}ClN_5$	$[M+H]^+$	188.06975	3.28	1.51
Desfuroylceftiofur cysteine disulfide (DCCD)	0.01	$C_{17}H_{20}N_6O_7S_4$	$[M+H]^+$	549.03491	/	-4.2
Desmedipham	0.01	$C_{16}H_{16}N_2O_4$	$[M+H]^+$	301.11828	5.78	3.39
Desmethyl norflurazon	0.01	$C_{11}H_7ClF_3N_3O$	$[M+H]^-$	290.03025	4.82	1.6**
Desmethyl-formamido-pirimicarb	0.01	$C_{11}H_{16}N_4O_3$	$[M+H]^+$	253.12952	4.36	0.9**
Desmetryn	0.01	$C_8H_{15}N_5S$	$[M+H]^+$	214.11209	4.36	2.38
Diafenthiuron	0.01	$C_{23}H_{32}N_2OS$	$[M+H]^+$	385.23081	8.52	6
Dialifos	0.01	$C_{14}H_{17}ClNO_4PS_2$	$[M+H]^+$	394.00979	7.6	4.69
Diazinon	0.01	$C_{12}H_{21}N_2O_3PS$	$[M+H]^+$	305.10833	7.39	3.81
Diazinon-O-analog	0.01	$C_{12}H_{21}N_2O_4P$	$[M+H]^+$	289.13117	5.37	2.07
Dibrom	0.01	$C_4H_7Br_2Cl_2O_4P$	$[M+H]^+$	380.7876	5.46	1.38
Dichlofenthion	0.01	$C_{10}H_{13}Cl_2O_3PS$	$[M+H]^+$	314.97729	8.17	5.14
Dichlormid	0.01	$C_8H_{11}Cl_2NO$	$[M+H]^+$	208.02905	5.21	1.84
Dichlorvos	0.01	$C_4H_7Cl_2O_4P$	$[M+H]^+$	220.95318	4.4	1.43
Diclazuril	0.01	$C_{17}H_9Cl_3N_4O_2$	$[M-H]^-$	406.98639	6.46	4.1
Diclobutrazol	0.01	$C_{15}H_{19}Cl_2N_3O$	$[M+H]^+$	328.09779	6.49	3.8
Diclocymet	0.01	$C_{15}H_{18}Cl_2N_2O$	$[M+H]^+$	313.0869	6.74	4.3**
Diclofénac	0.01	$C_{14}H_{11}Cl_2NO_2$	$[M+H]^+$	296.02396	6.26	4
Diclosulam	0.01	$C_{13}H_{10}Cl_2FN_5O_3S$	$[M+H]^+$	405.99382	5.5	0.85
Dicrotophos	0.01	$C_8H_{16}NO_5P$	$[M+H]^+$	238.08389	2.57	0
Diethatyl-ethyl	0.01	$C_{16}H_{22}ClNO_3$	$[M+H]^+$	312.1361	6.96	3.6
Diethofencarb	0.01	$C_{14}H_{21}NO_4$	$[M+H]^+$	268.15433	6.01	2.91
Difenoconazole (mixture of isomers)	0.01	$C_{19}H_{17}Cl_2N_3O_3$	$[M+H]^+$	406.07197	7.18	4.3
Difenoxurone	0.01	$C_{16}H_{18}N_2O_3$	$[M+H]^+$	287.13902	5.28	2.54
Difloxacin	0.01	$C_{21}H_{19}F_2N_3O_3$	$[M+H]^+$	400.14672	3.04	1.6
Diflubenzuron	0.01	$C_{14}H_9ClF_2N_2O_2$	$[M+H]^+$	311.03934	6.43	3.88

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Diflufenicen	0.01	$C_{19}H_{11}F_5N_2O_2$	$[M-H]^-$	395.08135	7.56	4.6**
Dimefox	0.01	$C_4H_{12}FN_2OP$	$[M+H]^+$	155.07441	2.66	-0.43
Dimefuron	0.01	$C_{15}H_{19}ClN_4O_3$	$[M+H]^+$	339.12184	5.64	2.51
Dimepiperate	0.01	$C_{15}H_{21}NOS$	$[M+H]^+$	264.14166	7.7	4.02
Dimethachlor	0.01	$C_{13}H_{18}ClNO_2$	$[M+H]^+$	256.10988	5.58	2.17
Dimethametryn	0.01	$C_{11}H_{21}N_5S$	$[M+H]^+$	256.15904	6.36	3.9
Dimethenamid	0.01	$C_{12}H_{18}ClNO_2S$	$[M+H]^+$	276.08195	6.11	2.15
Dimethirimol	0.01	$C_{11}H_{19}N_3O$	$[M+H]^+$	210.16009	3.01	1.5**
Dimethoate	0.01	$C_5H_{12}NO_3PS_2$	$[M+H]^+$	230.0069	3.33	0.78
Dimethomorph	0.01	$C_{21}H_{22}ClNO_4$	$[M+H]^+$	388.13101	5.85	2.68
Dimethylvinphos	0.01	$C_{10}H_{10}Cl_3O_4P$	$[M+H]^+$	330.94551	6.19	3.13
Dimetilan	0.01	$C_{10}H_{16}N_4O_3$	$[M+H]^+$	241.12952	3.41	0.27
Dimetridazole	0.01	$C_5H_7N_3O_2$	$[M+H]^+$	142.06110	2.36	0.1
Dimoxystrobin	0.01	$C_{19}H_{22}N_2O_3$	$[M+H]^+$	327.17032	6.75	3.9**
Diniconazole (E isomer)	0.01	$C_{15}H_{17}Cl_2N_3O$	$[M+H]^+$	326.08214	6.82	4.3
Diniconazole (Z isomer)	0.01	$C_{15}H_{17}Cl_2N_3O$	$[M-H]^+$	326.08214	6.82	4.3
Dinitramine	0.01	$C_{11}H_{13}F_3N_4O_4$	$[M+H]^-$	323.09617	7.18	4.3
Dinotefuran	0.01	$C_7H_{14}N_4O_3$	$[M+H]^+$	203.11387	1.83	-0.55
Dioxacarb	0.01	$C_{11}H_{13}NO_4$	$[M+H]^+$	224.09173	3.37	0.67
Dioxathion (mixture of isomers)	0.01	$C_{12}H_{26}O_6P_2S_4$	$[M+H]^+$	457.01603	6.02	3
Diphenamid	0.01	$C_{16}H_{17}NO$	$[M+H]^+$	240.13829	5.62	2.17
Diphenyl phosphate	0.01	$C_{12}H_{11}O_4P$	$[M+H]^+$	251.04677	8.52	1.4**
Diphenylamine	0.01	$C_{12}H_{11}N$	$[M+H]^+$	170.09643	6.57	3.5
Dipropetryn	0.01	$C_{11}H_{21}N_5S$	$[M+H]^+$	256.15904	6.37	3.81
Disosultap	0.01	$C_5H_{11}NNa_2O_6S4$	$[M+H]^+$	355.93374	/	/
Disulfoton sulfone	0.01	$C_8H_{19}O_4PS_3$	$[M+H]^+$	307.02559	5.65	1.87
Disulfoton sulfoxide	0.01	$C_8H_{19}O_3PS_3$	$[M+H]^+$	291.03067	5	1.73
Ditalimfos	0.01	$C_{12}H_{14}NO_4PS$	$[M+H]^+$	300.04539	6.63	3.48
Dithianon	0.01	$C_{14}H_4N_2O_2S_2$	$[M+H]^+$	296.9787	6.45	2.84
Dithiopyr	0.01	$C_{15}H_{16}F_5NO_2S_2$	$[M+H]^+$	402.06154	7.82	4.75
Diuron	0.01	$C_9H_{10}Cl_2N_2O$	$[M+H]^+$	233.02429	5.2	2.68
DMA	0.01	$C_8H_{11}N$	$[M+H]^+$	122.09643	2.55	1.8
DMF	0.01	$C_9H_{11}NO$	$[M+H]^+$	150.09134	3.98	1.5
DMPF	0.01	$C_{10}H_{14}N_2$	$[M+H]^+$	163.12298	2.43	1.7
DMST	0.01	$C_9H_{14}N_2O_2S$	$[M+H]^+$	215.08488	4.46	1.2**
Dodemorph	0.01	$C_{18}H_{35}NO$	$[M+H]^+$	282.27914	5.1	5.8**

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Dodine	0.01	$C_{15}H_{33}N_3O_2$	$[M+H]^+$	288.26455	/	1.15
Doramectin	0.01	$C_{50}H_{74}O_{14}$	$[M+Na]^+$	921.49708	9.18	4.4
Doxycycline	0.01	$C_{22}H_{24}N_2O_8$	$[M+H]^+$	445.16054	/	/
Dyfonate ™	0.01	$C_{10}H_{15}OPS_2$	$[M+H]^+$	247.03747	7.39	3.94
Edifenphos	0.01	$C_{14}H_{15}O_2PS_2$	$[M+H]^+$	311.03239	6.91	3.48
Emamectin	0.01	$C_{49}H_{75}NO_{13}$	$[M+H]^+$	886.53112	6.92	5
Emamectin B1a	0.01	$C_{49}H_{75}NO_{13}$	$[M+H]^+$	886.53112	8.12	4.1
Empenthrin	0.01	$C_{18}H_{26}O_2$	$[M+H]^+$	275.20056	8.82	/
Enrofloxacin	0.01	$C_{19}H_{22}FN_3O_3$	$[M+H]^+$	360.17180	2.71	-0.2
Epi CTC	0.01	$C_{22}H_{23}ClN_2O_8$	$[M+H]^+$	479.12157	/	/
Epi OTC	0.01	$C_{22}H_{24}N_2O_9$	$[M+H]^+$	461.15546	/	/
Epi tetra	0.01	$C_{22}H_{24}N_2O_8$	$[M+H]^+$	445.16054	/	/
Epn	0.01	$C_{14}H_{14}NO_4PS$	$[M+H]^+$	324.04539	7.56	4.78
Epoxiconazole (iso)	0.01	$C_{17}H_{13}ClFN_3O$	$[M+H]^+$	330.08039	6.29	3.44
Eprinomectin	0.01	$C_{50}H_{75}NO_{14}$	$[M+H]^+$	914.52603	8.46	5.7
Eprinomectin B1a	0.01	$C_{50}H_{75}NO_{14}$	$[M+H]^+$	914.52603	8.48	3.8
EPTC (S-ethyl dipropylthiocarbamate)	0.01	$C_9H_{19}NOS$	$[M+H]^+$	190.12601	6.91	3.21
Erythromycin	0.01	$C_{37}H_{67}NO_{13}$	$[M+H]^+$	734.46852	4.15	3.06
Erythromycin	0.01	$C_{37}H_{67}NO_{13}$	$[M+H]^+$	734.46852	4.30	2.7
Esbiol	0.01	$C_{19}H_{26}O_3$	$[M+H]^+$	303.19547	8.07	/
Esprocarb	0.01	$C_{15}H_{23}NOS$	$[M+H]^+$	266.15731	8.06	4.6
Etaconazole	0.01	$C_{14}H_{15}Cl_2N_3O_2$	$[M+H]^+$	328.06141	6.34	3.1
Ethaboxam	0.01	$C_{14}H_{16}N_4OS_2$	$[M+H]^+$	321.08383	5.1	/
Ethametsulfuron-methyl	0.01	$C_{15}H_{18}N_6O_6S$	$[M+H]^+$	411.10813	4.93	1.59
Ethephone	0.01	$C_2H_6ClO_3P$	$[M+H]^+$	144.98159	/	/
Ethidimuron	0.01	$C_7H_{12}N_4O_3S_2$	$[M+H]^+$	265.04236	3.07	/
Ethiofencarb	0.01	$C_{11}H_{15}NO_2S$	$[M+H]^+$	226.08963	5.05	2.04
Ethiofencarb sulfone	0.01	$C_{11}H_{15}NO_4S$	$[M+H]^+$	258.07946	3.03	/
Ethiofencarb sulfoxide	0.01	$C_{11}H_{15}NO_3S$	$[M+H]^+$	242.08454	2.95	/
Ethion	0.01	$C_9H_{22}O_4P_2S_4$	$[M+H]^+$	384.9949	8.22	5.07
Ethiozin	0.01	$C_9H_{16}N_4OS$	$[M+H]^+$	229.11176	5.19	2.08
Ethiprole	0.01	$C_{13}H_9Cl_2F_3N_4OS$	$[M-H]^-$	396.9899	5.85	2.9
Ethirimol	0.01	$C_{11}H_{19}N_3O$	$[M+H]^+$	210.16009	3.07	2.22
Ethofenprox	0.01	$C_{25}H_{28}O_3$	$[M+H]^+$	377.21112	/	7.05
Ethofumesate	0.01	$C_{13}H_{18}O_5S$	$[M+H]^+$	287.09477	6.28	2.7
Ethoprophos (prophos)	0.01	$C_8H_{19}O_2PS_2$	$[M+H]^+$	243.06369	6.38	3.59

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Ethoxyquin	0.01	$C_{14}H_{19}NO$	$[M+H]^+$	218.15394	6.19	4.05
Ethoxysulfuron	0.01	$C_{15}H_{18}N_4O_7S$	$[M+H]^+$	399.0969	6.07	/
Ethyclozate	0.01	$C_{11}H_{11}ClN_2O_2$	$[M+H]^+$	239.05818	5.28	/
Etobenzanid	0.01	$C_{16}H_{15}Cl_2NO_3$	$[M+H]^+$	340.05018	7.25	/
Etoxazole	0.01	$C_{21}H_{23}F_2NO_2$	$[M+H]^+$	360.17696	8.46	5.59
Etrimfos	0.01	$C_{10}H_{17}N_2O_4PS$	$[M+H]^+$	293.07194	7.21	/
Famoxadone	0.01	$C_{22}H_{18}N_2O_4$	$[M+H]^+$	375.13393	7.21	4.65
Famphur	0.01	$C_{10}H_{16}NO_5PS_2$	$[M+H]^+$	326.02803	5.8	2.2
Fenamidone	0.01	$C_{17}H_{17}N_3OS$	$[M+H]^+$	312.11651	6.19	2.8
Fenamiphos	0.01	$C_{13}H_{22}NO_3PS$	$[M+H]^+$	304.11308	6.17	3.23
Fenamiphos sulfone	0.01	$C_{13}H_{22}NO_5PS$	$[M+H]^+$	336.10291	4.58	/
Fenamiphos sulfoxide	0.01	$C_{13}H_{22}NO_4PS$	$[M+H]^+$	320.108	4.04	/
Fenarimol	0.01	$C_{17}H_{12}Cl_2N_2O$	$[M+H]^+$	331.03995	6.17	3.6
Fenazaflor	0.01	$C_{15}H_7Cl_2F_3N_2O_2$	$[M+H]^+$	374.99094	/	/
Fenazaquin	0.01	$C_{20}H_{22}N_2O$	$[M+H]^+$	307.18049	8.51	5.51
Fenazox	0.01	$C_{12}H_{10}N_2O$	$[M+H]^+$	199.08659	7.02	#N/A
Fenbendazole	0.01	$C_{15}H_{13}N_3O_2S$	$[M+H]^+$	300.08013	5.45	3.6
Fenbuconazole	0.01	$C_{19}H_{17}ClN_4$	$[M+H]^+$	337.12145	6.5	3.23
Fenchlorazol-ethyl	0.01	$C_{12}H_8Cl_5N_3O_2$	$[M+H]^+$	403.91031	7.51	/
Fenchlorphos-oxon	0.01	$C_8H_8Cl_3O_4P$	$[M+H]^+$	304.92986	6.17	/
Fenclorim	0.01	$C_{10}H_6Cl_2N_2$	$[M+H]^+$	224.99808	/	4.2**
Fenfuram	0.01	$C_{12}H_{11}NO_2$	$[M+H]^+$	202.08626	5.14	2.2**
Fenhexamid	0.01	$C_{14}H_{17}Cl_2NO_2$	$[M+H]^+$	302.07091	6.31	3.51
Fenitrothion	0.01	$C_9H_{12}NO_5PS$	$[M+H]^+$	278.02466	6.58	3.3
Fenobucarb	0.01	$C_{12}H_{17}NO_2$	$[M+H]^+$	208.13321	5.87	2.78
Fenothiocarb	0.01	$C_{13}H_{19}NO_2S$	$[M+H]^+$	254.12093	6.76	3.3
Fenoxanil	0.01	$C_{15}H_{18}Cl_2N_2O_2$	$[M+H]^+$	329.08181	6.89	4.5
Fenoxaprop	0.01	$C_{16}H_{12}ClNO_5$	$[M+H]^+$	334.04768	6.22	3.4**
Fenoxaprop-P-ethyl	0.01	$C_{18}H_{16}ClNO_5$	$[M+H]^+$	362.07898	7.7	4.1**
Fenoxycarb	0.01	$C_{17}H_{19}NO_4$	$[M+H]^+$	302.13868	5.94	4.3
Fenpiclonil	0.01	$C_{11}H_6Cl_2N_2$	$[M+H]^+$	236.99808	5.72	4.3**
Fenpropathrin	0.01	$C_{22}H_{23}NO_3$	$[M+H]^+$	350.17507	8.6	6
Fenpropidin	0.01	$C_{19}H_{31}N$	$[M+H]^+$	274.25293	5.25	5.5
Fenpropimorph	0.01	$C_{20}H_{33}NO$	$[M+H]^+$	304.26349	5.34	4.93
Fenpyroximate	0.01	$C_{24}H_{27}N_3O_4$	$[M+H]^+$	422.20743	8.46	5.01
Fensulfothion	0.01	$C_{11}H_{17}O_4PS_2$	$[M+H]^+$	309.03787	5.37	2.23
Fensulfothion-oxon	0.01	$C_{11}H_{17}O_5PS$	$[M+H]^+$	293.06071	3.56	1.4**

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Fensulfothion-oxon sulfone	0.01	$C_{11}H_{17}O_6PS$	$[M+H]^+$	309.05563	4.11	1.5**
Fensulfothion sulfone	0.01	$C_{11}H_{17}O_5PS_2$	$[M+H]^+$	325.03278	5.94	2.6**
Fenthion	0.01	$C_{10}H_{15}O_3PS_2$	$[M+H]^+$	279.0273	7.14	4.1
Fenthion-oxon	0.01	$C_{10}H_{15}O_4PS$	$[M+H]^+$	263.05015	5.37	2.4**
Fenthion-oxon sulfoxide	0.01	$C_{10}H_{15}O_5PS$	$[M+H]^+$	279.04506	3.03	1**
Fenthion sulfoxide	0.01	$C_{10}H_{15}O_4PS_2$	$[M+H]^+$	295.02222	4.76	2.7**
Fenthion-ethyl	0.01	$C_{12}H_{19}O_3PS_2$	$[M+H]^+$	307.0586	7.86	5**
Fenthion sulfone	0.01	$C_{10}H_{15}O_5PS_2$	$[M+H]^+$	311.01713	5.41	2.8**
Fenthoxon sulfone	0.01	$C_{10}H_{15}O_6PS$	$[M+H]^+$	295.03998	3.57	1.1**
Fentin acetate as Fentin	0.01	$C_{20}H_{18}O_2Sn$	$[M+H]^+$	411.04016	/	3.43
Fenuron	0.01	$C_9H_{12}N_2O$	$[M+H]^+$	165.10224	3.19	0.98
Ferimzone	0.01	$C_{15}H_{18}N_4$	$[M+H]^+$	255.16042	4.37	3.5**
Fipronil	0.01	$C_{12}H_4Cl_2F_6N_4OS$	$[M+H]^-$	436.94598	6.87	4
Fipronil sulfide	0.01	$C_{12}H_4Cl_2F_6N_4S$	$[M-H]^-$	420.95107	7.3	5.5**
Fipronil-desulfinyl	0.01	$C_{12}H_4Cl_2F_6N_4$	$[M+H]^-$	388.979	7.05	4.6**
Flamprop-isopropyl	0.01	$C_{19}H_{19}ClFNO_3$	$[M+H]^+$	364.11103	7.25	4**
Flamprop-methyl (Metaven)	0.01	$C_{17}H_{15}ClFNO_3$	$[M+H]^+$	336.07973	6.47	3.2**
Flamprop-M-isopropyl	0.01	$C_{19}H_{19}ClFNO_3$	$[M+H]^+$	364.11103	7.25	4**
Flazasulfuron	0.01	$C_{13}H_{12}F_3N_5O_5S$	$[M+H]^+$	408.0584	5.48	1.08
Fleroxacin	0.01	$C_{17}H_{18}F_3N_3O_3$	$[M+H]^+$	370.13730	2.43	-0.1
Flonicamid	0.01	$C_9H_6F_3N_3O$	$[M+H]^+$	230.05357	2.71	0.3
Florasulam	0.01	$C_{12}H_8F_3N_5O_3S$	$[M+H]^+$	360.03727	4.63	1.22
Florfénicol	0.01	$C_{12}H_{14}Cl_2FNO_4S$	$[M+H]^+$	375.03429	3.33	0.8
Florfenicol amine	0.01	$C_{10}H_{14}FNO_3S$	$[M+H]^+$	270.05706	/	/
Fluacrypyrim	0.01	$C_{20}H_{21}F_3N_2O_5$	$[M+H]^+$	427.14753	7.64	4.1**
Fluazifop	0.01	$C_{15}H_{12}F_3NO_4$	$[M+H]^+$	328.07912	5.77	2.9**
Fluazifop-butyl	0.01	$C_{19}H_{20}F_3NO_4$	$[M+H]^+$	384.14172	8.04	4.5
Fluazifop-P-butyl	0.01	$C_{19}H_{20}F_3NO_4$	$[M+H]^+$	384.14172	8.03	4.5**
Fluazinam	0.01	$C_{13}H_4Cl_2F_6N_4O_4$	$[M-H]^-$	464.95866	7.9	4.01
Fluazuron	0.01	$C_{20}H_{10}Cl_2F_5N_3O_3$	$[M+H]^+$	506.00921	7.89	6.1**
Flubendazole	0.01	$C_{16}H_{12}FN_3O_3$	$[M+H]^+$	314.09355	4.68	2.9
Flubendiamide	0.01	$C_{23}H_{22}F_7IN_2O_4S$	$[M+H]^+$	683.03061	6.88	4.2
Flucarbazone sodium	0.01	$C_{12}H_{10}F_3N_4NaO_6S$	$[M+H]^+$	419.02436	4.21	-1.85
Fluchloralin	0.01	$C_{12}H_{13}ClF_3N_3O_4$	$[M+H]^+$	356.06195	7.69	5.07
Flucycloxuron	0.01	$C_{25}H_{20}ClF_2N_3O_3$	$[M+H]^+$	484.1234	8.11	6.1**
Flucythrinate	0.01	$C_{26}H_{23}F_2NO_4$	$[M+H]^+$	452.16679	/	6.2
Fludioxonil	0.01	$C_{12}H_6F_2N_2O_2$	$[M-H]^-$	249.04701	8.21	4.12

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Flufenacet	0.01	$C_{14}H_{13}F_4N_3O_2S$	$[M+H]^+$	364.07374	6.7	3.2
Flufenoxuron	0.01	$C_{21}H_{11}ClF_6N_2O_3$	$[M+H]^+$	489.04352	8.09	6.16
Flumequine	0.01	$C_{14}H_{12}FNO_3$	$[M+H]^+$	262.08740	4.73	2.9
Flumestulam	0.01	$C_{12}H_9F_2N_5O_2S$	$[M-H]^-$	326.05178	7.76	0.21
Flumetralin	0.01	$C_{16}H_{12}ClF_4N_3O_4$	$[M+H]^+$	422.05252	8.23	5.2**
Flumiclorac-pentyl	0.01	$C_{21}H_{23}ClFNO_5$	$[M+NH_4]^+$	441.1587	7.88	4.8**
Flumioxazin	0.01	$C_{19}H_{15}FN_2O_4$	$[M+H]^+$	355.10886	5.84	2.55
Flumorph	0.01	$C_{21}H_{22}FNO_4$	$[M+H]^+$	372.16056	5.3	3.4**
Flunixin	0.01	$C_{14}H_{11}F_3N_2O_2$	$[M+H]^+$	297.08454	5.71	4.1
Fluoglycofene-ethyl	0.01	$C_{18}H_{13}ClF_3NO_7$	$[M+NH_4]^+$	465.06709	7.69	3.6**
Fluometuron	0.01	$C_{10}H_{11}F_3N_2O$	$[M-H]^-$	233.08962	5	2.42
Fluopicolide	0.01	$C_{14}H_8Cl_3F_3N_2O$	$[M+H]^+$	382.97271	6.41	3.26
Fluopyram	0.01	$C_{16}H_{11}ClF_6N_2O$	$[M+H]^+$	397.05369	6.46	4.5**
Fluorodifen	0.01	$C_{13}H_7F_3N_2O_5$	$[M+H]^+$	329.03798	7.01	3.7**
Fluotrimazol	0.01	$C_{22}H_{16}F_3N_3$	$[M+H]^+$	380.13691	/	5.7**
Fluoxastrobin	0.01	$C_{21}H_{16}ClFN_4O_5$	$[M+H]^+$	459.0866	6.69	2.86
Flupyradifurone	0.01	$C_{12}H_{11}ClF_2N_2O_2$	$[M+H]^+$	289.05499	3.72	2.3**
Flupyrsulfuron-methyl sodium	0.01	$C_{15}H_{13}F_3N_5NaO_7S$	$[M+H]^+$	488.04583	5.79	/
Fluquinconazole	0.01	$C_{16}H_8Cl_2FN_5O$	$[M+H]^+$	376.01627	6.34	3.24
Fluralaner	0.01	$C_{22}H_{17}Cl_2F_6N_3O_3$	$[M+H]^+$	556.06239	7.39	5.6
Flurenol-butyl	0.01	$C_{18}H_{18}O_3$	$[M+H]^+$	283.13287	/	3.6**
Flurenol-methyl	0.01	$C_{15}H_{12}O_3$	$[M+H]^+$	241.08592	4.36	2.3**
Fluridone	0.01	$C_{19}H_{14}F_3NO$	$[M+H]^+$	330.11003	5.86	1.87
Flurilazole	0.01	$C_{11}H_{13}Cl_2NO_3$	$[M+H]^+$	278.03453	3.66	2**
Flurochloridon (ISO)	0.01	$C_{12}H_{10}Cl_2F_3NO$	$[M+H]^+$	312.01643	6.56	3.4**
Fluroxypyr	0.01	$C_7H_5Cl_2FN_2O_3$	$[M+H]^+$	254.9734	4.03	2.2
Fluroxypyr-meptyl	0.01	$C_{15}H_{21}Cl_2FN_2O_3$	$[M+H]^+$	367.0986	8.43	5.4**
Flurprimidol	0.01	$C_{15}H_{15}F_3N_2O_2$	$[M+H]^+$	313.11584	5.92	3.3**
Flurtamone	0.01	$C_{18}H_{14}F_3NO_2$	$[M+H]^-$	334.10494	5.95	4.5**
Flusilazole	0.01	$C_{16}H_{15}F_2N_3Si$	$[M+H]^+$	316.10761	6.51	3.7
Fluthiacet-methyl	0.01	$C_{15}H_{15}ClFN_3O_3S_2$	$[M+H]^+$	404.03002	6.92	3.77
Flutolanil	0.01	$C_{17}H_{16}F_3NO_2$	$[M+H]^-$	324.12059	6.56	3.7
Flutriafol	0.01	$C_{16}H_{13}F_2N_3O$	$[M+H]^+$	302.10995	4.98	2.29
Fomesafen	0.01	$C_{15}H_{10}ClF_3N_2O_6S$	$[M-H]^-$	456.02385	6.13	2.4**
Foramsulfuron	0.01	$C_{17}H_{20}N_6O_7S$	$[M+H]^+$	453.1187	4.2	0.17
Forchlorfenuron	0.01	$C_{12}H_{10}ClN_3O$	$[M-H]^-$	248.05852	4.95	3.2
Formetanate HCl	0.01	$C_{11}H_{15}N_3O_2$	$[M+H]^+$	222.1237	0.95	/

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Fosthiazate	0.01	$C_9H_{18}NO_3PS_2$	$[M+H]^+$	284.05385	5.05	1.68
Fuberidazole	0.01	$C_{11}H_8N_2O$	$[M+H]^+$	185.07094	2.55	2.67
Furalaxyl	0.01	$C_{17}H_{19}NO_4$	$[M+H]^+$	302.13868	5.94	2.61
Furathiocarb	0.01	$C_{18}H_{26}N_2O_5S$	$[M+H]^+$	383.16352	7.97	4.7
Furmecyclox	0.01	$C_{14}H_{21}NO_3$	$[M+H]^+$	252.15942	6.94	3.1**
Fusidic acid	0.01	$C_{31}H_{48}O_6$	$[M+H]^-$	534.37892	7.46	5.5
Gamithromycin	0.01	$C_{40}H_{76}N_2O_{12}$	$[M+H]^+$	777.54710	3.89	4.9
Guthion-ethyl	0.01	$C_{12}H_{16}N_3O_3PS_2$	$[M+H]^+$	346.04435	6.67	3.4**
Guthion®	0.01	$C_{10}H_{12}N_3O_3PS_2$	$[M+H]^+$	318.01305	5.92	2.75
Halofenozide	0.01	$C_{18}H_{19}ClN_2O_2$	$[M+H]^+$	331.12078	5.99	3.22
Halofuginone	0.01	$C_{16}H_{17}BrClN_3O_3$	$[M+H]^+$	414.02146	3.40	1.4
Halosulfuron-methyl	0.01	$C_{13}H_{15}ClN_6O_7S$	$[M+H]^+$	435.04842	6.05	1.3**
Haloxyfop	0.01	$C_{15}H_{11}ClF_3NO_4$	$[M+H]^+$	362.04015	6.47	4.2**
Haloxyfop-2-ethoxyethyl	0.01	$C_{19}H_{19}ClF_3NO_5$	$[M+H]^+$	434.09766	7.81	4.7**
Haloxyfop-methyl	0.01	$C_{16}H_{13}ClF_3NO_4$	$[M+H]^+$	376.0558	7.51	4.5**
Haloxyfop-P-methyl	0.01	$C_{16}H_{13}ClF_3NO_4$	$[M+H]^+$	376.0558	7.52	4.5**
Heptenophos	0.01	$C_9H_{12}ClO_4P$	$[M+H]^+$	251.02345	5.31	2.32
Hexaconazole	0.01	$C_{14}H_{17}Cl_2N_3O$	$[M+H]^+$	314.08214	6.52	3.9
Hexaflumuron	0.01	$C_{16}H_8Cl_2F_6N_2O_3$	$[M+H]^-$	460.98889	7.37	5.68
Hexazinone	0.01	$C_{12}H_{20}N_4O_2$	$[M+H]^+$	253.1659	4.13	1.85
Hexythiazox	0.01	$C_{17}H_{21}ClN_2O_2S$	$[M+H]^+$	353.1085	8.23	5.57
HMMNI	0.01	$C_5H_7N_3O_3$	$[M+H]^+$	175.08257	1.81	-0.4
Hydroxy-flubendazole	0.01	$C_{16}H_{14}FN_3O_3$	$[M+H]^+$	316.10920	3.56	1.9
Hydroxy-mebendazole	0.01	$C_{16}H_{15}N_3O_3$	$[M+H]^+$	298.11862	3.30	2.3
Hydroxy-thiabendazole	0.01	$C_{10}H_7N_3OS$	$[M+H]^+$	218.03826	1.84	2.1
Hymexazole	0.01	$C_4H_5NO_2$	$[M+H]^+$	100.0393	1.73	0.1**
Imazalil	0.01	$C_{14}H_{14}Cl_2N_2O$	$[M+H]^+$	297.0556	4.47	3.82
Imazamethabenz-methyl	0.01	$C_{16}H_{20}N_2O_3$	$[M+H]^+$	289.15467	4.14	2.6**
Imazamox	0.01	$C_{15}H_{19}N_3O_4$	$[M+H]^+$	306.14483	3.19	0.73
Imazapic	0.01	$C_{14}H_{17}N_3O_3$	$[M+H]^+$	276.13427	3.3	0.39
Imazaquin	0.01	$C_{17}H_{17}N_3O_3$	$[M+H]^+$	312.13427	4.45	2.5**
Imazethapyr	0.01	$C_{15}H_{19}N_3O_3$	$[M+H]^+$	290.14992	3.95	1
Imazosulfuron	0.01	$C_{14}H_{13}ClN_6O_5S$	$[M+H]^+$	413.04294	5.53	1.49
Imibenconazole	0.01	$C_{17}H_{13}Cl_3N_4S$	$[M+H]^-$	410.99993	7.69	5.8**
Imidacloprid	0.01	$C_9H_{10}ClN_5O_2$	$[M+H]^+$	256.05958	3.19	0.57
Imidacloprid-olefin	0.01	$C_9H_8ClN_5O_2$	$[M+H]^+$	254.04393	2.6	2**
Imidocarb dipropionate	0.01	$C_{25}H_{32}N_6O_5$	$[M+H]^+$	497.25069	/	/

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Imiprothrin (mixture of isomers)	0.01	$C_{17}H_{22}N_2O_4$	$[M+H]^+$	319.16523	6.51	2.9
Inabenfide	0.01	$C_{19}H_{15}ClN_2O_2$	$[M+H]^+$	339.08948	5.55	3.7**
Indanofan	0.01	$C_{20}H_{17}ClO_3$	$[M+H]^+$	341.0939	5.47	4.1**
Indaziflam	0.01	$C_{16}H_{20}FN_5$	$[M+H]^+$	302.17755	5.78	3.2**
Indoxacarb	0.01	$C_{22}H_{17}ClF_3N_3O_7$	$[M+H]^+$	528.07799	7.52	4.65
Iodofenphos	0.01	$C_8H_8Cl_2IO_3PS$	$[M+H]^+$	412.84264	8.14	5.51
Iodosulfuron-methyl sodium	0.01	$C_{14}H_{13}IN_5NaO_6S$	$[M+H]^+$	529.96018	5.57	/
Ipconazole	0.01	$C_{18}H_{28}N_2O_3$	$[M+H]^+$	321.21727	6.08	4.1**
Iprobenfos	0.01	$C_{13}H_{21}O_3PS$	$[M+H]^+$	289.10218	6.61	3
Iprodione	0.01	$C_{13}H_{13}Cl_2N_3O_3$	$[M+H]^+$	330.04067	6.49	3.34
Ipronidazole	0.01	$C_7H_{11}N_3O_2$	$[M+H]^+$	170.09240	3.79	1.1
Ipronidazole OH	0.01	$C_7H_{11}N_3O_3$	$[M+H]^+$	186.08732	2.79	-0.5
Iprovalicarb	0.01	$C_{18}H_{28}N_2O_3$	$[M+H]^+$	321.21727	6.14	3.37**
Irgarol (cybutryne)	0.01	$C_{11}H_{19}N_5S$	$[M+H]^+$	254.14339	5.99	3.95
Isazophos	0.01	$C_9H_{17}ClN_3O_3PS$	$[M+H]^+$	314.04896	6.89	3.82
Isocarbamide	0.01	$C_8H_{15}N_3O_2$	$[M+H]^+$	186.1237	3.14	0.8**
Isofenphos	0.01	$C_{15}H_{24}NO_4PS$	$[M+H]^+$	346.12365	7.64	4.12
Isofenphos-methyl	0.01	$C_{14}H_{22}NO_4PS$	$[M+H]^+$	332.108	7.27	3.8**
Isofenphos-oxon	0.01	$C_{15}H_{24}NO_5P$	$[M+H]^+$	330.14649	6.02	2.4**
Isomethiozin	0.01	$C_{12}H_{20}N_4OS$	$[M+H]^+$	269.14306	6.2	3.5**
Isonoruron	0.01	$C_{13}H_{22}N_2O$	$[M+H]^+$	223.18049	5.46	2.3**
Isoprocarb	0.01	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.34	2.31
Isopropalin	0.01	$C_{15}H_{23}N_3O_4$	$[M+H]^+$	310.17613	8.73	5.6**
Isoprothiolane	0.01	$C_{12}H_{18}O_4S_2$	$[M+H]^+$	291.07193	6.59	2.88
Isoproturon	0.01	$C_{12}H_{18}N_2O$	$[M+H]^+$	207.14919	5.19	2.87
Isouron	0.01	$C_{10}H_{17}N_3O_2$	$[M+H]^+$	212.13935	4.34	1.6**
Isoxaben	0.01	$C_{18}H_{24}N_2O_4$	$[M+H]^+$	333.18088	6.4	3.94
Isoxadifen-ethyl	0.01	$C_{18}H_{17}NO_3$	$[M+H]^+$	296.12812	7.03	3.5
Isoxaflutole	0.01	$C_{15}H_{12}F_3NO_4S$	$[M+H]^+$	360.05119	6	2.32
Isoxathion	0.01	$C_{13}H_{16}NO_4PS$	$[M+H]^+$	314.06104	7.53	3.73
Ivermectin	0.01	$C_{48}H_{74}O_{14}$	$[M+Na]^+$	897.49708	9.69	5.83
Ivermectin B1a	0.01	$C_{48}H_{74}O_{14}$	$[M+Na]^+$	875.51513	9.74	3.8
Josamycin	0.01	$C_{42}H_{69}NO_{15}$	$[M+H]^+$	828.47400	5.49	2.9
Karbutilate	0.01	$C_{14}H_{21}N_3O_3$	$[M+H]^+$	280.16557	4.62	1.7**
Ketoprofen	0.01	$C_{16}H_{14}O_3$	$[M+H]^+$	255.10157	5.26	3.12
Ketotriclabendazole	0.01	$C_{13}H_7Cl_3N_2O_2$	$[M+H]^+$	328.96459	5.90	4

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Kresoxim-methyl	0.01	$C_{18}H_{19}NO_4$	$[M+H]^+$	314.13868	6.86	3.4
Lactofen	0.01	$C_{19}H_{15}ClF_3NO_7$	$[M+NH_4]^+$	479.08274	7.97	4.81
Lambda cyhalothrin	0.01	$C_{23}H_{19}ClF_3NO_3$	$[M+H]^+$	450.10783	/	7
Lasalocid A	0.01	$C_{34}H_{54}O_8$	$[M+NH_4]^+$	608.41569	9.37	6.4
Lenacil	0.01	$C_{13}H_{18}N_2O_2$	$[M-H]^-$	235.1441	4.59	1.7**
Leptophos	0.01	$C_{13}H_{10}BrCl_2O_2PS$	$[M+H]^+$	412.87485	8.86	6.3**
Levamisole	0.01	$C_{11}H_{12}N_2S$	$[M+H]^+$	205.07940	2.07	1.8
Levofloxacin	0.01	$C_{18}H_{20}FN_3O_4$	$[M+H]^+$	362.15106	2.32	-0.39
Lincomycin	0.01	$C_{18}H_{34}N_2O_6S$	$[M+H]^+$	407.22104	0.95	0.2
Linuron	0.01	$C_9H_{10}Cl_2N_2O_2$	$[M+H]^+$	249.01921	5.96	3.2
Lomefloxacin	0.01	$C_{17}H_{19}F_2N_3O_3$	$[M+H]^+$	352.14672	2.58	-0.8
Lontrel (clopyralid)	0.01	$C_6H_3Cl_2NO_2$	$[M+H]^+$	191.96136	/	1.06
Lufenuron	0.01	$C_{17}H_8Cl_2F_8N_2O_3$	$[M+H]^+$	510.9857	7.89	5.12
Maduramicin	0.01	$C_{47}H_{83}NO_{17}$	$[M+H]^+$	934.57338	10.58	4.3
Magnamycin A	0.01	$C_{42}H_{67}NO_{16}$	$[M+H]^+$	842.45326	/	/
Malaoxon	0.01	$C_{10}H_{19}O_7PS$	$[M+H]^+$	315.06619	4.68	0.6**
Malathion	0.01	$C_{10}H_{19}O_6PS_2$	$[M+H]^+$	331.04335	6.53	2.36
Mandipropamid	0.01	$C_{23}H_{22}ClNO_4$	$[M+H]^+$	412.13101	6.23	3.2
Marbofloxacin	0.01	$C_{17}H_{19}FN_4O_4$	$[M+H]^+$	363.14631	2.31	-0.5
Mebendazole	0.01	$C_{16}H_{13}N_3O_3$	$[M+H]^+$	296.10297	4.48	2.8
Mecarbam	0.01	$C_{10}H_{20}NO_5PS_2$	$[M+H]^+$	330.05933	6.84	2.29
Mefenacet	0.01	$C_{16}H_{14}N_2O_2S$	$[M+H]^+$	299.08488	6.26	3.23
Mefenamic acid	0.01	$C_{15}H_{15}NO_2$	$[M-H]^-$	242.11756	6.83	5.1
Mefenpyr-diethyl	0.01	$C_{16}H_{18}Cl_2N_2O_4$	$[M+H]^+$	373.07164	7.41	3.9**
Mefluidide	0.01	$C_{11}H_{13}F_3N_2O_3S$	$[M+H]^+$	311.06718	4.61	2.02
Meloxicam	0.01	$C_{14}H_{13}N_3O_4S_2$	$[M+H]^+$	352.04203	5.49	3
Mepanipyrim	0.01	$C_{14}H_{13}N_3$	$[M+H]^+$	224.11822	6.46	3.28
Mephosfolan	0.01	$C_8H_{16}NO_3PS_2$	$[M+H]^+$	270.0382	4.27	1**
Mepiquat chloride	0.01	$C_7H_{16}ClN$	$[M+H]^+$	150.1044	/	-2.82
Mepronil	0.01	$C_{17}H_{19}NO_2$	$[M+H]^+$	270.14886	6.49	3.66
Mesosulfuron-methyl	0.01	$C_{17}H_{21}N_5O_9S_2$	$[M+H]^+$	504.08535	4.96	-0.48
Mesotrione	0.01	$C_{14}H_{13}NO_7S$	$[M+H]^+$	340.04855	4.34	0.9
Metaflumizone	0.01	$C_{24}H_{16}F_6N_4O_2$	$[M-H]^-$	507.12502	7.8	6.2**
Metalaxyl	0.01	$C_{15}H_{21}NO_4$	$[M+H]^+$	280.15433	5.21	1.65
Metalaxyl-M	0.01	$C_{15}H_{21}NO_4$	$[M+H]^+$	280.15433	5.21	1.6**
Metamitron	0.01	$C_{10}H_{10}N_4O$	$[M+H]^+$	203.09274	3.03	0.83
Metazachlor	0.01	$C_{14}H_{16}ClN_3O$	$[M+H]^+$	278.10547	5.48	2.7**

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Metconazole	0.01	$C_{17}H_{22}ClN_3O$	$[M+H]^+$	320.15242	6.75	3.85
Methabenzthiazuron	0.01	$C_{10}H_{11}N_3OS$	$[M+H]^+$	222.06956	4.89	2.64
Methacrifos	0.01	$C_7H_{13}O_5PS$	$[M+H]^+$	241.02941	5.91	1.9**
Methamidophos	0.01	$C_2H_8NO_2PS$	$[M+H]^+$	142.00862	0.92	-0.8
Methazine	0.01	$C_{11}H_{19}N_7$	$[M+H]^+$	250.17747	/	/
Methfuroxam	0.01	$C_{14}H_{15}NO_2$	$[M+H]^+$	230.11756	5.91	3**
Methidathion	0.01	$C_6H_{11}N_2O_4PS_3$	$[M+H]^+$	302.96914	5.87	2.2
Methiocarb	0.01	$C_{11}H_{15}NO_2S$	$C_9H_{13}OS^+$	169.06816	5.82	2.92
Methiocarb sulfone	0.01	$C_{11}H_{15}NO_4S$	$[M+H]^+$	258.07946	3.67	1.6**
Methiocarb sulfoxide	0.01	$C_{11}H_{15}NO_3S$	$[M+H]^+$	242.08454	2.96	1.5**
Methomyl	0.01	$C_5H_{10}N_2O_2S$	$[M+H]^+$	163.05358	/	0.6
Methomyl oxime	0.01	C_3H_7NOS	$[M+H]^+$	106.03211	/	0.2**
Methoprotryne	0.01	$C_{11}H_{21}N_5OS$	$[M+H]^+$	272.15396	5.09	2.82
Methoxyfenozide	0.01	$C_{22}H_{28}N_2O_3$	$[M+H]^-$	313.15467	6.43	3.7
Methyl paraoxon	0.01	$C_8H_{10}NO_6P$	$[M+H]^+$	248.03185	4.27	1.3**
Methyl parathion	0.01	$C_8H_{10}NO_5PS$	$[M+H]^+$	264.00901	6.25	2.86
Metobromuron	0.01	$C_9H_{11}BrN_2O_2$	$[M+H]^+$	259.00767	5.34	2.38
Metolachlor	0.01	$C_{15}H_{22}ClNO_2$	$[M+H]^+$	284.14118	6.71	3.13
Metolcarb	0.01	$C_9H_{11}NO_2$	$[M+H]^+$	166.08626	4.32	1.7
(E)-Metominostrobin	0.01	$C_{16}H_{16}N_2O_3$	$[M+H]^+$	285.12337	5.52	3.2**
(Z)-Metominostrobin	0.01	$C_{16}H_{16}N_2O_3$	$[M+H]^+$	285.12337	5.58	3.2**
Metosulam	0.01	$C_{14}H_{13}Cl_2N_5O_4S$	$[M+H]^+$	418.01381	5.02	3.08
Metoxuron	0.01	$C_{10}H_{13}ClN_2O_2$	$[M+H]^+$	229.07383	3.99	1.6**
Metrafenone	0.01	$C_{19}H_{21}BrO_5$	$[M+H]^+$	409.06451	7.65	4.6**
Metribuzin	0.01	$C_8H_{14}N_4OS$	$[M+H]^+$	215.09611	4.49	1.7
Metronidazole	0.01	$C_6H_9N_3O_3$	$[M+H]^+$	172.07167	1.86	0
Metronidazole OH	0.01	$C_6H_9N_3O_4$	$[M+H]^+$	188.06658	0.95	/
Metsulfuron-methyl	0.01	$C_{14}H_{15}N_5O_6S$	$[M+H]^+$	382.08158	4.55	2.2
Mevinphos	0.01	$C_7H_{13}O_6P$	$C_6H_{10}O_5P^+$	193.02604	3.54	0.13
Mexacarbate	0.01	$C_{12}H_{18}N_2O_2$	$[M+H]^+$	223.1441	3.48	2.56
MGK-264 (mixture of isomers)	0.01	$C_{17}H_{25}NO_2$	$[M+H]^+$	276.19581	7.42	3.7
Molinate	0.01	$C_9H_{17}NOS$	$[M+H]^+$	188.11036	6.31	3.21
Monensin	0.01	$C_{36}H_{62}O_{11}$	$[M+NH_4]^+$	688.46304	9.94	4.2
Monepantel	0.01	$C_{20}H_{13}F_6N_3O_2S$	$[M+H]^+$	474.07054	7.23	5.2
Monepantel sulfone	0.01	$C_{20}H_{13}F_6N_3O_4S$	$[M-H]^-$	506.06037	6.85	3.9
Monocrotophos	0.01	$C_7H_{14}NO_5P$	$[M+H]^+$	224.06824	2.29	-0.2

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Monolinuron	0.01	$C_9H_{11}ClN_2O_2$	$[M+H]^+$	215.05818	5.14	2.3
Monuron	0.01	$C_9H_{11}ClN_2O$	$[M+H]^+$	199.06327	4.31	1.94
Morantel	0.01	$C_{12}H_{16}N_2S$	$[M+H]^+$	221.11070	3.07	1.9
Morpholine	0.01	C_4H_9NO	$[M+H]^+$	88.07569	/	-0.86
Moxidectin	0.01	$C_{37}H_{53}NO_8$	$[M+H]^+$	640.38439	9.31	4.3
N,N-Diethyl-*m*-toluamide (DEET)	0.01	$C_{12}H_{17}NO$	$[M+H]^+$	192.13829	5.23	2.02
N,N'-Ethylenethiourea	0.01	$C_3H_6N_2S$	$[M+H]^+$	103.03245	0.9	-0.5
Nafcillin	0.01	$C_{21}H_{22}N_2O_5S$	$[M-H]^-$	415.13222	5.22	2.9
Nalidixic acid	0.01	$C_{12}H_{12}N_2O_3$	$[M+H]^+$	233.09207	4.68	/
Naphthalophos (naftalofos)	0.01	$C_{16}H_{16}NO_6P$	$[M+H]^+$	350.0788	5.76	2.4**
Napropamide	0.01	$C_{17}H_{21}NO_2$	$[M+H]^+$	272.16451	6.49	3.36
Naproxen	0.01	$C_{14}H_{14}O_3$	$[M+H]^+$	231.10157	5.35	3.3
Naptalam	0.01	$C_{18}H_{13}NO_3$	$[M+H]^+$	292.09682	4.49	3.5**
Narasin	0.01	$C_{43}H_{72}O_{11}$	$[M+NH_4]^+$	782.54129	10.37	6.2
Neburon	0.01	$C_{12}H_{16}Cl_2N_2O$	$[M+H]^+$	275.07125	6.8	4.1
Neospiramycin	0.01	$C_{36}H_{62}N_2O_{11}$	$[M+H]^+$	716.46919	/	/
Nereistoxin oxalate	0.01	$C_7H_{13}NO_4S_2$	$[M+H]^+$	240.03588	/	/
Nicarbazin (DNC)	0.01	$C_{19}H_{18}N_6O_6$	$[M+H]^+$	444.16261	/	/
Nicosulfuron	0.01	$C_{15}H_{18}N_6O_6S$	$[M+H]^+$	411.10813	4.05	/
Nigericin	0.01	$C_{40}H_{68}O_{11}$	$[M+NH_4]^+$	742.50999	10.84	4.3
Nitenpyram (ISO)	0.01	$C_{11}H_{15}ClN_4O_2$	$[M+H]^+$	271.09563	2.25	-0.66
Nitralin	0.01	$C_{13}H_{19}N_3O_6S$	$[M+H]^+$	346.10673	6.84	3.7**
Nitrapyrin (2-chloro-6-(trichloromethyl)pyridine)	0.01	$C_6H_3Cl_4N$	$[M+H]^+$	231.9063	/	3.4
Nitroguanidine	0.01	$CH_4N_4O_2$	$[M+H]^+$	105.0407	/	-0.89
Nitroxinil	0.01	$C_7H_3IN_2O_3$	$[M+H]^+$	290.92612	4.37	2.3
Norfloxacin	0.01	$C_{16}H_{18}FN_3O_3$	$[M+H]^+$	320.14050	2.36	-1
Norflurazon	0.01	$C_{12}H_9ClF_3N_3O$	$[M+H]^+$	304.0459	5.34	2.3
Noruron	0.01	$C_{13}H_{22}N_2O$	$[M+H]^+$	223.18049	5.52	2.3**
Novaluron	0.01	$C_{17}H_9ClF_8N_2O_4$	$[M+H]^-$	493.01959	7.54	5.27
Novobiocin	0.01	$C_{31}H_{36}N_2O_{11}$	$[M-H]^-$	613.23919	6.88	3.3
Nuarimol	0.01	$C_{17}H_{12}ClFN_2O$	$[M+H]^+$	315.0695	5.62	3.18
O-Acetyltylosin	0.01	$C_{48}H_{79}NO_{18}$	$[M+H]^+$	958.53699	4.79	1.6
Ofloxacin	0.01	$C_{18}H_{20}FN_3O_4$	$[M+H]^+$	362.15106	2.43	-0.4
Ofurace	0.01	$C_{14}H_{16}ClNO_3$	$[M+H]^+$	282.08915	5.09	2.7**
Oleandomycin	0.01	$C_{35}H_{61}NO_{12}$	$[M+H]^+$	688.42665	4.29	1.7
Omethoate	0.01	$C_5H_{12}NO_4PS$	$[M+H]^+$	214.02974	0.92	-0.74

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Orbencarb	0.01	$C_{12}H_{16}ClNOS$	$[M+H]^+$	258.07139	7.36	3.4**
Orbifloxacin	0.01	$C_{19}H_{20}F_3N_3O_3$	$[M+H]^+$	396.15295	2.74	0.9
Ormetoprim	0.01	$C_{14}H_{18}N_4O_2$	$[M+H]^+$	275.15025	2.41	1.2
Orysastrobin	0.01	$C_{18}H_{25}N_5O_5$	$[M+H]^+$	392.19285	6.23	2.5**
Oryzalin	0.01	$C_{12}H_{18}N_4O_6S$	$[M-H]^-$	347.10198	6.47	3.73
Oxacillin	0.01	$C_{19}H_{19}N_3O_5S$	$[M-H]^-$	402.11182	4.72	2.4
Oxadiargyl	0.01	$C_{15}H_{14}Cl_2N_2O_3$	$[M+H]^+$	341.04542	7.35	4.1**
Oxadiazon	0.01	$C_{15}H_{18}Cl_2N_2O_3$	$[M+H]^+$	345.07672	8.15	4.8
Oxadixyl	0.01	$C_{14}H_{18}N_2O_4$	$[M+H]^+$	279.13393	4.24	0.8
Oxamyl	0.01	$C_7H_{13}N_3O_3S$	$[M+H]^+$	242.05698	2.93	-0.47
Oxasulfuron	0.01	$C_{17}H_{18}N_4O_6S$	$[M+H]^+$	407.10198	4.4	1.6**
Oxaziclomefone	0.01	$C_{20}H_{19}Cl_2NO_2$	$[M+H]^+$	376.08656	7.98	5.2**
Oxfendazole (fenbendazole sulfoxide)	0.01	$C_{15}H_{13}N_3O_3S$	$[M+H]^+$	316.07504	3.49	2.3
Oxfendazole sulfone (fenbendazole sulfone)	0.01	$C_{15}H_{13}N_3O_4S$	$[M+H]^+$	332.06995	4.15	2.3
Oxibendazole	0.01	$C_{12}H_{15}N_3O_3$	$[M+H]^+$	250.11862	3.79	2.4
Oximino oxamyl	0.01	$C_5H_{10}N_2O_2S$	$[M+H]^+$	163.05358	/	1.2**
Oxolinic acid	0.01	$C_{13}H_{11}NO_5$	$[M+H]^+$	262.07100	3.82	-0.2
Oxycarboxin	0.01	$C_{12}H_{13}NO_4S$	$[M+H]^+$	268.06381	3.84	0.77
Oxyclozanide	0.01	$C_{13}H_6Cl_5NO_3$	$[M-H]^-$	399.88631	6.83	5.7
Oxydemeton-methyl (demeton-*S*-)	0.01	$C_6H_{15}O_4PS_2$	$[M+H]^+$	247.02222	/	-0.74
Oxyfluorfen	0.01	$C_{15}H_{11}ClF_3NO_4$	$[M+H]^+$	362.04015	7.98	4.73
Oxyphenbutazone	0.01	$C_{19}H_{20}N_2O_3$	$[M-H]^-$	325.15467	5.36	2.7
Oxytetracycline	0.01	$C_{22}H_{24}N_2O_9$	$[M+H]^+$	461.15546	/	/
Paclobutrazol	0.01	$C_{15}H_{20}ClN_3O$	$[M+H]^+$	294.13677	5.83	3.2
Paraoxon-ethyl	0.01	$C_{10}H_{14}NO_6P$	$[M+H]^+$	276.06315	5.28	1.98
Parathion	0.01	$C_{10}H_{14}NO_5PS$	$[M+H]^+$	292.04031	7.1	3.83
Pebulate	0.01	$C_{10}H_{21}NOS$	$[M+H]^+$	204.14166	7.57	3.83
Penconazol	0.01	$C_{13}H_{15}Cl_2N_3$	$[M-H]^+$	284.07158	6.7	3.72
Pencycuron	0.01	$C_{19}H_{21}ClN_2O$	$[M+H]^-$	329.14152	7.42	4.8**
Pendimethalin	0.01	$C_{13}H_{19}N_3O_4$	$[M+H]^+$	282.14483	8.22	5.2
Penfluron	0.01	$C_{15}H_9F_5N_2O_2$	$[M+H]^-$	345.0657	6.73	4**
Penicillin-G	0.01	$C_{16}H_{18}N_2O_4S$	$[M-H]^-$	335.10601	4.07	1.8
Penicilllin-V^{+4}	0.01	$C_{16}H_{18}N_2O_5S$	$[M-H]^-$	351.10092	4.43	2.1
Penoxsulam	0.01	$C_{16}H_{14}F_5N_5O_5S$	$[M-H]^-$	484.07086	5.37	-0.354
Pentachlorocyanobenzene	0.01	C_7Cl_5N	$[M+H]^+$	275.85168	/	/

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Pentanochlor	0.01	$C_{13}H_{18}ClNO$	$[M+H]^+$	240.11497	6.89	4.3**
Penthiopyrad	0.01	$C_{16}H_{20}F_3N_3OS$	$[M-H]^-$	360.1352	7.03	4**
Pethoxamid	0.01	$C_{16}H_{22}ClNO_2$	$[M+H]^+$	296.14118	6.66	3.5**
Phenmedipham	0.01	$C_{16}H_{16}N_2O_4$	$[M+H]^+$	301.11828	5.78	3.6**
Phenothrin	0.01	$C_{23}H_{26}O_3$	$[M+H]^+$	351.19547	9.11	7.54
Phenthoate	0.01	$C_{12}H_{17}O_4PS_2$	$[M+H]^+$	321.03787	7.15	3.7**
Phénylbutazone	0.01	$C_{19}H_{20}N_2O_2$	$[M+H]^+$	309.15975	6.64	3.2
Phenylurea	0.01	$C_7H_8N_2O$	$[M+H]^+$	137.07094	2.34	0.8**
Phorate	0.01	$C_7H_{17}O_2PS_3$	$[M+H]^+$	261.02011	/	3.56
Phorate-oxon sulfoxide	0.01	$C_7H_{17}O_4PS_2$	$[M+H]^+$	261.03787	3.03	1.8**
Phorate sulfoxide	0.01	$C_7H_{17}O_3PS_3$	$[M+H]^+$	277.01502	5	3.5**
Phorate-oxon	0.01	$C_7H_{17}O_3PS$	$[M+H]^+$	213.07088	/	2.1**
Phorate-oxon sulfone	0.01	$C_7H_{17}O_5PS_2$	$[M+H]^+$	277.03278	3.66	2**
Phorat sulfone	0.01	$C_7H_{17}O_4PS_3$	$[M+H]^+$	293.00994	5.71	3.7**
Phosalone	0.01	$C_{12}H_{15}ClNO_4PS_2$	$[M+H]^+$	367.99414	7.45	4.38
Phosfolan	0.01	$C_7H_{14}NO_3PS_2$	$[M+H]^+$	256.02255	3.72	0.6**
Phosmet	0.01	$C_{11}H_{12}NO_4PS_2$	$[M+H]^+$	318.00182	6.03	2.95
Phosmet-oxon	0.01	$C_{11}H_{12}NO_5PS$	$[M+H]^+$	302.02466	4.07	1.1**
Phosphamidon	0.01	$C_{10}H_{19}ClNO_5P$	$[M+H]^+$	300.07622	4.11	0.8
Phospholan-methyl	0.01	$C_5H_{10}NO_3PS_2$	$[M+H]^+$	227.99125	2.58	1.1**
Phoxim	0.01	$C_{12}H_{15}N_2O_3PS$	$[M+H]^+$	299.06138	7.04	4.4**
Phthalylsulfathiazole (CAS)	0.01	$C_{17}H_{13}N_3O_5S_2$	$[M-H]^-$	404.03694	3.16	1.1
Picolinafen	0.01	$C_{19}H_{12}F_4N_2O_2$	$[M+H]^+$	377.09077	7.85	4.9**
Picoxystrobin	0.01	$C_{18}H_{16}F_3NO_4$	$[M+H]^+$	368.11042	7.03	3.6
Piperalin	0.01	$C_{16}H_{21}Cl_2NO_2$	$[M+H]^+$	330.10221	4.56	4.31
Piperonyl butoxide	0.01	$C_{19}H_{30}O_5$	$[M+NH_4]^+$	356.24315	7.92	4.75
Piperophos	0.01	$C_{14}H_{28}NO_3PS_2$	$[M+H]^+$	354.1321	7.59	4.2**
Pirimicarb	0.01	$C_{11}H_{18}N_4O_2$	$[M+H]^+$	239.15025	3.91	1.7
Pirimicarb-desmethyl	0.01	$C_{10}H_{16}N_4O_2$	$[M+H]^+$	225.1346	2.68	1.6**
Pirimiphos-methyl	0.01	$C_{11}H_{20}N_3O_3PS$	$[M+H]^+$	306.10358	7.47	4.12
Pirimiphos-ethyl	0.01	$C_{13}H_{24}N_3O_3PS$	$[M+H]^+$	334.13488	8.17	5
Pirimiphos-methyl-N-desethyl	0.01	$C_9H_{16}N_3O_3PS$	$[M+H]^+$	278.07228	5.36	3.7**
Pirlymycin	0.01	$C_{17}H_{31}ClN_2O_5S$	$[M+H]^+$	411.17150	3.09	1.7
Prallethrin	0.01	$C_{19}H_{24}O_3$	$[M+H]^+$	301.17982	7.58	4.49
Pretilachlor	0.01	$C_{17}H_{26}ClNO_2$	$[M+H]^+$	312.17248	7.69	4.1**
Primisulfuron-methyl	0.01	$C_{15}H_{12}F_4N_4O_7S$	$[M+H]^-$	469.04356	6.19	/
Probenazole	0.01	$C_{10}H_9NO_3S$	$[M+H]^+$	224.03759	4.96	1.4**

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Prochloraz	0.01	$C_{15}H_{16}Cl_3N_3O_2$	$[M+H]^+$	376.03809	6.62	4.1
Procyazine	0.01	$C_{10}H_{13}ClN_6$	$[M+H]^+$	253.0963	4.55	2.4**
Procymidone	0.01	$C_{13}H_{11}Cl_2NO_2$	$[M+H]^+$	284.02396	6.64	3**
Profenofos	0.01	$C_{11}H_{15}BrClO_3PS$	$[M+H]^+$	374.94017	7.68	4.68
Profoxydim lithium	0.01	$C_{24}H_{32}ClNO_4S$	$[M+H]^+$	466.18133	8.88	/
Prohydrojasmon	0.01	$C_{15}H_{26}O_3$	$[M+H]^+$	255.19547	7.5	3.6**
Promecarb	0.01	$C_{12}H_{17}NO_2$	$[M+H]^+$	208.13321	5.87	3.1
Prometon	0.01	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.41	2.99
Prometryn	0.01	$C_{10}H_{19}N_5S$	$[M+H]^+$	242.14339	5.88	3.51
Propachlor	0.01	$C_{11}H_{14}ClNO$	$[M+H]^+$	212.08367	5.49	2.18
Propamocarb	0.01	$C_9H_{20}N_2O_2$	$[M+H]^+$	189.15975	0.96	1.12
Propamocarb HCl	0.01	$C_9H_{21}ClN_2O_2$	$[M+H]^+$	225.13643	2.64	/
Propanil	0.01	$C_9H_9Cl_2NO$	$[M+H]^-$	218.0134	5.69	3.07
Propaphos	0.01	$C_{13}H_{21}O_4PS$	$[M+H]^+$	305.0971	6.75	3.67
Propaquizafop	0.01	$C_{22}H_{22}ClN_3O_5$	$[M+H]^+$	444.13208	7.84	4.6
Propargite	0.01	$C_{19}H_{26}O_4S$	$[M+NH_4]^+$	368.18901	8.36	5
Propazine	0.01	$C_9H_{16}ClN_5$	$[M+H]^+$	230.1167	6.53	2.93
Propazine-2-hydroxy	0.01	$C_9H_{17}N_5O$	$[M+H]^+$	212.15059	3.71	0.6**
Propetamphos	0.01	$C_{10}H_{20}NO_4PS$	$[M+H]^+$	282.09235	6.5	3.82
Propham	0.01	$C_{10}H_{13}NO_2$	$C_7H_8NO_2^+$	138.05496	5.41	2.6
Propiconazol (mixture of isomers)	0.01	$C_{15}H_{17}Cl_2N_3O_2$	$[M+H]^+$	342.07706	6.87	3.72
Propisochlor	0.01	$C_{15}H_{22}ClNO_2$	$[M+H]^+$	284.14118	6.71	3.9**
Propoxur	0.01	$C_{11}H_{15}NO_3$	$C_8H_{10}NO_3^+$	168.06552	4.65	1.52
Propyzamide (pronamide)	0.01	$C_{12}H_{11}Cl_2NO$	$[M+H]^+$	256.02905	6.31	3.43
Proquinazid	0.01	$C_{14}H_{17}IN_2O_2$	$[M+H]^+$	373.04076	8.68	3.7**
Prosulfocarb	0.01	$C_{14}H_{21}NOS$	$[M+H]^+$	252.14166	7.8	3.9**
Prosulfuron	0.01	$C_{15}H_{16}F_3N_5O_4S$	$[M+H]^+$	420.09479	5.87	-0.21
Prothioconazole	0.01	$C_{14}H_{15}Cl_2N_3OS$	$[M+H]^+$	344.03857	6.8	3.82
Prothioconazole-desthio	0.01	$C_{14}H_{15}Cl_2N_3O$	$[M+H]^+$	312.06649	6.24	2.7**
Pymetrozine	0.01	$C_{10}H_{11}N_5O$	$[M+H]^+$	218.10364	1.62	-0.18
Pyracarbolid	0.01	$C_{13}H_{15}NO_2$	$[M+H]^+$	218.11756	4.88	2.1**
Pyraclofos	0.01	$C_{14}H_{18}ClN_2O_3PS$	$[M+H]^+$	361.05371	7.16	3.8**
Pyraclostrobin	0.01	$C_{19}H_{18}ClN_3O_4$	$[M+H]^+$	388.10586	7.3	3.99
Pyraflufen-ethyl	0.01	$C_{15}H_{13}Cl_2F_3N_2O_4$	$[M+H]^+$	413.02772	7.12	3.49
Pyrantel	0.01	$C_{11}H_{14}N_2S$	$[M+H]^+$	207.09505	2.50	1.6
Pyrazolynate	0.01	$C_{19}H_{16}Cl_2N_2O_4S$	$[M+H]^+$	439.02806	7.48	3.8**

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Pyrazophos	0.01	$C_{14}H_{20}N_3O_5PS$	$[M+H]^+$	374.09341	7.27	3.1**
Pyrazosulfuron-ethyl	0.01	$C_{14}H_{18}N_6O_7S$	$[M+H]^+$	415.10305	5.93	0.7**
Pyrazoxyfen	0.01	$C_{20}H_{16}Cl_2N_2O_3$	$[M+H]^+$	403.06107	6.96	3.7**
Pyrethrin (mixture of isomers)	0.01	$C_{22}H_{28}O_5$	$[M+H]^+$	373.20095	7.57	4.3
Pyributicarb	0.01	$C_{18}H_{22}N_2O_2S$	$[M+H]^+$	331.14748	8.21	5.2**
Pyridaben	0.01	$C_{19}H_{25}ClN_2OS$	$[M+H]^+$	365.14489	8.82	6.37
Pyridafol	0.01	$C_{10}H_7ClN_2O$	$[M+H]^+$	207.03197	3.48	2.4**
Pyridalyl	0.01	$C_{18}H_{14}Cl_4F_3NO_3$	$[M+H]^+$	491.9725	9.59	7.59
Pyridaphenthion	0.01	$C_{14}H_{17}N_2O_4PS$	$[M+H]^+$	341.07194	6.32	3.3**
Pyridate	0.01	$C_{19}H_{23}ClN_2O_2S$	$[M+H]^+$	379.12415	9.25	6.6**
Pyrifenox (mixture of isomers)	0.01	$C_{14}H_{12}Cl_2N_2O$	$[M+H]^+$	295.03995	5.56	2.5**
Pyrimethanil	0.01	$C_{12}H_{13}N_3$	$[M+H]^+$	200.11822	5.49	2.84
Pyriproxyfen	0.01	$C_{20}H_{19}NO_3$	$[M+H]^+$	322.14377	8.11	5.37
Pyroquilon	0.01	$C_{11}H_{11}NO$	$[M+H]^+$	174.09134	4.07	1.57
Pyroxsulam	0.01	$C_{14}H_{13}F_3N_6O_5S$	$[M+H]^+$	435.0693	4.66	1.7**
Quinalphos	0.01	$C_{12}H_{15}N_2O_3PS$	$[M+H]^+$	299.06138	7.04	4.4**
Quinclorac	0.01	$C_{10}H_5Cl_2NO_2$	$[M+H]^+$	241.97701	3.81	2.97
Quinine	0.01	$C_{20}H_{24}N_2O_2$	$[M+H]^+$	325.19105	2.91	/
Quinine sulfate	0.01	$C_{40}H_{54}N_4O_{10}S$	$[M+H]^+$	783.36334	/	/
Quinmerac	0.01	$C_{11}H_8ClNO_2$	$[M+H]^+$	222.03163	3.21	2.7**
Quinoclamine	0.01	$C_{10}H_6ClNO_2$	$[M+H]^+$	208.01598	4.36	2.1**
Quinoline	0.01	C_9H_7N	$[M+H]^+$	130.06513	2.1	2.03
Quinoxyfen	0.01	$C_{15}H_8Cl_2FNO$	$[M+H]^+$	308.00397	8	4.66
Quizalofop	0.01	$C_{17}H_{13}ClN_2O_4$	$[M+H]^+$	345.06366	6.27	3.6**
Quizalofop-ethyl	0.01	$C_{19}H_{17}ClN_2O_4$	$[M+H]^+$	373.09496	7.75	4.28
Quizalofop-P-ethyl	0.01	$C_{19}H_{17}ClN_2O_4$	$[M+H]^+$	373.09496	7.74	4.3
Rafoxanide	0.01	$C_{19}H_{11}Cl_2I_2NO_3$	$[M+H]^+$	625.82783	/	7
Reserpine	0.01	$C_{33}H_{40}N_2O_9$	$[M+H]^+$	609.28066	4.84	3.2
Resmethrin	0.01	$C_{22}H_{26}O_3$	$[M+H]^+$	339.19547	8.89	5.43
Rifampicin	0.01	$C_{43}H_{58}N_4O_{12}$	$[M+H]^+$	823.41240	5.94	2.7
Rifamycin	0.01	$C_{37}H_{47}NO_{12}$	$[M+H]^+$	698.31710	/	/
Rifaximin	0.01	$C_{43}H_{51}N_3O_{11}$	$[M+H]^+$	786.35964	6.24	3.2
Rimsulfuron	0.01	$C_{14}H_{17}N_5O_7S_2$	$[M+H]^+$	432.06422	4.77	-1.47
Robenidine	0.01	$C_{15}H_{13}Cl_2N_5$	$[M+H]^+$	334.06208	5.57	3.8
Ronidazole	0.01	$C_6H_8N_4O_4$	$[M+H]^+$	201.06183	/	/
Rotenone	0.01	$C_{23}H_{22}O_6$	$[M+H]^+$	395.14892	6.72	4.1
Roxithromycin	0.01	$C_{41}H_{76}N_2O_{15}$	$[M+H]^+$	837.53185	4.99	1.7

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Saflufenacil	0.01	$C_{17}H_{17}ClF_4N_4O_5S$	$[M+H]^+$	501.06171	5.99	2.1**
Salinomycin	0.01	$C_{42}H_{70}O_{11}$	$[M+NH_4]^+$	768.52564	9.98	5.7
Sarafloxacin	0.01	$C_{20}H_{17}F_2N_3O_3$	$[M+H]^+$	386.13107	2.98	0.3
Schradan (DMPA)	0.01	$C_8H_{24}N_4O_3P_2$	$[M+H]^+$	287.13964	3.05	-0.3
Sebuthylazin	0.01	$C_9H_{16}ClN_5$	$[M+H]^+$	230.1167	5.9	3.1**
Sebuthylazin-desethyl	0.01	$C_7H_{12}ClN_5$	$[M+H]^+$	202.0854	3.98	2.2**
Secbumeton	0.01	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.45	3.2**
Selamectin impurity B	0.01	$C_{43}H_{63}NO_{11}$	$[M+H]^+$	770.44739	9.65	5.4**
Semduramicin	0.01	$C_{45}H_{76}O_{16}$	$[M+H]^+$	873.52061	7.59	/
Sethoxydim	0.01	$C_{17}H_{29}NO_3S$	$[M+H]^+$	328.19409	8.09	/
S-Hydroprene	0.01	$C_{17}H_{30}O_2$	$[M+H]^+$	267.23186	/	6.5
Siduron	0.01	$C_{14}H_{20}N_2O$	$[M+H]^+$	233.16484	5.77	3.8
Silthiofam	0.01	$C_{13}H_{21}NOSSi$	$[M+H]^+$	268.11859	/	/
Simazine	0.01	$C_7H_{12}ClN_5$	$[M+H]^+$	202.0854	4.4	2.18
Simeconazole	0.01	$C_{14}H_{20}FN_3OSi$	$[M+H]^+$	294.14325	6.16	/
Simeton	0.01	$C_8H_{15}N_5O$	$[M+H]^+$	198.13494	3.36	1.8
Simetryn	0.01	$C_8H_{15}N_5S$	$[M+H]^+$	214.11209	4.41	2.8
S-Metolachlor	0.01	$C_{15}H_{22}ClNO_2$	$[M+H]^+$	284.14118	6.72	3.1
Spinetoram (mixture of isomers)	0.01	$C_{42}H_{69}NO_{10}$	$[M+H]^+$	748.49942	6.94	5.9**
Spinosad (mixure of spinosyn A and D)	0.01	$C_{41}H_{65}NO_{10}$	$[M+H]^+$	732.46812	6.34	4.9**
Spiramycin	0.01	$C_{43}H_{74}N_2O_{14}$	$[M+H]^+$	843.52128	3.33	2.1
Spirodiclofen	0.01	$C_{21}H_{24}Cl_2O_4$	$[M+H]^+$	411.11244	8.81	5.1
Spiromesifen	0.01	$C_{23}H_{30}O_4$	$[M+H]^+$	371.22169	8.7	4.55
Spirotetramat	0.01	$C_{21}H_{27}NO_5$	$[M+H]^+$	374.1962	6.04	3.2**
Spirotetramat-enol	0.01	$C_{18}H_{23}NO_3$	$[M+H]^+$	302.17507	4.45	2.4**
Spirotetramat-enol-glucoside	0.01	$C_{24}H_{33}NO_8$	$[M+H]^+$	464.22789	2.38	0.5**
Spirotetramat-mono-hydroxy	0.01	$C_{21}H_{27}NO_5$	$[M+H]^+$	374.1962	6.04	2.1**
Spiroxamine (mixture of isomers)	0.01	$C_{18}H_{35}NO_2$	$[M+H]^+$	298.27406	5.39	4.2**
Sulbactam	0.01	$C_8H_{11}NO_5S$	$[M+NH_4]^+$	256.02502	/	/
Sulcotrione	0.01	$C_{14}H_{13}ClO_5S$	$[M+H]^+$	329.0245	4.61	1.5**
Sulfacetamide	0.01	$C_8H_{10}N_2O_3S$	$[M+H]^+$	215.04849	/	-1
Sulfachloropyridazine	0.01	$C_{10}H_9ClN_4O_2S$	$[M+H]^+$	285.02075	3.12	1
Sulfaclozine	0.01	$C_{10}H_9ClN_4O_2S$	$[M+H]^+$	285.02075	3.79	0.9
Sulfadiazine	0.01	$C_{10}H_{10}N_4O_2S$	$[M+H]^+$	251.05972	2.07	-0.1
Sulfadimerazine	0.01	$C_{12}H_{14}N_4O_2S$	$[M+H]^+$	279.09102	2.79	0.1

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Sulfadimethoxine	0.01	$C_{12}H_{14}N_4O_4S$	$[M+H]^+$	311.08085	3.86	1.6
Sulfadoxine	0.01	$C_{12}H_{14}N_4O_4S$	$[M+H]^+$	311.08085	3.35	0.7
Sulfaguanidine	0.01	$C_7H_{10}N_4O_2S$	$[M+H]^+$	215.05972	0.95	-0.7
Sulfallate	0.01	$C_8H_{14}ClNS_2$	$[M+H]^+$	224.0329	7.25	3.15
Sulfamerazine	0.01	$C_{11}H_{12}N_4O_2S$	$[M+H]^+$	265.07537	2.46	0.14
Sulfamerazine	0.01	$C_{11}H_{12}N_4O_2S$	$[M+H]^+$	265.07537	2.46	0.1
Sulfamethizole	0.01	$C_9H_{10}N_4O_2S_2$	$[M+H]^+$	271.03180	2.64	2.9
Sulfamethoxazole	0.01	$C_{10}H_{11}N_3O_3S$	$[M+H]^+$	254.05939	3.25	0.9
Sulfamethoxypyridazine	0.01	$C_{11}H_{12}N_4O_3S$	$[M+H]^+$	281.07029	2.98	0.3
Sulfamonomethoxine	0.01	$C_{11}H_{12}N_4O_3S$	$[M+H]^+$	281.07029	3	0.8
Sulfamonomethoxine	0.01	$C_{11}H_{12}N_4O_3S$	$[M+H]^+$	281.07029	2.72	0.7
Sulfanilamide	0.01	$C_6H_8N_2O_2S$	$[M+H]^+$	173.03793	/	-0.6
Sulfaphenazole	0.01	$C_{15}H_{14}N_4O_2S$	$[M+H]^+$	315.09102	3.93	1.5
Sulfaquinoxaline	0.01	$C_{14}H_{12}N_4O_2S$	$[M+H]^+$	301.07537	3.89	1.7
Sulfathiazole	0.01	$C_9H_9N_3O_2S_2$	$[M+H]^+$	256.02090	2.13	0.1
Sulfentrazone	0.01	$C_{11}H_{10}Cl_2F_2N_4O_3S$	$[M+H]^+$	386.98915	4.91	0.99
Sulfisoxazole	0.01	$C_{11}H_{13}N_3O_3S$	$[M+H]^+$	268.07504	3.44	1
Sulfometuron-methyl	0.01	$C_{15}H_{16}N_4O_5S$	$[M+H]^+$	365.09142	4.73	1.2
Sulfosulfuron	0.01	$C_{16}H_{18}N_6O_7S_2$	$[M+H]^+$	471.07512	5.3	-0.77
Sulfoxaflor	0.01	$C_{10}H_{10}F_3N_3OS$	$[M+H]^+$	278.05695	3.91	0.8
Sulfluramid	0.01	$C_{10}H_6F_{17}NO_2S$	$[M-H]^-$	527.99206	8.32	5.6**
Sulprofos sulfoxide	0.01	$C_{12}H_{19}O_3PS_3$	$[M+H]^+$	339.03067	6.37	3.5**
Systhane™	0.01	$C_{15}H_{17}ClN_4$	$[M+H]^+$	289.12145	6.16	2.94
Tau-fluvalinate	0.01	$C_{26}H_{22}ClF_3N_2O_3$	$[M+H]^+$	503.13438	9.02	7.7**
TDCPP	0.01	$C_9H_{15}Cl_6O_4P$	$[M+H]^+$	430.88829	6.89	3.65
Tebuconazole (Folicur®)	0.01	$C_{16}H_{22}ClN_3O$	$[M+H]^+$	308.15242	6.49	3.7
Tebufenozide	0.01	$C_{22}H_{28}N_2O_2$	$C_{18}H_{21}N_2O_2^+$	297.15975	6.82	4.25
Tebufenpyrad	0.01	$C_{18}H_{24}ClN_3O$	$[M+H]^+$	334.16807	7.86	4.61
Tebupirimfos	0.01	$C_{13}H_{23}N_2O_3PS$	$[M+H]^+$	319.12398	8.21	4.2
Tebutam	0.01	$C_{15}H_{23}NO$	$[M+H]^+$	234.18524	6.72	3.4**
Tebuthiuron	0.01	$C_9H_{16}N_4OS$	$[M+H]^+$	229.11176	4.06	1.79
Teflubenzuron	0.01	$C_{14}H_6Cl_2F_4N_2O_2$	$[M+H]^+$	380.98152	7.46	4.56
Telithromycin	0.01	$C_{43}H_{65}N_5O_{10}$	$[M+H]^+$	812.48042	3.89	4.2
Tembotrione	0.01	$C_{17}H_{16}ClF_3O_6S$	$[M+NH_4]^+$	458.06465	5.97	-1.09
Tepraloxydim	0.01	$C_{17}H_{24}ClNO_4$	$[M+H]^-$	342.14666	6.44	2.6**
Terbufos	0.01	$C_9H_{21}O_2PS_3$	$[M+H]^+$	289.05141	8.09	4.48
Terbufos sulfone	0.01	$C_9H_{21}O_4PS_3$	$[M+H]^+$	321.04124	6.33	2.5**

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Terbufos sulfoxide	0.01	$C_9H_{21}O_3PS_3$	$[M+H]^+$	305.04633	5.74	2.2**
Terbumeton	0.01	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.41	3.1**
Terbumeton-desethyl	0.01	$C_8H_{15}N_5O$	$[M+H]^+$	198.13494	3.27	2.1**
Terbutaline sulfate	0.01	$C_{24}H_{40}N_2O_{10}S$	$[M+H]^+$	549.24764	/	/
Terbuthylazine	0.01	$C_9H_{16}ClN_5$	$[M+H]^+$	230.1167	5.96	3.4
Terbuthylazine-desethyl	0.01	$C_7H_{12}ClN_5$	$[M+H]^+$	202.0854	4.4	2**
Terbutol (terbucarb)	0.01	$C_{17}H_{27}NO_2$	$[M+H]^+$	278.21146	7.52	5.2**
Terbutryn	0.01	$C_{10}H_{19}N_5S$	$[M+H]^+$	242.14339	5.88	3.74
Terbutylazine-2-hydroxy	0.01	$C_9H_{17}N_5O$	$[M+H]^+$	212.15059	2.69	0.3**
Tetrachlorvinphos (ISO)	0.01	$C_{10}H_9Cl_4O_4P$	$[M+H]^+$	366.90367	6.65	3.53
Tetraconazole	0.01	$C_{13}H_{11}Cl_2F_4N_3O$	$[M+H]^+$	372.02881	6.33	3.56
Tetracycline	0.01	$C_{22}H_{24}N_2O_8$	$[M+H]^+$	445.16054	/	/
Tetraethyl dithiopyrophosphate	0.01	$C_8H_{20}O_5P_2S_2$	$[M+H]^+$	323.03002	7.36	3.99
Tetraethyl pyrophosphate	0.01	$C_8H_{20}O_7P_2$	$[M+H]^+$	291.07571	4.04	/
Tetramethrin	0.01	$C_{19}H_{25}NO_4$	$[M+H]^+$	332.18564	7.96	4.73
Thenylchlor	0.01	$C_{16}H_{18}ClNO_2S$	$[M+H]^+$	324.08195	6.69	3.8**
Thiabendazole	0.01	$C_{10}H_7N_3S$	$[M+H]^+$	202.04335	2.43	2.47
Thiacloprid	0.01	$C_{10}H_9ClN_4S$	$[M+H]^+$	253.03092	3.9	1.26
Thiamethoxam	0.01	$C_8H_{10}ClN_5O_3S$	$[M+H]^+$	292.02657	2.63	-0.13
Thiamphenicol	0.01	$C_{12}H_{15}Cl_2NO_5S$	$[M+H]^+$	373.03863	2.48	-0.3
Thiazafluron	0.01	$C_6H_7F_3N_4OS$	$[M+H]^+$	241.03654	4.41	0.8**
Thiazopyr	0.01	$C_{16}H_{17}F_5N_2O_2S$	$[M+H]^+$	397.10037	7.3	3.89
Thidiazuron	0.01	$C_9H_8N_4OS$	$[M+H]^-$	221.04916	4.09	1.77
Thiencarbazone-methyl	0.01	$C_{12}H_{14}N_4O_7S_2$	$[M+H]^+$	391.03767	4.54	1.2**
Thifensulfuron-methyl	0.01	$C_{12}H_{13}N_5O_6S_2$	$[M+H]^+$	388.038	4.41	/
Thifluzamide	0.01	$C_{13}H_6Br_2F_6N_2O_2S$	$[M+H]^+$	528.84733	6.91	6**
Thiobencarb	0.01	$C_{12}H_{16}ClNOS$	$[M+H]^+$	258.07139	7.36	3.4
Thiocarbazyl	0.01	$C_{16}H_{25}NOS$	$[M+H]^+$	280.17296	8.55	/
Thiocyclam hydrogen oxalate	0.01	$C_7H_{13}NO_4S_3$	$[M+H]^+$	272.00795	/	/
Thiodicarb	0.01	$C_{10}H_{18}N_4O_4S_3$	$[M+H]^+$	355.0563	4.71	1.62
Thiofanox	0.01	$C_9H_{18}N_2O_2S$	$[M+Na]^+$	241.09812	5.02	2.2**
Thiofanox sulfone	0.01	$C_9H_{18}N_2O_4S$	$[M+H]^+$	251.10601	3.38	0.9**
Thiofanox sulfoxide	0.01	$C_9H_{18}N_2O_3S$	$[M+H]^+$	235.11109	2.8	0.8**
Thionazin (Zinophos™)	0.01	$C_8H_{13}N_2O_3PS$	$[M+H]^+$	249.04573	5.66	2**
Thiophanate-methyl	0.01	$C_{12}H_{14}N_4O_4S_2$	$[M+H]^+$	343.05293	4.48	2.6**
Thiophanate-ethyl	0.01	$C_{14}H_{18}N_4O_4S_2$	$[M+H]^+$	371.08423	5.49	3.3**

Compound	MRL (mg.kg^{-1})*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Tiadinil	0.01	$C_{11}H_{10}ClN_3OS$	$[M+H]^-$	268.03059	6.13	3**
Tiamulin	0.01	$C_{28}H_{47}NO_4S$	$[M+H]^+$	494.32986	4.86	4.5
Tiamulin fumarate	0.01	$C_{32}H_{51}NO_8S$	$[M+H]^+$	610.34082	/	/
Ticarcillin	0.01	$C_{15}H_{16}N_2O_6S_2$	$[M+H]^+$	385.05226	/	/
Tildipirosin	0.01	$C_{41}H_{71}N_3O_8$	$[M+H]^+$	751.55794	/	/
Tilmicosin	0.01	$C_{46}H_{80}N_2O_{13}$	$[M+Na]^+$	891.55526	9.33	/
Tokuthion®	0.01	$C_{11}H_{15}Cl_2O_2PS_2$	$[M+H]^+$	344.97009	8.96	4.9**
Tolclofos-methyl	0.01	$C_9H_{11}Cl_2O_3PS$	$[M+H]^+$	300.96164	7.47	4.56
Tolfenamic acid	0.01	$C_{14}H_{12}ClNO_2$	$[M-H]^-$	262.06293	7.02	5.2
Tolfenpyrade	0.01	$C_{21}H_{22}ClN_3O_2$	$[M+H]^+$	384.14733	7.84	4.7**
Toltrazuril	0.01	$C_{18}H_{14}F_3N_3O_4S$	$[M+H]^+$	426.07299	6.76	2.9
Toltrazuril sulfone	0.01	$C_{18}H_{14}F_3N_3O_6S$	$[M+H]^+$	458.06282	6.09	2.7
Tolylfluanid	0.01	$C_{10}H_{13}Cl_2FN_2O_2S_2$	$[M+H]^+$	346.98523	7.35	3.9
Topramezone	0.01	$C_{16}H_{17}N_3O_5S$	$[M+H]^+$	364.09617	3.57	1.44
Tralkoxydim	0.01	$C_{20}H_{27}NO_3$	$[M+H]^+$	330.20637	8.24	4.1**
Triadimefon	0.01	$C_{14}H_{16}ClN_3O_2$	$[M+H]^+$	294.10038	6.27	2.77
Triadimenol (Baytan®)	0.01	$C_{14}H_{18}ClN_3O_2$	$[M+H]^+$	296.11603	5.78	3.56
Triallate	0.01	$C_{10}H_{16}Cl_3NOS$	$[M+H]^+$	304.0091	8.5	4.6
Triasulfuron	0.01	$C_{14}H_{16}ClN_5O_5S$	$[M+H]^+$	402.06334	4.75	-0.59
Triazamate	0.01	$C_{13}H_{22}N_4O_3S$	$[M+H]^+$	315.14854	6.69	2.7**
Triaziflam	0.01	$C_{17}H_{24}FN_5O$	$[M+H]^+$	334.20377	6.12	3.5**
Triazophos	0.01	$C_{12}H_{16}N_3O_3PS$	$[M+H]^+$	314.07228	6.58	3.34
Triazoxid	0.01	$C_{10}H_6ClN_5O$	$[M+H]^+$	248.03336	4.56	0.9**
Tribenuron-methyl	0.01	$C_{15}H_{17}N_5O_6S$	$[M+H]^+$	396.09723	5.55	0.78
Tribufos (defiolant)	0.01	$C_{12}H_{27}OPS_3$	$[M+H]^+$	315.10345	8.89	3.2**
Trichlorfon	0.01	$C_4H_8Cl_3O_4P$	$[M+H]^+$	256.92986	2.9	0.51
Triclabendazole	0.01	$C_{14}H_9Cl_3N_2OS$	$[M+H]^+$	358.95739	6.97	5.5
Triclabendazole sulfone	0.01	$C_{14}H_9Cl_3N_2O_3S$	$[M+H]^+$	390.94722	6.50	4.5
Triclabendazole sulfoxide	0.01	$C_{14}H_9Cl_3N_2O_2S$	$[M+H]^+$	374.95231	6.16	4.4
Tricyclazole	0.01	$C_9H_7N_3S$	$[M+H]^+$	190.04335	3.57	1.7
Tridemorph (mixture of isomers)	0.01	$C_{19}H_{39}NO$	$[M+H]^+$	298.31044	6.43	6.9**
Tridiphane	0.01	$C_{10}H_7Cl_5O$	$[M+H]^+$	320.89832	/	4.7**
Trietazine	0.01	$C_9H_{16}ClN_5$	$[M+H]^+$	230.1167	6.58	3.34
Trifloxystrobin	0.01	$C_{20}H_{19}F_3N_2O_4$	$[M+H]^+$	409.13697	7.64	4.5
Trifloxystrobin metabolite	0.01	$C_{19}H_{17}F_3N_2O_4$	$[M+H]^+$	395.12132	6.71	4.3**
Trifloxysulfuron sodium	0.01	$C_{14}H_{13}F_3N_5NaO_6S$	$[M+H]^+$	460.05091	5.07	/

Compound	MRL ($mg.kg^{-1}$)*	Formula [M]	Ion	Theoretical m/z	T_R (min)	LogP
Triflumizole	0.01	$C_{15}H_{15}ClF_3N_3O$	$[M+H]^+$	346.09285	7.12	2.9
Triflumuron	0.01	$C_{15}H_{10}ClF_3N_2O_3$	$[M+H]^+$	359.04048	7	4.91
Trifluralin	0.01	$C_{13}H_{16}F_3N_3O_4$	$[M+H]^+$	336.11657	8.17	5.34
Triflusulfuron-methyl	0.01	$C_{17}H_{19}F_3N_6O_6S$	$[M+H]^+$	493.11117	6.22	3.1**
Triforine	0.01	$C_{10}H_{14}Cl_6N_4O_2$	$[M+H]^+$	434.92917	5.3	2.2
Trimethoprim	0.01	$C_{14}H_{18}N_4O_3$	$[M+H]^+$	291.14517	2.20	0.4
Trinexapac-ethyl	0.01	$C_{13}H_{16}O_5$	$[M+H]^+$	253.10705	5.52	0.9**
Triphenyl phosphorothionate	0.01	$C_{18}H_{15}O_3PS$	$[M+H]^+$	343.05523	8.21	6.3**
Tris(2-chloroethyl) phosphate (TRCP)	0.01	$C_6H_{12}Cl_3O_4P$	$[M+H]^+$	284.96116	4.71	1.78
Tri-*o*-cresyl phosphate (TCP)	0.01	$C_{21}H_{21}O_4P$	$[M+H]^+$	369.12502	8.28	6.34
Triticonazole	0.01	$C_{17}H_{20}ClN_3O$	$[M+H]^+$	318.13677	6.03	3.29
Tritosulfuron	0.01	$C_{13}H_9F_6N_5O_4S$	$[M-H]^-$	446.03522	5.93	3.1**
Trovafloxacin	0.01	$C_{20}H_{15}F_3N_4O_3$	$[M+H]^+$	417.11690	3.33	0.3
Tulathromycin	0.01	$C_{41}H_{79}N_3O_{12}$	$[M+H]^+$	806.57365	/	/
Tylosin	0.01	$C_{46}H_{77}NO_{17}$	$[M+H]^+$	916.52643	4.55	1
Tylvalosin	0.01	$C_{53}H_{87}NO_{19}$	$[M+H]^+$	1042.59451	/	/
Uniconazole	0.01	$C_{15}H_{18}ClN_3O$	$[M+H]^+$	292.12112	6.22	3.6**
Valnemulin	0.01	$C_{31}H_{52}N_2O_5S$	$[M+H]^+$	565.36697	5.17	5.3
Vamidothion	0.01	$C_8H_{18}NO_4PS_2$	$[M+H]^+$	288.04877	2.92	0.16
Vamidothion sulfoxide	0.01	$C_8H_{18}NO_5PS_2$	$[M+H]^+$	304.04368	0.93	-1.1
Vedaprofen	0.01	$C_{19}H_{22}O_2$	$[M+H]^+$	300.19581	7.62	5.7
Vernolate	0.01	$C_{10}H_{21}NOS$	$[M+H]^+$	204.14166	7.57	/
Virginiamycin M1	0.01	$C_{28}H_{35}N_3O_7$	$[M+H]^+$	526.25478	5.1	2.5
XMC (3,5-xylyl methylcarbamate)	0.01	$C_{10}H_{13}NO_2$	$[M+H]^+$	180.10191	4.97	2.23
Z-mevinphos	0.01	$C_7H_{13}O_6P$	$[M+H]^+$	193.02604	3.06	1.2**
Zoxamide	0.01	$C_{14}H_{16}Cl_3NO_2$	$[M+H]^+$	336.03194	7.2	3.76

***** General default maximum residue limit (MRL) value in seafood matrices

****** LogP predicted by XLogP3 (PubChem)

Table S2. Taguchi L9 orthogonal array (TOA) used for optimization of sample preparation (3 factors, 3 levels).

Experiment	Factor		
	Extraction solvent	dSPE sorbent	Dilution
1	1	1	1
2	1	2	3
3	1	3	2
4	2	1	3
5	2	2	2
6	2	3	1
7	3	1	2
8	3	2	1
9	3	3	3

Table S3. Ultra-high performance liquid chromatography-quadrupole time-of-flight mass spectrometry (UHPLC-Q-TOF-MS) conditions.

Instrument	Parameter	Condition		
UHPLC	Column temperature	50°C		
	Injection volume	10 µL		
	Flow rate	0.5 $mL.min^{-1}$		
	Mobile phase	A: H_2O containing 0.01% formic acid		
		B: ACN containing 0.01% formic acid		
		Time (min)	% A	% B
		0	90	10
		9	0	100
		12	0	100
		12.1	90	10
		16	90	10
Q-TOF-MS	Ion source type	ESI		
	Ion spray voltage floating (ISVF)	(+) 5500 V, (-) 4500 V		
	Source temperature (TEM)	500 °C		
	Curtain gas (CUR)	30 psi		
	Nebulising gas (GS1)	40 psi		
	Heater gas (GS2)	45 psi		

ACN, acetonitrile

Table S4. Pesticide detection rates observed in the L9 orthogonal array used for the optimisation of sample preparation.

Experiment	Factor			Mean detection rate (%)	SD
	Extraction solvent	dSPE sorbent	Dilution		
1	1	1	1	96.08	0.85
2	1	2	3	65.52	0.75
3	1	3	2	78.43	8.36
4	2	1	3	72.88	5.93
5	2	2	2	80.88	3.21
6	2	3	1	83.66	1.50
7	3	1	2	57.03	3.44
8	3	2	1	82.84	2.98
9	3	3	3	56.54	2.21
K1*	80.01	76.42	87.53		
K2	79.14	75.33	72.11		
K3	65.47	72.88	64.98		
R**	14.54	3.54	22.55		
***F*-value**	15.01	0.74	29.97		
p*-value**	< 0.05	> 0.05	< 0.05		

* The average detection rate for each level (Ki), used to select the best level for each factor.

** The range of detection rates, used to rank factors by their impact on the detection rate. The higher this value, the greater the impact of the given parameter on the response.

*** One-way ANOVA test

Table S5. Veterinary drug detection rates of L9 orthogonal array (TOA) for the optimisation of sample preparation.

Experiment	Factor			Mean detection rate (%)	SD
	Extraction solvent	dSPE sorbent	Dilution		
1	1	1	1	53.75	1.25
2	1	2	3	54.17	1.57
3	1	3	2	59.58	4.52
4	2	1	3	57.29	4.25
5	2	2	2	67.92	2.82
6	2	3	1	82.71	0.72
7	3	1	2	51.88	6.53
8	3	2	1	63.75	3.31
9	3	3	3	38.33	0.95
K1*	55.83	54.31	66.74		
K2	69.31	61.94	59.79		
K3	51.32	60.21	49.93		
R**	17.99	7.64	16.81		
***F*-value**	24.24	4.44	19.74		
p*-value**	< 0.05	< 0.05	< 0.05		

* The average detection rate for each level (Ki), used to select the best level for each factor.
** The range of detection rates, used to rank the factors by their impact on the detection rate. The higher this value, the greater the impact of the given parameter on the response.
*** One-way ANOVA test

Table S6. Validation results for 850 contaminants across 24 samples spiked at 0.001, 0.01 and 0.1 mg.kg^{-1} with corresponding screening detection limit (SDL) and limit of identification (LOI).

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
1-(3,4-Dichlorophenyl)-3-methylurea	24	24	24	0.001	24	24	24	0.001
1-(4-Nitrophenyl)-3-propylure	24	24	24	0.001	24	24	24	0.001
1,2-Benzisothiazol-3(*2H*)-one	24	24	24	0.001	22	24	24	0.01
1,3-Diphenylurea	24	24	24	0.001	24	24	24	0.001
2,3,5-Trimethacarb	24	24	24	0.001	24	24	24	0.001
2,4-Dimethylaniline	24	24	24	0.001	24	24	24	0.001
2,6-Dichlorobenzamide	24	24	24	0.001	13	22	24	0.1
2,6-Diethylaniline	24	24	24	0.001	22	24	24	0.01
2-Ethylhexyl diphenyl phosphate	24	24	24	0.001	24	23	24	0.001
2-N-Octyl-4-isothiazolin-3-one	3	24	24	0.01	0	23	24	0.01
3,4-Dichloroaniline	24	24	24	0.001	23	24	24	0.001
3,4,5-Trimethacarb	24	24	24	0.001	24	24	24	0.001
3-Hydroxycarbofuran	24	24	24	0.001	24	24	24	0.001
3-Ketocarbofuran	24	24	24	0.001	8	20	24	0.1
4-Acethylaminoantipyrine	24	24	24	0.001	24	24	24	0.001
4-Aminoantipyrine	20	22	24	0.1	10	22	24	0.1
4-Bromo-3,5-dimethylphenyl-N-methylcarbamate	24	24	24	0.001	19	24	23	0.01
4-Dimethylaminoantipyrine	17	24	24	0.01	12	24	24	0.01
4-Formylaminoantipyrine	23	24	24	0.001	16	24	24	0.01
4-Methylaminoantipyrine	10	24	24	0.01	10	24	24	0.01
5-Hydroxy-flunixin	24	24	24	0.001	24	24	24	0.001
8-Hydroxy-mutilin	23	24	24	0.001	0	0	13	> 0.1
Abamectin	22	23	24	0.01	0	0	0	> 0.1
Abamectin B1a	22	22	23	0.1	18	22	23	0.1
Abamectin B1b	17	21	24	0.1	9	16	24	0.1
Abate® (temephos)	24	24	24	0.001	24	24	24	0.001
Acephate	24	24	24	0.001	2	3	21	> 0.1
Acetamiprid	24	24	24	0.001	24	24	24	0.001
Acibenzolar-*S*-methyl	24	24	24	0.001	24	24	24	0.001
Aclonifen	24	24	24	0.001	0	0	0	> 0.1
Aconitine	24	24	24	0.001	24	24	24	0.001
Akton	21	24	24	0.01	3	16	22	> 0.1
Alachlor	24	24	24	0.001	0	0	0	> 0.1

Compounds	No. of detections			SDL ($mg.kg^{-1}$)	No. of identifications			LOI ($mg.kg^{-1}$)
	0.001 $mg.kg^{-1}$	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$		0.001 $mg.kg^{-1}$	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$	
Albendazole	24	24	24	0.001	24	24	24	0.001
Albendazole amino sulfone	24	24	24	0.001	24	24	24	0.001
Albendazole sulfone	24	24	24	0.001	24	24	24	0.001
Albendazole sulfoxide	24	24	24	0.001	24	24	24	0.001
Aldicarb	24	24	24	0.001	11	22	24	0.1
Aldicarb sulfone	24	24	24	0.001	24	24	24	0.001
Aldicarb sulfoxide	5	2	4	> 0.1	1	0	0	> 0.1
Allethrin	24	24	24	0.001	4	21	22	> 0.1
Allidochlor	24	24	24	0.001	0	12	24	0.1
Alloxydim sodium	22	23	24	0.01	3	21	24	0.1
Alpha-cypermethrin	0	0	1	> 0.1	0	0	0	> 0.1
Ametoctradin	24	24	24	0.001	24	24	24	0.001
Ametryne	24	24	24	0.001	24	24	24	0.001
Amicarbazone	24	24	24	0.001	22	24	23	0.01
Amidosulfuron	24	24	24	0.001	24	24	24	0.001
Amino flubendazole	24	24	24	0.001	24	24	24	0.001
Amino mebendazole	22	24	24	0.01	22	23	24	0.01
Aminocarb	22	22	24	0.1	22	22	24	0.1
Amitraze	2	24	24	0.01	2	24	24	0.01
Amoxicillin	20	24	24	0.01	0	4	20	> 0.1
Ampicillin +4	24	23	24	0.001	19	21	23	0.1
Ancymidol	24	24	24	0.001	2	11	24	0.1
Anilazine	24	24	24	0.001	7	14	13	> 0.1
Anilofos	24	24	24	0.001	24	24	24	0.001
Antipyrine phenazone	24	24	24	0.001	24	24	24	0.001
Aspon ™	24	24	24	0.001	24	24	24	0.001
Asulam	24	24	24	0.001	24	24	24	0.001
Atraton	24	24	24	0.001	24	24	24	0.001
Atrazine	21	22	24	0.1	20	21	23	0.1
Atrazine desisopropyl	24	24	24	0.001	13	22	24	0.1
Azaconazole	24	24	24	0.001	24	24	24	0.001
Azadirachtin (technical)	17	20	18	> 0.1	0	0	0	> 0.1
Azamethiphos	24	24	24	0.001	24	24	24	0.001
Azimsulfuron	24	24	24	0.001	24	24	24	0.001
Aziprotryne	24	24	24	0.001	24	23	23	0.001
Azoxystrobin	24	24	24	0.001	24	24	24	0.001
Barban	0	3	5	> 0.1	0	0	0	> 0.1

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Beflubutamid	24	24	24	0.001	24	24	24	0.001
Benalaxyl	24	24	24	0.001	24	24	24	0.001
Benazolin	24	24	24	0.001	0	0	0	> 0.1
Benfluralin (benefin)	2	0	0	> 0.1	0	0	0	> 0.1
Benfuresate	12	16	18	> 0.1	0	1	0	> 0.1
Benodanil	24	24	24	0.001	24	24	24	0.001
Benomyl	11	13	19	> 0.1	3	6	5	> 0.1
Benoxacor	24	24	24	0.001	1	12	10	> 0.1
Bensulfuron-methyl	24	24	24	0.001	24	24	24	0.001
Bensulide	24	24	24	0.001	22	24	24	0.01
Bentazon	24	24	24	0.001	24	24	24	0.001
Bentazon-methyl	1	0	0	> 0.1	1	0	0	> 0.1
Benthiavalicarb-isopropyl	24	24	24	0.001	24	24	24	0.001
Benzoximate	24	24	24	0.001	24	24	24	0.001
Benzoylprop ethyl	24	24	24	0.001	23	24	24	0.001
Benzthiazuron	24	24	24	0.001	24	24	24	0.001
Bioresmethrin	24	24	24	0.001	22	24	24	0.01
Bitertanole (mixture of isomers)	24	24	24	0.001	15	24	24	0.01
Bixafen	24	24	24	0.001	23	24	24	0.001
Bladex	24	24	24	0.001	24	24	24	0.001
Boscalid	24	24	24	0.001	24	24	24	0.001
Bromacil	24	24	24	0.001	24	24	24	0.001
Bromofenvinphos-ethyl	24	24	24	0.001	24	24	24	0.001
Bromophos-methyl	2	18	19	> 0.1	0	0	0	> 0.1
Bromuconazole (mixture of isomers)	24	24	24	0.001	24	24	24	0.001
Bupirimate	24	24	24	0.001	24	24	24	0.001
Buprofezin	24	24	24	0.001	24	24	24	0.001
Butachlor	24	24	24	0.001	20	23	24	0.01
Butafenacil	24	24	24	0.001	24	24	24	0.001
Butocarboxim	0	1	0	> 0.1	0	0	0	> 0.1
Butocarboxim sulfoxide	2	3	2	> 0.1	1	0	0	> 0.1
Butoxycarboxim	24	24	24	0.001	24	24	24	0.001
Butroxydim	24	24	24	0.001	23	24	24	0.001
Buturon	24	24	24	0.001	24	24	24	0.001
Butylate	24	24	24	0.001	18	24	24	0.01
Cadusafos	24	24	24	0.001	24	24	24	0.001
Cafenstrole	23	24	24	0.001	16	21	21	> 0.1

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Carbaryl	24	24	24	0.001	21	24	24	0.01
Carbendazim	24	24	24	0.001	24	24	24	0.001
Carbetamide	24	24	24	0.001	24	24	24	0.001
Carbofuran	24	24	24	0.001	24	24	24	0.001
Carbophenothion	2	24	24	0.01	0	22	23	0.1
Carboxine	24	24	24	0.001	24	24	23	0.001
Carfentrazone-ethyl	24	24	24	0.001	24	24	24	0.001
Carprofen	24	24	24	0.001	24	24	24	0.001
Carpropamid	24	24	24	0.001	24	24	24	0.001
Cefalexine	24	24	24	0.001	9	24	24	0.01
Cefapirine	1	1	23	0.1	0	0	22	> 0.1
Cefazolin	24	24	24	0.001	2	4	17	> 0.1
Cefoperazone	24	24	24	0.001	24	24	24	0.001
Ceftiofur +4	24	24	24	0.001	24	24	24	0.001
Cefuroxim	24	24	24	0.001	17	11	18	> 0.1
Chinomethionate	24	24	24	0.001	23	24	24	0.001
Chlorantraniliprole	24	24	24	0.001	24	24	24	0.001
Chlorbromuron	24	24	24	0.001	17	24	24	0.01
Chlordimeform	24	24	24	0.001	23	24	24	0.001
Chlorfenapyr	7	19	20	> 0.1	0	1	14	> 0.1
Chlorfenvinphos (mixture of Z and E)	24	24	24	0.001	24	24	24	0.001
Chlorfluazuron	24	24	24	0.001	24	24	24	0.001
Chloridazon	24	24	24	0.001	24	24	24	0.001
Chlorimuron-ethyl	24	24	24	0.001	24	24	24	0.001
Chlorobenzuron	24	24	24	0.001	23	24	24	0.001
Chlorosulfuron	24	24	24	0.001	24	24	24	0.001
Chlorotoluron	24	24	24	0.001	24	24	24	0.001
Chloroxuron	24	24	24	0.001	24	24	24	0.001
Chlorpyrifos	23	24	24	0.001	19	24	24	0.01
Chlorpyrifos-methyl	22	24	24	0.01	1	13	20	> 0.1
Chlorpyrifos-oxon	24	24	24	0.001	24	24	24	0.001
Chlorthiamid	0	0	1	> 0.1	0	0	0	> 0.1
Chlorthiophos	20	24	24	0.01	0	0	0	> 0.1
Chromafenozide	24	24	24	0.001	24	24	24	0.001
Cinidon-ethyl	23	24	24	0.001	11	18	3	> 0.1
Cinmethylin	24	23	24	0.001	20	21	24	0.1
Cinosulfuron	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Cinoxacin	24	24	24	0.001	19	23	24	0.01
Ciprofloxacin	24	24	24	0.001	21	24	24	0.01
Clarithromycin	24	24	24	0.001	24	24	23	0.001
Clethodim	24	24	24	0.001	21	24	23	0.01
Climbazol	24	24	24	0.001	20	24	24	0.01
Clindamycin	24	24	24	0.001	24	24	24	0.001
Clodinafop (acid-free)	24	24	24	0.001	19	24	24	0.01
Clodinafop-propargyl	24	24	24	0.001	24	24	24	0.001
Clofentezine	24	24	24	0.001	24	24	24	0.001
Clomeprop	24	24	24	0.001	24	24	24	0.001
Cloquintocet-mexyl	24	24	24	0.001	24	24	24	0.001
Cloransulam-methyl	24	24	24	0.001	24	24	24	0.001
Clorsulon	24	24	24	0.001	24	24	24	0.001
Closantel	24	24	24	0.001	24	24	24	0.001
Clothianidin	24	24	24	0.001	24	24	24	0.001
Cloxacillin	24	24	24	0.001	19	23	24	0.01
Command (clomazone)	24	24	24	0.001	24	24	24	0.001
Coumaphos	24	24	24	0.001	23	24	24	0.001
Coumaphos-oxon	24	24	24	0.001	24	24	24	0.001
Crimidine	24	24	24	0.001	24	24	24	0.001
Crotoxyphos	24	24	24	0.001	5	10	3	> 0.1
Cumyluron	24	24	24	0.001	24	22	24	0.001
Cyanofenphos	0	6	13	> 0.1	0	2	2	> 0.1
Cyanophos	24	24	24	0.001	0	0	0	> 0.1
Cyantraniliprole	24	24	24	0.001	24	24	24	0.001
Cyazofamid	24	24	24	0.001	24	23	24	0.001
Cyclanilide	24	24	24	0.001	24	24	24	0.001
Cycloate	24	24	24	0.001	8	24	24	0.01
Cyclohexamide	24	24	24	0.001	1	4	23	0.1
Cycloprothrin	0	3	8	> 0.1	0	0	0	> 0.1
Cyclosulfamuron	24	24	24	0.001	24	24	24	0.001
Cycloxidim	24	24	24	0.001	19	24	24	0.01
Cycluron	24	24	24	0.001	24	23	24	0.001
Cyflufenamid	24	24	23	0.001	23	24	23	0.001
Cyhalofop-butyl	9	14	23	0.1	3	5	11	> 0.1
Cymiazole	24	24	24	0.001	24	24	24	0.001
Cymoxanil	24	24	24	0.001	1	12	24	0.1

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Cypermethrin (mixture of isomers)	0	2	5	> 0.1	0	0	0	> 0.1
Cyphenothrin	12	22	23	0.1	0	6	15	> 0.1
Cyprazine	23	24	24	> 0.1	18	20	22	> 0.1
Cyproconazole (mixture of isomers)	24	24	24	0.001	24	23	24	0.001
Cyprodinil	24	24	24	0.001	24	24	24	0.001
Cyprofuram	24	24	24	0.001	24	24	24	0.001
Cyprosulfamide	24	24	24	0.001	24	24	24	0.001
Cyromazine	22	23	24	0.01	5	15	24	0.1
Cythioate	24	24	24	0.001	0	2	2	> 0.1
Daimuron	24	24	24	0.001	22	24	24	0.01
Daminozide	19	24	24	0.01	0	1	7	> 0.1
Danitol	21	23	24	0.01	14	17	22	> 0.1
Danofloxacin	24	24	24	0.001	23	24	24	0.001
Dapsone	24	24	24	0.001	23	24	24	0.001
Dazomet	5	21	21	> 0.1	0	0	7	> 0.1
Dementon-*S*-methyl sulfone	24	24	24	0.001	24	24	24	0.001
Demeton S	23	24	24	0.001	18	20	19	> 0.1
Demeton-*S*-methyl	13	16	20	> 0.1	0	0	0	> 0.1
Deoxynivalenol	4	4	0	> 0.1	0	0	0	> 0.1
Desethyl atrazine	24	24	24	0.001	22	24	24	0.01
Desfuroylceftiofur cysteine disulfide (DCCD)	22	24	24	0.01	5	12	16	> 0.1
Desmedipham	24	24	24	0.001	24	24	24	0.001
Desmethyl norflurazon	24	24	24	0.001	24	24	24	0.001
Desmethyl-formamido-pirimicarb	24	24	24	0.001	24	24	24	0.001
Desmetryn	9	24	24	0.01	9	24	24	0.01
Diafenthiuron	0	0	1	> 0.1	0	0	0	> 0.1
Dialifos	24	24	24	0.001	21	22	24	0.1
Diazinon	24	24	24	0.001	24	24	24	0.001
Diazinon-O-analog	24	24	24	0.001	24	24	24	0.001
Dibrom	17	24	23	0.01	0	0	0	> 0.1
Dichlofenthion	18	24	24	0.01	1	8	19	> 0.1
Dichlormid	24	24	24	0.001	10	15	23	0.1
Dichlorvos	24	24	24	0.001	2	14	24	0.1
Diclazuril	23	24	24	0.001	23	24	24	0.001
Diclobutrazol (mixture of stereo isomers)	24	24	24	0.001	24	23	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Diclocymet	24	24	24	0.001	24	24	24	0.001
Diclofenac	24	24	24	0.001	24	24	24	0.001
Diclosulam	24	24	24	0.001	24	24	24	0.001
Dicrotophos	24	24	24	0.001	24	24	24	0.001
Diethatyl-ethyl	24	24	24	0.001	24	24	24	0.001
Diethofencarb	24	24	24	0.001	24	24	24	0.001
Difenoconazole (mixture of isomers)	24	24	24	0.001	24	24	24	0.001
Difenoxurone	24	24	24	0.001	24	24	24	0.001
Difloxacin	24	24	24	0.001	24	24	24	0.001
Diflubenzuron	24	24	24	0.001	24	24	24	0.001
Diflufenicen	24	24	24	0.001	24	24	24	0.001
Dimefox	24	24	24	0.001	11	11	19	> 0.1
Dimefuron	24	24	24	0.001	24	24	24	0.001
Dimepiperate	24	24	24	0.001	24	24	23	0.001
Dimethachlor	24	24	24	0.001	24	24	24	0.001
Dimethametryn	24	24	24	0.001	24	24	24	0.001
Dimethenamid	24	24	24	0.001	24	24	24	0.001
Dimethirimol	24	24	24	0.001	24	24	24	0.001
Dimethoate	24	24	24	0.001	24	24	24	0.001
Dimethomorph	24	24	24	0.001	24	24	24	0.001
Dimethylvinphos	24	24	24	0.001	24	24	24	0.001
Dimetilan	24	24	24	0.001	24	24	24	0.001
Dimetridazole	24	24	24	0.001	24	24	24	0.001
Dimoxystrobin	24	24	24	0.001	24	24	24	0.001
Diniconazole (E isomer)	24	24	24	0.001	24	24	24	0.001
Diniconazole (Z isomer)	24	24	24	0.001	24	24	24	0.001
Dinitramine	24	24	24	0.001	24	24	24	0.001
Dinotefuran	24	24	24	0.001	24	24	24	0.001
Dioxacarb	24	24	24	0.001	24	24	24	0.001
Dioxathion (mixture of isomers)	0	1	0	> 0.1	0	0	0	> 0.1
Diphenamid	24	24	24	0.001	24	24	24	0.001
Diphenyl phosphate	1	0	2	> 0.1	0	0	0	> 0.1
Diphenylamine	24	24	24	0.001	24	24	24	0.001
Dipropetryn	24	24	24	0.001	24	24	24	0.001
Disulfoton sulfone	24	24	24	0.001	13	22	23	0.1
Disulfoton sulfoxide	24	24	24	0.001	24	24	24	0.001
Ditalimfos	24	24	24	0.001	23	24	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Dithianon	0	11	18	> 0.1	0	0	3	> 0.1
Dithiopyr	24	24	24	0.001	24	24	24	0.001
Diuron	24	24	24	0.001	24	24	24	0.001
DMA	24	24	24	0.001	24	24	24	0.001
DMF	24	24	24	0.001	22	24	24	0.01
DMPF	24	24	24	0.001	24	24	24	0.001
Dodemorph	24	24	24	0.001	24	24	24	0.001
Doramectin	24	24	24	0.001	23	24	24	0.001
Dyfonate™	24	24	24	0.001	17	24	23	0.01
Edifenphos	24	24	24	0.001	24	24	24	0.001
Emamectin	7	24	24	0.01	0	24	24	0.01
Emamectin B1a	24	24	24	0.001	24	24	24	0.001
Empenthrin	9	24	24	0.01	0	3	9	> 0.1
Enrofloxacin	24	24	24	0.001	24	24	24	0.001
Epn	24	24	24	0.001	2	11	21	> 0.1
Epoxiconazole (iso)	24	24	24	0.001	24	24	24	0.001
Eprinomectin	23	24	24	0.001	21	24	24	0.01
Eprinomectin B1a	23	24	24	0.001	21	24	24	0.01
EPTC (S-ethyl dipropylthiocarbamate)	24	24	24	0.001	1	2	5	> 0.1
Erythromycin	24	24	24	0.001	24	24	24	0.001
Erythromycin	24	24	24	0.001	24	24	24	0.001
Esbiol	24	24	24	0.001	4	21	22	> 0.1
Esprocarb	24	24	24	0.001	24	24	24	0.001
Etaconazole	24	24	24	0.001	24	24	24	0.001
Ethaboxam	24	24	24	0.001	24	24	24	0.001
Ethametsulfuron-methyl	24	24	24	0.001	24	24	24	0.001
Ethidimuron	24	24	24	0.001	23	24	24	0.001
Ethiofencarb	24	24	24	0.001	24	24	24	0.001
Ethiofencarb sulfone	24	24	24	0.001	24	24	23	0.001
Ethiofencarb sulfoxide	24	24	24	0.001	24	24	24	0.001
Ethion	24	24	24	0.001	23	23	23	0.001
Ethiozin	17	22	22	> 0.1	14	20	20	> 0.1
Ethiprole	24	24	24	0.001	24	24	24	0.001
Ethirimol	24	24	24	0.001	24	24	24	0.001
Ethofumesate	24	24	24	0.001	0	0	0	> 0.1
Ethoprophos (prophos)	24	24	24	0.001	24	24	24	0.001
Ethoxyquin	6	19	24	0.1	3	15	22	> 0.1

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Ethoxysulfuron	24	24	24	0.001	21	21	24	0.1
Ethyclozate	24	24	24	0.001	24	24	24	0.001
Etobenzanid	24	24	24	0.001	22	24	24	0.01
Etoxazole	24	24	24	0.001	24	24	24	0.001
Etrimfos	24	24	24	0.001	24	24	24	0.001
Famoxadone	5	0	2	> 0.1	2	0	0	> 0.1
Famphur	24	24	24	0.001	23	24	24	0.001
Fenamidone	24	24	24	0.001	24	24	24	0.001
Fenamiphos	24	24	24	0.001	24	24	24	0.001
Fenamiphos sulfone	24	24	24	0.001	24	24	24	0.001
Fenamiphos sulfoxide	24	24	24	0.001	15	8	1	> 0.1
Fenarimol	24	24	24	0.001	24	24	24	0.001
Fenazaquin	24	24	24	0.001	24	24	24	0.001
Fenazox	24	24	24	0.001	8	20	22	> 0.1
Fenbendazole	24	24	24	0.001	24	24	24	0.001
Fenbuconazole	24	24	24	0.001	24	24	24	0.001
Fenchlorazol-ethyl	24	24	24	0.001	23	24	24	0.001
Fenchlorphos-oxon	24	24	24	0.001	22	24	24	0.01
Fenclorim	3	1	5	> 0.1	0	0	0	> 0.1
Fenfuram	24	24	24	0.001	24	24	24	0.001
Fenhexamid	24	24	24	0.001	24	24	24	0.001
Fenitrothion	20	23	24	0.01	7	22	24	0.1
Fenobucarb	23	24	24	0.001	23	23	24	0.001
Fenothiocarb	24	24	24	0.001	24	24	24	0.001
Fenoxanil	24	24	24	0.001	24	24	24	0.001
Fenoxaprop	24	24	24	0.001	24	24	24	0.001
Fenoxaprop-P-ethyl	24	24	24	0.001	24	24	24	0.001
Fenoxycarb	24	24	24	0.001	24	24	24	0.001
Fenpiclonil	24	24	24	0.001	24	24	24	0.001
Fenpropathrin	21	23	24	0.01	14	17	23	0.1
Fenpropidin	24	24	24	0.001	24	24	24	0.001
Fenpropimorph	24	24	24	0.001	24	24	24	0.001
Fenpyroximate	24	24	24	0.001	24	24	24	0.001
Fensulfothion	24	24	24	0.001	24	24	24	0.001
Fensulfothion-oxon	24	24	24	0.001	24	24	24	0.001
Fensulfothion-oxon sulfone	24	24	24	0.001	24	24	24	0.001
Fensulfothion sulfone	24	24	24	0.001	7	20	24	0.1

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Fenthion	24	24	24	0.001	1	19	24	0.1
Fenthion-oxon	24	24	24	0.001	24	24	24	0.001
Fenthion-oxon sulfoxide	24	24	24	0.001	24	24	23	0.001
Fenthion sulfoxide	24	24	24	0.001	24	24	24	0.001
Fenthion-ethyl	24	24	24	0.001	3	24	24	0.01
Fenthion sulfone	24	24	24	0.001	1	6	17	> 0.1
Fenthoxon sulfone	24	24	24	0.001	24	24	24	0.001
Fenuron	24	24	24	0.001	24	24	24	0.001
Ferimzone	10	24	24	0.01	6	23	23	0.01
Fipronil	24	24	24	0.001	22	18	24	0.1
Fipronil sulfide	23	24	24	0.001	22	24	24	0.01
Fipronil-desulfinyl	24	24	24	0.001	22	24	24	0.01
Flamprop-isopropyl	24	24	24	0.001	24	24	24	0.001
Flamprop-methyl (Metaven)	24	24	24	0.001	9	17	20	> 0.1
Flamprop-M-isopropyl	24	24	24	0.001	24	24	24	0.001
Flazasulfuron	24	24	24	0.001	3	6	4	> 0.1
Fleroxacin	24	24	24	0.001	24	24	24	0.001
Flonicamid	24	24	24	0.001	24	24	24	0.001
Florasulam	24	24	24	0.001	24	24	24	0.001
Florfénicol	24	24	24	0.001	24	24	24	0.001
Fluacrypyrim	24	24	24	0.001	23	24	24	0.001
Fluazifop	24	24	24	0.001	24	24	24	0.001
Fluazifop-butyl	24	24	24	0.001	24	24	24	0.001
Fluazifop-P-butyl	24	24	24	0.001	24	24	24	0.001
Fluazinam	24	24	24	0.001	24	24	24	0.001
Fluazuron	24	24	24	0.001	24	24	23	0.001
Flubendazole	24	24	24	0.001	24	24	24	0.001
Flubendiamide	24	24	24	0.001	24	24	24	0.001
Flucarbazone sodium	22	24	24	0.01	10	20	23	0.1
Fluchloralin	1	17	24	0.1	0	1	0	> 0.1
Flucycloxuron	24	24	24	0.001	24	24	24	0.001
Fludioxonil	10	10	20	> 0.1	0	0	0	> 0.1
Flufenacet	24	24	24	0.001	23	24	24	0.001
Flufenoxuron	24	24	24	0.001	24	24	24	0.001
Flumequine	23	23	23	0.001	23	23	23	0.001
Flumestulam	24	24	24	0.001	24	24	24	0.001
Flumetralin	2	20	22	> 0.1	0	0	0	> 0.1

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Flumiclorac-pentyl	24	24	24	0.001	24	24	24	0.001
Flumioxazin	24	24	24	0.001	22	24	24	0.01
Flumorph	24	24	24	0.001	24	24	24	0.001
Flunixin	24	24	24	0.001	24	24	24	0.001
Fluoglycofene-ethyl	22	24	23	0.01	14	15	16	> 0.1
Fluometuron	24	24	24	0.001	24	24	24	0.001
Fluopicolide	24	24	24	0.001	24	24	24	0.001
Fluopyram	24	24	24	0.001	24	24	24	0.001
Fluorodifen	1	1	0	> 0.1	1	1	0	> 0.1
Fluoxastrobin	24	24	24	0.001	24	24	24	0.001
Flupyradifurone	24	24	24	0.001	23	24	24	0.001
Flupyrsulfuron-methyl sodium	20	24	24	0.01	0	0	0	> 0.1
Fluquinconazole	24	24	24	0.001	24	24	24	0.001
Fluralaner	23	24	24	0.001	23	24	24	0.001
Fluridone	24	24	24	0.001	24	24	24	0.001
Flurilazole	22	18	23	0.1	0	2	19	> 0.1
Flurochloridon (iso)	24	24	24	0.001	17	24	24	0.01
Fluroxypyr	24	24	24	0.001	24	24	24	0.001
Fluroxypyr-meptyl	24	24	24	0.001	18	24	24	0.01
Flurprimidol	24	24	24	0.001	24	24	24	0.001
Flurtamone	24	24	24	0.001	24	24	24	0.001
Flusilazole	24	24	24	0.001	24	24	24	0.001
Fluthiacet-methyl	24	24	24	0.001	24	24	24	0.001
Flutolanil	24	24	24	0.001	24	24	24	0.001
Flutriafol	24	24	24	0.001	24	24	24	0.001
Fomesafen	23	24	24	0.001	22	20	24	0.1
Foramsulfuron	24	24	24	0.001	24	24	24	0.001
Forchlorfenuron	24	24	24	0.001	24	24	24	0.001
Formetanate HCl	6	0	24	0.1	0	0	24	0.1
Fosthiazate	24	24	24	0.001	24	24	24	0.001
Fuberidazole	24	24	24	0.001	24	24	24	0.001
Furalaxyl	24	24	24	0.001	24	24	24	0.001
Furathiocarb	24	24	24	0.001	24	24	24	0.001
Furmecyclox	24	24	24	0.001	24	24	24	0.001
Fusidic acid	23	24	24	0.001	23	24	23	0.001
Gamithromycin	24	24	24	0.001	23	24	24	0.001
Guthion-ethyl	21	17	24	0.1	1	5	8	> 0.1

Compounds	No. of detections			SDL ($mg.kg^{-1}$)	No. of identifications			LOI ($mg.kg^{-1}$)
	0.001 $mg.kg^{-1}$	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$		0.001 $mg.kg^{-1}$	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$	
Guthion®	2	0	11	> 0.1	0	0	5	> 0.1
Halofenozide	24	24	24	0.001	24	24	24	0.001
Halofuginone	24	24	24	0.001	24	24	24	0.001
Halosulfuron-methyl	24	24	24	0.001	24	24	24	0.001
Haloxyfop	9	18	3	> 0.1	0	6	0	> 0.1
Haloxyfop-2-ethoxyethyl	24	24	24	0.001	24	24	24	0.001
Haloxyfop-methyl	24	24	24	0.001	24	24	24	0.001
Haloxyfop-P-methyl	24	24	24	0.001	24	24	24	0.001
Heptenophos	24	24	24	0.001	22	24	24	0.01
Hexaconazole	24	24	24	0.001	24	24	24	0.001
Hexaflumuron	24	24	24	0.001	23	24	24	0.001
Hexazinon	24	24	24	0.001	24	24	24	0.001
Hexythiazox	24	24	24	0.001	24	24	24	0.001
HMMNI	23	24	24	0.001	20	23	24	0.01
Hydroxy-flubendazole	24	24	24	0.001	24	24	24	0.001
Hydroxy-mebendazole	24	24	24	0.001	24	24	24	0.001
Hydroxy-thiabendazole	24	24	24	0.001	24	24	24	0.001
Hymexazole	19	22	24	0.1	0	0	0	> 0.1
Imazalil	24	24	24	0.001	24	24	24	0.001
Imazamethabenz-methyl	24	24	24	0.001	24	24	24	0.001
Imazamox	24	24	24	0.001	24	24	24	0.001
Imazapic	24	24	24	0.001	24	24	24	0.001
Imazaquin	24	24	24	0.001	24	24	24	0.001
Imazethapyr	24	24	24	0.001	24	24	24	0.001
Imazosulfuron	24	24	24	0.001	24	24	24	0.001
Imibenconazole	24	24	24	0.001	24	24	24	0.001
Imidacloprid	24	24	24	0.001	24	24	24	0.001
Imidacloprid-olefin	24	24	24	0.001	22	24	24	0.01
Inabenfide	24	24	24	0.001	24	24	24	0.001
Indaziflam	24	24	24	0.001	24	24	24	0.001
Indoxacarb	24	24	24	0.001	24	24	24	0.001
Iodofenphos	5	18	19	> 0.1	0	2	9	> 0.1
Iodosulfuron-methyl sodium	18	24	23	0.01	1	16	19	> 0.1
Ipconazole	24	24	24	0.001	24	24	24	0.001
Iprobenfos	24	24	24	0.001	24	24	24	0.001
Iprodione	20	24	24	0.01	1	6	10	> 0.1
Ipronidazole	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Ipronidazole OH	24	24	24	0.001	18	24	24	0.01
Iprovalicarb	24	24	24	0.001	24	24	24	0.001
Irgarol (cybutryne)	24	24	24	0.001	24	24	24	0.001
Isazophos	24	24	24	0.001	24	24	24	0.001
Isocarbamide	24	24	24	0.001	14	21	24	0.1
Isofenphos	24	24	24	0.001	24	24	24	0.001
Isofenphos-methyl	22	23	24	0.01	19	19	24	0.1
Isofenphos-oxon	24	24	24	0.001	24	24	24	0.001
Isomethiozin	24	24	24	0.001	24	24	24	0.001
Isonoruron	24	24	24	0.001	24	24	24	0.001
Isoprocarb	24	24	24	0.001	24	24	24	0.001
Isopropalin	24	24	24	0.001	8	22	23	0.1
Isoprothiolane	24	24	24	0.001	24	24	24	0.001
Isoproturon	24	24	24	0.001	24	24	24	0.001
Isouron	24	24	24	0.001	23	24	24	0.001
Isoxaben	24	24	24	0.001	24	24	24	0.001
Isoxadifen-ethyl	24	24	24	0.001	23	24	24	0.001
Isoxaflutole	24	24	24	0.001	20	23	23	0.01
Isoxathion	24	24	24	0.001	23	24	24	0.001
Ivermectin	24	24	24	0.001	0	0	0	> 0.1
Ivermectin B1a	24	24	24	0.001	0	16	21	> 0.1
Josamycin	24	24	23	0.001	24	24	23	0.001
Karbutilate	24	24	24	0.001	22	24	24	0.01
Ketoprofen	24	24	24	0.001	24	24	24	0.001
Ketotriclabendazole	24	24	24	0.001	24	24	24	0.001
Kresoxim Methyl	18	24	24	0.01	18	23	24	0.01
Lactofen	22	24	24	0.01	15	22	23	0.1
Lasalocid A	24	24	24	0.001	24	24	24	0.001
Lenacil	24	24	24	0.001	23	24	24	0.001
Leptophos	7	21	22	> 0.1	1	11	20	> 0.1
Levamisole	22	24	24	0.01	22	24	24	0.01
Levofloxacin	24	24	24	0.001	23	24	23	0.001
Lincomycin	24	24	24	0.001	24	24	24	0.001
Linuron	24	24	24	0.001	24	24	24	0.001
Lomefloxacin	24	24	24	0.001	24	24	24	0.001
Lufenuron	24	24	24	0.001	23	24	24	0.001
Maduramicin	19	22	23	0.1	19	22	23	0.1

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Malaoxon	24	24	24	0.001	23	23	24	0.001
Malathion	24	24	24	0.001	20	22	24	0.1
Mandipropamid	24	24	24	0.001	24	24	24	0.001
Marbofloxacin	24	24	24	0.001	21	24	24	0.01
Mebendazole	24	24	24	0.001	24	24	24	0.001
Mefenacet	24	24	24	0.001	24	24	24	0.001
Mefenamic acid	24	24	24	0.001	24	24	24	0.001
Mefenpyr-diethyl	24	24	24	0.001	24	24	24	0.001
Mefluidide	24	24	24	0.001	24	24	24	0.001
Meloxicam	24	24	24	0.001	24	24	24	0.001
Mepanipyrim	24	24	24	0.001	24	24	24	0.001
Mephosfolan	24	24	24	0.001	24	24	24	0.001
Mepronil	24	24	24	0.001	24	24	23	0.001
Mesosulfuron-methyl	24	24	24	0.001	24	24	24	0.001
Mesotrione	24	24	24	0.001	23	23	24	0.001
Metaflumizone	24	24	24	0.001	24	24	24	0.001
Metalaxyl	24	24	24	0.001	24	24	24	0.001
Metalaxyl-m	24	24	24	0.001	24	24	24	0.001
Metamitron	24	24	24	0.001	18	24	24	0.01
Metazachlor	24	24	24	0.001	24	24	24	0.001
Metconazole	24	24	24	0.001	24	24	24	0.001
Methabenzthiazuron	24	24	24	0.001	24	24	24	0.001
Methacrifos	8	20	21	> 0.1	0	0	0	> 0.1
Methfuroxam	24	24	24	0.001	24	24	24	0.001
Methidathion	24	24	24	0.001	4	17	23	0.1
Methiocarb	24	24	24	0.001	18	19	24	0.1
Methiocarb sulfone	24	24	24	0.001	19	21	24	0.1
Methiocarb sulfoxide	24	24	24	0.001	24	24	24	0.001
Methoprotryne	24	24	24	0.001	24	24	24	0.001
Methoxyfenozide	24	24	24	0.001	24	24	24	0.001
Methyl paraoxon	24	24	24	0.001	16	24	24	0.01
Methyl parathion	23	24	24	0.001	0	0	0	> 0.1
Metobromuron	24	24	24	0.001	24	24	24	0.001
Metolachlor	24	24	24	0.001	24	24	24	0.001
Metolcarb	22	24	24	0.01	17	23	24	0.01
(E)-Metominostrobin	24	24	24	0.001	24	24	24	0.001
(Z)-Metominostrobin	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Metosulam	24	24	24	0.001	24	24	24	0.001
Metoxuron	24	24	24	0.001	24	24	23	0.001
Metrafenone	24	24	24	0.001	24	24	24	0.001
Metribuzin	24	24	24	0.001	24	24	24	0.001
Metronidazole	24	24	24	0.001	20	24	23	0.01
Metsulfuron-methyl	24	24	24	0.001	24	24	24	0.001
Mevinphos	24	24	24	0.001	24	24	24	0.001
Mexacarbate	24	24	24	0.001	24	24	24	0.001
MGK-264 (mixture of isomers)	24	24	24	0.001	15	24	24	0.01
Molinate	24	24	24	0.001	9	21	24	0.1
Monensin	24	24	24	0.001	24	24	24	0.001
Monepantel	24	24	24	0.001	23	24	24	0.001
Monepantel sulfone	24	24	24	0.001	24	24	24	0.001
Monocrotophos	24	24	24	0.001	23	24	24	0.001
Monolinuron	24	24	24	0.001	24	24	24	0.001
Monuron	24	24	24	0.001	24	24	24	0.001
Morantel	24	24	24	0.001	24	24	24	0.001
Moxidectin	24	24	24	0.001	15	24	24	0.01
N,N-Diethyl-*m*-toluamide (DEET)	24	24	24	0.001	24	24	24	0.001
N,N'-Ethylenethiourea	0	0	3	> 0.1	0	0	0	> 0.1
Nafcillin	24	24	24	0.001	22	23	24	0.01
Naphthalophos (naftalofos)	24	24	24	0.001	24	24	24	0.001
Napropamide	24	24	24	0.001	24	24	24	0.001
Naproxen	23	24	24	0.001	20	24	23	0.01
Naptalam	24	24	24	0.001	23	24	24	0.001
Narasin	24	24	24	0.001	24	24	24	0.001
Neburon	24	24	24	0.001	24	24	24	0.001
Nicosulfuron	24	24	24	0.001	23	24	24	0.001
Nigericin	24	24	24	0.001	24	24	24	0.001
Nitenpyram (ISO)	24	24	24	0.001	21	24	24	0.01
Nitralin	23	23	24	0.001	0	0	0	> 0.1
Nitroguanidine	12	20	24	0.1	0	0	0	> 0.1
Nitroxinil	24	24	24	0.001	24	24	24	0.001
Norfloxacin	24	24	24	0.001	24	24	23	0.001
Norflurazon	24	24	24	0.001	24	24	24	0.001
Noruron	24	24	24	0.001	24	24	24	0.001
Novaluron	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Novobiocin	24	24	24	0.001	23	24	24	0.001
Nuarimol	24	24	24	0.001	24	24	24	0.001
O-Acetyltylosin	24	24	24	0.001	24	24	24	0.001
Ofloxacin	24	24	24	0.001	23	24	23	0.001
Ofurace	24	24	24	0.001	24	24	24	0.001
Oleandomycin	24	24	24	0.001	22	24	24	0.01
Omethoate	1	1	0	> 0.1	0	0	0	> 0.1
Orbencarb	24	24	24	0.001	24	24	24	0.001
Orbifloxacin	24	24	24	0.001	24	24	24	0.001
Ormetoprime	24	24	24	0.001	24	24	24	0.001
Orysastrobin	24	24	24	0.001	24	24	24	0.001
Oryzalin	24	24	24	0.001	24	24	24	0.001
Oxacillin	24	24	24	0.001	24	24	24	0.001
Oxadiargyl	24	24	24	0.001	0	12	16	> 0.1
Oxadiazon	22	23	24	0.01	13	22	23	0.1
Oxadixyl	24	24	24	0.001	24	24	24	0.001
Oxasulfuron	24	24	24	0.001	24	24	24	0.001
Oxaziclomefone	24	24	24	0.001	24	24	24	0.001
Oxfendazole (fenbendazole sulfoxide)	24	24	24	0.001	24	24	24	0.001
Oxfendazole sulfone (fenbendazole sulfone)	24	24	24	0.001	24	24	24	0.001
Oxibendazole	24	24	24	0.001	24	24	24	0.001
Oxolinic acid	24	24	24	0.001	23	23	24	0.001
Oxycarboxin	24	24	24	0.001	24	24	24	0.001
Oxyclozanide	24	24	24	0.001	23	24	24	0.001
Oxyfluorfen	15	22	24	0.1	1	8	21	> 0.1
Oxyphenbutazone	24	24	24	0.001	24	24	24	0.001
Paclobutrazol (mixture of stereo isomers)	24	24	24	0.001	24	24	24	0.001
Paraoxon-ethyl	24	24	24	0.001	23	24	24	0.001
Parathion	24	24	24	0.001	1	6	17	> 0.1
Pebulate	24	24	24	0.001	0	12	24	0.1
Penconazol	24	24	24	0.001	24	24	24	0.001
Pencycuron	24	24	24	0.001	24	24	24	0.001
Pendimethalin	24	24	24	0.001	9	20	23	0.1
Penfluron	23	24	24	0.001	23	24	24	0.001
Pénicillin-G	24	24	24	0.001	21	24	24	0.01
Penicilllin-V^{+4}	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Penoxsulam	24	24	24	0.001	24	24	24	0.001
Pentanochlor	24	24	24	0.001	24	24	24	0.001
Penthiopyrad	24	24	24	0.001	24	24	24	0.001
Pethoxamid	24	24	24	0.001	24	24	24	0.001
Phenmedipham	24	24	24	0.001	24	24	24	0.001
Phenothrin	1	24	24	0.01	0	18	23	0.1
Phenthoate	24	24	24	0.001	6	20	21	> 0.1
Phenylbutazone	24	24	24	0.001	21	24	24	0.01
Phenylurea	23	24	24	0.001	23	24	24	0.001
Phorate-oxon sulfoxide	24	24	24	0.001	4	15	15	> 0.1
Phorate sulfoxide	24	24	24	0.001	24	24	24	0.001
Phorate-oxon sulfone	24	24	24	0.001	24	24	24	0.001
Phorat sulfone	24	24	24	0.001	6	19	23	0.1
Phosalone	24	24	24	0.001	19	22	22	> 0.1
Phosfolan	24	24	24	0.001	24	24	24	0.001
Phosmet	24	24	24	0.001	23	24	24	0.001
Phosmet-oxon	24	24	24	0.001	24	24	24	0.001
Phosphamidon	24	24	24	0.001	24	24	24	0.001
Phospholan-methyl	24	24	24	0.001	23	24	24	0.001
Phoxim	24	24	24	0.001	24	24	24	0.001
Phthalylsulfathiazole (CAS)	24	24	24	0.001	24	24	24	0.001
Picolinafen	24	24	24	0.001	7	9	9	> 0.1
Picoxystrobin	24	24	24	0.001	24	24	24	0.001
Piperalin	24	24	24	0.001	24	24	24	0.001
Piperonyl butoxide	24	24	24	0.001	24	24	24	0.001
Piperophos	24	24	24	0.001	24	24	24	0.001
Pirimicarb	24	24	24	0.001	24	24	24	0.001
Pirimicarb-desmethyl	24	24	24	0.001	24	24	24	0.001
Pirimiphos-methyl	24	24	24	0.001	24	24	24	0.001
Pirimiphos-ethyl	24	24	24	0.001	24	24	24	0.001
Pirimiphos-methyl-N-desethyl	24	24	24	0.001	24	24	24	0.001
Pirlymycin	24	24	24	0.001	24	24	24	0.001
Prallethrin	24	24	24	0.001	2	15	24	0.1
Pretilachlor	24	24	24	0.001	24	24	24	0.001
Primisulfuron-methyl	24	24	24	0.001	24	24	24	0.001
Probenazole	24	24	24	0.001	6	16	22	> 0.1
Prochloraz	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL ($mg.kg^{-1}$)	No. of identifications			LOI ($mg.kg^{-1}$)
	0.001 $mg.kg^{-1}$	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$		0.001 $mg.kg^{-1}$	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$	
Procyazine	24	24	24	0.001	24	24	24	0.001
Procymidone	20	24	24	0.01	18	23	23	0.01
Profenofos	24	24	24	0.001	21	20	23	0.1
Profoxydim lithium	24	24	24	0.001	21	24	24	0.01
Prohydrojasmon	7	24	24	0.01	0	5	19	> 0.1
Promecarb	23	24	24	0.001	23	23	24	0.001
Prometon	24	24	24	0.001	24	24	24	0.001
Prometryn	24	24	24	0.001	24	24	24	0.001
Propachlor	24	24	24	0.001	24	24	24	0.001
Propanil	24	24	24	0.001	24	24	24	0.001
Propaphos	24	24	24	0.001	24	24	24	0.001
Propaquizafop	24	24	24	0.001	24	24	24	0.001
Propargite	24	24	24	0.001	23	24	24	0.001
Propazine	24	24	24	0.001	24	24	24	0.001
Propazine-2-hydroxy	24	24	24	0.001	24	24	24	0.001
Propetamphos	14	21	23	0.1	0	0	0	> 0.1
Propham	24	24	24	0.001	23	24	24	0.001
Propiconazol (mixture of isomers)	24	24	24	0.001	24	24	24	0.001
Propisochlor	24	24	24	0.001	24	24	24	0.001
Propoxur	24	24	24	0.001	23	24	24	0.001
Propyzamide (pronamide)	24	24	24	0.001	24	24	24	0.001
Proquinazid	24	24	24	0.001	24	24	24	0.001
Prosulfocarb	24	24	24	0.001	24	24	24	0.001
Prosulfuron	24	24	24	0.001	24	24	24	0.001
Prothioconazole-desthio	24	24	24	0.001	24	24	24	0.001
Pymetrozine	22	24	24	0.01	22	24	24	0.01
Pyracarbolid	24	24	24	0.001	24	24	24	0.001
Pyraclofos	24	24	24	0.001	23	24	24	0.001
Pyraclostrobin	24	24	24	0.001	24	24	24	0.001
Pyraflufen-ethyl	24	24	24	0.001	24	24	24	0.001
Pyrantel	24	24	24	0.001	24	24	24	0.001
Pyrazolynate	24	24	24	0.001	24	24	24	0.001
Pyrazophos	24	24	24	0.001	24	24	24	0.001
Pyrazosulfuron-ethyl	24	24	24	0.001	24	24	24	0.001
Pyrazoxyfen	24	24	24	0.001	24	24	24	0.001
Pyrethrin (mixture of isomers)	2	4	0	> 0.1	0	0	0	> 0.1
Pyributicarb	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Pyridaben	24	24	24	0.001	24	24	24	0.001
Pyridafol	24	24	24	0.001	24	24	24	0.001
Pyridalyl	24	24	24	0.001	24	24	24	0.001
Pyridaphenthion	24	24	24	0.001	24	24	24	0.001
Pyridate	24	24	24	0.001	24	24	24	0.001
Pyrifenox (mixture of isomers))	24	24	24	0.001	24	24	24	0.001
Pyrimethanil	24	24	24	0.001	24	24	24	0.001
Pyriproxyfen	24	24	24	0.001	24	24	24	0.001
Pyroquilon	24	24	24	0.001	24	24	24	0.001
Pyroxsulam	24	24	24	0.001	24	24	24	0.001
Quinalphos	24	24	24	0.001	24	24	24	0.001
Quinclorac	24	24	24	0.001	23	24	24	0.001
Quinmerac	16	24	24	0.01	16	24	24	0.01
Quinoclamine	24	24	24	0.001	22	24	24	0.01
Quinoline	24	24	24	0.001	24	24	24	0.001
Quinoxyfen	24	24	24	0.001	24	24	24	0.001
Quizalofop	24	24	24	0.001	23	24	24	0.001
Quizalofop-ethyl	24	24	24	0.001	24	24	24	0.001
Quizalofop-P-ethyl	24	24	24	0.001	24	24	24	0.001
Rafoxanide	23	24	24	0.001	22	24	24	0.01
Reserpine	24	24	24	0.001	23	24	23	0.001
Resmethrin	24	24	24	0.001	22	24	24	0.01
Rifampicin	5	16	20	> 0.1	2	14	17	> 0.1
Rifaximine	20	22	24	0.1	18	22	24	0.1
Rimsulfuron	24	24	24	0.001	20	24	23	0.01
Robenidine	24	24	24	0.001	24	24	24	0.001
Rotenone	24	24	23	0.001	24	24	23	0.001
Roxithromycin	24	24	23	0.001	24	24	23	0.001
Saflufenacil	24	24	24	0.001	21	24	24	0.01
Salinomycin	24	24	24	0.001	24	24	24	0.001
Sarafloxacin	24	24	24	0.001	24	24	24	0.001
Schradan (DMPA)	24	24	24	0.001	24	24	24	0.001
Sebuthylazin	22	24	23	0.01	22	24	24	0.01
Sebuthylazin-desethyl	24	24	24	0.001	24	24	24	0.001
Secbumeton	1	24	24	0.01	1	24	24	0.01
Selamectin impurity B	24	24	24	0.001	24	24	24	0.001
Sethoxydim	24	24	24	0.001	18	23	24	0.01

Compounds	No. of detections			SDL ($mg.kg^{-1}$)	No. of identifications			LOI ($mg.kg^{-1}$)
	0.001 $mg.kg^{-1}$	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$		0.001 $mg.kg^{-1}$	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$	
Siduron	24	24	24	0.001	24	24	24	0.001
Simazine	24	24	24	0.001	24	24	24	0.001
Simeconazole	24	24	24	0.001	23	24	24	0.001
Simetone	24	24	24	0.001	24	24	24	0.001
Simetryn	9	24	24	0.01	9	24	24	0.01
S-Metolachlor	24	24	24	0.001	24	24	24	0.001
Spinetoram (mixture of isomers)	1	24	24	0.01	0	24	24	0.01
Spinosad (mixure Of spinosyn A and B)	2	24	24	0.01	0	24	24	0.01
Spiramycin	24	24	24	0.001	22	24	24	0.01
Spirodiclofen	24	24	23	0.001	24	24	23	0.001
Spiromesifen	24	24	24	0.001	24	24	24	0.001
Spirotetramat	24	24	24	0.001	24	24	24	0.001
Spirotetramat-enol	24	24	24	0.001	24	24	24	0.001
Spirotetramat-enol-glucoside	24	24	24	0.001	24	23	24	0.001
Spirotetramat-mono-hydroxy	24	24	24	0.001	24	24	24	0.001
Spiroxamine (mixture of isomers)	24	24	24	0.001	24	24	24	0.001
Sulcotrione	24	24	24	0.001	7	8	7	> 0.1
Sulfacetamide	24	24	24	0.001	24	24	24	0.001
Sulfachloropyridazine	24	24	24	0.001	24	24	24	0.001
Sulfaclozine	24	24	24	0.001	24	24	24	0.001
Sulfadiazine	24	24	24	0.001	22	24	24	0.01
Sulfadimerazine	24	24	24	0.001	24	24	24	0.001
Sulfadimethoxine	24	24	24	0.001	24	24	24	0.001
Sulfadoxine	24	24	24	0.001	24	24	24	0.001
Sulfaguanidine	21	23	24	0.01	2	4	24	0.1
Sulfallate	22	24	24	0.01	8	9	18	> 0.1
Sulfamerazine	24	24	24	0.001	24	24	24	0.001
Sulfamethizole	24	24	24	0.001	24	24	24	0.001
Sulfamethoxazole	24	24	24	0.001	24	24	24	0.001
Sulfamethoxypyridazine	24	24	24	0.001	24	24	24	0.001
Sulfamonomethoxine	24	24	24	0.001	24	24	24	0.001
Sulfamonomethoxine	24	24	24	0.001	24	24	24	0.001
Sulfanilamide	24	24	24	0.001	1	13	16	> 0.1
Sulfaphenazole	24	24	24	0.001	24	24	24	0.001
Sulfaquinoxaline	24	24	24	0.001	24	24	24	0.001
Sulfathiazole	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Sulfentrazone	24	24	24	0.001	24	24	24	0.001
Sulfisoxazole	24	24	24	0.001	24	24	24	0.001
Sulfometuron-methyl	24	24	24	0.001	24	24	24	0.001
Sulfosulfuron	24	24	24	0.001	24	24	24	0.001
Sulfoxaflor	24	24	24	0.001	24	24	24	0.001
Sulfuramid	19	18	24	0.1	19	18	24	0.1
Sulprofos sulfoxide	24	24	24	0.001	24	24	24	0.001
Systhane™	24	24	24	0.001	24	24	24	0.001
Tau-fluvalinate	20	22	22	> 0.1	15	19	21	> 0.1
TDCPP	23	24	24	0.001	11	5	12	> 0.1
Tebuconazol (Folicur®)	24	24	24	0.001	24	24	24	0.001
Tebufenozide	24	24	24	0.001	24	24	24	0.001
Tebufenpyrad	24	24	24	0.001	24	24	24	0.001
Tebupirimfos	24	24	24	0.001	24	24	24	0.001
Tebutam	24	24	24	0.001	24	24	24	0.001
Tebuthiuron	24	24	24	0.001	24	24	24	0.001
Teflubenzuron	24	24	24	0.001	21	24	24	0.01
Telithromycin	24	24	24	0.001	24	24	24	0.001
Tembotrione	24	24	24	0.001	19	22	22	> 0.1
Tepraloxydim	24	24	24	0.001	23	23	24	0.001
Terbufos	1	7	6	> 0.1	0	0	0	> 0.1
Terbufos sulfone	24	24	24	0.001	24	24	24	0.001
Terbufos sulfoxide	24	24	24	0.001	24	24	24	0.001
Terbumeton	24	24	24	0.001	24	24	24	0.001
Terbumeton-desethyl	24	24	24	0.001	24	24	24	0.001
Terbuthylazine	22	24	23	0.01	22	24	24	0.01
Terbuthylazine-desethyl	24	24	24	0.001	24	24	24	0.001
Terbutol (terbucarb)	24	24	24	0.001	24	24	24	0.001
Terbutryne	24	24	24	0.001	24	24	24	0.001
Terbutylazine-2-hydroxy	24	24	24	0.001	24	24	24	0.001
Tetrachlorvinphos (ISO)	24	24	24	0.001	0	0	0	> 0.1
Tetraconazole	24	24	24	0.001	24	24	24	0.001
Tetraethyl dithiopyrophosphate	24	24	24	0.001	24	24	24	0.001
Tetraethyl pyrophosphate	24	24	24	0.001	24	24	24	0.001
Tetramethrin	24	24	23	0.001	24	24	23	0.001
Thenylchlor	24	24	24	0.001	11	13	24	0.1
Thiabendazole	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Thiacloprid	24	24	24	0.001	24	24	24	0.001
Thiamethoxam	24	24	24	0.001	24	24	24	0.001
Thiamphenicol	24	24	24	0.001	24	23	24	0.001
Thiazafluron	24	24	24	0.001	24	24	24	0.001
Thiazopyr	24	24	24	0.001	24	24	24	0.001
Thidiazuron	24	24	24	0.001	24	24	24	0.001
Thiencarbazone-methyl	24	24	24	0.001	24	24	24	0.001
Thifensulfuron-methyl	24	24	24	0.001	24	24	24	0.001
Thifluzamide	24	24	24	0.001	0	0	0	> 0.1
Thiobencarb	24	24	24	0.001	24	24	24	0.001
Thiocarbazyl	24	24	24	0.001	24	24	24	0.001
Thiodicarb	24	24	24	0.001	24	24	24	0.001
Thiofanox	24	24	24	0.001	4	11	23	0.1
Thiofanox-sulfone	24	24	24	0.001	13	18	24	0.1
Thiofanox-sulfoxide	24	24	24	0.001	0	1	6	> 0.1
Thionazin (Zinophos^{TM})	24	24	24	0.001	22	24	24	0.01
Thiophanate-methyl	24	24	24	0.001	20	24	24	0.01
Thiophanate-ethyl	24	24	24	0.001	13	16	18	> 0.1
Tiadinil	24	24	24	0.001	24	24	24	0.001
Tiamulin	24	24	24	0.001	24	24	24	0.001
Tokuthion®	19	23	24	0.01	0	1	5	> 0.1
Tolclofos-methyl	21	23	24	0.01	1	18	23	0.1
Tolfenamic acid	24	24	24	0.001	24	24	24	0.001
Tolfenpyrade	24	24	24	0.001	23	24	24	0.001
Toltrazuril	24	24	24	0.001	5	6	18	> 0.1
Toltrazuril sulfone	23	24	24	0.001	22	23	24	0.01
Tolylfluanid	1	1	1	> 0.1	0	1	0	> 0.1
Topramezone	0	4	1	> 0.1	0	0	0	> 0.1
Tralkoxydim	24	24	24	0.001	24	24	24	0.001
Triadimefon	24	24	24	0.001	24	24	24	0.001
Triadimenol (Baytan®)	15	21	24	0.1	15	21	24	0.1
Triallate	24	24	24	0.001	8	22	24	0.1
Triasulfuron	24	24	24	0.001	24	24	24	0.001
Triazamate	24	24	24	0.001	24	24	24	0.001
Triaziflam	24	24	24	0.001	24	24	24	0.001
Triazophos	23	24	24	0.001	21	22	23	0.1
Triazoxid	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL (mg.kg^{-1})	No. of identifications			LOI (mg.kg^{-1})
	0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}		0.001 mg.kg^{-1}	0.01 mg.kg^{-1}	0.1 mg.kg^{-1}	
Tribenuron-methyl	24	24	24	0.001	0	0	0	> 0.1
Tribufos (defoliant)	24	24	24	0.001	24	24	24	0.001
Trichlorfon	24	24	24	0.001	10	19	22	> 0.1
Triclabendazole	24	24	24	0.001	24	24	24	0.001
Triclabendazole sulfone	24	24	24	0.001	24	24	24	0.001
Triclabendazole sulfoxide	24	24	24	0.001	24	24	24	0.001
Tricyclazole	24	24	24	0.001	24	24	24	0.001
Tridemorph (mixture of isomers)	0	24	0	0.01	0	21	0	> 0.1
Tridiphane	0	1	0	> 0.1	0	0	0	> 0.1
Trietazine	24	24	24	0.001	24	24	24	0.001
Trifloxystrobin	24	24	24	0.001	24	24	24	0.001
Trifloxystrobin metabolite	24	24	24	0.001	24	24	24	0.001
Trifloxysulfuron sodium	23	24	23	0.001	0	0	0	> 0.1
Triflumizole	24	24	24	0.001	24	24	24	0.001
Triflumuron	24	24	24	0.001	24	24	24	0.001
Trifluralin	2	0	1	> 0.1	0	0	0	> 0.1
Triflusulfuron-methyl	24	24	24	0.001	24	24	24	0.001
Triforine	23	24	24	0.001	16	24	24	0.01
Trimethoprim	24	24	24	0.001	24	24	24	0.001
Trinexapac-ethyl	24	24	24	0.001	2	18	20	> 0.1
Triphenyl phosphorothionate	24	24	24	0.001	9	20	24	0.1
Tris(2-chloroethyl) phosphate (TRCP)	24	24	24	0.001	5	15	23	0.1
Tri-*o*-cresyl phosphate (TCP)	24	24	24	0.001	24	24	24	0.001
Triticonazole	24	24	24	0.001	24	24	24	0.001
Tritosulfuron	24	24	24	0.001	22	24	24	0.01
Trovafloxacin	24	24	24	0.001	23	24	24	0.001
Tylosin	24	24	23	0.001	24	24	23	0.001
Uniconazole	24	24	24	0.001	24	23	24	0.001
Valnemulin	24	24	24	0.001	24	24	24	0.001
Vamidothion	24	24	24	0.001	24	24	24	0.001
Vamidothion sulfoxide	1	3	2	> 0.1	0	0	0	> 0.1
Vedaprofen	23	24	24	0.01	17	21	24	0.1
Vernolate	24	24	24	0.001	0	12	24	0.1
Virginiamycin M1	24	24	24	0.001	22	24	24	0.01
XMC (3,5-xylyl methylcarbamate)	21	24	24	0.01	1	11	23	0.1
Z-mevinphos	24	24	24	0.001	24	24	24	0.001

Compounds	No. of detections			SDL ($mg.kg^{-1}$)	No. of identifications			LOI ($mg.kg^{-1}$)
	0.001 $mg.kg^{-1}$	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$		0.001 $mg.kg^{-1}$	0.01 $mg.kg^{-1}$	0.1 $mg.kg^{-1}$	
Zoxamide	24	24	24	0.001	24	24	24	0.001

Table S7. Comparison of the results of the present study with those in the literature for the analysis of organic contaminants in seafood matrices. SDL, screening detection limit; LOI, limit of identification; LOQ, limit of quantification

Contaminants (number)	Method	% of contaminants SDL < 0.01 $mg{\cdot}kg^{-1}$	% of contaminants LOI < 0.01 $mg{\cdot}kg^{-1}$	% of contaminants LOQ < 0.01 $mg{\cdot}kg^{-1}$	Reference
Pesticides, metabolites, veterinary drugs and industrial chemicals (**850**)	QuEChUP/LC-QToF-MS	92	78	-	Preset study
Pesticides, veterinary drugs, persistent organic pollutants (POPs) and marine toxins (**756**)	QuEChERS/LC-QtoF-MS	93	-	90	(Bai et al., 2022)
Pesticides (**204**)	QuEChUP/LC-QtoF-MS	66	37	-	(Diallo et al., 2022)
Pesticides, veterinary drugs and personal care products (**182**)	QuEChERS/LC-QtoF-MS	63	54	62	(Munaretto et al., 2016)
Pesticides (**109**)	ASE[b]/GC-MS/MS	-	-	88	(Wu et al., 2011)
Pesticides and veterinary drugs (**106**)	QuEChERS/LC-MS/MS	-	-	100	(Castilla-Fernández et al., 2021)
Veterinary drugs (**96**)	QuEChERS/LC-MS/MS	-	-	96	(Park et al., 2022)
Herbicides and veterinary drugs (**84**)	QuEChERS/LC and GC-MS/MS	-	-	89	(Chang et al., 2016)
Veterinary drugs (**80**)	QuEChERS/LC-MS/MS	-	-	99	(Zhao et al., 2017)
Pesticides (**52**)	QuEChERS/LC-MS/MS	-	-	85	(Barbieri et al., 2019)
Pesticides (**50**)	GLME-MA-dSPE[c]/GC-MS/MS	-	-	76	(Kaw et al., 2021)

a '-' indicates 'not provided'
b ASE = Accelerated solvent extraction
c GLME-MA-dSPE = gas-liquid microextraction and magnetic-assisted dispersive solid phase extraction

Table S8. Target analysis results, summarising the estimated mean concentration of each identified contaminant and the concentration range for each species and for all the tested samples, expressed in mg.kg^{-1} wet weight (w.w.), along with the frequency of appearance (%FoA) of each identified contaminants through target analysis in the 24 real seafood samples. SDL; screening detection limit

Compound	LogP	SDL (mg.kg^{-1})	Positif sample	Estimated mean concentration (*range*) (mg.kg^{-1} w.w.)						%FoA in all samples
				Calibration strategy A		Calibration strategy B		Calibration strategy C		
Pesticides and their TPs										
1-(3,4-Dichlorophenyl)-3-methyl urea	2.9	0.001	Oysters (n=6)	**0.043**	*(0.031-0.063)*	**0.039**	*(0.027-0.056)*	**0.038**	*(0.027-0.056)*	63
			Mussels (n=6)	**0.048**	*(0.025-0.065)*	**0.043**	*(0.023-0.058)*	**0.045**	*(0.023-0.058)*	
			Spiny lobster (n=3)	**0.009**	*(0.003-0.012)*	**0.009**	*(0.002-0.014)*	**0.008**	*(0.001-0.013)*	
Azimsulfuron	0.7	0.001	Crayfish (n=3)	**0.007**	*(0.004-0.007)*	**0.008**	*(0.005-0.010)*	**0.009**	*(0.006-0.012)*	13
Bupirimate	2.7	0.001	Spiny lobster (n=3)	**0.001**	*(0.001-0.002)*	**<SDL**	*(<SDL-0.002)*	**<SDL**	*(<SDL-0.001)*	13
Butroxydim	1.9	0.001	Oysters (n=6)	**0.014**	*(0.012-0.019)*	**0.007**	*(0.005-0.011)*	**0.008**	*(0.006-0.011)*	50
			Mussels (n=6)	**0.016**	*(0.011-0.019)*	**0.008**	*(0.004-0.012)*	**0.007**	*(0.003-0.011)*	
Cyprazine	3.1	0.001	Mussels (n=6)	**0.009**	*(0.001-0.018)*	**0.011**	*(0.002-0.021)*	**0.009**	*(0.001-0.018)*	25
DEET	2.0	0.001	Oysters (n=6)	**0.008**	*(0.006-0.011)*	**0.008**	*(0.006-0.011)*	**0.008**	*(0.006-0.011)*	100
			Mussels (n=6)	**0.008**	*(0.007-0.010)*	**0.008**	*(0.007-0.009)*	**0.007**	*(0.006-0.009)*	
			Sole (n=3)	**0.008**	*(0.004-0.011)*	**0.006**	*(0.001-0.011)*	**0.006**	*(0.001-0.011)*	
			Horse mackerel (n=3)	**0.006**	*(0.003-0.011)*	**0.003**	*(<SDL-0.011)*	**0.003**	*(<SDL-0.011)*	
			Spiny lobster (n=3)	**0.021**	*(0.016-0.026)*	**0.026**	*(0.019-0.032)*	**0.025**	*(0.018-0.030)*	
			Crayfish (n=3)	**0.036**	*(0.031-0.047)*	**0.046**	*(0.039-0.060)*	**0.047**	*(0.039-0.062)*	
Diazinon	3.8	0.001	Oysters (n=6)	**<SDL**	*(<SDL-0.004)*	**0.001**	*(<SDL-0.004)*	**0.004**	*(0.003-0.006)*	50
			Mussels (n=6)	**<SDL**	*(<SDL-0.002)*	**<SDL**	*(<SDL-0.002)*	**<SDL**	*(<SDL-0.001)*	
Diflufenicen	4.6	0.001	Oysters (n=6)	**<SDL**	*(<SDL-0.003)*	**0.001**	*(<SDL-0.004)*	**0.003**	*(0.002-0.006)*	50
			Mussels (n=6)	**0.011**	*(0.008-0.011)*	**0.011**	*(0.008-0.013)*	**0.009**	*(0.006-0.012)*	
Diphenylamine	3.5	0.001	Oysters (n=6)	**0.005**	*(0.004-0.006)*	**0.005**	*(0.004-0.006)*	**0.006**	*(0.006-0.007)*	100
			Mussels (n=6)	**0.006**	*(0.004-0.008)*	**0.005**	*(0.004-0.008)*	**0.005**	*(0.003-0.007)*	
			Sole (n=3)	**0.007**	*(0.005-0.009)*	**0.008**	*(0.006-0.010)*	**0.008**	*(0.006-0.010)*	

			Horse mackerel (n=3)	**0.006**	*(0.004-0.007)*	**0.006**	*(0.005-0.007)*	**0.006**	*(0.005-0.007)*	
			Spiny lobster (n=3)	**0.007**	*(0.006-0.009)*	**0.007**	*(0.006-0.009)*	**0.007**	*(0.005-0.009)*	
			Crayfish (n=3)	**0.008**	*(0.005-0.011)*	**0.008**	*(0.005-0.012)*	**0.009**	*(0.006-0.012)*	
Diuron	2.7	0.001	Oysters (n=6)	**0.055**	*(0.037-0.080)*	**0.050**	*(0.034-0.072)*	**0.050**	*(0.034-0.071)*	63
			Mussels (n=6)	**0.076**	*(0.064-0.086)*	**0.069**	*(0.059-0.078)*	**0.070**	*(0.059-0.078)*	
			Spiny lobster (n=3)	**0.008**	*(0.007-0.010)*	**0.009**	*(0.008-0.011)*	**0.008**	*(0.007-0.010)*	
Fenpropimorph	4.9	0.001	Oysters (n=6)	**0.008**	*(0.004-0.013)*	**0.008**	*(0.004-0.012)*	**0.009**	*(0.005-0.013)*	25
Prosulfocarb	3.9	0.001	Oysters (n=6)	**0.012**	*(0.005-0.015)*	**0.012**	*(0.005-0.015)*	**0.012**	*(0.005-0.015)*	50
			Mussels (n=6)	**<SDL**	*(<SDL)*	**<SDL**	*(<SDL)*	**<SDL**	*(<SDL)*	
Pyroxsulam	1.7	0.001	Spiny lobster (n=3)	**<SDL**	*(<SDL)*	**<SDL**	*(<SDL)*	**<SDL**	*(<SDL)*	13
Spiroxamine	4.2	0.001	Oysters (n=6)	**<SDL**	*(<SDL-0.004)*	**0.001**	*(<SDL-0.004)*	**0.003**	*(0.002-0.006)*	50
			Mussels (n=6)	**0.009**	*(0.006-0.014)*	**0.009**	*(0.006-0.013)*	**0.008**	*(0.006-0.013)*	
Tebuconazole	3.7	0.001	Spiny lobster (n=3)	**0.004**	*(0.002-0.005)*	**0.004**	*(0.002-0.005)*	**0.004**	*(0.001-0.005)*	13
Thiabendazole	2.5	0.001	Crayfish (n=3)	**0.002**	-	**0.002**	-	**0.002**	*(0.002-0.003)*	13
Veterinary drugs and their TPs										
4-Dimethylaminoantipyrine	1.0	0.001	Crayfish (n=3)	**0.010**	*(0.008-0.013)*	**0.012**	*(0.010-0.016)*	**0.011**	*(0.009-0.016)*	13
Amino flubendazole	1.6	0.001	Mussels (n=6)	**0.011**	*(0.006-0.016)*	**0.010**	*(0.006-0.014)*	**0.009**	*(0.005-0.013)*	25
Clarithromycin	3.2	0.001	Oysters (n=6)	**0.015**	*(0.006-0.028)*	**0.016**	*(0.007-0.027)*	**0.015**	*(0.007-0.025)*	50
			Mussels (n=6)	**0.004**	*(<SDL-0.011)*	**0.006**	*(0.002-0.012)*	**0.005**	*(0.001-0.012)*	
Dapsone	1	0.001	Oysters (n=6)	**0.012**	*(0.005-0.015)*	**0.012**	*(0.006-0.014)*	**0.012**	*(0.007-0.015)*	50
			Mussels (n=6)	**0.017**	*(0.002-0.033)*	**0.016**	*(0.003-0.030)*	**0.015**	*(0.001-0.031)*	
Diclofenac	4	0.001	Oysters (n=6)	**0.052**	*(0.038-0.068)*	**0.044**	*(0.032-0.057)*	**0.043**	*(0.032-0.054)*	50
			Mussels (n=6)	**0.068**	*(0.045-0.091)*	**0.057**	*(0.038-0.075)*	**0.060**	*(0.039-0.079)*	
Vedaprofen	5.7	0.001	Sole (n=3)	**0.029**	*(0.017-0.044)*	**0.042**	*(0.026-0.062)*	**0.042**	*(0.026-0.062)*	50
			Horse mackerel (n=3)	**0.027**	*(0.018-0.034)*	**0.040**	*(0.027-0.049)*	**0.040**	*(0.027-0.049)*	
			Spiny lobster (n=3)	**0.030**	*(0.022-0.037)*	**0.039**	*(0.030-0.049)*	**0.035**	*(0.026-0.043)*	

			Crayfish (n=3)	**0.030**	*(0.026-0.034)*	**0.040**	*(0.035-0.045)*	**0.046**	*(0.041-0.051)*	
Industrial chemicals										
2-Ethylhexyl diphenyl phosphate	6.3	0.001	Oysters (n=6)	**0.018**	*(0.014-0.028)*	**0.016**	*(0.013-0.024)*	**0.017**	*(0.014-0.025)*	63
			Mussels (n=6)	**0.017**	*(0.014-0.020)*	**0.015**	*(0.012-0.018)*	**0.014**	*(0.011-0.017)*	
			Spiny lobster (n=3)	**0.005**	*(0.004-0.006)*	**0.005**	*(0.005-0.007)*	**0.005**	*(0.005-0.006)*	
Triphenyl phosphorothionate	6.3	0.001	Oysters (n=6)	**0.004**	*(0.002-0.008)*	**0.005**	*(0.004-0.009)*	**0.003**	*(0.001-0.007)*	75
			Mussels (n=6)	**0.007**	*(0.003-0.009)*	**0.008**	*(0.004-0.010)*	**0.010**	*(0.006-0.012)*	
			Sole (n=3)	**<SDL**	*(<SDL)*	**<SDL**	*(<SDL)*	**<SDL**	*(<SDL)*	
			Crayfish (n=3)	**<SDL**	*(<SDL)*	**<SDL**	*(<SDL)*	**<SDL**	*(<SDL)*	
Tris(2-chloroethyl) phosphate (TRCP)	1.8	0.001	Oysters (n=6)	**0.010**	*(0.004-0.018)*	**0.010**	*(0.005-0.017)*	**0.010**	*(0.006-0.017)*	100
			Mussels (n=6)	**0.009**	*(0.007-0.014)*	**0.009**	*(0.007-0.013)*	**0.008**	*(0.006-0.013)*	
			Sole (n=3)	**0.002**	*(0.001-0.002)*	**0.002**	*(0.001-0.003)*	**0.002**	*(0.001-0.003)*	
			Horse mackerel (n=3)	**<SDL**	*(<SDL-0.002)*	**<SDL**	*(<SDL-0.002)*	**<SDL**	*(<SDL-0.002)*	
			Spiny lobster (n=3)	**0.001**	-	**<SDL**	*(<SDL)*	**<SDL**	*(<SDL)*	
			Crayfish (n=3)	**0.002**	*(0.001-0.002)*	**<SDL**	*(<SDL-0.001)*	**<SDL**	*(<SDL-0.001)*	
Tri-*o*-cresyl phosphate (TCP)	6.3	0.001	Oysters (n=6)	**0.004**	*(0.003-0.005)*	**0.004**	*(0.004-0.005)*	**0.005**	*(0.005-0.006)*	100
			Mussels (n=6)	**0.004**	*(0.003-0.005)*	**0.004**	*(0.004-0.006)*	**0.003**	*(0.003-0.005)*	
			Sole (n=3)	**0.006**	*(0.005-0.006)*	**0.005**	*(0.004-0.006)*	**0.005**	*(0.004-0.006)*	
			Horse mackerel (n=3)	**0.003**	*(0.003-0.004)*	**0.001**	*(0.001-0.002)*	**0.001**	*(0.001-0.002)*	
			Spiny lobster (n=3)	**0.003**	*(0.003-0.004)*	**0.003**	-	**<SDL**	*(<SDL)*	
			Crayfish (n=3)	**0.004**	*(0.003-0.004)*	**0.003**	*(0.003-0.004)*	**0.004**	-	

Table S9. Suspect screening results and frequency of appearance (%FoA).

Compound	Class	Positive seafood species	%FoA
17alpha-Methyltestosterone	Antineoplastic agent	Mussels	25
2,6-Xylidine	Metabolite of lindocaine (anesthetic)	Sole	13
4-Hydroxybenzoic acid	Personal care product	Mussels	25
Allopurinol	Antigout agent	Crayfish	13
Benzocaine	Anesthetic	Crayfish	13
Betaine	Nutrient	Oysters, mussels, spiny lobster, crayfish, sole	88
Bisphenol S	Industrial chemical	Crayfish	13
Canrenone	Antimineralocorticoid	Oysters, mussels, spiny lobster, crayfish, horse mackerel	88
Chlordecone	Insecticide	Spiny lobster, crayfish	25
Chlordecole	Metabolite of chlordecone (insecticide)	Crayfish	13
Cordycepin	Antineoplastic	Oysters	25
Cytisin	Partial agonist	Mussels	25
delta9-Tetrahydrocannabinol	Cannabinoid	Oysters, mussels	50
Digitoxigenin	Cardionic agent	Oysters	25
Dihydromuronic acid	Personal care product	Crayfish	13
Dinoterb	Herbicide	Crayfish	13
Diosgenin	Antioxidant	Spiny lobster	13
Ethambutol	Antibiotic	Spiny lobster, crayfish	25
Etofylline	Lipid regulatror	Spiny lobster, crayfish	25
Fexofenadine	Antihistamine	Oysters	25
Flufenacet ESA	Metabolite of flufenacet (herbicide)	Mussels	25
Galaxolidone	Personal care product	Oysters, mussels, spiny lobster, crayfish, horse mackerel	88
Gemfibrozil	Fibrate	Oysters	25
Hydroquinidine	Antiarrhythmic agent	Horse mackerel	13
Ibuprofen	Non-steroidal anti-inflammatory drug	Oysters, mussels	50
Imidocarb	Antiprotozoal agent	Crayfish, sole, horse mackerel	38
Laurocapram	Personal care product	Spiny lobster, sole	25
Metamitron-desamino	Metabolite of metamitron (herbicide)	Mussels	25
Methylprednisolone	Immunosuppressive and anti-inflammatory drugs	Horse mackerel	13
N-ethylperfluorooctane sulfonamidoacetic acid (N-EtFOSAA)	PFOS precursor	Mussels	13
Norethindrone	Hormonal agents (progestins)	Oysters, mussels	50
Oxypurinol	Metabolite of allopunol (Antigout agent)	Crayfish	13
Phenylacetaldehyde	Personal care product	Horse mackerel	13
Progesterone	Hormonal agents (progestins)	Oysters, mussels	50
Propafenone	Antiarrhythmic agent	Mussels	25
Prostaglandin E1	Vasodilator	Oysters	25

Compound	Class	Positive seafood species	%FoA
Salicylic acid	Non-steroidal anti-inflammatory drug	Mussels	25
Sclareol	Anti-inflammatory, cholagogic and anti-cancer	Oysters	25
Tocainide	Antiarrhythmic agent	Spiny lobster, crayfish	25
Triethylene glycol bis (2-ethylhexanoate)	Industrial chemical	Spiny lobster, horse mackerel	25
Tri-isobutylphosphate	Industrial chemical	Sole	13
Tris(1,3-dichloro-2-propyl)phosphate	Industrial chemical	Mussels, crayfish, Sole	50
Tris(1-chloro-2-propyl)phosphate	Industrial chemical	Oysters, mussels, spiny lobster, crayfish, sole, horse mackerel	100
Velvione	Personal care product	Mussels, crayfish, horse mackerel	50

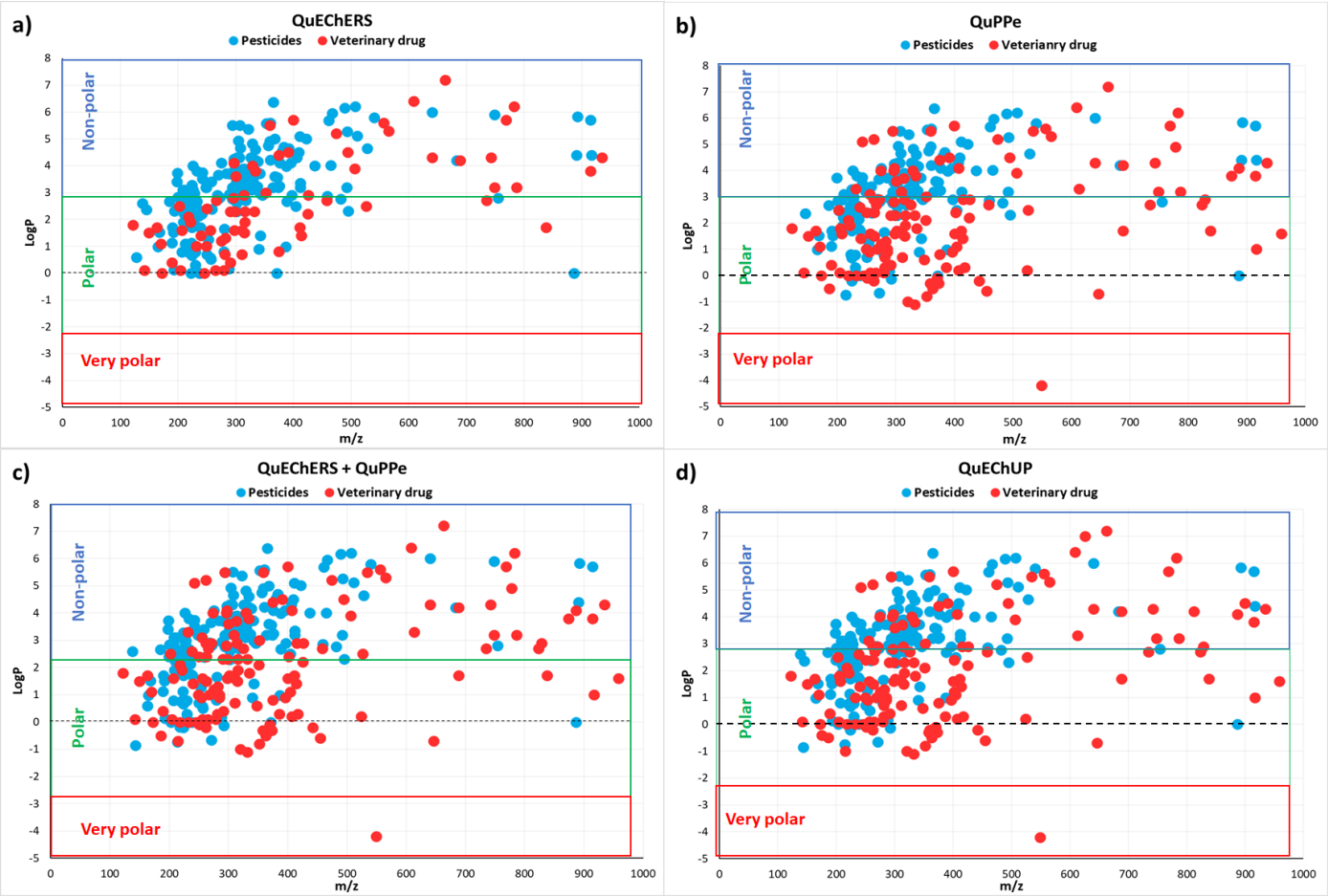

Fig. S1. Chemical coverage obtained for the QuEChERS (a), QuPPe (b), QuEChERS + QuPPe (c) and QuEChUP (d) sample preparation methods.

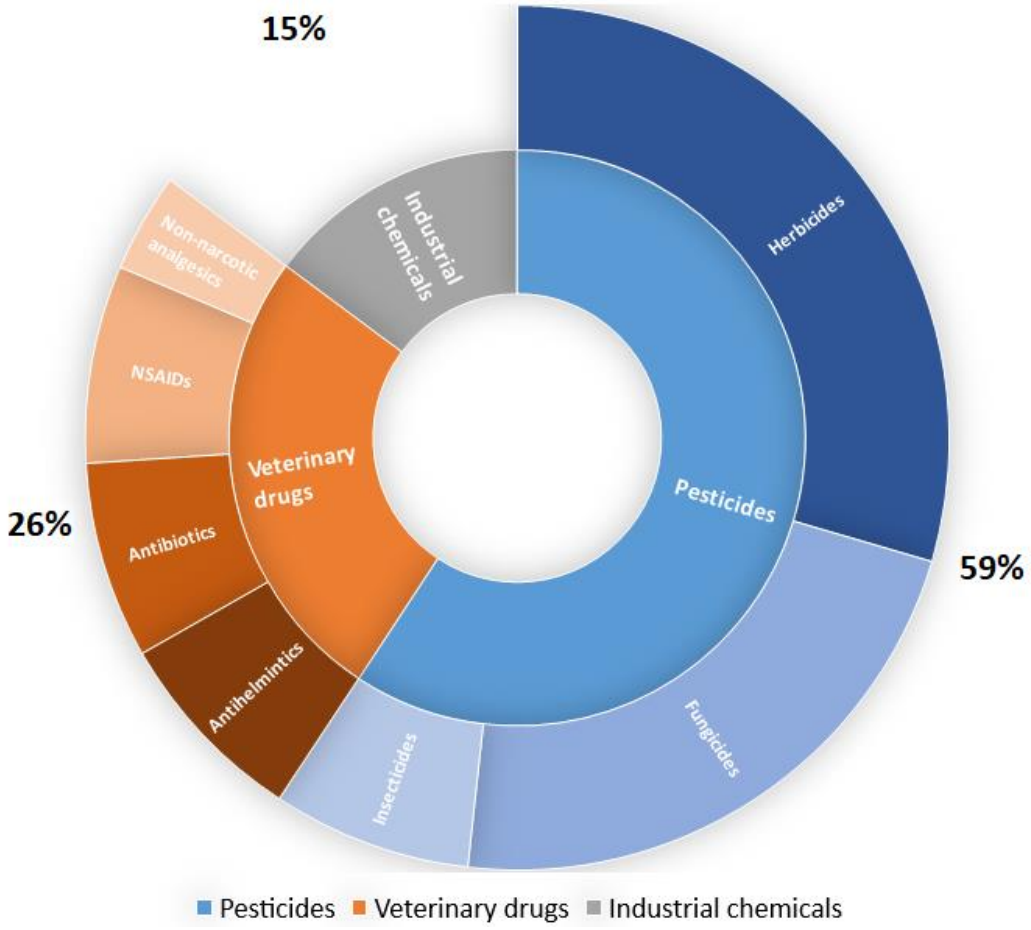

Fig. S2. Classification of the identified compounds in seafood samples by target screening based on their main use. NSAID, non-steroidal anti-inflammatory drug**.**

CHAPTER 3: The versatility of HRMS: targeted, suspected and non-targeted analyses

Article 5 (Makni et al., 2023b): "A proof-of-concept study on the versatility of liquid chromatography coupled to high-resolution mass spectrometry to screen for various contaminants and highlight markers of floral and geographical origin for different honeys"

Table S1: List of the 52 honey samples included in the study with their associated metadata

Sample	ID	Floral origin	Geographical origin	Texture	Production method*
Honey	#1	chestnut	France	liquid	OF
	#2	chestnut	France	liquid	NOF
	#3	chestnut	France	liquid	NOF
	#4	chestnut	France	liquid	NOF
	#5	chestnut	France	creamy	NOF
	#6	chestnut	France	liquid	NOF
	#7	chestnut	France	liquid	NOF
	#8	chestnut	France	liquid	NOF
	#9	chestnut	Italy	liquid	NOF
	#10	chestnut	Italy	liquid	OF
	#11	chestnut	Italy	liquid	OF
	#12	chestnut	Italy	liquid	OF
	#13	chestnut	Italy	liquid	OF
	#14	chestnut	Italy	liquid	OF
	#15	chestnut	Spain	liquid	NOF
	#16	chestnut	Spain	liquid	NOF
	#17	chestnut	Spain	liquid	NOF
	#18	chestnut	Spain	liquid	OF
	#19	lavender	France	creamy	NOF
	#20	lavender	France	creamy	NOF
	#21	lavender	France	solid	OF
	#22	lavender	Spain	solid	NOF
	#23	lavender	Spain	solid	NOF
	#24	lemon tree	Italy	creamy	OF
	#25	lemon tree	Italy	solid	OF
	#26	lemon tree	Spain	liquid	NOF
	#27	lemon tree	Spain	liquid	NOF
	#28	lemon tree	Spain	liquid	NOF
	#29	orange tree	Italy	liquid	OF
	#30	orange tree	Italy	solid	OF
	#31	orange tree	Italy	solid	OF

Sample	ID	Floral origin	Geographical origin	Texture	Production method*
	#32	orange tree	Spain	liquid	NOF
	#33	orange tree	Spain	solid	NOF
Urban honey	#34	unspecified	Canada	liquid	NOF
	#35	unspecified	Canada	liquid	NOF
	#36	unspecified	Canada	liquid	NOF
	#37	unspecified	Canada	liquid	NOF
	#38	unspecified	Canada	liquid	NOF
	#39	unspecified	Canada	liquid	NOF
	#40	unspecified	Canada	liquid	NOF
	#41	unspecified	Canada	liquid	NOF
	#42	unspecified	Canada	liquid	NOF
	#43	unspecified	Canada	liquid	NOF
	#44	unspecified	Canada	liquid	NOF
	#45	unspecified	Canada	liquid	NOF
	#46	unspecified	Canada	liquid	NOF
	#47	unspecified	Canada	liquid	NOF
	#48	unspecified	France	liquid	NOF
	#49	unspecified	France	liquid	NOF
	#50	unspecified	France	liquid	NOF
	#51	unspecified	France	liquid	NOF
	#52	unspecified	France	liquid	NOF

*organic farming (OF) or non-organic farming (NOF)

Table S2. Analytical parameters

Instrument	Parameter	Condition		
UHPLC	Column temperature	50 °C		
	Injection volume	10 µL		
	Flow rate	0.5 mL.min^{-1}		
	Mobile phase	A: H_2O containing 0.01% formic acid		
		B: ACN containing 0.01% formic acid		
		Time (min)	% A	% B
		0	90	10
		9	0	100
		12	0	100
		12.1	90	10
		16	90	10
Q-TOF-MS (ESI+/ESI-)	Ion source type	ESI		
	Ion spray voltage floating (ISVF)	(+) 5500 V, (-) 4500 V		
	Source temperature (TEM)	500 °C		
	Curtain gas (CUR)	30 psi		
	Nebulizing gas (GS1)	40 psi		
	Heater gas (GS2)	45psi		
	Declustering potential (DP)	(+/-) 80 eV		
	Acquisition mode	IDA		
	No. of precursor ions	10 (*Top10*)		
	TOF MS range (Da)	50-1000		
	Full scan collision energy (CE)	(+/-) 10 eV		
	MS accumulation time (ms)	490		
	TOF MS/MS range (Da)	50-1000		
	Collision energy (CE) for MS/MS	(+/-) 40 ± 20 eV		
	MS/MS accumulation time (ms)	40		
	Cycle time (ms)	940		

Table S3. List of the 694 targeted contaminants correctly detected in solvent (among the initial mixture of 746 contaminants), including in the quality assurance (QA) sample, with their corresponding formula, adduct or in-source fragment, theoretical *m/z* and retention time (t_R).

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
1-(3,4-Dichlorophenyl)-3-methyl Urea	TP*	$C_8H_8Cl_2N_2O$	$[M-H]^-$	216.99409	4.78
1-(4-Nitrophenyl)-3-propylure	Industrial contaminant	$C_{10}H_{13}N_3O_3$	$[M-H]^-$	222.08842	4.69
1,2-Benzisothiazol-3(2h)-one	Fungicide	C_7H_5NOS	$[M+H]^+$	152.01646	2.78
1,3-Diphenylurea	Plant hormone	$C_{13}H_{12}N_2O$	$[M+H]^+$	213.10224	5.19
2,3,5-Trimethacarb	Insecticide	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.35
2,4-Dimethylaniline (DMA)	TP*	$C_8H_{11}N$	$[M+H]^+$	122.09643	2.47
2,6-Dichlorobenzamide	TP*	$C_7H_5Cl_2NO$	$[M+H]^+$	189.98210	2.71
2,6-Diethylaniline	TP*	$C_{10}H_{15}N$	$[M+H]^+$	150.12773	5.75
2-Ethylhexyl diphenyl phosphate	Industrial contaminant	$C_{20}H_{27}O_4P$	$[M+H]^+$	363.17197	8.64
2-n-Octyl-4-isothiazolin-3-one	Antimicrobial agent	$C_{11}H_{19}NOS$	$[M+H]^+$	214.12601	6.29
3,4-Dichloroaniline	Industrial contaminant	$C_6H_5Cl_2N$	$[M+H]^+$	161.98718	5.32
3,4,5-Trimethacarb	Insecticide	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.28
3-Hydroxycarbofuran	TP*	$C_{12}H_{15}NO_4$	$C_{12}H_{14}NO_3^+$	220.09682	3.08
3-Ketocarbofuran	TP*	$C_{12}H_{13}NO_4$	$[M+H]^+$	236.09173	4.03
4-Bromo-3,5-dimethylphenyl-N-methlycarbamate?	Insecticide	$C_{10}H_{12}BrNO_2$	$[M+H]^+$	258.01242	5.91
Abamectin	Acaricide/Insecticide	$C_{48}H_{72}O_{14}$	$[M+Na]^+$	895.48143	8.78
Abate® (temephos)	Insecticide	$C_{16}H_{20}O_6P_2S_3$	$[M+H]^+$	466.99701	8.03
Acephate	Insecticide	$C_4H_{10}NO_3PS$	$C_2H_8O_3PS^+$	142.99263	0.96
Acetamiprid	Insecticide	$C_{10}H_{11}ClN_4$	$[M+H]^+$	223.07450	3.44
Acibenzolar-s-methyl	Fungicide	$C_8H_6N_2OS_2$	$[M+H]^+$	210.99943	6.07
Aclonifen	Herbicide	$C_{12}H_9ClN_2O_3$	$[M+H]^+$	265.03745	6.93
Aconitine	Plant toxin	$C_{34}H_{47}NO_{11}$	$[M+H]^+$	646.32219	4.71
Akton	Insecticide	$C_{12}H_{14}Cl_3O_3PS$	$[M+H]^+$	374.95396	8.30
Alachlor	Herbicide	$C_{14}H_{20}ClNO_2$	$[M+H]^+$	270.12553	6.68
Aldicarb	Insecticide	$C_7H_{14}N_2O_2S$	$[M+Na]^+$	213.06682	3.80
Aldicarb sulphone	TP*	$C_7H_{14}N_2O_4S$	$[M+H]^+$	223.07471	3.44
Aldicarb sulphoxide	TP*	$C_7H_{14}N_2O_3S$	$[M+H]^+$	207.07979	0.94
Allethrin	Insecticide	$C_{19}H_{26}O_3$	$[M+H]^+$	303.19547	8.08
Allidochlor	Herbicide	$C_8H_{12}ClNO$	$[M+H]^+$	174.06802	4.23
Alloxydim sodium	Herbicide	$C_{17}H_{24}NNaO_5$	$[M+H]^+$	346.16249	7.12
Ametoctradin	Fungicide	$C_{15}H_{25}N_5$	$[M-H]^-$	274.20372	6.57
Ametryn	Herbicide	$C_9H_{17}N_5S$	$[M+H]^+$	228.12774	5.03
Amicarbazone	Herbicide	$C_{10}H_{19}N_5O_2$	$[M+H]^+$	242.16115	4.06
Amidosulfuron	Herbicide	$C_9H_{15}N_5O_7S_2$	$[M+H]^+$	370.04857	4.77

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Aminocarb	Insecticide	$C_{11}H_{16}N_2O_2$	$[M+H]^+$	209.12845	1.71
Ancymidol	Rodenticide	$C_{15}H_{16}N_2O_2$	$[M+H]^+$	257.12845	4.26
Anilazine	Fungicide	$C_9H_5Cl_3N_4$	$[M+H]^+$	274.96526	6.26
Anilofos	Herbicide	$C_{13}H_{19}ClNO_3PS_2$	$[M+H]^+$	368.03053	7.12
Aspon™	Insecticide	$C_{12}H_{28}O_5P_2S_2$	$[M+H]^+$	379.09262	8.73
Asulam	Herbicide	$C_8H_{10}N_2O_4S$	$[M+H]^+$	231.04341	2.25
Atraton	Herbicide	$C_9H_{17}N_5O$	$[M+H]^+$	212.15059	3.75
Atrazine	Herbicide	$C_8H_{14}ClN_5$	$[M+H]^+$	216.10105	5.12
Atrazine desisopropyl	TP*	$C_5H_8ClN_5$	$[M+H]^+$	174.05410	2.51
Azaconazole	Fungicide	$C_{12}H_{11}Cl_2N_3O_2$	$[M+H]^+$	300.03011	5.21
Azadirachtin	Insecticide	$C_{35}H_{44}O_{16}$	$[M+H]^+$	721.27021	5.01
Azamethiphos	Insecticide	$C_9H_{10}ClN_2O_5PS$	$[M+H]^+$	324.98094	4.44
Azimsulfuron	Herbicide	$C_{13}H_{16}N_{10}O_5S$	$[M+H]^+$	425.10986	5.03
Aziprotryne	Herbicide	$C_7H_{11}N_7S$	$[M+H]^+$	226.08694	6.15
Azoxystrobin	Fungicide	$C_{22}H_{17}N_3O_5$	$[M+H]^+$	404.12410	6.16
Beflubutamid	Herbicide	$C_{18}H_{17}F_4NO_2$	$[M+H]^+$	356.12682	6.96
Benalaxyl	Fungicide	$C_{20}H_{23}NO_3$	$[M+H]^+$	326.17507	7.04
Benazolin	Herbicide	$C_9H_6ClNO_3S$	$[M+H]^+$	243.98297	3.88
Benodanil	Fungicide	$C_{13}H_{10}INO$	$[M+H]^+$	323.98799	5.67
Benomyl	Fungicide	$C_{14}H_{18}N_4O_3$	$[M+H]^+$	291.14517	6.10
Benoxacor	Herbicide	$C_{11}H_{11}Cl_2NO_2$	$[M+H]^+$	260.02396	6.06
Bensulfuron-methyl	Herbicide	$C_{16}H_{18}N_4O_7S$	$[M+H]^+$	411.09690	5.44
Bensulide	Herbicide	$C_{14}H_{24}NO_4PS_3$	$[M+H]^+$	398.06779	7.09
Bentazon	Herbicide	$C_{10}H_{12}N_2O_3S$	$[M+H]^+$	241.06414	4.48
Benthiavalicarb-isopropyl	Fungicide	$C_{18}H_{24}FN_3O_3S$	$[M+H]^+$	382.15952	5.93
Benzoximate	Acaricide	$C_{18}H_{18}ClNO_5$	$C_9H_8ClO_3^+$	199.01565	7.53
Benzoylprop-ethyl	Herbicide	$C_{18}H_{17}Cl_2NO_3$	$[M+H]^+$	366.06583	7.28
Benzthiazuron	Herbicide	$C_9H_9N_3OS$	$[M-H]^-$	206.03936	3.88
Bioresmethrin	Insecticide	$C_{22}H_{26}O_3$	$[M+H]^+$	339.19547	8.89
Bitertanole (mixture of isomers)	Fungicide	$C_{20}H_{23}N_3O_2$	$[M+H]^+$	338.18630	6.65
Bixafen	Fungicide	$C_{18}H_{12}Cl_2F_3N_3O$	$[M-H]^-$	412.02368	6.69
Bladex	Herbicide	$C_9H_{13}ClN_6$	$[M+H]^+$	241.09630	4.40
Boscalid	Fungicide	$C_{18}H_{12}Cl_2N_2O$	$[M+H]^+$	343.03995	6.32
Bromacil	Herbicide	$C_9H_{13}BrN_2O_2$	$[M-H]^-$	259.00876	4.18
Bromofenvinphos-ethyl	Insecticide	$C_{12}H_{14}BrCl_2O_4P$	$[M+H]^+$	404.92397	7.03
Bromophos-methyl	Insecticide	$C_8H_8BrCl_2O_3PS$	$[M+H]^+$	366.85409	8.06
Bromuconazole (mixture of isomers)	Fungicide	$C_{13}H_{12}BrCl_2N_3O$	$[M+H]^+$	377.95902	6.12
Bupirimate	Fungicide	$C_{13}H_{24}N_4O_3S$	$[M+H]^+$	317.16419	6.49
Buprofezin	Insecticide	$C_{16}H_{23}N_3OS$	$[M+H]^+$	306.16346	7.96

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Butachlor	Herbicide	$C_{17}H_{26}ClNO_2$	$[M+H]^+$	312.17248	8.11
Butafenacil	Herbicide	$C_{20}H_{18}ClF_3N_2O_6$	$[M+NH_4]^+$	492.11437	6.72
Butocarboxim sulphoxide	TP*	$C_7H_{14}N_2O_3S$	$[M+Na]^+$	229.06174	0.96
Butoxycarboxim	Insecticide	$C_7H_{14}N_2O_4S$	$[M+H]^+$	223.07471	3.44
Butroxydim	Herbicide	$C_{24}H_{33}NO_4$	$[M+H]^+$	400.24824	8.14
Buturon	Herbicide	$C_{12}H_{13}ClN_2O$	$[M+H]^+$	237.07892	5.57
Butylate	Herbicide	$C_{11}H_{23}NOS$	$[M+H]^+$	218.15731	7.97
Cadusafos	Insecticide	$C_{10}H_{23}O_2PS_2$	$[M+H]^+$	271.09499	7.33
Cafenstrole	Herbicide	$C_{16}H_{22}N_4O_3S$	$[M+H]^+$	351.14854	6.62
Carbaryl	Insecticide	$C_{12}H_{11}NO_2$	$C_{10}H_9O^+$	145.06479	4.89
Carbendazim	Fungicide	$C_9H_9N_3O_2$	$[M+H]^+$	192.07675	2.19
Carbetamide	Herbicide	$C_{12}H_{16}N_2O_3$	$[M+H]^+$	237.12337	4.04
Carbofuran	Insecticide	$C_{12}H_{15}NO_3$	$[M+H]^+$	222.11247	4.75
Carbophenothion	Insecticide	$C_{11}H_{16}ClO_2PS_3$	$[M+H]^+$	342.98114	8.39
Carboxin	Fungicide	$C_{12}H_{13}NO_2S$	$[M+H]^+$	236.07398	5.07
Carfentrazone-ethyl	Herbicide	$C_{15}H_{14}Cl_2F_3N_3O_3$	$[M+H]^+$	412.04371	6.93
Carpropamid	Fungicide	$C_{15}H_{18}Cl_3NO$	$[M+H]^+$	334.05267	7.10
Chinomethionate	Acaricide/Fungicide	$C_{10}H_6N_2OS_2$	$[M+H]^+$	234.99943	7.38
Chlorantraniliprole	Acaricide/Insecticide	$C_{18}H_{14}BrCl_2N_5O_2$	$[M+H]^+$	483.97579	5.68
Chlorbromuron	Herbicide	$C_9H_{10}BrClN_2O_2$	$[M+H]^+$	294.96648	6.10
Chlordimeform	Insecticide	$C_{10}H_{13}ClN_2$	$[M+H]^+$	197.08400	2.64
Chlorfenapyr	Insecticide	$C_{15}H_{11}BrClF_3N_2O$	$[M+H]^+$	408.97465	7.93
Chlorfenvinphos (mixture of Z and E)	Insecticide	$C_{12}H_{14}Cl_3O_4P$	$[M+H]^+$	358.97681	6.93
Chlorfluazuron	Insecticide	$C_{20}H_9Cl_3F_5N_3O_3$	$[M-H]^-$	537.95569	8.30
Chloridazon	Herbicide	$C_{10}H_8ClN_3O$	$[M+H]^+$	222.04287	3.19
Chlorimuron-ethyl	Herbicide	$C_{15}H_{15}ClN_4O_6S$	$[M+H]^+$	415.04736	6.06
Chlorobenzuron	Insecticide	$C_{14}H_{10}Cl_2N_2O_2$	$[M+H]^+$	309.01921	6.64
Chlorosulfuron	Herbicide	$C_{12}H_{12}ClN_5O_4S$	$[M+H]^+$	358.03713	4.80
Chlorotoluron	Herbicide	$C_{10}H_{13}ClN_2O$	$[M+H]^+$	213.07892	4.93
Chloroxuron	Herbicide	$C_{15}H_{15}ClN_2O_2$	$[M+H]^+$	291.08948	6.07
Chlorpyrifos	Insecticide	$C_9H_{11}Cl_3NO_3PS$	$[M+H]^+$	349.93356	8.21
Chlorpyrifos-methyl	Insecticide	$C_7H_7Cl_3NO_3PS$	$[M+H]^+$	321.90226	7.49
Chlorpyrifos-oxon	TP*	$C_9H_{11}Cl_3NO_4P$	$[M+H]^+$	333.95641	6.48
Chlorthiophos	Insecticide	$C_{11}H_{15}Cl_2O_3PS_2$	$[M+H]^+$	360.96501	8.36
Chromafenozide	Insecticide	$C_{24}H_{30}N_2O_3$	$[M-H]^-$	393.21837	6.65
Cinidon-ethyl	Herbicide	$C_{19}H_{17}Cl_2NO_4$	$[M+H]^+$	394.06074	7.85
Cinmethylin	Herbicide	$C_{18}H_{26}O_2$	$[M+NH_4]^+$	292.22711	8.08
Cinosulfuron	Herbicide	$C_{15}H_{19}N_5O_7S$	$[M+H]^+$	414.10780	4.57
Clarithromycin	Antibiotic	$C_{38}H_{69}NO_{13}$	$[M+H]^+$	748.48417	4.89
Clethodim	Herbicide	$C_{17}H_{26}ClNO_3S$	$[M+H]^+$	360.13947	7.86

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Climbazol	Antifungal	$C_{15}H_{17}ClN_2O_2$	$[M+H]^+$	293.10513	5.02
Clodinafop (acid-free)	Herbicide	$C_{14}H_{11}ClFNO_4$	$[M+H]^+$	312.04334	5.76
Clodinafop-propargyl	Herbicide	$C_{17}H_{13}ClFNO_4$	$[M+H]^+$	350.05899	7.11
Clofentezine	Acaricide	$C_{14}H_8Cl_2N_4$	$[M+H]^+$	303.01988	7.39
Clomeprop	Herbicide	$C_{16}H_{15}Cl_2NO_2$	$[M-H]^-$	322.04071	7.76
Cloquintocet-mexyl	Herbicide	$C_{18}H_{22}ClNO_3$	$[M+H]^+$	336.13610	7.90
Cloransulam-methyl	Herbicide	$C_{15}H_{13}ClFN_5O_5S$	$[M+H]^+$	430.03827	5.41
Clothianidin	Insecticide	$C_6H_8ClN_5O_2S$	$[M+H]^+$	250.01600	3.03
Command (clomazone)	Herbicide	$C_{12}H_{14}ClNO_2$	$[M+H]^+$	240.07858	5.69
Coumaphos	Insecticide	$C_{14}H_{16}ClO_5PS$	$[M+H]^+$	363.02174	7.33
Coumaphos-oxon	Insecticide	$C_{14}H_{16}ClO_6P$	$[M+H]^+$	347.04458	5.69
Crimidine	Rodenticide	$C_7H_{10}ClN_3$	$[M+H]^+$	172.06360	3.73
Crotoxyphos	Insecticide	$C_{14}H_{19}O_6P$	$[M+NH_4]^+$	332.12575	5.89
Crufomate	Insecticide	$C_{12}H_{19}ClNO_3P$	$[M+H]^+$	292.08639	6.23
Cumyluron	Herbicide	$C_{17}H_{19}ClN_2O$	$[M+H]^+$	303.12587	6.15
Cyanofenphos	Insecticide	$C_{15}H_{14}NO_2PS$	$[M+H]^+$	304.05557	7.17
Cyanophos	Insecticide	$C_9H_{10}NO_3PS$	$[M+H]^+$	244.01918	5.85
Cyantraniliprole	Insecticide	$C_{19}H_{14}BrClN_6O_2$	$[M+H]^+$	475.01020	5.17
Cyazofamid	Fungicide	$C_{13}H_{13}ClN_4O_2S$	$[M+H]^+$	325.05205	6.92
Cyclanilide	Plant growth regulator	$C_{11}H_9Cl_2NO_3$	$[M+H]^+$	274.00323	5.71
Cycloate	Herbicide	$C_{11}H_{21}NOS$	$[M+H]^+$	216.14166	7.62
Cyclohexamide	Antifungal	$C_{15}H_{23}NO_4$	$[M+H]^+$	282.16998	3.79
Cycloprothrin	Insecticide	$C_{26}H_{21}Cl_2NO_4$	$[M+H]^+$	482.09204	8.52
Cyclosulfamuron	Herbicide	$C_{17}H_{19}N_5O_6S$	$[M+H]^+$	422.11288	6.36
Cycloxidim	Herbicide	$C_{17}H_{27}NO_3S$	$[M+H]^+$	326.17844	7.78
Cycluron	Herbicide	$C_{11}H_{22}N_2O$	$[M+H]^+$	199.18049	5.12
Cyflufenamid	Fungicide	$C_{20}H_{17}F_5N_2O_2$	$[M+H]^+$	413.12830	7.55
Cyhalofop-butyl	Herbicide	$C_{20}H_{20}FNO_4$	$[M+H]^+$	358.14491	7.75
Cymiazole	Veterinary drug	$C_{12}H_{14}N_2S$	$[M+H]^+$	219.09505	3.19
Cymoxanil	Fungicide	$C_7H_{10}N_4O_3$	$C_4H_6N_3O_2^+$	128.04545	3.66
Cyphenothrin	Insecticide	$C_{24}H_{25}NO_3$	$[M+H]^+$	376.19072	8.89
Cyprazine	Herbicide	$C_9H_{14}ClN_5$	$[M+H]^+$	228.10105	5.13
Cyproconazole (mixture of isomers)	Fungicide	$C_{15}H_{18}ClN_3O$	$[M+H]^+$	292.12112	6.17
Cyprodinil	Fungicide	$C_{14}H_{15}N_3$	$[M+H]^+$	226.13387	6.48
Cyprofuram	Fungicide	$C_{14}H_{14}ClNO_3$	$[M+H]^+$	280.07350	5.23
Cyprosulfamide	Herbicide	$C_{18}H_{18}N_2O_5S$	$[M+H]^+$	375.10092	4.73
Cyromazine	Insecticide	$C_6H_{10}N_6$	$[M+H]^+$	167.10397	0.94
Cythioate	Insecticide	$C_8H_{12}NO_5PS_2$	$[M+H]^+$	297.99673	4.41
Daimuron	Herbicide	$C_{17}H_{20}N_2O$	$[M+H]^+$	269.16484	6.22

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Daminozide	Plant growth regulator	$C_6H_{12}N_2O_3$	$[M+H]^+$	161.0921	0.90
Danitol	Acaricide	$C_{22}H_{23}NO_3$	$[M+H]^+$	350.17507	8.59
Dazomet	Fungicide/Herbicide	$C_5H_{10}N_2S_2$	$[M+H]^+$	163.03582	2.51
Demeton-s-methyl-sulphone	TP*	$C_6H_{15}O_5PS_2$	$[M+H]^+$	263.01713	2.55
Demeton O	Insecticide	$C_8H_{19}O_3PS_2$	$[M+H]^+$	259.05860	7.05
Demeton S	Insecticide	$C_8H_{19}O_3PS_2$	$[M+H]^+$	259.05860	5.51
Demeton-s-methyl	TP*	$C_6H_{15}O_3PS_2$	$[M+H]^+$	231.02730	4.48
Deoxynivalenol	Mycotoxin	$C_{15}H_{20}O_6$	$[M+H]^+$	297.13327	0.93
Desethyl atrazine	TP*	$C_6H_{10}ClN_5$	$[M+H]^+$	188.06975	3.28
Desmedipham	Herbicide	$C_{16}H_{16}N_2O_4$	$[M+H]^+$	301.11828	5.78
Desmethyl norflurazon	TP*	$C_{11}H_7ClF_3N_3O$	$[M-H]^-$	288.01570	4.82
Desmethyl-formamido-pirimicarb	TP*	$C_{11}H_{16}N_4O_3$	$[M+H]^+$	253.12952	4.36
Desmetryn	Herbicide	$C_8H_{15}N_5S$	$[M+H]^+$	214.11209	4.36
Dialifos	Insecticide	$C_{14}H_{17}ClNO_4PS_2$	$[M+H]^+$	394.00979	7.60
Diazinon	Insecticide	$C_{12}H_{21}N_2O_3PS$	$[M+H]^+$	305.10833	7.39
Diazinon-O analog	TP*	$C_{12}H_{21}N_2O_4P$	$[M+H]^+$	289.13117	5.37
Dibrom	Acaricide/Insecticide	$C_4H_7Br_2Cl_2O_4P$	$[M+H]^+$	380.78760	5.46
Dichlofenthion	Nematicide	$C_{10}H_{13}Cl_2O_3PS$	$[M+H]^+$	314.97729	8.17
Dichlormid	Herbicide	$C_8H_{11}Cl_2NO$	$[M+H]^+$	208.02905	5.21
Dichlorvos	Acaricide/Insecticide	$C_4H_7Cl_2O_4P$	$[M+H]^+$	220.95318	4.40
Diclobutrazol (mixture of stereo isomers)	Fungicide	$C_{15}H_{19}Cl_2N_3O$	$[M+H]^+$	328.09779	6.49
Diclocymet	Insecticide	$C_{15}H_{18}Cl_2N_2O$	$[M+H]^+$	313.08690	6.74
Diclosulam	Herbicide	$C_{13}H_{10}Cl_2FN_5O_3S$	$[M+H]^+$	405.99382	5.50
Dicrotophos	Insecticide	$C_8H_{16}NO_5P$	$[M+H]^+$	238.08389	2.57
Diethatyl-ethyl	Herbicide	$C_{16}H_{22}ClNO_3$	$[M+H]^+$	312.13610	6.96
Diethofencarb	Fungicide	$C_{14}H_{21}NO_4$	$[M+H]^+$	268.15433	6.01
Difenoconazole (mixture of isomers)	Fungicide	$C_{19}H_{17}Cl_2N_3O_3$	$[M+H]^+$	406.07197	7.18
Difenoxurone	Herbicide	$C_{16}H_{18}N_2O_3$	$[M+H]^+$	287.13902	5.28
Diflubenzuron	Insecticide	$C_{14}H_9ClF_2N_2O_2$	$[M+H]^+$	311.03934	6.43
Diflufenicen	Herbicide	$C_{19}H_{11}F_5N_2O_2$	$[M-H]^-$	393.06679	7.56
Dimefox	Acaricide/Insecticide	$C_4H_{12}FN_2OP$	$[M+H]^+$	155.07441	2.66
Dimefuron	Herbicide	$C_{15}H_{19}ClN_4O_3$	$[M+H]^+$	339.12184	5.64
Dimepiperate	Herbicide	$C_{15}H_{21}NOS$	$[M+H]^+$	264.14166	7.70
Dimethachlor	Herbicide	$C_{13}H_{18}ClNO_2$	$[M+H]^+$	256.10988	5.58
Dimethametryn	Herbicide	$C_{11}H_{21}N_5S$	$[M+H]^+$	256.15904	6.36
Dimethenamid	Herbicide	$C_{12}H_{18}ClNO_2S$	$[M+H]^+$	276.08195	6.11
Dimethirimol	Fungicide	$C_{11}H_{19}N_3O$	$[M+H]^+$	210.16009	3.01

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Dimethoate	Acaricide/Insecticide	$C_5H_{12}NO_3PS_2$	$[M+H]^+$	230.00690	3.33
Dimethomorph	Fungicide	$C_{21}H_{22}ClNO_4$	$[M+H]^+$	388.13101	5.85
Dimethylvinphos	Insecticide	$C_{10}H_{10}Cl_3O_4P$	$[M+H]^+$	330.94551	6.19
Dimetilan	Insecticide	$C_{10}H_{16}N_4O_3$	$[M+H]^+$	241.12952	3.41
Dimoxystrobin	Fungicide	$C_{19}H_{22}N_2O_3$	$[M+H]^+$	327.17032	6.75
Diniconazole (E-isomer)	Fungicide	$C_{15}H_{17}Cl_2N_3O$	$[M+H]^+$	326.08214	6.82
Diniconazole (Z-isomer)	Fungicide	$C_{15}H_{17}Cl_2N_3O$	$[M+H]^+$	326.08214	6.82
Dinitramine	Herbicide	$C_{11}H_{13}F_3N_4O_4$	$[M-H]^-$	321.08161	7.18
Dinotefuran	Insecticide	$C_7H_{14}N_4O_3$	$[M+H]^+$	203.11387	1.83
Dioxacarb	Insecticide	$C_{11}H_{13}NO_4$	$[M+H]^+$	224.09173	3.37
Diphenamid	Herbicide	$C_{16}H_{17}NO$	$[M+H]^+$	240.13829	5.62
Diphenylamine	Fungicide	$C_{12}H_{11}N$	$[M+H]^+$	170.09643	6.57
Dipropetryn	Herbicide	$C_{11}H_{21}N_5S$	$[M+H]^+$	256.15904	6.37
Disulfoton sulphone	TP*	$C_8H_{19}O_4PS_3$	$[M+H]^+$	307.02559	5.65
Disulfoton sulphoxide	TP*	$C_8H_{19}O_3PS_3$	$[M+H]^+$	291.03067	5.00
Ditalimfos	Fungicide	$C_{12}H_{14}NO_4PS$	$[M+H]^+$	300.04539	6.63
Dithianon	Fungicide	$C_{14}H_4N_2O_2S_2$	$[M+H]^+$	296.9787	6.45
Dithiopyr	Herbicide	$C_{15}H_{16}F_5NO_2S_2$	$[M+H]^+$	402.06154	7.82
Diuron	Herbicide	$C_9H_{10}Cl_2N_2O$	$[M-H]^-$	231.00974	5.20
Dodemorph	Fungicide	$C_{18}H_{35}NO$	$[M+H]^+$	282.27914	5.10
Doramectin	Veterinary drug	$C_{50}H_{74}O_{14}$	$[M+Na]^+$	921.49708	9.18
Dyfonate™	Insecticide	$C_{10}H_{15}OPS_2$	$[M+H]^+$	247.03747	7.39
Edifenphos	Fungicide	$C_{14}H_{15}O_2PS_2$	$[M+H]^+$	311.03239	6.91
Emamectin	Insecticide	$C_{49}H_{75}NO_{13}$	$[M+H]^+$	886.53112	6.92
Empenthrin	Insecticide	$C_{18}H_{26}O_2$	$[M+H]^+$	275.20056	8.82
Epn	Insecticide	$C_{14}H_{14}NO_4PS$	$[M+H]^+$	324.04539	7.56
Epoxiconazole (iso)	Fungicide	$C_{17}H_{13}ClFN_3O$	$[M+H]^+$	330.08039	6.29
Eprinomectin	Veterinary drug	$C_{50}H_{75}NO_{14}$	$[M+H]^+$	914.52603	8.46
EPTC (s-ethyl dipropylthiocarbamate)	Herbicide	$C_9H_{19}NOS$	$[M+H]^+$	190.12601	6.91
Erythromycin	Antibiotic	$C_{37}H_{67}NO_{13}$	$[M+H]^+$	734.46852	4.15
Esbiol	Insecticide	$C_{19}H_{26}O_3$	$[M+H]^+$	303.19547	8.07
Esprocarb	Herbicide	$C_{15}H_{23}NOS$	$[M+H]^+$	266.15731	8.06
Etaconazole	Fungicide	$C_{14}H_{15}Cl_2N_3O_2$	$[M+H]^+$	328.06141	6.34
Ethaboxam	Fungicide	$C_{14}H_{16}N_4OS_2$	$[M+H]^+$	321.08383	5.10
Ethametsulfuron-methyl	Herbicide	$C_{15}H_{18}N_6O_6S$	$[M+H]^+$	411.10813	4.93
Ethidimuron	Herbicide	$C_7H_{12}N_4O_3S_2$	$[M+H]^+$	265.04236	3.07
Ethiofencarb	Insecticide	$C_{11}H_{15}NO_2S$	$[M+H]^+$	226.08963	5.05
Ethiofencarb sulphone	TP*	$C_{11}H_{15}NO_4S$	$[M+H]^+$	258.07946	3.03
Ethiofencarb sulphoxide	TP*	$C_{11}H_{15}NO_3S$	$[M+H]^+$	242.08454	2.95

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Ethion	Acaricide/Insecticide	$C_9H_{22}O_4P_2S_4$	$[M+H]^+$	384.9949	8.22
Ethiozin	Herbicide	$C_9H_{16}N_4OS$	$[M+H]^+$	229.11176	5.19
Ethiprole	Insecticide	$C_{13}H_9Cl_2F_3N_4OS$	$[M-H]^-$	394.97535	5.85
Ethirimol	Fungicide	$C_{11}H_{19}N_3O$	$[M+H]^+$	210.16009	3.07
Ethofumesate	Herbicide	$C_{13}H_{18}O_5S$	$[M+H]^+$	287.09477	6.28
Ethoprophos (prophos)	Nematicide	$C_8H_{19}O_2PS_2$	$[M+H]^+$	243.06369	6.38
Ethoxyquin	Industrial contaminant	$C_{14}H_{19}NO$	$[M+H]^+$	218.15394	6.19
Ethoxysulfuron	Herbicide	$C_{15}H_{18}N_4O_7S$	$[M+H]^+$	399.09690	6.07
Ethyclozate	Plant hormone	$C_{11}H_{11}ClN_2O_2$	$[M+H]^+$	239.05818	5.28
Etobenzanid	Herbicide	$C_{16}H_{15}Cl_2NO_3$	$[M+H]^+$	340.05018	7.25
Etoxazole	Acaricide	$C_{21}H_{23}F_2NO_2$	$[M+H]^+$	360.17696	8.46
Etrimfos	Insecticide	$C_{10}H_{17}N_2O_4PS$	$[M+H]^+$	293.07194	7.21
Famphur	Insecticide	$C_{10}H_{16}NO_5PS_2$	$[M+H]^+$	326.02803	5.80
Fenamidone	Fungicide	$C_{17}H_{17}N_3OS$	$[M+H]^+$	312.11651	6.19
Fenamiphos	Insecticide	$C_{13}H_{22}NO_3PS$	$[M+H]^+$	304.11308	6.17
Fenamiphos sulphone	TP*	$C_{13}H_{22}NO_5PS$	$[M+H]^+$	336.10291	4.58
Fenamiphos sulphoxide	TP*	$C_{13}H_{22}NO_4PS$	$[M+H]^+$	320.10800	4.04
Fenarimol	Fungicide	$C_{17}H_{12}Cl_2N_2O$	$[M+H]^+$	331.03995	6.17
Fenazaquin	Acaricide	$C_{20}H_{22}N_2O$	$[M+H]^+$	307.18049	8.51
Fenazox	Insecticide	$C_{12}H_{10}N_2O$	$[M+H]^+$	199.08659	7.02
Fenbuconazole	Fungicide	$C_{19}H_{17}ClN_4$	$[M+H]^+$	337.12145	6.50
Fenchlorazol-ethyl	Herbicide	$C_{12}H_8Cl_5N_3O_2$	$[M+H]^+$	403.91031	7.51
Fenchlorphos-oxon	TP*	$C_8H_8Cl_3O_4P$	$[M+H]^+$	304.92986	6.17
Fenfuram	Fungicide	$C_{12}H_{11}NO_2$	$[M+H]^+$	202.08626	5.14
Fenhexamid	Fungicide	$C_{14}H_{17}Cl_2NO_2$	$[M+H]^+$	302.07091	6.31
Fenitrothion	Insecticide	$C_9H_{12}NO_5PS$	$[M+H]^+$	278.02466	6.58
Fenobucarb	Insecticide	$C_{12}H_{17}NO_2$	$[M+H]^+$	208.13321	5.87
Fenothiocarb	Acaricide	$C_{13}H_{19}NO_2S$	$[M+H]^+$	254.12093	6.76
Fenoxanil	Fungicide	$C_{15}H_{18}Cl_2N_2O_2$	$[M+H]^+$	329.08181	6.89
Fenoxaprop	Herbicide	$C_{16}H_{12}ClNO_5$	$[M+H]^+$	334.04768	6.22
Fenoxaprop-P-ethyl	Herbicide	$C_{18}H_{16}ClNO_5$	$[M+H]^+$	362.07898	7.70
Fenoxycarb	Insecticide	$C_{17}H_{19}NO_4$	$[M+H]^+$	302.13868	5.94
Fenpiclonil	Fungicide	$C_{11}H_6Cl_2N_2$	$[M+H]^+$	236.99808	5.72
Fenpropathrin	Acaricide	$C_{22}H_{23}NO_3$	$[M+H]^+$	350.17507	8.60
Fenpropidin	Fungicide	$C_{19}H_{31}N$	$[M+H]^+$	274.25293	5.25
Fenpropimorph	Fungicide	$C_{20}H_{33}NO$	$[M+H]^+$	304.26349	5.34
Fenpyroximate	Acaricide/Insecticide	$C_{24}H_{27}N_3O_4$	$[M+H]^+$	422.20743	8.46
Fensulfothion	Insecticide/Nematicide	$C_{11}H_{17}O_4PS_2$	$[M+H]^+$	309.03787	5.37
Fensulfothion-oxon	TP*	$C_{11}H_{17}O_5PS$	$[M+H]^+$	293.06071	3.56

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Fensulfothion-oxon sulphone	TP*	$C_{11}H_{17}O_6PS$	$[M+H]^+$	309.05563	4.11
Fensulfothion sulphone	TP*	$C_{11}H_{17}O_5PS_2$	$[M+H]^+$	325.03278	5.94
Fenthion	Insecticide	$C_{10}H_{15}O_3PS_2$	$[M+H]^+$	279.02730	7.14
Fenthion-oxon	TP*	$C_{10}H_{15}O_4PS$	$[M+H]^+$	263.05015	5.37
Fenthion-oxon sulphoxide	TP*	$C_{10}H_{15}O_5PS$	$[M+H]^+$	279.04506	3.03
Fenthion sulphoxide	TP*	$C_{10}H_{15}O_4PS_2$	$[M+H]^+$	295.02222	4.76
Fenthion-ethyl	Insecticide	$C_{12}H_{19}O_3PS_2$	$[M+H]^+$	307.05860	7.86
Fenthion sulphone	TP*	$C_{10}H_{15}O_5PS_2$	$[M+H]^+$	311.01713	5.41
Fenthoxon sulphone	TP*	$C_{10}H_{15}O_6PS$	$[M+H]^+$	295.03998	3.57
Fenuron	Herbicide	$C_9H_{12}N_2O$	$[M+H]^+$	165.10224	3.19
Ferimzone	Fungicide	$C_{15}H_{18}N_4$	$[M+H]^+$	255.16042	4.37
Fipronil	Acaricide/Insecticide	$C_{12}H_4Cl_2F_6N_4OS$	$[M-H]^-$	434.93143	6.87
Fipronil sulfide	TP*	$C_{12}H_4Cl_2F_6N_4S$	$[M-H]^-$	418.93652	7.30
Fipronil-desulfinyl	TP*	$C_{12}H_4Cl_2F_6N_4$	$[M-H]^-$	386.96444	7.05
Flamprop-isopropyl	Herbicide	$C_{19}H_{19}ClFNO_3$	$[M+H]^+$	364.11103	7.25
Flamprop-methyl (Metaven)	TP*	$C_{17}H_{15}ClFNO_3$	$[M+H]^+$	336.07973	6.47
Flamprop-m-isopropyl	Herbicide	$C_{19}H_{19}ClFNO_3$	$[M+H]^+$	364.11103	7.25
Flazasulfuron	Herbicide	$C_{13}H_{12}F_3N_5O_5S$	$[M+H]^+$	408.05840	5.48
Flonicamid	Insecticide	$C_9H_6F_3N_3O$	$[M+H]^+$	230.05357	2.71
Florasulam	Herbicide	$C_{12}H_8F_3N_5O_3S$	$[M+H]^+$	360.03727	4.63
Fluacrypyrim	Acaricide	$C_{20}H_{21}F_3N_2O_5$	$[M+H]^+$	427.14753	7.64
Fluazifop	Herbicide	$C_{15}H_{12}F_3NO_4$	$[M+H]^+$	328.07912	5.77
Fluazifop-butyl	Herbicide	$C_{19}H_{20}F_3NO_4$	$[M+H]^+$	384.14172	8.04
Fluazifop-P-butyl	Herbicide	$C_{19}H_{20}F_3NO_4$	$[M+H]^+$	384.14172	8.03
Fluazinam	Fungicide	$C_{13}H_4Cl_2F_6N_4O_4$	$[M-H]^-$	462.94410	7.90
Fluazuron	Acaricide	$C_{20}H_{10}Cl_2F_5N_3O_3$	$[M+H]^+$	506.00921	7.89
Flubendiamide	Insecticide	$C_{23}H_{22}F_7IN_2O_4S$	$[M-H]^-$	681.01605	6.88
Flucarbazone sodium	Herbicide	$C_{12}H_{10}F_3N_4NaO_6S$	$[M+H]^+$	419.02436	4.21
Fluchloralin	Herbicide	$C_{12}H_{13}ClF_3N_3O_4$	$[M+H]^+$	356.06195	7.69
Flucycloxuron	Acaricide/Insecticide	$C_{25}H_{20}ClF_2N_3O_3$	$[M+H]^+$	484.12340	8.11
Fludioxonil	Fungicide	$C_{12}H_6F_2N_2O_2$	$[M-H]^-$	248.03973	8.21
Flufenacet	Herbicide	$C_{14}H_{13}F_4N_3O_2S$	$[M+H]^+$	364.07374	6.70
Flufenoxuron	Insecticide	$C_{21}H_{11}ClF_6N_2O_3$	$[M+H]^+$	489.04352	8.09
Flumestulam	Herbicide	$C_{12}H_9F_2N_5O_2S$	$[M-H]^-$	324.03723	7.76
Flumetralin	Herbicide	$C_{16}H_{12}ClF_4N_3O_4$	$[M+H]^+$	422.05252	8.23
Flumiclorac-pentyl	Herbicide	$C_{21}H_{23}ClFNO_5$	$[M+NH_4]^+$	441.15870	7.88
Flumioxazin	Herbicide	$C_{19}H_{15}FN_2O_4$	$[M+H]^+$	355.10886	5.84
Flumorph	Fungicide	$C_{21}H_{22}FNO_4$	$[M+H]^+$	372.16056	5.30
Fluoglycofene-ethyl	Herbicide	$C_{18}H_{13}ClF_3NO_7$	$[M+NH_4]^+$	465.06709	7.69
Fluometuron	Herbicide	$C_{10}H_{11}F_3N_2O$	$[M-H]^-$	231.07507	5.00

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Fluopicolide	Fungicide	$C_{14}H_8Cl_3F_3N_2O$	$[M+H]^+$	382.97271	6.41
Fluopyram	Fungicide	$C_{16}H_{11}ClF_6N_2O$	$[M+H]^+$	397.05369	6.46
Fluoxastrobin	Fungicide	$C_{21}H_{16}ClFN_4O_5$	$[M+H]^+$	459.08660	6.69
Flupyradifurone	Insecticide	$C_{12}H_{11}ClF_2N_2O_2$	$[M+H]^+$	289.05499	3.72
Flupyrsulfuron-methyl sodium	Herbicide	$C_{15}H_{13}F_3N_5NaO_7S$	$[M+H]^+$	488.04583	5.79
Fluquinconazole	Fungicide	$C_{16}H_8Cl_2FN_5O$	$[M+H]^+$	376.01627	6.34
Fluridone	Herbicide	$C_{19}H_{14}F_3NO$	$[M+H]^+$	330.11003	5.86
Flurilazole	Herbicide	$C_{11}H_{13}Cl_2NO_3$	$[M+H]^+$	278.03453	3.66
Flurochloridon (ISO)	Herbicide	$C_{12}H_{10}Cl_2F_3NO$	$[M+H]^+$	312.01643	6.56
Fluroxypyr	Herbicide	$C_7H_5Cl_2FN_2O_3$	$[M+H]^+$	254.97340	4.03
Fluroxypyr-meptyl	Herbicide	$C_{15}H_{21}Cl_2FN_2O_3$	$[M+H]^+$	367.09860	8.43
Flurprimidol	Plant growth regulator	$C_{15}H_{15}F_3N_2O_2$	$[M+H]^+$	313.11584	5.92
Flurtamone	Herbicide	$C_{18}H_{14}F_3NO_2$	$[M-H]^-$	332.09039	5.95
Flusilazole	Fungicide	$C_{16}H_{15}F_2N_3Si$	$[M+H]^+$	316.10761	6.51
Fluthiacet-methyl	Herbicide	$C_{15}H_{15}ClFN_3O_3S_2$	$[M+H]^+$	404.03002	6.92
Flutolanil	Fungicide	$C_{17}H_{16}F_3NO_2$	$[M-H]^-$	322.10604	6.56
Flutriafol	Fungicide	$C_{16}H_{13}F_2N_3O$	$[M+H]^+$	302.10995	4.98
Fomesafen	Herbicide	$C_{15}H_{10}ClF_3N_2O_6S$	$[M-H]^-$	436.98274	6.13
Foramsulfuron	Herbicide	$C_{17}H_{20}N_6O_7S$	$[M+H]^+$	453.11870	4.20
Forchlorfenuron	Plant growth regulator	$C_{12}H_{10}ClN_3O$	$[M-H]^-$	246.04396	4.95
Formetanate	Acaricide/Insecticide	$C_{11}H_{15}N_3O_2$	$[M+H]^+$	222.12370	0.95
Fosthiazate	Nematicide	$C_9H_{18}NO_3PS_2$	$[M+H]^+$	284.05385	5.05
Fuberidazole	Fungicide	$C_{11}H_8N_2O$	$[M+H]^+$	185.07094	2.55
Furalaxyl	Fungicide	$C_{17}H_{19}NO_4$	$[M+H]^+$	302.13868	5.94
Furathiocarb	Insecticide	$C_{18}H_{26}N_2O_5S$	$[M+H]^+$	383.16352	7.97
Furmecyclox	Fungicide	$C_{14}H_{21}NO_3$	$[M+H]^+$	252.15942	6.94
Guthion-ethyl	Insecticide	$C_{12}H_{16}N_3O_3PS_2$	$[M+H]^+$	346.04435	6.67
Halofenozide	Insecticide	$C_{18}H_{19}ClN_2O_2$	$[M+H]^+$	331.12078	5.99
Halosulfuron-methyl	Insecticide	$C_{13}H_{15}ClN_6O_7S$	$[M+H]^+$	435.04842	6.05
Haloxyfop	Herbicide	$C_{15}H_{11}ClF_3NO_4$	$[M+H]^+$	362.04015	6.47
Haloxyfop-2-ethoxyethyl	Herbicide	$C_{19}H_{19}ClF_3NO_5$	$[M+H]^+$	434.09766	7.81
Haloxyfop-methyl	TP*	$C_{16}H_{13}ClF_3NO_4$	$[M+H]^+$	376.05580	7.51
Haloxyfop-P-methyl	TP*	$C_{16}H_{13}ClF_3NO_4$	$[M+H]^+$	376.05580	7.52
Heptenophos	Insecticide	$C_9H_{12}ClO_4P$	$[M+H]^+$	251.02345	5.31
Hexaconazole	Fungicide	$C_{14}H_{17}Cl_2N_3O$	$[M+H]^+$	314.08214	6.52
Hexaflumuron	Acaricide/Insecticide	$C_{16}H_8Cl_2F_6N_2O_3$	$[M-H]^-$	458.97434	7.37
Hexazinone	Herbicide	$C_{12}H_{20}N_4O_2$	$[M+H]^+$	253.16590	4.13
Hexythiazox	Acaricide	$C_{17}H_{21}ClN_2O_2S$	$[M+H]^+$	353.10850	8.23
Hymexazole	Fungicide	$C_4H_5NO_2$	$[M+H]^+$	100.03930	1.73

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Imazalil	Fungicide	$C_{14}H_{14}Cl_2N_2O$	$[M+H]^+$	297.05560	4.47
Imazamethabenz-methyl	Herbicide	$C_{16}H_{20}N_2O_3$	$[M+H]^+$	289.15467	4.14
Imazamox	Herbicide	$C_{15}H_{19}N_3O_4$	$[M+H]^+$	306.14483	3.19
Imazapic	Herbicide	$C_{14}H_{17}N_3O_3$	$[M+H]^+$	276.13427	3.30
Imazaquin	Herbicide	$C_{17}H_{17}N_3O_3$	$[M+H]^+$	312.13427	4.45
Imazethapyr	Herbicide	$C_{15}H_{19}N_3O_3$	$[M+H]^+$	290.14992	3.95
Imazosulfuron	Herbicide	$C_{14}H_{13}ClN_6O_5S$	$[M+H]^+$	413.04294	5.53
Imibenconazole	Fungicide	$C_{17}H_{13}Cl_3N_4S$	$[M-H]^-$	408.98538	7.69
Imidacloprid	Insecticide	$C_9H_{10}ClN_5O_2$	$[M+H]^+$	256.05958	3.19
Imidacloprid-olefin	TP*	$C_9H_8ClN_5O_2$	$[M+H]^+$	254.04393	2.60
Imiprothrin (mixture of isomers)	Insecticide	$C_{17}H_{22}N_2O_4$	$[M+H]^+$	319.16523	6.51
Inabenfide	Insecticide	$C_{19}H_{15}ClN_2O_2$	$[M+H]^+$	339.08948	5.55
Indaziflam	Herbicide	$C_{16}H_{20}FN_5$	$[M+H]^+$	302.17755	5.78
Indoxacarb	Insecticide	$C_{22}H_{17}ClF_3N_3O_7$	$[M+H]^+$	528.07799	7.52
Iodofenphos	Acaricide/Insecticide	$C_8H_8Cl_2IO_3PS$	$[M+H]^+$	412.84264	8.14
Iodosulfuron-methyl sodium	Herbicide	$C_{14}H_{13}IN_5NaO_6S$	$[M+H]^+$	529.96018	5.57
Ipconazole	Fungicide	$C_{18}H_{28}N_2O_3$	$[M+H]^+$	321.21727	6.08
Iprobenfos	Fungicide	$C_{13}H_{21}O_3PS$	$[M+H]^+$	289.10218	6.61
Iprodione	Fungicide	$C_{13}H_{13}Cl_2N_3O_3$	$[M+H]^+$	330.04067	6.49
Iprovalicarb	Fungicide	$C_{18}H_{28}N_2O_3$	$[M+H]^+$	321.21727	6.14
Irgarol (cybutryne)	Algaecide	$C_{11}H_{19}N_5S$	$[M+H]^+$	254.14339	5.99
Isazophos	Insecticide	$C_9H_{17}ClN_3O_3PS$	$[M+H]^+$	314.04896	6.89
Isocarbamide	Herbicide	$C_8H_{15}N_3O_2$	$[M+H]^+$	186.12370	3.14
Isofenphos	Insecticide	$C_{15}H_{24}NO_4PS$	$[M+H]^+$	346.12365	7.64
Isofenphos-methyl	TP*	$C_{14}H_{22}NO_4PS$	$[M+H]^+$	332.10800	7.27
Isofenphos-oxon	TP*	$C_{15}H_{24}NO_5P$	$[M+H]^+$	330.14649	6.02
Isomethiozin	Herbicide	$C_{12}H_{20}N_4OS$	$[M+H]^+$	269.14306	6.20
Isonoruron	Herbicide	$C_{13}H_{22}N_2O$	$[M+H]^+$	223.18049	5.46
Isoprocarb	Insecticide	$C_{11}H_{15}NO_2$	$[M+H]^+$	194.11756	5.34
Isopropalin	Herbicide	$C_{15}H_{23}N_3O_4$	$[M+H]^+$	310.17613	8.73
Isoprothiolane	Fungicide	$C_{12}H_{18}O_4S_2$	$[M+H]^+$	291.07193	6.59
Isoproturon	Herbicide	$C_{12}H_{18}N_2O$	$[M+H]^+$	207.14919	5.19
Isouron	Herbicide	$C_{10}H_{17}N_3O_2$	$[M+H]^+$	212.13935	4.34
Isoxaben	Herbicide	$C_{18}H_{24}N_2O_4$	$[M+H]^+$	333.18088	6.40
Isoxadifen-ethyl	Herbicide	$C_{18}H_{17}NO_3$	$[M+H]^+$	296.12812	7.03
Isoxaflutole	Herbicide	$C_{15}H_{12}F_3NO_4S$	$[M+H]^+$	360.05119	6.00
Isoxathion	Insecticide	$C_{13}H_{16}NO_4PS$	$[M+H]^+$	314.06104	7.53
Ivermectin	Veterinary drug	$C_{48}H_{74}O_{14}$	$[M+Na]^+$	897.49708	9.69
Karbutilate	Insecticide	$C_{14}H_{21}N_3O_3$	$[M+H]^+$	280.16557	4.62

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Ketoprofen	Anti-inflammatory drug	$C_{16}H_{14}O_3$	$[M+H]^+$	255.10157	5.26
Kresoxim-methyl	Fungicide	$C_{18}H_{19}NO_4$	$[M+H]^+$	314.13868	6.86
Lactofen	Fungicide/Herbicide	$C_{19}H_{15}ClF_3NO_7$	$[M+NH_4]^+$	479.08274	7.97
Lambda-cyhalothrin	Insecticide	$C_{23}H_{19}ClF_3NO_3$	$[M+H]^+$	450.10783	8.71
Lenacil	Herbicide	$C_{13}H_{18}N_2O_2$	$[M-H]^-$	233.12955	4.59
Leptophos	Fungicide	$C_{13}H_{10}BrCl_2O_2PS$	$[M+H]^+$	412.87485	8.86
Levofloxacin	Antibiotic	$C_{18}H_{20}FN_3O_4$	$[M+H]^+$	362.15106	2.32
Linuron	Herbicide	$C_9H_{10}Cl_2N_2O_2$	$[M+H]^+$	249.01921	5.96
Lontrel (clopyralid)	Herbicide	$C_6H_3Cl_2NO_2$	$[M+H]^+$	191.96136	1.72
Lufenuron	Fungicide/Insecticide	$C_{17}H_8Cl_2F_8N_2O_3$	$[M+H]^+$	510.98570	7.89
Malaoxon	TP*	$C_{10}H_{19}O_7PS$	$[M+H]^+$	315.06619	4.68
Malathion	Insecticide	$C_{10}H_{19}O_6PS_2$	$[M+H]^+$	331.04335	6.53
Mandipropamid	Fungicide	$C_{23}H_{22}ClNO_4$	$[M+H]^+$	412.13101	6.23
Mecarbam	Acaricide/Insecticide	$C_{10}H_{20}NO_5PS_2$	$[M+H]^+$	330.05933	6.84
Mefenacet	Herbicide	$C_{16}H_{14}N_2O_2S$	$[M+H]^+$	299.08488	6.26
Mefenpyr-diethyl	Plant protection agent	$C_{16}H_{18}Cl_2N_2O_4$	$[M+H]^+$	373.07164	7.41
Mefluidide	Plant growth regulator	$C_{11}H_{13}F_3N_2O_3S$	$[M+H]^+$	311.06718	4.61
Mepanipyrim	Fungicide	$C_{14}H_{13}N_3$	$[M+H]^+$	224.11822	6.46
Mephosfolan	Acaricide/Insecticide	$C_8H_{16}NO_3PS_2$	$[M+H]^+$	270.03820	4.27
Mepronil	Fungicide	$C_{17}H_{19}NO_2$	$[M+H]^+$	270.14886	6.49
Mesosulfuron-methyl	Herbicide	$C_{17}H_{21}N_5O_9S_2$	$[M+H]^+$	504.08535	4.96
Mesotrione	Herbicide	$C_{14}H_{13}NO_7S$	$[M+H]^+$	340.04855	4.34
Metaflumizone	Insecticide	$C_{24}H_{16}F_6N_4O_2$	$[M-H]^-$	505.11047	7.80
Metalaxyl	Fungicide	$C_{15}H_{21}NO_4$	$[M+H]^+$	280.15433	5.21
Metalaxyl-M	Fungicide	$C_{15}H_{21}NO_4$	$[M+H]^+$	280.15433	5.21
Metamitron	Herbicide	$C_{10}H_{10}N_4O$	$[M+H]^+$	203.09274	3.03
Metazachlor	Herbicide	$C_{14}H_{16}ClN_3O$	$[M+H]^+$	278.10547	5.48
Metconazole	Fungicide	$C_{17}H_{22}ClN_3O$	$[M+H]^+$	320.15242	6.75
Methabenzthiazuron	Herbicide	$C_{10}H_{11}N_3OS$	$[M+H]^+$	222.06956	4.89
Methacrifos	Insecticide	$C_7H_{13}O_5PS$	$[M+H]^+$	241.02941	5.91
Methamidophos	Insecticide	$C_2H_8NO_2PS$	$[M+H]^+$	142.00862	0.92
Methfuroxam	Fungicide	$C_{14}H_{15}NO_2$	$[M+H]^+$	230.11756	5.91
Methidathion	Insecticide	$C_6H_{11}N_2O_4PS_3$	$[M+H]^+$	302.96914	5.87
Methiocarb	Acaricide/Insecticide	$C_{11}H_{15}NO_2S$	$C_9H_{13}OS^+$	169.06816	5.82
Methiocarb sulphone	TP*	$C_{11}H_{15}NO_4S$	$[M+H]^+$	258.07946	3.67
Methiocarb sulphoxide	TP*	$C_{11}H_{15}NO_3S$	$[M+H]^+$	242.08454	2.96
Methomyl	Insecticide	$C_5H_{10}N_2O_2S$	$[M+H]^+$	163.05358	2.40

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Methomyl-oxime	TP*	C_3H_7NOS	$[M+H]^+$	106.03211	1.81
Methoprotryne	Herbicide	$C_{11}H_{21}N_5OS$	$[M+H]^+$	272.15396	5.09
Methoxyfenozide	Insecticide	$C_{22}H_{28}N_2O_3$	$[M-H]^-$	367.20272	6.43
Methyl paraoxon	TP*	$C_8H_{10}NO_6P$	$[M+H]^+$	248.03185	4.27
Methyl parathion	TP*	$C_8H_{10}NO_5PS$	$[M+H]^+$	264.00901	6.25
Metobromuron	Herbicide	$C_9H_{11}BrN_2O_2$	$[M+H]^+$	259.00767	5.34
Metolachlor	Herbicide	$C_{15}H_{22}ClNO_2$	$[M+H]^+$	284.14118	6.71
Metolcarb	Acaricide/Insecticide	$C_9H_{11}NO_2$	$[M+H]^+$	166.08626	4.32
Metominostrobin (E-isomer)	Fungicide	$C_{16}H_{16}N_2O_3$	$[M+H]^+$	285.12337	5.52
Metominostrobin (Z-type)	Fungicide	$C_{16}H_{16}N_2O_3$	$[M+H]^+$	285.12337	5.58
Metosulam	Herbicide	$C_{14}H_{13}Cl_2N_5O_4S$	$[M+H]^+$	418.01381	5.02
Metoxuron	Herbicide	$C_{10}H_{13}ClN_2O_2$	$[M+H]^+$	229.07383	3.99
Metrafenone	Fungicide	$C_{19}H_{21}BrO_5$	$[M+H]^+$	409.06451	7.65
Metribuzin	Herbicide	$C_8H_{14}N_4OS$	$[M+H]^+$	215.09611	4.49
Metsulfuron-methyl	Herbicide	$C_{14}H_{15}N_5O_6S$	$[M+H]^+$	382.08158	4.55
Mevinphos	Insecticide	$C_7H_{13}O_6P$	$C_6H_{10}O_5P^+$	193.02604	3.54
Mexacarbate	Insecticide	$C_{12}H_{18}N_2O_2$	$[M+H]^+$	223.14410	3.48
MGK-264 (mixture of isomers)	Synergist	$C_{17}H_{25}NO_2$	$[M+H]^+$	276.19581	7.42
Molinate	Herbicide	$C_9H_{17}NOS$	$[M+H]^+$	188.11036	6.31
Monocrotophos	Insecticide	$C_7H_{14}NO_5P$	$[M+H]^+$	224.06824	2.29
Monolinuron	Algaecide	$C_9H_{11}ClN_2O_2$	$[M+H]^+$	215.05818	5.14
Monuron	Herbicide	$C_9H_{11}ClN_2O$	$[M+H]^+$	199.06327	4.31
Moxidectin	Veterinary drug	$C_{37}H_{53}NO_8$	$[M+H]^+$	640.38439	9.33
N,N-Diethyl-*m*-toluamide (DEET)	Insect repellent	$C_{12}H_{17}NO$	$[M+H]^+$	192.13829	5.23
N,N'-Ethylenethiourea	Industrial contaminant	$C_3H_6N_2S$	$[M+H]^+$	103.03245	0.90
Naphthalophos (naftalofos)	Veterinary drug	$C_{16}H_{16}NO_6P$	$[M+H]^+$	350.07880	5.76
Napropamide	Herbicide	$C_{17}H_{21}NO_2$	$[M+H]^+$	272.16451	6.49
Naptalam	Herbicide	$C_{18}H_{13}NO_3$	$[M+H]^+$	292.09682	4.49
Neburon	Herbicide	$C_{12}H_{16}Cl_2N_2O$	$[M+H]^+$	275.07125	6.80
Nicosulfuron	Herbicide	$C_{15}H_{18}N_6O_6S$	$[M+H]^+$	411.10813	4.05
Nitenpyram (ISO)	Insecticide/Veterinary drug	$C_{11}H_{15}ClN_4O_2$	$[M+H]^+$	271.09563	2.25
Nitralin	Herbicide	$C_{13}H_{19}N_3O_6S$	$[M+H]^+$	346.10673	6.84
Norflurazon	Herbicide	$C_{12}H_9ClF_3N_3O$	$[M+H]^+$	304.04590	5.34
Noruron	Pesticide	$C_{13}H_{22}N_2O$	$[M+H]^+$	223.18049	5.52
Novaluron	Insecticide	$C_{17}H_9ClF_8N_2O_4$	$[M-H]^-$	491.00503	7.54
Nuarimol	Fungicide	$C_{17}H_{12}ClFN_2O$	$[M+H]^+$	315.06950	5.62
Ofurace	Fungicide	$C_{14}H_{16}ClNO_3$	$[M+H]^+$	282.08915	5.09
Omethoate	Insecticide	$C_5H_{12}NO_4PS$	$[M+H]^+$	214.02974	0.92

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Orbencarb	Herbicide	$C_{12}H_{16}ClNOS$	$[M+H]^+$	258.07139	7.36
Orysastrobin	Fungicide	$C_{18}H_{25}N_5O_5$	$[M+H]^+$	392.19285	6.23
Oryzalin	Herbicide	$C_{12}H_{18}N_4O_6S$	$[M-H]^-$	345.08743	6.47
Oxadiargyl	Herbicide	$C_{15}H_{14}Cl_2N_2O_3$	$[M+H]^+$	341.04542	7.35
Oxadiazon	Herbicide	$C_{15}H_{18}Cl_2N_2O_3$	$[M+H]^+$	345.07672	8.15
Oxadixyl	Fungicide	$C_{14}H_{18}N_2O_4$	$[M+H]^+$	279.13393	4.24
Oxasulfuron	Herbicide	$C_{17}H_{18}N_4O_6S$	$[M+H]^+$	407.10198	4.40
Oxaziclomefone	Herbicide	$C_{20}H_{19}Cl_2NO_2$	$[M+H]^+$	376.08656	7.98
Oximino oxamyl	Nematicide	$C_5H_{10}N_2O_2S$	$[M+H]^+$	163.05358	1.77
Oxycarboxin	Fungicide	$C_{12}H_{13}NO_4S$	$[M+H]^+$	268.06381	3.84
Oxydemeton-methyl	Acaricide/Insecticide	$C_6H_{15}O_4PS_2$	$[M+H]^+$	247.02222	2.14
Oxyfluorfen	Herbicide	$C_{15}H_{11}ClF_3NO_4$	$[M+H]^+$	362.04015	7.98
Paclobutrazol (mixture of stereoisomers)	Fungicide	$C_{15}H_{20}ClN_3O$	$[M+H]^+$	294.13677	5.83
Paraoxon-ethyl	Insecticide	$C_{10}H_{14}NO_6P$	$[M+H]^+$	276.06315	5.28
Parathion	Insecticide	$C_{10}H_{14}NO_5PS$	$[M+H]^+$	292.04031	7.10
Pebulate	Herbicide	$C_{10}H_{21}NOS$	$[M+H]^+$	204.14166	7.57
Penconazole	Fungicide	$C_{13}H_{15}Cl_2N_3$	$[M+H]^+$	284.07158	6.70
Pencycuron	Fungicide	$C_{19}H_{21}ClN_2O$	$[M-H]^-$	327.12696	7.42
Pendimethalin	Herbicide	$C_{13}H_{19}N_3O_4$	$[M+H]^+$	282.14483	8.22
Penfluron	Insecticide	$C_{15}H_9F_5N_2O_2$	$[M-H]^-$	343.05114	6.73
Penoxsulam	Herbicide	$C_{16}H_{14}F_5N_5O_5S$	$[M-H]^-$	482.05631	5.37
Pentanochlor	Herbicide	$C_{13}H_{18}ClNO$	$[M+H]^+$	240.11497	6.89
Penthiopyrad	Fungicide	$C_{16}H_{20}F_3N_3OS$	$[M-H]^-$	358.12064	7.03
Pethoxamid	Herbicide	$C_{16}H_{22}ClNO_2$	$[M+H]^+$	296.14118	6.66
Phenmedipham	Herbicide	$C_{16}H_{16}N_2O_4$	$[M+H]^+$	301.11828	5.78
Phenothrin	Insecticide	$C_{23}H_{26}O_3$	$[M+H]^+$	351.19547	9.11
Phenthoate	Insecticide	$C_{12}H_{17}O_4PS_2$	$[M+H]^+$	321.03787	7.15
Phenylurea	Herbicide	$C_7H_8N_2O$	$[M+H]^+$	137.07094	2.34
Phorate-oxon sulphoxide	TP*	$C_7H_{17}O_4PS_2$	$[M+H]^+$	261.03787	3.03
Phorate sulphoxide	TP*	$C_7H_{17}O_3PS_3$	$[M+H]^+$	277.01502	5.00
Phorate-oxon sulphone	TP*	$C_7H_{17}O_5PS_2$	$[M+H]^+$	277.03278	3.66
Phorat sulphone	TP*	$C_7H_{17}O_4PS_3$	$[M+H]^+$	293.00994	5.71
Phosalone	Acaricide/Insecticide	$C_{12}H_{15}ClNO_4PS_2$	$[M+H]^+$	367.99414	7.45
Phosfolan	Insecticide	$C_7H_{14}NO_3PS_2$	$[M+H]^+$	256.02255	3.72
Phosmet	Insecticide	$C_{11}H_{12}NO_4PS_2$	$[M+H]^+$	318.00182	6.03
Phosmet-oxon	TP*	$C_{11}H_{12}NO_5PS$	$[M+H]^+$	302.02466	4.07
Phosphamidon	Insecticide	$C_{10}H_{19}ClNO_5P$	$[M+H]^+$	300.07622	4.11
Phospholan-methyl	TP*	$C_5H_{10}NO_3PS_2$	$[M+H]^+$	227.99125	2.58
Phoxim	Insecticide	$C_{12}H_{15}N_2O_3PS$	$[M+H]^+$	299.06138	7.04

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Picolinafen	Herbicide	$C_{19}H_{12}F_4N_2O_2$	$[M+H]^+$	377.09077	7.85
Picoxystrobin	Fungicide	$C_{18}H_{16}F_3NO_4$	$[M+H]^+$	368.11042	7.03
Piperalin	Fungicide	$C_{16}H_{21}Cl_2NO_2$	$[M+H]^+$	330.10221	4.56
Piperonyl butoxide	Synergise	$C_{19}H_{30}O_5$	$[M+NH_4]^+$	356.24315	7.92
Piperophos	Herbicide	$C_{14}H_{28}NO_3PS_2$	$[M+H]^+$	354.13210	7.59
Pirimicarb	Insecticide	$C_{11}H_{18}N_4O_2$	$[M+H]^+$	239.15025	3.91
Pirimicarb-desmethyl	TP*	$C_{10}H_{16}N_4O_2$	$[M+H]^+$	225.13460	2.68
Pirimiphos-methyl	TP*	$C_{11}H_{20}N_3O_3PS$	$[M+H]^+$	306.10358	7.47
Pirimiphos-ethyl	TP*	$C_{13}H_{24}N_3O_3PS$	$[M+H]^+$	334.13488	8.17
Pirimiphos-methyl-N-desethyl	TP*	$C_9H_{16}N_3O_3PS$	$[M+H]^+$	278.07228	5.36
Prallethrin	Insecticide	$C_{19}H_{24}O_3$	$[M+H]^+$	301.17982	7.58
Pretilachlor	Herbicide	$C_{17}H_{26}ClNO_2$	$[M+H]^+$	312.17248	7.69
Primisulfuron-methyl	TP*	$C_{15}H_{12}F_4N_4O_7S$	$[M-H]^-$	467.02901	6.19
Probenazole	Fungicide	$C_{10}H_9NO_3S$	$[M+H]^+$	224.03759	4.96
Prochloraz	Fungicide	$C_{15}H_{16}Cl_3N_3O_2$	$[M+H]^+$	376.03809	6.62
Procyazine	Herbicide	$C_{10}H_{13}ClN_6$	$[M+H]^+$	253.09630	4.55
Procymidone	Fungicide	$C_{13}H_{11}Cl_2NO_2$	$[M+H]^+$	284.02396	6.64
Profenofos	Insecticide	$C_{11}H_{15}BrClO_3PS$	$[M+H]^+$	374.94017	7.68
Profoxydim lithium	Herbicide	$C_{24}H_{32}ClNO_4S$	$[M+H]^+$	466.18133	8.88
Prohydrojasmon	Plant growth retardant	$C_{15}H_{26}O_3$	$[M+H]^+$	255.19547	7.50
Promecarb	Insecticide	$C_{12}H_{17}NO_2$	$[M+H]^+$	208.13321	5.87
Prometon	Herbicide	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.41
Prometryn	Herbicide	$C_{10}H_{19}N_5S$	$[M+H]^+$	242.14339	5.88
Propachlor	Herbicide	$C_{11}H_{14}ClNO$	$[M+H]^+$	212.08367	5.49
Propamocarb	Fungicide	$C_9H_{20}N_2O_2$	$[M+H]^+$	189.15975	0.96
Propanil	Herbicide	$C_9H_9Cl_2NO$	$[M-H]^-$	215.99884	5.69
Propaphos	Insecticide	$C_{13}H_{21}O_4PS$	$[M+H]^+$	305.09710	6.75
Propaquizafop	Herbicide	$C_{22}H_{22}ClN_3O_5$	$[M+H]^+$	444.13208	7.84
Propargite	Insecticide	$C_{19}H_{26}O_4S$	$[M+NH_4]^+$	368.18901	8.36
Propazine	Herbicide	$C_9H_{16}ClN_5$	$[M+H]^+$	230.11670	6.53
Propazine-2-hydroxy	TP*	$C_9H_{17}N_5O$	$[M+H]^+$	212.15059	3.71
Propetamphos	Insecticide	$C_{10}H_{20}NO_4PS$	$[M+H]^+$	282.09235	6.50
Propham	Herbicide	$C_{10}H_{13}NO_2$	$C_7H_8NO_2^+$	138.05496	5.41
Propiconazole (mixture of isomers)	Fungicide	$C_{15}H_{17}Cl_2N_3O_2$	$[M+H]^+$	342.07706	6.87
Propisochlor	Herbicide	$C_{15}H_{22}ClNO_2$	$[M+H]^+$	284.14118	6.71
Propoxur	Insecticide	$C_{11}H_{15}NO_3$	$C_8H_{10}NO_3^+$	168.06552	4.65
Propyzamide (pronamide)	Herbicide	$C_{12}H_{11}Cl_2NO$	$[M+H]^+$	256.02905	6.31
Proquinazid	Fungicide	$C_{14}H_{17}IN_2O_2$	$[M+H]^+$	373.04076	8.68
Prosulfocarb	Herbicide	$C_{14}H_{21}NOS$	$[M+H]^+$	252.14166	7.80
Prosulfuron	Herbicide	$C_{15}H_{16}F_3N_5O_4S$	$[M+H]^+$	420.09479	5.87

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Prothioconazole-desthio	TP*	$C_{14}H_{15}Cl_2N_3O$	$[M+H]^+$	312.06649	6.24
Pymetrozine	Insecticide	$C_{10}H_{11}N_5O$	$[M+H]^+$	218.10364	1.62
Pyracarbolid	Fungicide	$C_{13}H_{15}NO_2$	$[M+H]^+$	218.11756	4.88
Pyraclofos	Insecticide	$C_{14}H_{18}ClN_2O_3PS$	$[M+H]^+$	361.05371	7.16
Pyraclostrobin	Fungicide	$C_{19}H_{18}ClN_3O_4$	$[M+H]^+$	388.10586	7.30
Pyraflufen-ethyl	TP*	$C_{15}H_{13}Cl_2F_3N_2O_4$	$[M+H]^+$	413.02772	7.12
Pyrazolynate	Herbicide	$C_{19}H_{16}Cl_2N_2O_4S$	$[M+H]^+$	439.02806	7.48
Pyrazophos	Fungicide	$C_{14}H_{20}N_3O_5PS$	$[M+H]^+$	374.09341	7.27
Pyrazosulfuron-ethyl	TP*	$C_{14}H_{18}N_6O_7S$	$[M+H]^+$	415.10305	5.93
Pyrazoxyfen	Herbicide	$C_{20}H_{16}Cl_2N_2O_3$	$[M+H]^+$	403.06107	6.96
Pyrethrin (mixture of isomers)	Insecticide	$C_{22}H_{28}O_5$	$[M+H]^+$	373.20095	7.57
Pyributicarb	Insecticide	$C_{18}H_{22}N_2O_2S$	$[M+H]^+$	331.14748	8.21
Pyridaben	Insecticide	$C_{19}H_{25}ClN_2OS$	$[M+H]^+$	365.14489	8.82
Pyridafol	Herbicide	$C_{10}H_7ClN_2O$	$[M+H]^+$	207.03197	3.48
Pyridalyl	Insecticide	$C_{18}H_{14}Cl_4F_3NO_3$	$[M+H]^+$	491.97250	9.59
Pyridaphenthion	Insecticide	$C_{14}H_{17}N_2O_4PS$	$[M+H]^+$	341.07194	6.32
Pyridate	Herbicide	$C_{19}H_{23}ClN_2O_2S$	$[M+H]^+$	379.12415	9.25
Pyrifenox (mixture of isomers))	Fungicide	$C_{14}H_{12}Cl_2N_2O$	$[M+H]^+$	295.03995	5.56
Pyrimethanil	Fungicide	$C_{12}H_{13}N_3$	$[M+H]^+$	200.11822	5.49
Pyriproxyfen	Insecticide	$C_{20}H_{19}NO_3$	$[M+H]^+$	322.14377	8.11
Pyroquilon	Fungicide	$C_{11}H_{11}NO$	$[M+H]^+$	174.09134	4.07
Pyroxsulam	Herbicide	$C_{14}H_{13}F_3N_6O_5S$	$[M+H]^+$	435.06930	4.66
Quinalphos	Insecticide	$C_{12}H_{15}N_2O_3PS$	$[M+H]^+$	299.06138	7.04
Quinclorac	Herbicide	$C_{10}H_5Cl_2NO_2$	$[M+H]^+$	241.97701	3.81
Quinmerac	Herbicide	$C_{11}H_8ClNO_2$	$[M+H]^+$	222.03163	3.21
Quinoclamine	Herbicide	$C_{10}H_6ClNO_2$	$[M+H]^+$	208.01598	4.36
Quinoline	Antimicrobial agent	C_9H_7N	$[M+H]^+$	130.06513	2.10
Quinoxyfen	Fungicide	$C_{15}H_8Cl_2FNO$	$[M+H]^+$	308.00397	8.00
Quizalofop	Herbicide	$C_{17}H_{13}ClN_2O_4$	$[M+H]^+$	345.06366	6.27
Quizalofop-ethyl	TP*	$C_{19}H_{17}ClN_2O_4$	$[M+H]^+$	373.09496	7.75
Quizalofop-p-ethyl	TP*	$C_{19}H_{17}ClN_2O_4$	$[M+H]^+$	373.09496	7.74
Reserpine	Antihypertensive	$C_{33}H_{40}N_2O_9$	$[M+H]^+$	609.28066	4.84
Resmethrin	Insecticide	$C_{22}H_{26}O_3$	$[M+H]^+$	339.19547	8.89
Rimsulfuron	Herbicide	$C_{14}H_{17}N_5O_7S_2$	$[M+H]^+$	432.06422	4.77
Rotenone	Insecticide	$C_{23}H_{22}O_6$	$[M+H]^+$	395.14892	6.72
Roxithromycin	Antibiotic	$C_{41}H_{76}N_2O_{15}$	$[M+H]^+$	837.53185	4.99
Saflufenacil	Herbicide	$C_{17}H_{17}ClF_4N_4O_5S$	$[M+H]^+$	501.06171	5.99
Schradan (DMPA)	Herbicide	$C_8H_{24}N_4O_3P_2$	$[M+H]^+$	287.13964	3.05
Sebuthylazin	Herbicide	$C_9H_{16}ClN_5$	$[M+H]^+$	230.11670	5.90
Sebuthylazin-desethyl	TP*	$C_7H_{12}ClN_5$	$[M+H]^+$	202.08540	3.98
Secbumeton	Herbicide	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.45

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Selamectin impurity B	Veterinary drug	$C_{43}H_{63}NO_{11}$	$[M+H]^+$	770.44739	9.65
Sethoxydim	Herbicide	$C_{17}H_{29}NO_3S$	$[M+H]^+$	328.19409	8.09
S-Hydroprene	Insecticide	$C_{17}H_{30}O_2$	$[M+H]^+$	267.23186	10.05
Siduron	Herbicide	$C_{14}H_{20}N_2O$	$[M+H]^+$	233.16484	5.77
Silthiofam	Fungicide	$C_{13}H_{21}NOSSi$	$[M+H]^+$	268.11859	0.00
Simazine	Herbicide	$C_7H_{12}ClN_5$	$[M+H]^+$	202.08540	4.40
Simeconazole	Fungicide	$C_{14}H_{20}FN_3OSi$	$[M+H]^+$	294.14325	6.16
Simetone	Herbicide	$C_8H_{15}N_5O$	$[M+H]^+$	198.13494	3.36
Simetryn	Herbicide	$C_8H_{15}N_5S$	$[M+H]^+$	214.11209	4.41
S-Metolachlor	Herbicide	$C_{15}H_{22}ClNO_2$	$[M+H]^+$	284.14118	6.72
Spinetoram (mixture of isomers)	Insecticide	$C_{42}H_{69}NO_{10}$	$[M+H]^+$	748.49942	6.94
Spinosad (mixure of spinosyn A And D)	Insecticide	$C_{41}H_{65}NO_{10}$	$[M+H]^+$	732.46812	6.34
Spirodiclofen	Insecticide	$C_{21}H_{24}Cl_2O_4$	$[M+H]^+$	411.11244	8.81
Spiromesifen	Insecticide	$C_{23}H_{30}O_4$	$[M+H]^+$	371.22169	8.70
Spirotetramat	Insecticide	$C_{21}H_{27}NO_5$	$[M+H]^+$	374.19620	6.04
Spirotetramat-enol	TP*	$C_{18}H_{23}NO_3$	$[M+H]^+$	302.17507	4.45
Spirotetramat-enol glucoside	TP*	$C_{24}H_{33}NO_8$	$[M+H]^+$	464.22789	2.38
Spirotetramat-mono-hydroxy	TP*	$C_{21}H_{27}NO_5$	$[M+H]^+$	374.19620	6.04
Spiroxamine (mixture of isomers)	Fungicide	$C_{18}H_{35}NO_2$	$[M+H]^+$	298.27406	5.39
Sulcotrione	Herbicide	$C_{14}H_{13}ClO_5S$	$[M+H]^+$	329.02450	4.61
Sulfallate	Herbicide	$C_8H_{14}ClNS_2$	$[M+H]^+$	224.03290	7.25
Sulfamerazine	Antibacterial agent	$C_{11}H_{12}N_4O_2S$	$[M+H]^+$	265.07537	2.46
Sulfamonomethoxine	Antibacterial agent	$C_{11}H_{12}N_4O_3S$	$[M+H]^+$	281.07029	3.00
Sulfentrazone	Herbicide	$C_{11}H_{10}Cl_2F_2N_4O_3S$	$[M+H]^+$	386.98915	4.91
Sulfometuron-methyl	Herbicide	$C_{15}H_{16}N_4O_5S$	$[M+H]^+$	365.09142	4.73
Sulfosulfuron	Herbicide	$C_{16}H_{18}N_6O_7S_2$	$[M+H]^+$	471.07512	5.30
Sulfoxaflor	Insecticide	$C_{10}H_{10}F_3N_3OS$	$[M+H]^+$	278.05695	3.91
Sulfuramid	Insecticide	$C_{10}H_6F_{17}NO_2S$	$[M-H]^-$	525.97750	8.32
Sulprofos sulphoxide	TP*	$C_{12}H_{19}O_3PS_3$	$[M+H]^+$	339.03067	6.37
Systhane™	Fungicide	$C_{15}H_{17}ClN_4$	$[M+H]^+$	289.12145	6.16
Tau-Fluvalinate	Insecticide	$C_{26}H_{22}ClF_3N_2O_3$	$[M+H]^+$	503.13438	9.02
TDCPP	Industrial contaminant	$C_9H_{15}Cl_6O_4P$	$[M+H]^+$	430.88829	6.89
Tebuconazole (folicur)	Fungicide	$C_{16}H_{22}ClN_3O$	$[M+H]^+$	308.15242	6.49
Tebufenozide	Insecticide	$C_{22}H_{28}N_2O_2$	$C_{18}H_{21}N_2O_2^+$	297.15975	6.82
Tebufenpyrad	Acaricide	$C_{18}H_{24}ClN_3O$	$[M+H]^+$	334.16807	7.86
Tebupirimfos	Insecticide	$C_{13}H_{23}N_2O_3PS$	$[M+H]^+$	319.12398	8.21
Tebutam	Herbicide	$C_{15}H_{23}NO$	$[M+H]^+$	234.18524	6.72
Tebuthiuron	Herbicide	$C_9H_{16}N_4OS$	$[M+H]^+$	229.11176	4.06

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Teflubenzuron	Insecticide	$C_{14}H_6Cl_2F_4N_2O_2$	$[M+H]^+$	380.98152	7.46
Tembotrione	Herbicide	$C_{17}H_{16}ClF_3O_6S$	$[M+NH_4]^+$	458.06465	5.97
Tepraloxydim	Herbicide	$C_{17}H_{24}ClNO_4$	$[M-H]^-$	340.13211	6.44
Terbufos sulphone	TP*	$C_9H_{21}O_4PS_3$	$[M+H]^+$	321.04124	6.33
Terbufos sulphoxide	TP*	$C_9H_{21}O_3PS_3$	$[M+H]^+$	305.04633	5.74
Terbumeton	Herbicide	$C_{10}H_{19}N_5O$	$[M+H]^+$	226.16624	4.41
Terbumeton-desethyl	TP*	$C_8H_{15}N_5O$	$[M+H]^+$	198.13494	3.27
Terbuthylazine	Herbicide	$C_9H_{16}ClN_5$	$[M+H]^+$	230.11670	5.96
Terbuthylazine-desethyl	TP*	$C_7H_{12}ClN_5$	$[M+H]^+$	202.08540	4.40
Terbutol (terbucarb)	Insecticide	$C_{17}H_{27}NO_2$	$[M+H]^+$	278.21146	7.52
Terbutryne	Herbicide	$C_{10}H_{19}N_5S$	$[M+H]^+$	242.14339	5.88
Terbutylazine-2-hydroxy	TP*	$C_9H_{17}N_5O$	$[M+H]^+$	212.15059	2.69
Tetrachlorvinphos (ISO)	Insecticide	$C_{10}H_9Cl_4O_4P$	$[M+H]^+$	366.90367	6.65
Tetraconazole	Fungicide	$C_{13}H_{11}Cl_2F_4N_3O$	$[M+H]^+$	372.02881	6.33
Tetraethyl dithiopyrophosphate	Insecticide	$C_8H_{20}O_5P_2S_2$	$[M+H]^+$	323.03002	7.36
Tetraethyl pyrophosphate	Insecticide	$C_8H_{20}O_7P_2$	$[M+H]^+$	291.07571	4.04
Tetramethrin	Insecticide	$C_{19}H_{25}NO_4$	$[M+H]^+$	332.18564	7.96
Thenylchlor	Herbicide	$C_{16}H_{18}ClNO_2S$	$[M+H]^+$	324.08195	6.69
Thiabendazole	Anthelmintic/Fungicide	$C_{10}H_7N_3S$	$[M+H]^+$	202.04335	2.43
Thiacloprid	Insecticide	$C_{10}H_9ClN_4S$	$[M+H]^+$	253.03092	3.90
Thiamethoxam	Insecticide	$C_8H_{10}ClN_5O_3S$	$[M+H]^+$	292.02657	2.63
Thiazafluron	Herbicide	$C_6H_7F_3N_4OS$	$[M+H]^+$	241.03654	4.41
Thiazopyr	Herbicide	$C_{16}H_{17}F_5N_2O_2S$	$[M+H]^+$	397.10037	7.30
Thidiazuron	Herbicide	$C_9H_8N_4OS$	$[M-H]^-$	219.03461	4.09
Thiencarbazone-methyl	Herbicide	$C_{12}H_{14}N_4O_7S_2$	$[M+H]^+$	391.03767	4.54
Thifensulfuron-methyl	Herbicide	$C_{12}H_{13}N_5O_6S_2$	$[M+H]^+$	388.03800	4.41
Thifluzamide	Fungicide	$C_{13}H_6Br_2F_6N_2O_2S$	$[M+H]^+$	528.84733	6.91
Thiobencarb	Herbicide	$C_{12}H_{16}ClNOS$	$[M+H]^+$	258.07139	7.36
Thiocarbazyl	Herbicide	$C_{16}H_{25}NOS$	$[M+H]^+$	280.17296	8.55
Thiodicarb	Insecticide	$C_{10}H_{18}N_4O_4S_3$	$[M+H]^+$	355.05630	4.71
Thiofanox	Insecticide	$C_9H_{18}N_2O_2S$	$[M+Na]^+$	241.09812	5.02
Thiofanox sulfone	TP*	$C_9H_{18}N_2O_4S$	$[M+H]^+$	251.10601	3.38
Thiofanox sulfoxide	TP*	$C_9H_{18}N_2O_3S$	$[M+H]^+$	235.11109	2.80
Thionazine (Zinophos™)	Insecticide	$C_8H_{13}N_2O_3PS$	$[M+H]^+$	249.04573	5.66
Thiophanate-methyl	Fungicide	$C_{12}H_{14}N_4O_4S_2$	$[M+H]^+$	343.05293	4.48
Thiophanate-ethyl	Fungicide	$C_{14}H_{18}N_4O_4S_2$	$[M+H]^+$	371.08423	5.49
Tiadinil	Fungicide	$C_{11}H_{10}ClN_3OS$	$[M-H]^-$	266.01604	6.13
Tokuthion®	Insecticide	$C_{11}H_{15}Cl_2O_2PS_2$	$[M+H]^+$	344.97009	8.96
Tolclofos-methyl	Fungicide	$C_9H_{11}Cl_2O_3PS$	$[M+H]^+$	300.96164	7.47
Tolfenpyrade	Herbicide	$C_{21}H_{22}ClN_3O_2$	$[M+H]^+$	384.14733	7.84

Compound	Class	Formula [M]	Ion	Theoretical m/z	t_R (min)
Tolylfluanid	Fungicide	$C_{10}H_{13}Cl_2FN_2O_2S_2$	$[M+H]^+$	346.98523	7.35
Topramezone	Herbicide	$C_{16}H_{17}N_3O_5S$	$[M+H]^+$	364.09617	3.57
Tralkoxydim	Herbicide	$C_{20}H_{27}NO_3$	$[M+H]^+$	330.20637	8.24
Triadimefon	Fungicide	$C_{14}H_{16}ClN_3O_2$	$[M+H]^+$	294.10038	6.27
Triallate	Herbicide	$C_{10}H_{16}Cl_3NOS$	$[M+H]^+$	304.00910	8.50
Triasulfuron	Herbicide	$C_{14}H_{16}ClN_5O_5S$	$[M+H]^+$	402.06334	4.75
Triazamate	Insecticide	$C_{13}H_{22}N_4O_3S$	$[M+H]^+$	315.14854	6.69
Triaziflam	Herbicide	$C_{17}H_{24}FN_5O$	$[M+H]^+$	334.20377	6.12
Triazophos	Insecticide	$C_{12}H_{16}N_3O_3PS$	$[M+H]^+$	314.07228	6.58
Triazoxid	Fungicide	$C_{10}H_6ClN_5O$	$[M+H]^+$	248.03336	4.56
Tribenuron-methyl	Herbicide	$C_{15}H_{17}N_5O_6S$	$[M+H]^+$	396.09723	5.55
Tribufos (defoliant)	Herbicide	$C_{12}H_{27}OPS_3$	$[M+H]^+$	315.10345	8.89
Trichlorfon	Insecticide	$C_4H_8Cl_3O_4P$	$[M+H]^+$	256.92986	2.90
Tricyclazole	Fungicide	$C_9H_7N_3S$	$[M+H]^+$	190.04335	3.57
Tridemorph (mixture of isomers)	Fungicide	$C_{19}H_{39}NO$	$[M+H]^+$	298.31044	6.43
Trietazine	Herbicide	$C_9H_{16}ClN_5$	$[M+H]^+$	230.11670	6.58
Trifloxystrobin	Fungicide	$C_{20}H_{19}F_3N_2O_4$	$[M+H]^+$	409.13697	7.64
Trifloxystrobin metabolite	TP*	$C_{19}H_{17}F_3N_2O_4$	$[M+H]^+$	395.12132	6.71
Trifloxysulfuron sodium	Herbicide	$C_{14}H_{13}F_3N_5NaO_6S$	$[M+H]^+$	460.05091	5.07
Triflumizole	Fungicide	$C_{15}H_{15}ClF_3N_3O$	$[M+H]^+$	346.09285	7.12
Triflumuron	Insecticide	$C_{15}H_{10}ClF_3N_2O_3$	$[M+H]^+$	359.04048	7.00
Triflusulfuron-methyl	Herbicide	$C_{17}H_{19}F_3N_6O_6S$	$[M+H]^+$	493.11117	6.22
Triforine	Fungicide	$C_{10}H_{14}Cl_6N_4O_2$	$[M+H]^+$	434.92917	5.30
Trinexapac-ethyl	Plant growth regulator	$C_{13}H_{16}O_5$	$[M+H]^+$	253.10705	5.52
Triphenyl phosphorothionate	Industrial contaminant	$C_{18}H_{15}O_3PS$	$[M+H]^+$	343.05523	8.21
Tris(2-chloroethyl) phosphate	Industrial contaminant	$C_6H_{12}Cl_3O_4P$	$[M+H]^+$	284.96116	4.71
Tri-*o*-cresyl phosphate	Industrial contaminant	$C_{21}H_{21}O_4P$	$[M+H]^+$	369.12502	8.28
Triticonazole	Fungicide	$C_{17}H_{20}ClN_3O$	$[M+H]^+$	318.13677	6.03
Tritosulfuron	Herbicide	$C_{13}H_9F_6N_5O_4S$	$[M-H]^-$	444.02067	5.93
Uniconazole	Plant growth regulator	$C_{15}H_{18}ClN_3O$	$[M+H]^+$	292.12112	6.22
Vamidothion	Insecticide	$C_8H_{18}NO_4PS_2$	$[M+H]^+$	288.04877	2.92
Vamidothion sulfoxide	Insecticide	$C_8H_{18}NO_5PS_2$	$[M+H]^+$	304.04368	0.93
Vernolate	Herbicide	$C_{10}H_{21}NOS$	$[M+H]^+$	204.14166	7.57
XMC (3,5-xylyl methylcarbamate)	Insecticide	$C_{10}H_{13}NO_2$	$[M+H]^+$	180.10191	4.97
Z-Mevinphos	Insecticide	$C_7H_{13}O_6P$	$[M+H]^+$	193.02604	3.06
Zoxamide	Fungicide	$C_{14}H_{16}Cl_3NO_2$	$[M+H]^+$	336.03194	7.20

*Transformation product

Table S4: Results of the targeted and suspected screening of anthropic contaminants in the 52 honey samples.

		Origin		Target screening	Suspect screening
Sample	ID	Floral	Geographical	Unequivocally identified contaminants[a]	Tentatively identified contaminants [b]
Honey	**#1**	**chestnut**	**France**	tebuconazole, tebufenozide, prothioconazole-desthio, fluopyram	2HBzN, 24MoBT, DEP, DBP, DBS,
	#2	**chestnut**	**France**	DMF	24MoBT, DBP
	#3	**chestnut**	**France**	chlorfenvinphos, DMF, tris(1,3-dichloro-2-propyl)phosphate (TDCPP)	24MoBT, DBP, ATBC, benzoic acid (-) , MEP (-)
	#4	**chestnut**	**France**	fluopyram, DMF	2HBzN, TEP, 24MoBT, DBP, DBS, PNA
	#5	**chestnut**	**France**	DMF	2HBzN, EP, DBP, PNA
	#6	**chestnut**	**France**	tebuconazole	2HBzN, 24MoBT, DEP, DBP, PNA, paracetamol (-)
	#7	**chestnut**	**France**	DMF	DBP, 2HBzN, 24MoBT, DEP, ATBC, DBS
	#8	**chestnut**	**France**	fluopyram, prothioconazole-desthio, DMF	2HBzN, 24MoBT, DBP, DBS
	#9	**chestnut**	**Italy**		2HBzN, 24MoBT, MiBP, DBP, PNA
	#10	**chestnut**	**Italy**	acetamiprid, coumaphos, hexythiazox	2HBzN, 2-naphthylamine, 24MoBT, DEP, DBP, PNA
	#11	**chestnut**	**Italy**		2HBzN, DEP, DBP, MTSK, 4MBP
	#12	**chestnut**	**Italy**		2HBzN, DEP, DBP, DBS
	#13	**chestnut**	**Italy**		2HBzN, NBBS, DEP, DBP, DBS
	#14	**chestnut**	**Italy**		2HBzN, MTSK, DEP, DBP
	#15	**chestnut**	**Spain**	acetamiprid, coumaphos, DMA, DMF	2HBzN, 24MoBT, DBP, DBS, MEP (-)
	#16	**chestnut**	**Spain**	coumaphos, DMA, DMF	2HBzN, 24MoBT, NBBS, DBP
	#17	**chestnut**	**Spain**	coumaphos, DMA, piperonyl butoxide	2HBzN, DEP, DBP
	#18	**chestnut**	**Spain**	etoxazole, propiconazole	MTSK, 24MoBT, EP, DBP, DBS
	#19	**lavender**	**France**		EP, DBP, DBS
	#20	**lavender**	**France**	DMF	24MoBT, DBP, MEP (-)
	#21	**lavender**	**France**	DEET	24MoBT, DEP, DBP
	#22	**lavender**	**Spain**	coumaphos, DMA, DMF	DEP, DBP, DBS, MEP (-)
	#23	**lavender**	**Spain**	coumaphos, DMA, DMF, DMPF, propiconazole	DEP, DBP, DBS, MEP (-)
	#24	**lemon tree**	**Italy**	tris(1,3-dichloro-2-propyl)phosphate (TDCPP)	2HBzN, 24MoBT, DEP, DBP, DBS
	#25	**lemon tree**	**Italy**	chlorfenvinphos, hexythiazox	2HBzN, 24MoBT, DEP, DBP, DBS
	#26	**lemon tree**	**Spain**	acetamiprid, DMA, DMF, flonicamid, metalaxyl	2HBzN, DEP, EP, DBP, DBS, MEP (-)
	#27	**lemon tree**	**Spain**	acetamiprid, coumaphos, DMA, DMF, flonicamid, tebuconazole	2HBzN, DEP, TPHP, DBP
	#28	**lemon tree**	**Spain**	acetamiprid, coumaphos, DMA, DMF, DMPF, metalaxyl, myclobutanil, flonicamid, fluopyram	2HBzN, 24MoBT, DEP, DBP, DBS
	#29	**orange tree**	**Italy**	imidacloprid	DDAO, 2HBzN, 24MoBT, DBP, DBS, 4-acetamidophenol sulfate (-), MEP (-)
	#30	**orange tree**	**Italy**	acetamiprid, chlorfenvinphos, dimethoate	DDAO, DEP, DBP, DBS

		Origin		Target screening	Suspect screening
Sample	ID	Floral	Geographical	Unequivocally identified contaminants[a]	Tentatively identified contaminants [b]
Urban honey	**#31**	**orange tree**	**Italy**	acetamiprid, dimethoate, DMF	2HBzN, 24MoBT, DEP, DBP, DBS, , MEP (-)
	#32	**orange tree**	**Spain**	acetamiprid, chlorfenvinphos, coumaphos, dimethoate, DMF, propiconazole, metalaxyl-m	2HBzN, DEP, N,N-dimethyltetradecylamine, DBP
	#33	**orange tree**	**Spain**	acetamiprid, coumaphos, DMA, DMF, DMPF, piperonyl butoxide, chlorfenvinphos	2HBzN, 24MoBT, TiBP, DBP, DBS
	#34	**unspecified**	**Canada**	acetamiprid, DMA, DMF, DMPF	24MoBT, TPHP, DBP, DPHP, DBS, , MEP (-)
	#35	**unspecified**	**Canada**		DEP, TPHP, DBP, ATBC, MEP (-)
	#36	**unspecified**	**Canada**	DMF	TPHP, DBP, DBS
	#37	**unspecified**	**Canada**		24MoBT, DEP, EP, TPHP, DBP, DBS, myristamidopropyl betaine
	#38	**unspecified**	**Canada**		TEP, DEP, EP, DBP
	#39	**unspecified**	**Canada**		DBP, 2HBzN, MTSK, 24MoBT, EP, TPHP
	#40	**unspecified**	**Canada**		DP, 2HBzN, TEP, 24MoBT, DEP, N,N-dimethyltetradecylamine, EP, DBP, DBS, MEP (-), 3-ethoxy-4-hydroxybenzaldehyde (-)
	#41	**unspecified**	**Canada**		2HBzN, 24MoBT, EP, TPHP, DBP, ATBC, acamprosate (-)
	#42	**unspecified**	**Canada**		2HBzN, 24MoBT, DEP, EP, DBP, ATBC
	#43	**unspecified**	**Canada**		2HBzN, DP, DEP, EP, DBP, DPHP
	#44	**unspecified**	**Canada**		DP, DDAO, 24MoBT, DEP, EP, TBEP, DBP
	#45	**unspecified**	**Canada**		2HBzN, DDAO, 24MoBT, DEP, EP, DBP, DBS
	#46	**unspecified**	**Canada**	fluopyram, flupyradifurone, prothioconazole-desthio	24MoBT, EP, DBP, benzoic acid (-), MPP (-), MEP (-)
	#47	**unspecified**	**Canada**		24MoBT, EP, TPHP, BBP, DBP
	#48	**unspecified**	**France**	DMA, DMF	MTSK, 2HBzN, TPHP, DBP, DBS
	#49	**unspecified**	**France**	DMF, fluopyram, prothioconazole-desthio, thiacloprid	2HBzN, 24MoBT, DBP, DBS
	#50	**unspecified**	**France**		MTSK, 2HBzN, DDAO, 24MoBT, DBP , MEP (-)
	#51	**unspecified**	**France**	coumaphos, DMF	2HBzN, MTSK, 24MoBT, DBP
	#52	**unspecified**	**France**	fluopyram, prothioconazole-desthio, DMF	2HBzN, 24MoBT, DBP

[a]Unequivocal identification using the analytical standard with a confidence level 1 according to Schymanski et al. (2014)

[b]Tentative identification with a confidence level 2a according to Schymanski et al. (2014)

Table S5: Type of contaminant found by targeted and suspected analysis, as well as their usage and frequency of appearance (FoA).

Type of analysis	Type of contaminant	Compound	**Usage**	FoA (%)
Target screening[a]	Industrial chemical	tris(1,3-dichloro-2-propyl)phosphate (TDCPP)	**Flame retardant**	4
	Pesticide residue	acetamiprid	**Insecticide**	19
		chlorfenvinphos	**Insecticide**	10
		coumaphos	**Acaricide / Insecticide**	21
		dimethoate	**Acaricide / Insecticide**	6
		etoxazole	**Acaricide**	2
		flonicamid	**Insecticide**	6
		fluopyram	**Fungicide**	13
		flupyradifurone	**Insecticide**	2
		hexythiazox	**Acaricide**	4
		imidacloprid	**Insecticide**	2
		metalaxyl	**Fungicide**	6
		myclobutanil	**Fungicide**	2
		n,n-diethyl-m-toluamide (DEET)	**Insect repellent**	2
		propiconazole	**Fungicide**	6
		tebuconazole	**Fungicide**	6
		tebufenozide	**Insecticide**	2
		thiacloprid	**Insecticide**	2
	Synergist	piperonyl butoxide	**Insecticide synergist**	4
	Transformation product	2,4-dimethylaniline (DMA)		21
		2,4-dimethylformamidine (DMF)		44
		n-(2,4-dimethylphenyl)-n-methylformamidine (DMPF)		8
		prothioconazole-desthio		10
Suspect screening[b]	Industrial chemical	2-(4-morpholinyl)benzothiazole (24MoBT)	**Accelerator of vulcanisation**	65
		2-hydroxybenzonitrile (2HBzN)	**Disinfectant / Pesticide / Preservative / Starting agent**	67
		2-naphthylamine	**Antioxidant / Precursor agent**	2
		3-ethoxy-4-hydroxybenzaldehyde	**Additive**	2
		4-methylbenzophenone (4MBP)	**Coating agent**	2
		acetyl tributyl citrate (ATBC)	**Plasticizer**	10
		benzoic acid	**Preservative**	4
		benzyl butyl phthalate (BBP)	**Plasticiser**	2
		dibutyl phthalate (DP)	**Plasticiser**	6
		dibutyl sebacate (DBS)	**Plasticiser**	50
		diethyl phthalate (DEP)	**Plasticiser**	54
		dibutyl phthalate (DBP)	**Plasticiser**	100
		diphenyl phosphate (DPHP)	**Protective agent**	4
		ethylparaben (EP)	**Preservative**	46

Type of analysis	Type of contaminant	Compound	**Usage**	FoA (%)
Suspect screening[b]	Industrial chemical	methyl trans-styryl ketone (MTSK)	**Additive**	13
		methylparaben (MEP)	**Preservative**	23
		monoethyl phthalate (MEP)	**Plasticiser**	2
		mono-iso-butyl phthalate (MiBP)	**Plasticiser**	2
		monomethyl phthalate (MPP)	**Plasticiser**	2
		myristamidopropyl betaine	**Personal care product**	2
		n,n-dimethyldodecylamine N-oxide (DDAO)	**Personal care product**	10
		n,n-dimethyltetradecylamine	**Personal care product**	4
		n-butylbenzenesulfonamide (NBBS)	**Plasticiser**	4
		n-phenyl-2-naphthylamine (PNA)	**Antioxidant / Lubricant**	10
		tributoxyethyl Phosphate (TBEP)	**Plasticiser**	2
		tri-isobutyl phosphate (TiBP)	**Anti-foaming / Anti-freezing agent**	2
		triethyl phosphate (TEP)	**Flame retardant / Plasticiser**	6
		triphenyl phosphate (TPHP)	**Flame retardant / Plasticiser**	17
	Pharmaceutical	4-acetamidophenol sulfate	**Analgesic / Antipyretic**	2
		acamprosate	**Alcohol-dependant patient treatment**	2
		paracetamol	**Analgesic / Antipyretic**	2

[a]Unequivocal identification using the analytical standard with a confidence-level 1 according to Schymanski et al. (20

[b]Tentative identification with a confidence-level 2a according to Schymanski et al. (2014)

Table S6: Discriminant features influencing the separation of the 52 honey samples according to their type and floral origin.

		Features				
Ionization	Honey group	*m/z*	tR (min)	fold change	p-value	Tentative annotation
ESI^+	*Chestnut*	146.0598	2.97	39	1.75E-15	**2-Quinolone**
		164.0706	3.73	Infinity*	3.69E-09	nott annotated
		187.087	3.05	42	1.28E-12	**Deoxyvasicinone**
		188.0704	2.75	73	3.42E-14	**Indoleacrylic acid**
		213.1019	1.63	44	1.18E-16	not annotated
		233.129	3.59	Infinity*	4.42E-11	not annotated
		241.0969	3	80	3.19E-16	not annotated
		482.1879	2.99	Infinity*	2.89E-09	not annotated
		677.1853	3.76	Infinity*	3.72E-07	not annotated
	Citrus	130.0647	4.44	103	2.63E-20	**Indole-3-Carbinol**
		134.06	2.98	116	2.08E-26	**2-Oxindole**
		195.088	2.2	100	1.40E-06	**Caffeine**
		314.1227	2.8	195	2.02E-17	not annotated
		471.2007	5.42	24	3.88E-20	not annotated
		496.221	4.44	Infinity*	5.10E-12	not annotated
		795.4759	5.95	190	1.78E-12	not annotated
	Lavender	227.1276	3.81	42	7.78E-12	not annotated
		295.1448	5.75	19	4.99E-08	not annotated
		310.1283	2.99	1403	1.36E-11	not annotated
	Urban	316.3205	5.74	10	3.66E-11	not annotated
ESI^-	*Chestnut*	164.0356	3	Infinity*	1.73E-12	not annotated
		174.0201	3.75	207	2.63E-12	not annotated
		200.0363	2.71	37	3.51E-14	not annotated
		239.0829	2.98	56	4.13E-19	not annotated
		241.0992	2.54	111	6.46E-16	not annotated
		242.1019	2.53	Infinity*	1.03E-15	not annotated
		307.0724	2.8	35	7.52E-11	not annotated
		337.0836	3.75	326	3.37E-11	not annotated
		343.0459	4.33	Infinity*	2.78E-17	not annotated
		375.0988	4.52	Infinity*	3.34E-08	not annotated
		501.1539	2.99	60	1.58E-21	not annotated
		535.1083	4.34	103	3.38E-16	not annotated
		675.1731	3.75	Infinity*	2.68E-08	not annotated
	Citrus	377.1495	4.07	Infinity*	3.03E-12	not annotated
		657.2685	4.44	Infinity*	3.20E-15	not annotated
		839.4665	5.95	135	5.53E-13	not annotated
		975.3564	5.42	Infinity*	1.24E-17	not annotated
	Lavender	161.0458	3.12	14	2.47E-11	not annotated
		301.1239	3.29	451	1.99E-06	not annotated
		343.1541	6.34	128	2.18E-10	not annotated
		344.0894	2.99	499	2.79E-11	not annotated
		354.1189	2.99	159	1.96E-11	not annotated
		355.1216	2.99	Infinity*	1.95E-10	not annotated
		469.1915	3.29	Infinity*	1.60E-09	not annotated
		471.2071	3.13	Infinity*	7.88E-10	not annotated
		523.2736	3.8	Infinity*	1.82E-08	not annotated
		781.4276	8.73	99	3.56E-15	not annotated
		791.4581	8.73	82	2.57E-14	not annotated
		749.4462	8.1	18	3.09E-13	not annotated

		Features				
Ionization	Honey group	*m/z*	tR (min)	fold change	p-value	Tentative annotation
	Urban	285.0772	5.24	Infinity*	6.65E-05	not annotated
		293.1162	2.44	73	7.42E-08	not annotated
		301.1298	2.51	Infinity*	2.62E-06	not annotated
		513.268	2.94	222	2.99E-03	not annotated
		344.0852	5.61	21	3.34E-09	not annotated
		375.0862	6.95	14	2.81E-08	not annotated
		393.1756	2.63	Infinity*	1.25E-06	not annotated
		687.1723	5.62	Infinity*	5.81E-07	not annoteatd

*When the feature was totally absent (no peak detected) in the other honey groups

Table S7: Discriminant features influencing the separation of chestnut honey samples according to their geographical origin.

Ionization	Chestnut honey group	Features			
		m/z	tR (min)	fold change	p-value
ESI^+	*France*	292.1747	0.99	10	1.62E-03
		326.1412	3.45	26	7.54E-03
		356.1131	3.94	15	1.04E-02
	Italy	282.2694	8.97	Infinity*	3.04E-03
		559.5176	8.95	Infinity*	1.29E-03
ESI^-	*France*	306.1199	1.84	52	9.51E-03
		419.1473	6.69	Infinity*	9.72E-03
	Italy	261.0073	3.49	605	1.13E-02
		651.1741	3.88	91	1.54E-05
	Spain	283.0604	4.06	1672	4.40E-04
		299.1178	0.98	14	2.10E-04
		303.1084	1	30	6.69E-03
		310.1286	2.61	232	2.11E-03
		311.056	4.78	Infinity*	5.40E-04
		319.2278	7.53	196	1.09E-03
		323.2581	7.97	Infinity*	6.97E-06
		337.1072	6.5	Infinity*	3.40E-04
		381.1019	0.94	82	6.50E-06
		389.1173	0.98	Infinity*	7.07E-09
		424.1235	0.97	62	3.47E-07
		455.3539	8.98	2757	1.17E-03
		501.359	9.04	Infinity*	1.15E-03

*When the feature was totally absent (no peak detected) in the other honey groups

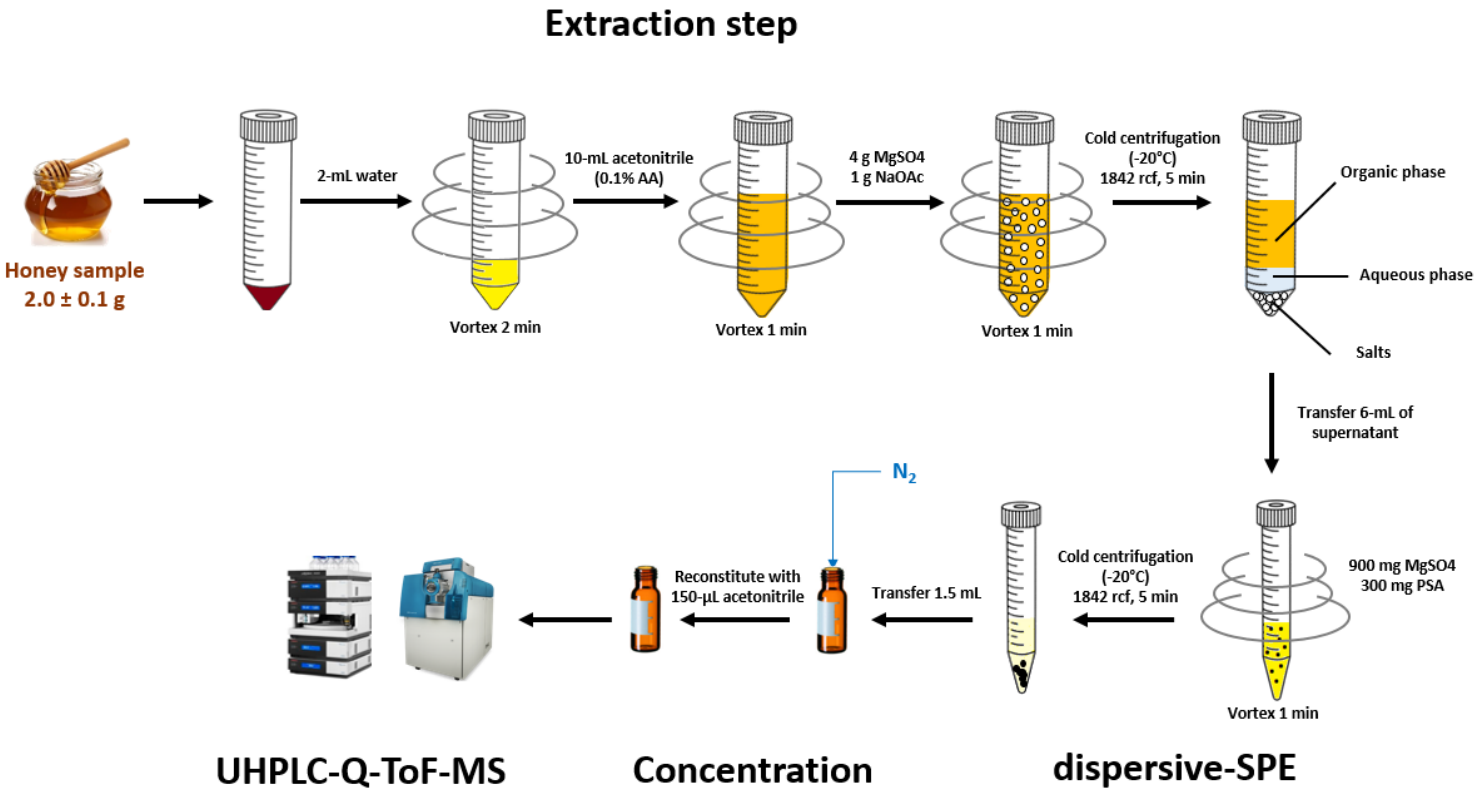

Fig. S1: Modified QuEChERS-based protocol for the preparation of honey samples.

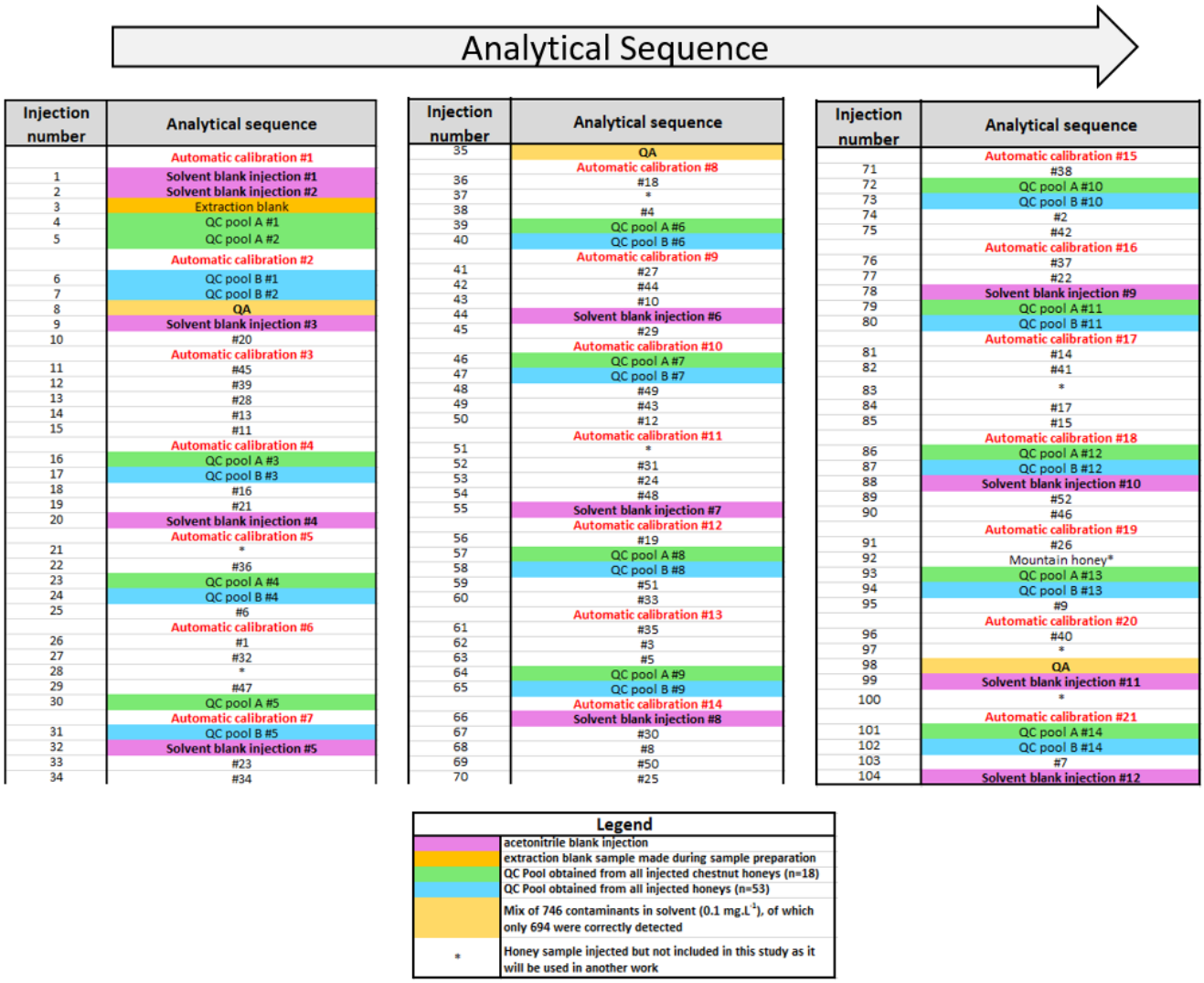

Fig. S2: Analytical sequence designed for this study, along with the quality assurance (QA) and quality control (QC) procedures implemented to meet quality standard requirements of metabolomics-like studies.

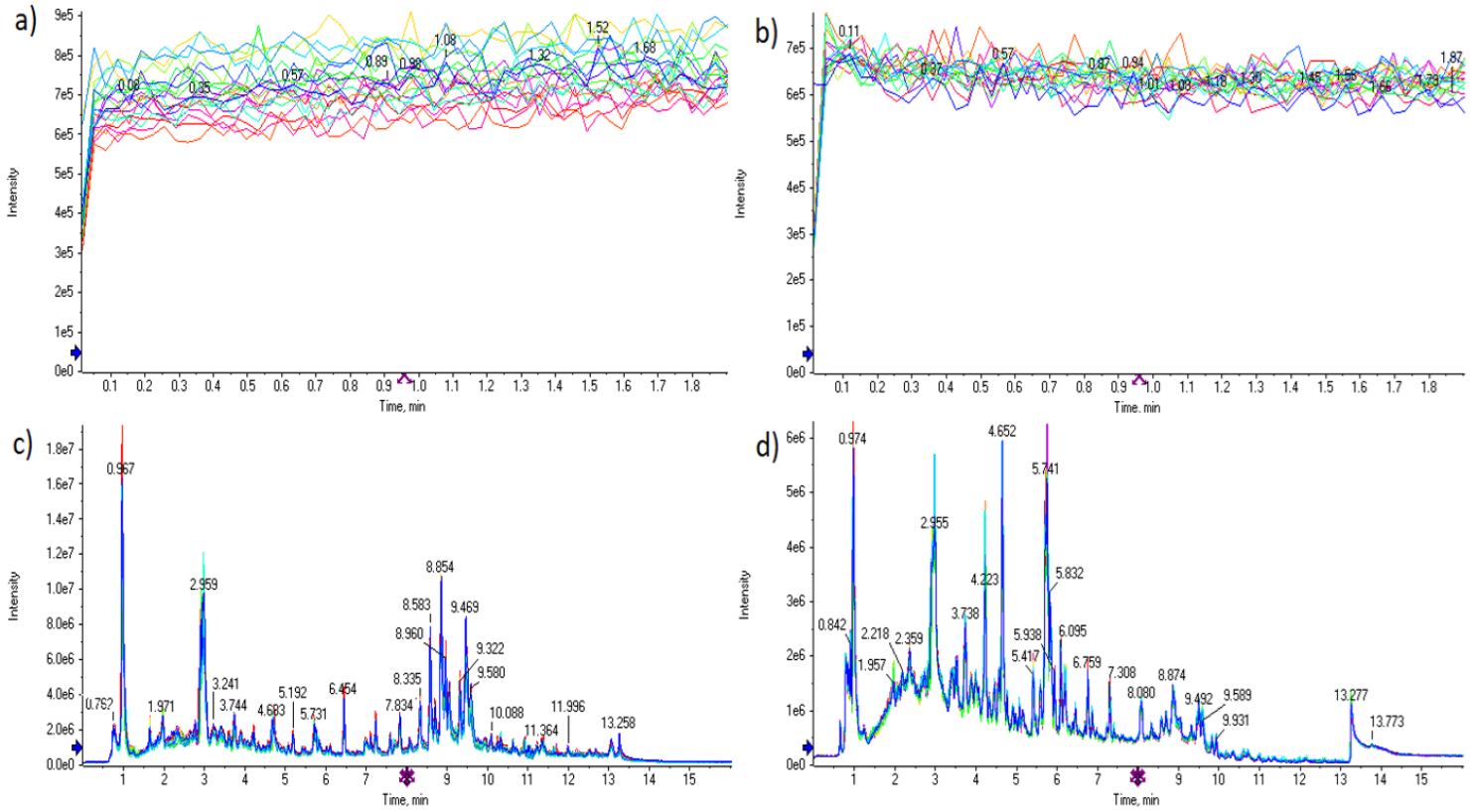

Fig.S3: Control and monitoring of instrument signal variation over time during the analytical sequence. (a) superposition of the automatic calibrations signal (n=21) in ESI+; (b) superposition of automatic calibrations signal (n=21) in ESI-; (c) superposition of QC-pooled samples TIC (n=14) in ESI+; (d) superposition of QC-pooled samples TIC (n=14) in ESI-.

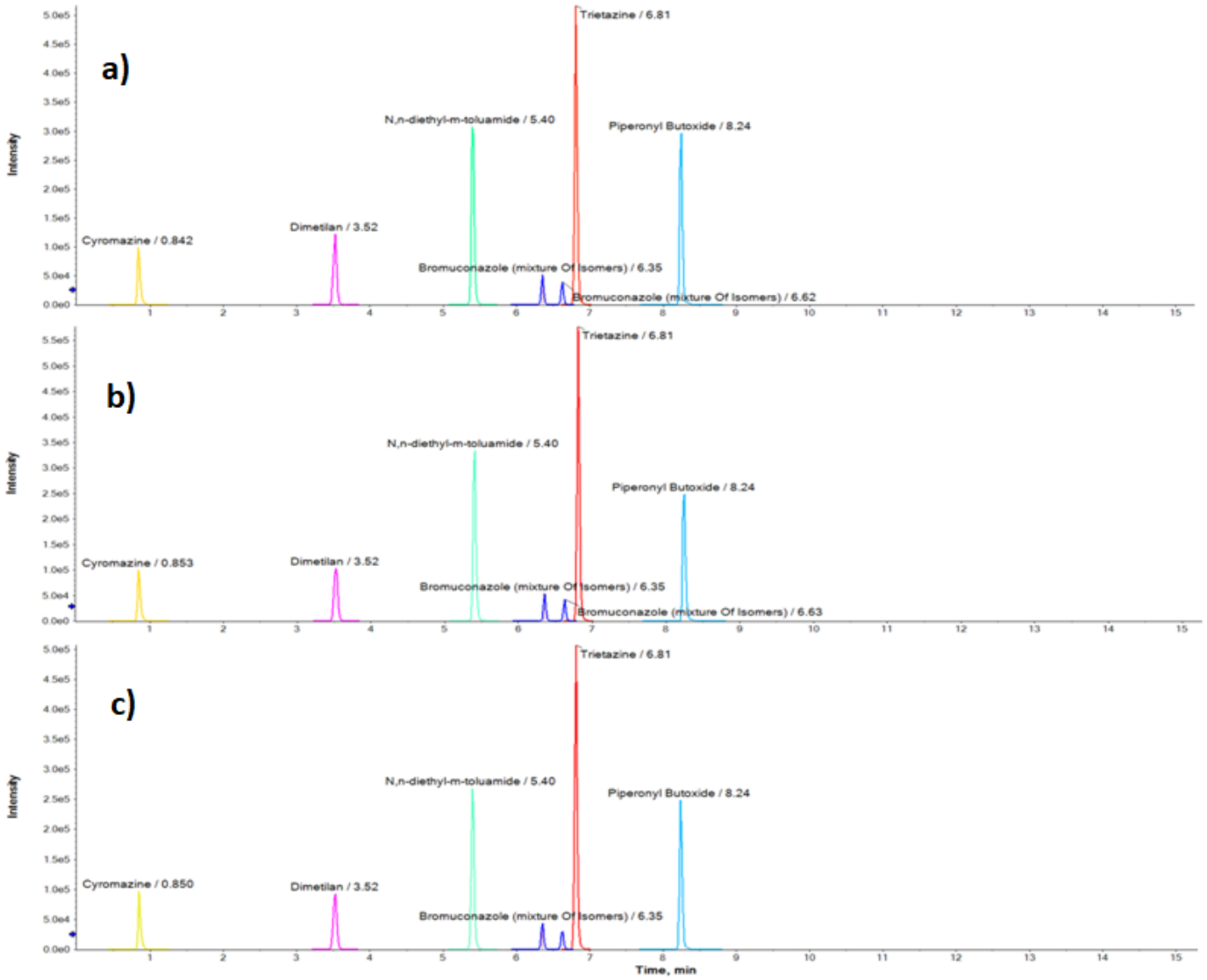

Fig. S4: Control and monitoring of chromatographic parameter stability over time using the quality assurance (QA) sample (a) injected at the beginning, (b) in the middle (c) and at the end of the analytical sequence.

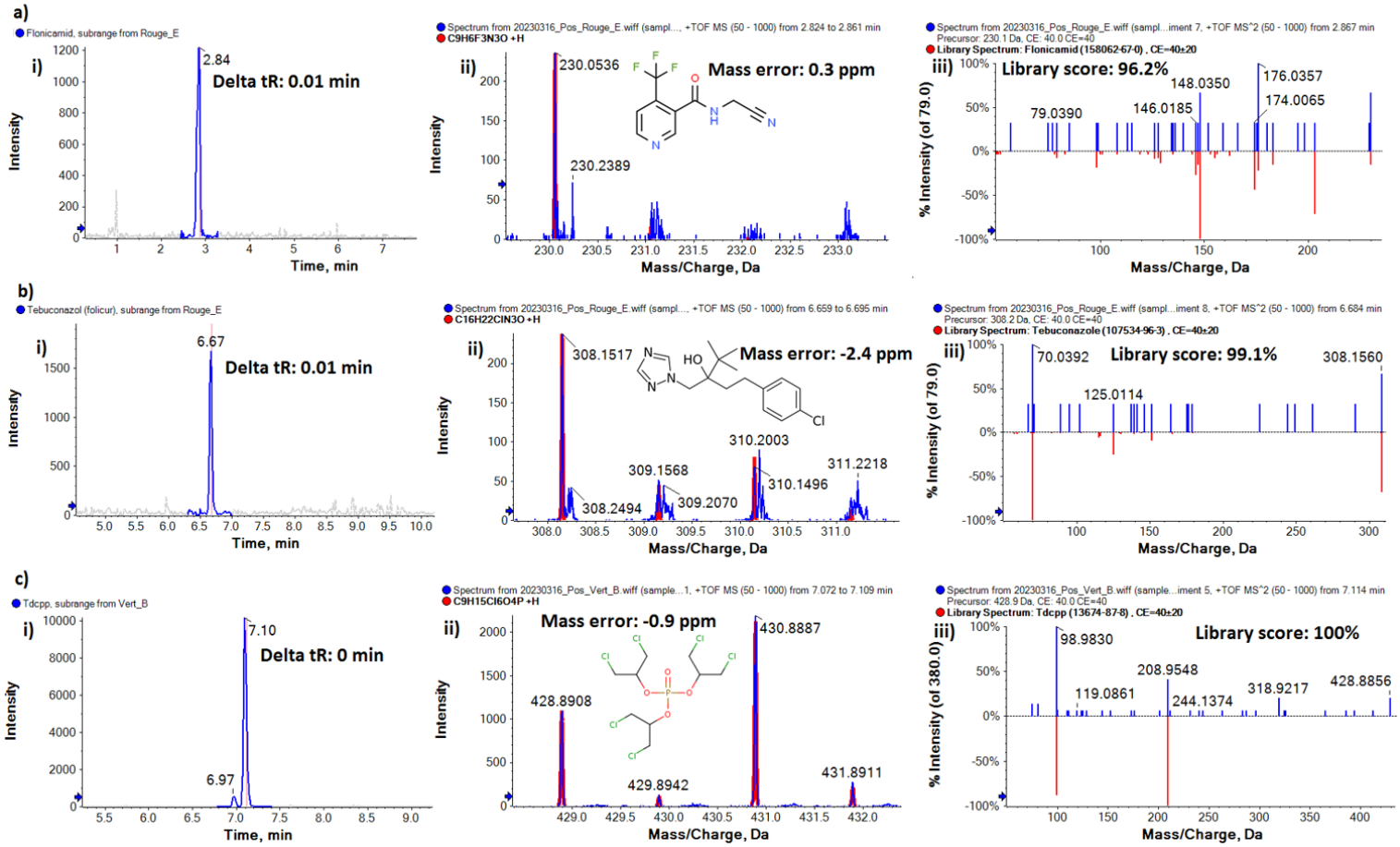

Fig. S5: Simultaneous and unequivocal identification in a Spanish lemon tree honey of **(a)** flonicamid; **(b)** tebuconazole and **(c)** TDCPP. **(i)** Extracted ion chromatogram; **(ii)** Isotopic pattern and mass error of the precursor ion; **(iii)** Experimental fragmentation spectrum (in blue) matched against the library spectrum produced by the injecting standard in solvent (in red).

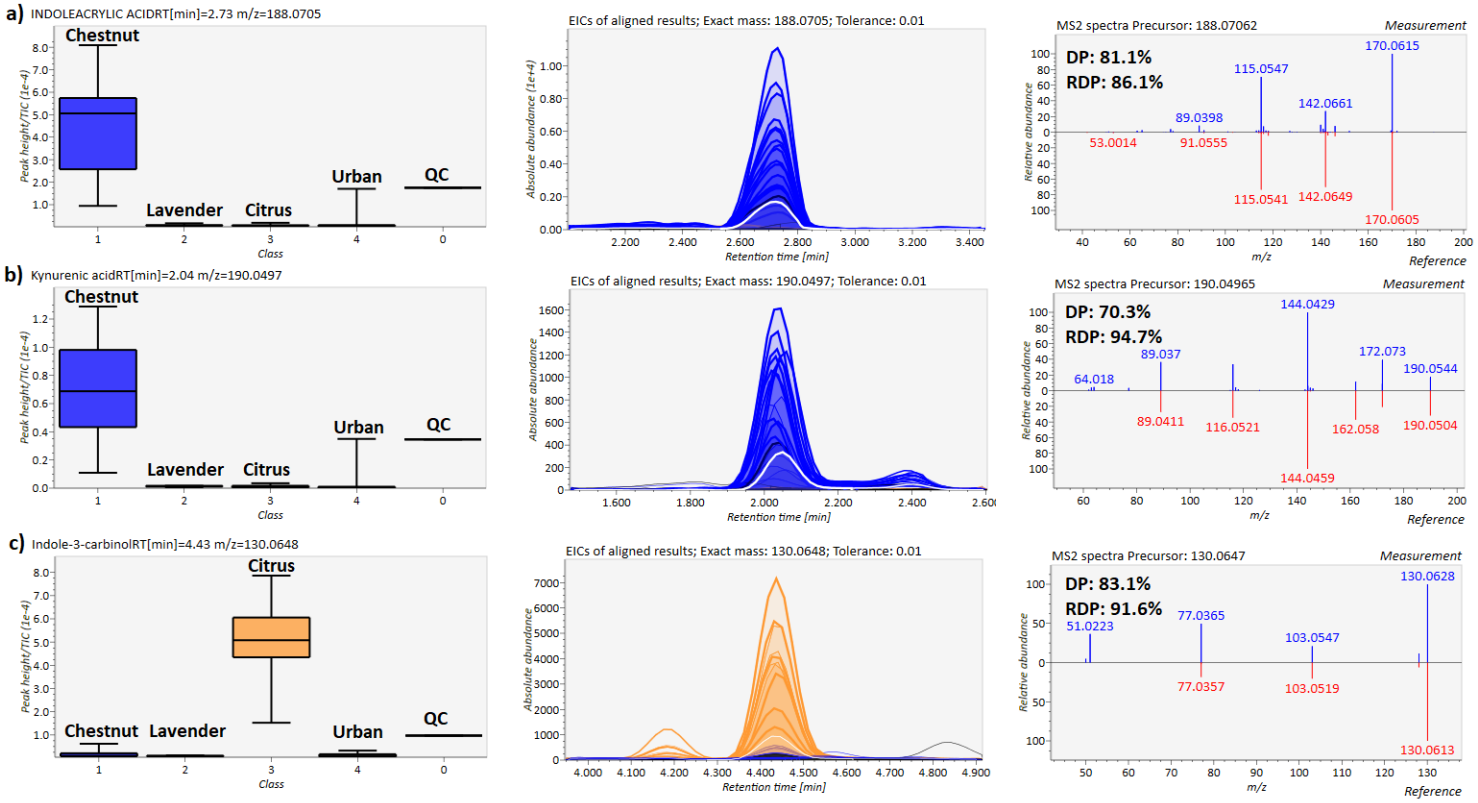

Fig. S6: Tentative identification in ESI$^+$ of potential markers of floral origin: (a) indoleacrylic acid in the chestnut honey group; (b) kynurenic acid in the chestnut honey group; (c) indole-3-carbinol in the citrus honey group. From left to right: the expression profile of the compounds between the different honey groups and the quality control (QC) sample; the extracted ion chromatograms of the compound in the different samples; experimental fragmentation spectrum (in blue) matched against an external and available fragmentation spectrum acquired in other analytical conditions (in red).

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CHAPTER 1: State of the art on consumer exposure to chemical substances and their analysis in food products

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CHAPTER 2: Development of analytical methods for the multiresidue and large-scale screening of contaminants in food samples

Article 1: "Improving the monitoring of multi-class pesticides in baby foods using QuEChERS-UHPLC-Q-TOF with automated identification based on MS/MS similarity algorithms"

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CHAPITRE 3: The versatility of HRMS: targeted, suspected and non-targeted analyses

Article 5: "A proof-of-concept study on the versatility of UHPLC-Q-ToF-MS to screen for various contaminants and highlight markers of floral and geographical origin for different honeys"

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ITERATIVE EVALUATION OF THE MULTIPLE POTENTIALS OF LIQUID CHROMATOGRAPHY COMBINED WITH HIGH-RESOLUTION MASS SPECTROMETRY FOR THE BROAD-SPECTRUM DETECTION OF MULTIRESIDUES IN FOOD: A TOOL FOR THE EXPOSOME AND FOOD SAFETY OF TOMORROW

The actual exposure of consumers to chemical contaminants in foodstuffs, and the risks they represent for human health, require a strengthening of the food monitoring system. Currently, liquid or gas chromatography coupled with tandem mass spectrometry (LC/GC-MS/MS) is used for food monitoring. These techniques are highly sensitive, but lack completeness. Indeed, all molecules for which analytical standards are not available, and which are not included in the initial screening list, are excluded from the analysis. If a hazardous chemical substance not considered for analysis were to be found in the food sample, this might represent a risk for the consumer. Recently, LC/GC coupled with high-resolution mass spectrometry (LC/GC-HRMS) has emerged as a promising technique for improving food monitoring, as it can broaden the analytical scope. However, HRMS is not recognized as a reference tool for food control. As part of my thesis, we used LC-HRMS to demonstrate its value for food monitoring. We developed multiresidue methods for the screening of hundreds of contaminants in various food matrices. The methods we developped were sensitive enough to identify monitored and oftenly researched contaminants, well below regulatory limits, and enabled us to highlight emerging and little-sought-after contaminants. This work contributed to show the reliability and effectiveness of HRMS for better characterizing the real state of consumers exposure and the mixtures of contaminants to which they are exposed. Integrated officially for routine applications, HRMS could help identify misuse and emerging contamination, as well as providing a more accurate and exhaustive characterization of the French food exposome.

Keywords

High-resolution mass spectrometry
Ultra-high-performance liquid chromatography
Method development
Food exposome
Food safety
Chemicals

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EVALUATION ITERATIVE DES POTENTIALITES MULTIPLES DE LA CHROMATOGRAPHIE LIQUIDE COUPLEE A LA SPECTROMETRIE DE MASSE A HAUTE RESOLUTION POUR LA RECHERCHE A LARGE SPECTRE DE MULTIRESIDUS DANS LES ALIMENTS : UN OUTIL AU SERVICE DE L'EXPOSOME ET DE LA SECURITE ALIMENTAIRE DE DEMAIN

L'exposition réelle des consommateurs aux contaminants chimiques présents dans les denrées alimentaires et les risques qu'ils représentent pour la santé humaine, impliquent un renforcement du dispositif de surveillance alimentaire. Actuellement, c'est la chromatographie liquide ou gazeuse couplée à la spectrométrie de masse en tandem (LC/GC-MS/MS), qui est utilisée pour le contrôle des denrées alimentaires. Ces techniques sont très sensibles, mais manquent d'exhaustivité. En effet, toutes les molécules dont on ne dispose pas des étalons analytiques, ou qui ne sont pas incluses dans la liste de criblage de départ, sont exclues de l'analyse. Dans le cas où une substance chimique dangereuse non considérée pour l'analyse se retrouverait dans l'échantillon alimentaire, cela pourrait poser un risque pour le consommateur. Récemment, la LC/GC couplée à la spectrométrie de masse à haute résolution (LC/GC-HRMS) s'impose comme une technique prometteuse pour améliorer la surveillance alimentaire car elle permet d'élargir le champ de surveillance. Cependant, la HRMS n'est pas reconnue comme méthode de référence pour le contrôle des denrées alimentaires. Dans le cadre de ma thèse, nous avons utilisé la LC-HRMS pour mettre en avant ses potentialités pour la surveillance alimentaire. Par itérations successives, nous avons développé des méthodes permettant l'analyse de centaines de contaminants dans différentes matrices alimentaires, très souvent bien en deçà des seuils réglementaires. De plus, ces méthodes nous ont également permis de détecter et caractériser des contaminants émergents ou peu recherchés. Ces travaux auront permis de mettre en avant que la HRMS est un système fiable et efficace qui permettrait, d'un point de vue qualitatif, de mieux caractériser l'état d'exposition réel du consommateur et les mélanges de contaminants auxquels il est exposé. Intégrée en routine, la HRMS pourrait également identifier d'éventuels mésusages, contaminations émergentes, et contribuer ainsi à mieux caractériser l'exposome alimentaire des français.

MOTS-CLÉS

Spectrométrie de masse à haute résolution
Chromatographie liquide à ultra-haute performance
Développement de méthodes
Exposome alimentaire
Sécurité alimentaire
Produits chimiques

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