Chapter 4

Pesticides and Their Degradation Products Including Metabolites: Chromatography-Mass Spectrometry Methods

Renata Raina-Fulton, Nicole Dunn and Zhen Xie

Additional information is available at the end of the chapter

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Abstract

This chapter reviews the selection of chromatography-mass spectrometry methods for the analysis of organophosphorus pesticides, pyrethroid insecticides, carbamates, and phenylureas. Options with different GC-MS, GC-MS/MS, and LC-MS/MS methods will be discussed for inclusion of the targeted pesticides. In addition, methods for the analysis of metabolites of these chemical classes of pesticides are investigated, including the feasibility of simultaneous analysis with parent pesticides. In some cases, a targeted approach is required for the analyses of metabolites. These methods apply to a wide variety of sample matrices including environmental (air, water, and soil), food (fruits, vegetation, or food products), and biological samples (urine and blood). The focus of the chapter is on MS detection approaches with consideration of the chromatographic separation conditions as required. A short discussion of multiresidue analysis methods and/or where feasible, other chemical classes or selected pesticides from these chemical classes can be analyzed in existing methods is included.

Keywords: gas chromatography-mass spectrometry (GC-MS), gas chromatography-tandem mass spectrometry (GC-MS/MS), liquid chromatography-tandem mass spectrometry (LC-MS/MS), carbamates, organophosphorus pesticides (OPs), phenylureas, pyrethroids, metabolites, degradation products

1. Introduction

Organophosphorus pesticides, pyrethroids, carbamates, and phenylureas remain important chemical classes of pesticides that require chemical analysis by gas chromatography-mass

spectrometry (GC-MS), gas chromatography-tandem mass spectrometry (GC-MS/MS), or liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods. The most diverse range of chromatography-mass spectrometry methods is available for these chemical classes of pesticides with method selection often based upon sensitivity and selectivity needs (see **Figure 1**). The chapter will discuss selection of methods for chemical analysis for each of these chemical classes of pesticides along with the feasibility of separate or simultaneous

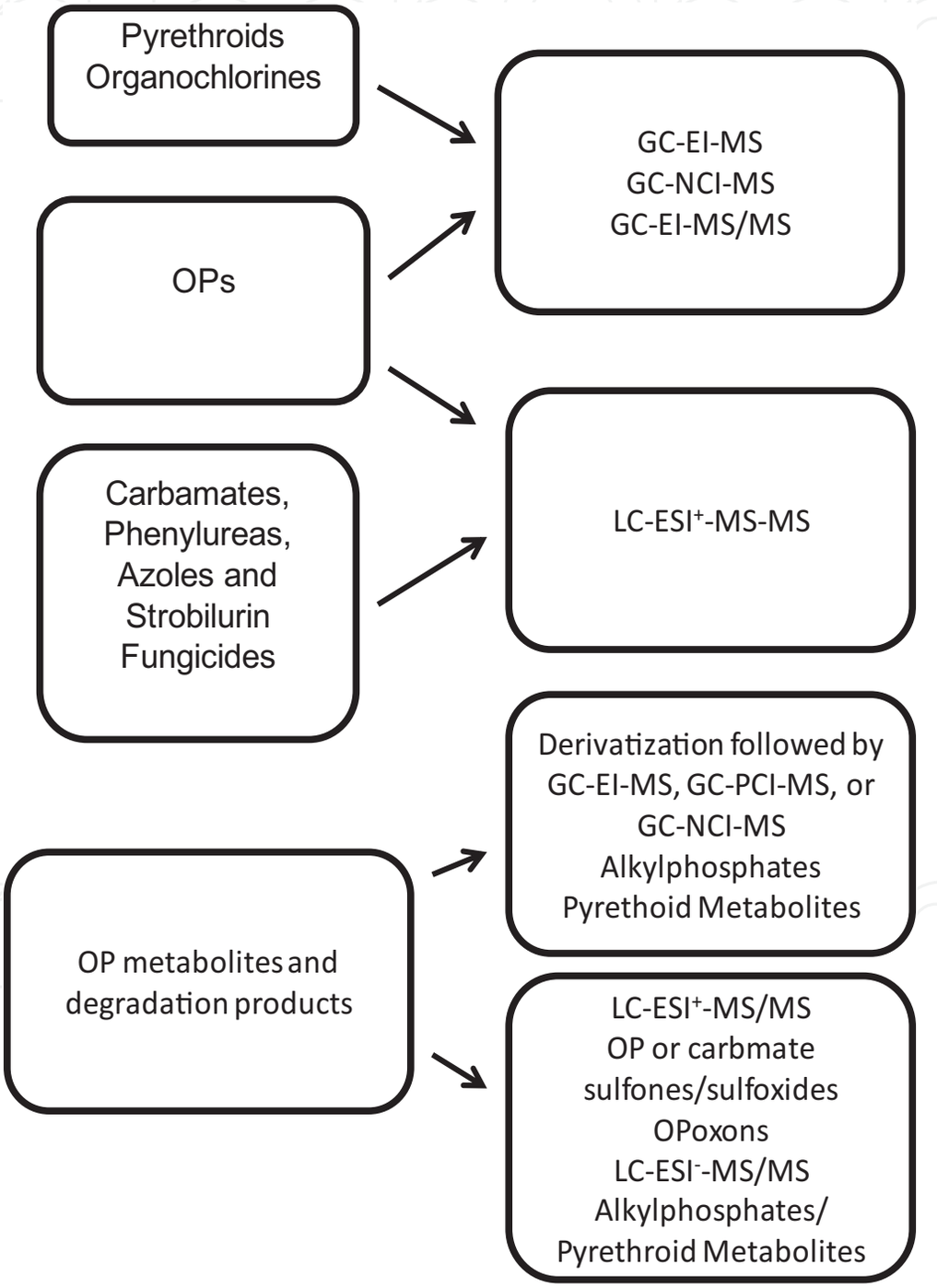

Figure 1. Options for the chromatography-mass spectrometric analysis of major chemical classes of pesticides and their metabolites or degradation products.

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analysis of metabolites and degradation products of these parent pesticides. The focus of this chapter is on the chromatography-mass spectrometry aspects of the methods. Extraction and clean-up or pre-concentration procedures for the target analytes from sample matrices will also influence the magnitude of matrix enhancement or suppression in the MS detection and column choice (or separation conditions used) to minimize the influence of matrix peaks. Further discussion on sample preparation procedures has been recently reviewed [1, 2].

2. Organophosphorus pesticides and their degradation products or metabolites

Organophosphorus pesticides (OPs) include both organophosphates ($(RO)_3PO$) and organothio phosphates ($(R_1O)_3PS$, $R(R_1O)_2PS$, $RS(R_1O)_2PS$ with OR_1 typically methoxy or ethoxy group) as shown in **Figure 1**. Common organophosphates analyzed include bromofenvinphos, chlorfenvinphos, dichlorvos, mevinphos, and tetrachlorvinphos [3–6]. The majority of OPs analyzed (see **Table 1**) are organothiophosphates including aliphatic organothiophosphates (chlormephos, demephion-O and S, disulfoton, ethion, ethoprofos, malathion, phorate, and sulfotep) [3–10], aliphatic amide organothiophosphates (dimethoate, o-methoate) [4, 6, 9, 10], heterocyclic organothiophosphates (coumaphos, azinphos-methyl, azinphos-ethyl, phosmet, pyrazophos, chlorpyrifos-methyl, chlorpyrifos-ethyl, diazinon, pirimiphos) [3–10], phenyl organothiophosphates (bromophos-methyl, bromophos-ethyl, carbophenothion, dichlofenthion, fenchlorphos, fenitrothion, fenthion, parathion-methyl, parathion-ethyl, prothiofos, sulprofos) [3, 5–9] and phosphonothioates (fonofos, trichloronat, cyanofenphos, leptophos, fenamiphos, and acephate) [3, 4, 6, 7].

OP	Molecular formula	SIM *m/z* (quantitative, confirmation)	Ref.	SRM *m/z* (quantitative, confirmation)	Ref.
Acephate		136	[10]	136→42, 136→94	[3]
Aspon		211, 253	[1]	378→210, 378→115	[7]
Azinphos-methyl				160→105, 160→132	[3]
				132→104	[6]
Azinphos-ethyl				160→105, 160→132	[3]
				132→04	[6]
Bromfenvinphos-methyl				295→295	[5]
Bromfenvinphos-ethyl				267→159	[5]
Bromophos-ethyl				359→303, 359→331	[3, 6]
				359→303	[5]
Bromophos-methyl				331→286, 331→316	[3, 6]
				331→331	[5]
Carbofenothion		157, 342	[1]	342→157, 342→143	[7]

OP	Molecular formula	SIM *m*/*z* (quantitative, confirmation)	Ref.	SRM *m*/*z* (quantitative, confirmation)	Ref.
Chlormefos				234→121, 234→154	[3]
				243→121	[5]
				235→171, 235→199	[6]
Chlorphenvinphos				267→159, 323→267	[3]
				323→267	[5]
				267→159	[6]
Chlorpyrifos-methyl		286, 125	[1]	321→268, 321→208	[7]
		286	[10]	286→136, 286→241	[3]
		286, 288, 125	[17]	286→93	[5]
				286→208, 286→286	[6]
Chlorpyrifos-ethyl		97, 197	[1]	349→208, 349→40	[7]
		199	[10]	314→258, 314→286	[3, 6]
		97, 197	[11]	314→258	[5]
Coumaphos		362	[10]		
Cyanofenphos				185→157, 157→110	[3]
				157→139, 157→110	[6]
Demeton-o		88, 60	[11]		
Diazinon		137, 179	[1]	304→179, 304→137	[7]
		304	[10]	304→137, 304→179	[3]
		137, 304	[11]	304→179	[5, 6]
		287, 302, 288	[17]		
Diazinon-d_{10}		314	[1]	314→185	[7]
Dichlofenthion		223, 97	[1]	314→223, 319→81	[7]
				279→222, 279→251	[3]
				279→223	[5]
				279→223, 279→251	[6]
Dichlorvos		185	[10]	185→93	[5]
				221→141, 221→145	[6]
Dimethoate		125	[10]	230→199	[6]
		87, 125	[11]		
		87, 93, 125	[17]		
Disulfoton		88, 60	[11]	274→88	[5]

OP	Molecular formula	SIM *m*/*z* (quantitative, confirmation)	Ref.	SRM *m*/*z* (quantitative, confirmation)	Ref.
Dyfonate		109, 137	[1]	246→137, 246→109	[7]
Ethion		231, 97	[1]	384→231, 384→203	[7]
		231, 384	[11]	231→175, 231→203	[3]
Ethoprophos				158→97, 158→114	[3]
				158→97	[5]
				243→131, 243→173	[6]
Fenamiphos				303→154, 303→180	[3]
Fenchlorphos		125, 287	[1]	320→285, 320→204	[7]
				285→270	[5]
Fenitrothion		277, 125	[1]	277→260, 277→109	[7]
		109, 125	[11]	260→109, 260→125	[3]
				277→260	[5]
				260→125	[6]
Fenthion		278, 125	[11]	278→125, 278→245	[3]
				278→109	[5]
				278→135	[6]
Fonophos				246→109, 246→137	[3]
				246→137, 246→109	[6]
Leptophos		171, 377	[1]		
Malathion		173, 125	[1]	173→ 99	[5]
		173, 125, 93	[17]	173→127	[6]
		93, 125	[11]		
o-methoate		156	[10]		
Mevinphos		192	[10]	192→127, 192→164	[3]
				192→127	[5]
				193→127	[3]
Parathion ethyl		97, 291	[1]	291→109, 291→137	[12]
		291, 109	[11]	291→91, 291→109	[8]
				291→109	[3]
				291→263, 291→143	[18]
Parathion methyl		109, 125	[11]	263→79, 263→109	[8]
				263→109	[3]
				263→136, 263→246	[18]

OP	Molecular formula	SIM *m*/*z* (quantitative, confirmation)	Ref.	SRM *m*/*z* (quantitative, confirmation)	Ref.
Phorate		121, 75	[1]	260→75, 263→231	[12]
				231→129	[3]
Phosmet		160	[10]	160→77	[3]
Pirimiphos-ethyl				333→163, 333→168	[3]
				316→166	[5]
				318→182, 318→166, 318→246	[6]
Pirimiphos-methyl				290→125, 290→151	[3]
				290→125	[5]
				290→151	[6]
Prothiofos				309→221, 309→239	[3]
				162→63	[5]
				309→239, 309→281	[6]
Pyrazophos				265→138, 265→210	[3]
				221→93	[5]
				265→210	[6]
Quinalphos				298→156, 298→190	[3]
				146→91	[5]
				146→118	[11]
Sulfoprofos		140, 322	[1]	322→156, 322→97	[7]
				322→156, 322→139	[3]
Sulfotep		322, 202	[1]	322→202, 322→146	[7]
		322, 97	[11]	322→146, 322→266	[3]
				322→146	[5]
Tetrachlorvinphos				329→109	[3, 5]
				331→109	[6]
Tokuthion		113, 267	[1]	344→328, 344→73	[7]
Tolclophos methyl				265→220, 265→250	[3]
				265→250	[5]
				265→220, 265→215	[6]
Tributylphosphorotrithioite		169, 57	[1]	314→115, 314→113	[7]
Trichloronate		109, 297	[1]		

Table 1. Selected ion monitoring (SIM) or selected reaction monitoring (SRM) transitions for organophosphorus pesticides (OPs) by GC-EI-MS or GC-EI-MS/MS methods.

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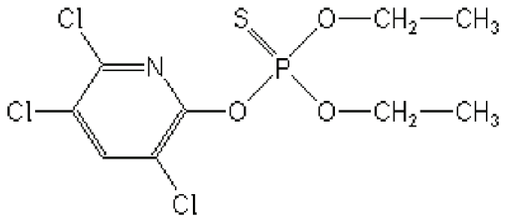
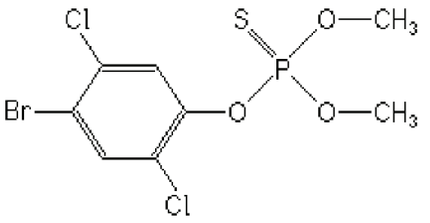
OPs are both GC-MS and LC-MS/MS amenable and the choice often depends upon instrument availability, what other pesticide chemical classes are analyzed for and whether there is a need to also analyze degradation products or metabolites of OPs [9, 12, 13]. In general, a greater diversity of OPs has been analyzed simultaneously by GC-MS or GC-MS/MS methods as compared to LC-MS/MS. For analysis of OPs by GC-MS methods, electron impact ionization (EI) remains the most widely used due to its ease of operation and ability to provide spectral library matches (see **Table 1**) [3–10]. Other pesticide classes that are most frequently analyzed with OPs by GC-MS include OCs, pyrethroids, and a few selected azole fungicides, strobilurin fungicides and carbamates [3, 5, 7, 9, 14].

Selection ion monitoring (SIM) with EI does not always meet sensitivity or selectivity needs or provide information on the molecular weight for some OPs due to the high amount of fragmentation in the EI source. OPs are prone to fragmentation in the EI source such that the molecular ion is often too low in abundance to monitor such that fragment ions are used for quantitation and confirmation analysis [3–7, 9, 10]. Positive or negative chemical ionization may be selected to obtain molecular weight confirmation, however, even with negative chemical ionization (NCI) significant amount of fragmentation of OPs may occur in the ion source although typically few fragment ions are observed in NCI as compared to EI [7, 10]. Electron capture in NCI can occur by dissociate electron capture and the structure of the OP may lead to more stable negatively charged fragment ions than the molecular ion. PCI is generally not selected for quantitative analysis as it does not provide significant improvements in selectivity over EI, while NCI is used for OPs, organochlorines (OCs), and pyrethroids when additional sensitivity or selectivity is required [7, 10]. OPs, organochlorines, and pyrethroids that contain halogen atoms or nitro groups often have lower detection limits with NCI than EI. For example, diazinon and malathion (see structures in **Figure 2**) have better sensitivity with GC-EI-MS than GC-NCI-MS, while chlorpyrifos-ethyl (chlorinated) and parathion-ethyl (contains a nitro group) have good sensitivity with GC-NCI-MS [7]. The ^{37}Cl or ^{81}Br isotopes of the molecular ion or fragment ions can be used for confirmation analysis with GC-EI-MS such as for chlorpyrifos methyl (m/z = 288); however, as there is a high degree of fragmentation of OPs with EI, generally more than two fragment ions of higher abundance than the isotope ions can be selected for quantitation and confirmation [3, 5–7, 9, 10].

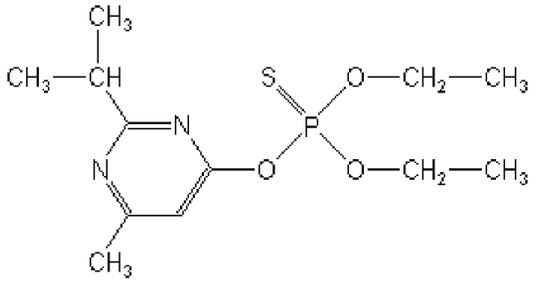
Most halogenated OPs observed better sensitivity with GC-NCI-MS than GC-EI-MS or GC-EI-MS/MS [7]. To provide additional selectivity, GC-EI-MS/MS has been used; however, when the molecular ion is selected as the precursor ion for collision-induced dissociation (CID), the sensitivity is lower than when NCI in SIM mode is used [7]. If the OR_1 group is an ethoxy group, CID of the molecular ion may lead to loss of ethene (C_2H_4) from the ethoxy group and if the OP is halogenated, the loss of halogen radical (e.g., Cl radical) is also frequently observed [6]. For example, the SRM 349→286 of chlorpyrifos corresponds to CID of the molecular ion ($M^{+\bullet}$) to form fragment ion F^+ ($Cl_2NC_4HOPS(OC_2H_5)(OH)^+$) as a result of loss of C_2H_2 from an ethoxy group and Cl radical from the aromatic R group. Phorate observes loss of ethyl from the aliphatic R group (SRM: 260→231) to form ($^+SCH_2SPS(OC_2H_5)_2$) [5, 7]. As phorate has an aliphatic R group, fragmentation within the R group can result in a stable fragment ion $CH_3CH_2SCH_2^+$ at m/z = 75 (SRM: 260→75). The fragment ion at m/z = 231 can undergo further fragmentation through loss of two molecules of ethene from the two ethoxy groups



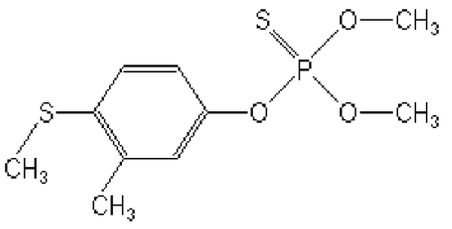
chlorpyrifos-ethyl



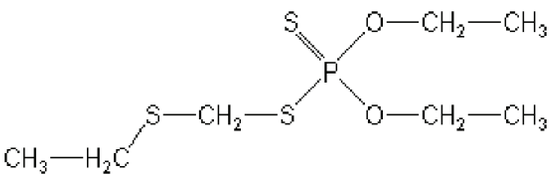
bromophos



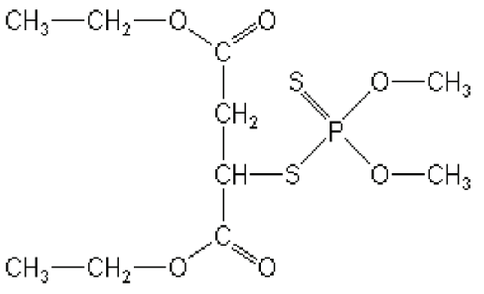
diazinon



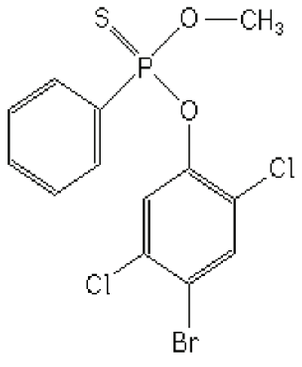
fenthion



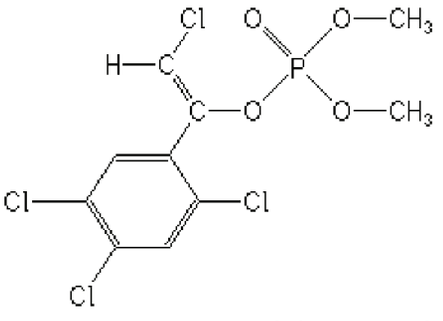
phorate



malathion



leptophos



tetrachlorvinphos

Figure 2. Structures of common organophosphorus pesticides (OPs) from different subclasses. OP subclasses include organophosphates (tetrachlorvinphos), aliphatic organothiophosphates (malathion, phorate), heterocyclic organothiophosphates (chlorpyrifos ethyl and diazinon), phenyl organothiophosphates (bromophos), and phosphonothioates (leptophos).

and neutral loss of SCH_2 to form $SPS(OH)_2^+$ corresponding to ion at *m*/*z*=129 (SRM: 231→129 observed). For $(RO)PS(OR_1)_2$ where OR_1 is methoxy, CID of the molecular ion will either form $[PS(OR_1)_2]^+$ with loss of OR radical or a thiono-thiolo rearrangement may occur such that $[PO(OR_1)_2]^+$ is formed with loss of SR radical as observed for fenthion 278→125 and 278→109, respectively [3, 5]. Thiono-thiolo rearrangements have been proposed for fragmentation of diazinon in LC-MS/MS [15].

To improve the sensitivity of GC-EI-MS/MS, the precursor ion can be selected as an abundant fragment ion rather than the molecular ion (see **Table 1**). For bromophos-methyl (monoisotopic mass 364) and bromophos-ethyl (monoisotopic mass 392), the fragment ions at *m*/*z* = 331 and *m*/*z* = 359, respectively are selected for precursor ions (SRM 331→286 and 359→303, respectively; see **Table 1**) and correspond to the either the ^{37}Cl or ^{81}Br isotope of $[M\text{-}Cl]^+$[3, 6]. The R groups of OPs vary substantially and can play a significant role in the fragmentation pathway that dominates. For some OPs, the most abundant fragment ion available for CID is R+. For example, azinphos-methyl and azinphos-ethyl fragmentation at S-R bond of $RS(OR_1)_2PS$ to produce R^+ and ion at *m*/*z* = 160 is the dominant fragment ion formed by loss of the $S(OR_1)_2PS$ radical in the EI ion source. Both azinphos-ethyl and azinphos-methyl monitor the SRM transitions at *m*/*z* of 160→105, and 160→132 for quantitation and confirmation analysis [3, 6]. The *m*/*z* = 160 fragment ion undergoes collision-induced dissociation through loss of N_3CH or C_2H_2 to give fragment ions at 105 and 132, respectively.

Metabolite or degradation product analysis has become of increasing importance for biological monitoring studies (urine or blood) and environmental studies (atmosphere or surface water) [8, 14, 16–21]. Organophosphorus pesticides can be grouped into organophosphates and organothiophosphates with different R-group substituents. Alkylphosphates (dimethylphosphate and diethylphosphate) and alkylthiophosphates (dimethylthiophosphate, dimethylethylthiophosphate, dimethyldithiophosphate, and dimethyldithiophosphates) are formed from metabolism of OPs. They can be analyzed by GC-MS methods following a derivatization step with N-(*tert*-butyldimethylsilyl)-N-methyltrifluoroacetamide (MTBSTFA) to form *tert*-butyldimethylsilyl derivatives (GC-EI-MS); 2,3,4,5,6-pentafluorobenzylbromide (PFBBr) to form pentafluorobenzylbromide derivatives (GC-NCI-MS); and 1-chloro-3-iodropane (CIP) to form chloropropyl ethers (GC-PCI-MS) (see **Table 2**) [3, 14, 16, 17]. There has been a gradual shift from use of MTBSTFA derivatives that are analyzed by GC-EI-MS to PFBBr-derivatives that can be analyzed by negative chemical ionization for added sensitivity and selectivity, and CIP derivatives that are analyzed with positive chemical ionization.

The analysis of OPs by LC-ESI^+-MS/MS has grown [11, 22–39]. OPs that are amenable to electrospray ionization often have lower detection limits than with GC-MS methods particularly for those OPs most widely studied, including azinphos-methyl, chlorpyrifos, diazinon, and malathion [7, 8, 11]. Since electrospray ionization is a much softer ionization process than EI, the protonated molecular ion can be selected as the precursor ion for LC-ESI^+-MS/MS and generally two fragments of significant abundance are observed such that two SRM transitions are available for quantitative and confirmation analysis (see **Table 3**). Organochlorines have poor sensitivity with LC-ESI^+-MS/MS such that GC-MS methods are selected over LC-ESI^+-MS/MS if organochlorines (OCs) are targeted along with OPs in a multiclass method (see **Figure 1**). However, LC-ESI^+-MS/MS is also

OP degradation product, derivatization agent	Parent	SIM *m*/*z* (quantitative, confirmation) EI	Ref	SRM *m*/*z* (quantitative, confirmation)	Ref
Diazinon oxon (oxadiazinon)	diazinon			175→112, 258→112	[7]
Dibutylphosphate, PFBBr (IS)	OP	335, 279	[12, 13, 20]	209→79^{NCI}	[14]
2,4-Dichlorophenol, MTBSTFA	dichlofenthion	219, 221	[8]		
2,5-Dichlorophenol, MTBSTFA	p-dichlorobenzene	221, 219	[8]		
Diethyldithiophosphate, PFBBr	OP	366, 185	[18]	185→111, 185→157^{NCI}	[14]
Diethyldithiophosphate, CIP	OP	366, 185, 157	[12, 13, 20]	263→153, 265→153^{PCI}	[16, 17]
Diethylphosphate, MTBSTFA	OP	211, 155	[8]	153→79, 153→125	[14]
Diethylphosphate, PFBBr	OP	258, 334	[18]	231→127, 233→127^{PCI}	[16, 17]
Diethylphosphate, CIP	OP	334, 278, 258	[12, 13, 20]		
Diethylthiophosphate, MTBSTFA	OP	227, 199	[8]	169→95, 169→141^{NCI}	[14]
Diethylthiophosphate, PFBBr	OP	350, 274	[18]	247→191, 249→191^{PCI}	[16, 17]
Diethylthiophosphate, CIP	OP	350, 274, 169	[12, 13, 20]		
Diisopropylphosphate (IS), MTBSTFA	OP	155, 239	[8]		
Dimethyldithiophosphate, PFBBr	OP	338, 157	[12, 13, 20]	157→112, 157→142^{NCI}	[14]
Dimethyldithiophophate, CIP	OP			235→125, 235→125^{PCI}	[16, 17]
Dimethylphosphate, MTBSTFA	OP	183, 153	[18]	125→63, 125→79^{NCI}	[14]
Dimethylphosphate, PFBBr	OP	306, 110	[18]	203→127, 205→127^{PCI}	[16, 17]
Dimethylphosphate, CIP	OP	306, 307, 194	[12, 13, 20]		
Dimethylthiophosphate, MTBSTFA	OP	199, 169	[8]	141→126, 141→96^{NCI}	[14]
Dimethylthiophosphate, PFBBr	OP	322, 211, 110	[12, 13, 20]	219→143, 221→143^{PCI}	[16, 17]
Dimethylthiophosphate, CIP	OP				

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OP degradation product, derivatization agent	Parent	SIM *m*/*z* (quantitative, confirmation) EI	Ref	SRM *m*/*z* (quantitative, confirmation)	Ref
Fenamiphos sulfone	fenamiphos			292→213, 320→292	[3]
Fenamiphos sulfoxide	fenamiphos			304→122, 304→196	[3]
2-Isopropyl-6-methyl-4-pyrimidinol, MTBSTFA	diazinon	209, 210	[19]		
3-Methyl-4-(methylthio)phenol, MTBSTFA	fenthion	268, 196	[14]		
6-Methyl-2-(1-methylethyl)4(1H)-pyrimidinone	diazinon	137, 152, 124	[19]		
3-Methyl-4-nitrophenol, MTBSTFA	fenitrothion	267, 210	[8]	152→122, 152→107^{NCI}	[14]
3-Methyl-4-nitrophenol, PFBBr	fenitrothion				
3,5,6-Trichloro-2-pyridinol, MTBSTFA	chlorpyrifos	254, 258	[8]	196→35, 198→35^{NCI}	[14]
3,5,6-Trichloro-2-pyridinol, PFBBr	chlorpyrifos	256, 254, 258	[21]		
Paraoxon methyl	parathion methyl			230→106, 230→136	[3]
Phosmet oxon	phosmet			160→77, 160→133	[3]

Electron ionization unless noted.

MTBSTFA, N-(*tert*-butyldimethylsilyl)-N-methyltrifluoroacetamide forms *tert*-butyldimethylsilyl derivatives; PFBBr, 2,3,4,5,6-pentafluorobenzylbromide forms pentafluorobenzylbromide derivatives; CIP, 1-chloro-3-iodropane forms chloropropyl ethers; NCI, negative chemical ionization; PCI, positive chemical ionization.

Table 2. Selected ion monitoring (SIM) or selected reaction monitoring (SRM) transitions for organophosphorus pesticides (OPs) degradation products including metabolites by GC/MS or GC/MS/MS methods.

OP	Organic modifier, additives in MP; column	SRM (quantitative, confirmation)	Ref
Acephate	MeOH, 10mM CH_3COONH_4; XTerra MS C18	182	[25]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	184→113, 184→95	[35]
	ACN, 0.1% HCOOH; C18	184→143	[4]
Azamethiphos	MeOH, 5 mM $HCOONH_4$; XDB-C18	325→183, 325→139	[23]
Azinphos-ethyl	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	346→160, 346→132	[11]
Azinphos-methyl	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	318→160, 318→132	[11]
	ACN, 0.1% HCOOH; C18	318→125, 318→132	[28]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	318→160, 318→132	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	318→132, 318→160	[37]
Chlorpyrifos-ethyl	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	352→97, 352→125	[11]
	MeOH, 5 mM $HCOONH_4$; XDB-C18	352→200, 352→97	[23]
	ACN, 0.1% HCOOH; C18	352→97, 352→200	[28]
	ACN, 20 mM CH_3COOH (pH 6.45-7.45); mixed mode RP/WAX	352→200, 352→115	[24]
	ACN, 0.025% HCOOH; Zorbax Extended C8	352→200	[29]
	ACN, 0.1% HCOOH; C18	350→198, 350→125, 352→200, 352→125	[30]
	ACN, 0.025% HCOOH; XDB-C8	352→200	[32]
	MeOH, 0.1% CH_3COOH; XSELECT™ CSH™C18	350→198, 352→200	[33]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	350→198, 350→97	[35]
	MeOH, 20 mM CH_3COONH_4; C18	350→198, 350→294	[36]
	MeOH, 5 mM $HCOONH_4$; ODS-4	350→198, 350→97	[37]
	MeOH, 2 mM CH_3COONH_4; C18	350→198, 352→200	[38]
	ACN, 20 mM CH_3COONH_4, RP18	350→125, 352→198	[39]
	ACN, 0.1% HCOOH; C18	352→198	[4]
Chlorpyrifos-methyl	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	322→125, 324→125	[4]
	MeOH, 5 mM HCOONH4; XDB-C18	322→125, 322→290	[26]
	MeOH, 0.1% CH_3COOH; XSELECT™ CSH™C18	322→125, 324→125	[36]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	322→125, 322→290	[38]

OP	Organic modifier, additives in MP; column	SRM (quantitative, confirmation)	Ref
	MeOH, 5 mM $HCOONH_4$; ODS-4	322→125, 322→290	[40]
	ACN, 0.1% HCOOH; C18	322→290	[4]
Coumaphos	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	363→227, 363→307	[6]
	MeOH, 0.1% HCOOH; Acquity UPLC™BEH C18	363→303, 363→289	[6]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	363→227, 363→307	[35]
Cyanophos	MeOH, 10mM CH_3COONH_4; XTerra MS C18	228	[25]
Demeton-S-methyl	MeOH, 0.1% HCOOH; Acquity UPLC™BEH C18	231→89, 231→61	[6]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	231→89, 231→61	[35]
Diazinon	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	305→169, 305→153	[11]
	MeOH, 5 mM $HCOONH_4$; XDB-C18	305→169, 305→153	[23]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	305→169, 305→97	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	305→169, 305→153	[37]
	MeOH, 2 mM CH_3COONH_4; C18	305→169, 305→153	[38]
	ACN, 20 mM CH_3COONH_4, RP18	305→169, 305→153	[39]
	ACN, 0.1% HCOOH; C18	322→290	[4]
	ACN, 0.1% HCOOH; XDB-C18	305.103, 277.077, 249.047, 169.077, 153.102*	[22]
	MeOH, 0.1 % HCOOH; X-Terra C18	305.1089→169.0799, 305.1089→153.1028*	[27]
Diazinon-d10 (IS)	MeOH, 0.1% HCOOH and 2 Mm CH_3COONH_4; C_6phenyl	315→170, 315→154	[11]
Dichlorvos	MeOH, 5 mM HCOONH4; XDB-C18	221→109, 221→127	[23]
	MeOH, 5 mM $HCOONH_4$; ODS-4	221→109, 221→127	[37]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	221→127, 221→109	[35]
	ACN, 0.1% HCOOH; C18	221→127	[4]
Dichlorvinphos	MeOH, 0.1% HCOOH; Acquity UPLC™BEH C18	238→112, 238→193	[6]
Dicrotophos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	238→112, 238→127	[35]
Dimethoate	MeOH, 0.1% HCOOH and 2 Mm CH_3COONH_4; C_6phenyl	230→199, 230→125	[11]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	230→199, 230→125	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	230→199, 230→125	[37]

OP	Organic modifier, additives in MP; column	SRM (quantitative, confirmation)	Ref
	MeOH, 2 mM CH_3COONH_4; C18	230→125, 230→143	[38]
	ACN, 0.1% HCOOH; C18	221→127	[4]
Disulfoton	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	275→89, 275→61	[35]
Ethion	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	385→199, 385→171	[35]
Ethoprofos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	243→131, 243→97	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	243→97, 243→131	[37]
Fenamiphos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	304→217, 304→202	[35]
Fenchlorphos	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	321→125, 321→109	[11]
Fenitrothion	MeOH, 10mM CH_3COONH_4; XTerra MS C18	262	[25]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	278→125, 278→109	[35]
Fensulfothion	MeOH, 0.1% HCOOH; Acquity UPLC™BEH C18	309→281, 309→157	[6]
Fenthion	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	279→169, 279→247	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	279→169, 279→247	[37]
	MeOH, 2 mM CH_3COONH_4; C18	279→169, 279→105	[38]
Malathion	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	331→127, 331→285	[11]
	MeOH, 10mM CH_3COONH_4; XTerra MS C18	315	[25]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	331→127, 331→99	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	331→127, 331→99	[37]
	ACN, 20 mM CH_3COONH_4, RP18	331→127, 331→285	[39]
Mevinphos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	225→127, 225→193	[35]
Methamidophos	MeOH, 5 mM HCOONH4; XDB-C18	142→94, 142→125	[23]
Monocrotophos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	224→127, 224→98	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	331→127, 331→99	[37]
Naled	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	398→127, 398→109	[35]
Parathion-ethyl	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	292→236, 292→97	[35]
Parathion-methyl	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	264→125, 264→232	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	264→125, 264→109	[37]
Phorate	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	261→75, 261→47	[11]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	261→75, 261→171	[35]

OP	Organic modifier, additives in MP; column	SRM (quantitative, confirmation)	Ref
Phosmet	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	318→160, 318→133	[35]
Pirimiphos methyl	MeOH, 5 mM HCOONH4; XDB-C18	306→164, 306→108	[23]
	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	306→164, 306→108	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	306→164, 306→108	[37]
Prothiophos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	345→241,345→133	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	345→241,345→133	[37]
Pyrazophos	MeOH, 5 mM $HCOONH_4$; ODS-4	374→222, 374→194	[37]
Quinalphos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	299→163, 299→147	[35]
Tebufos	MeOH, 0.1% HCOOH; Acquity UPLC™BEH C18	289→103, 289→57	[6]*
		289→57, 289→103	[35]
Temephos	ACN, CH_3COONH_4; C18	484, 523	[26]
Tetrachlorvinphos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	367→127, 367→241	[35]
Triazophos	MeOH, 0.1% HCOOH; Acquity UPLC™BEH C18	314→162, 314→119	[6]
		314→162, 314→119	[35]
Trichlorfon	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	274→109, 274→221	[35]
	MeOH, 5 mM $HCOONH_4$; ODS-4	257→109, 257→221	[37]

*LC-ESI$^+$-QTOF-MS.

Table 3. Selected ion monitoring (SIM) or selected reaction monitoring (SRM) transitions for organophosphorus pesticides (OPs) products by LC-ESI$^+$-MS/MS methods.

more amenable to a wider range of other pesticides included in multiclass methods, including azole fungicides, carbamates, phenylureas, and strobilurin fungicides (see **Figure 1**). Either chemical class-specific or multiclass separations can be achieved on reversed-phase stationary phases including C8, C12, C18, C6phenyl. OPs, OPoxons, OPsulfoxides, and OPsulfones observed better sensitivity with methanol rather than acetonitrile as the organic modifier in the mobile phase. Generally, ammonium acetate or ammonium formate is selected as an additive and pending the target list of OPs and their degradation products, 0.1% formic acid may also be added to the mobile phase to improve sensitivity. Only a few OP sulfones, sulfoxides, and oxons have been analyzed by GC-EI-MS/MS methods (**Table 2**) often due to the poor sensitivity, poor peak shapes, or poor chromatographic separation of these analytes due to their more polar nature such that LC-ESI$^+$-MS/MS are preferred (see **Table 4**) [4, 6, 11, 19, 22–41].

An additional reason why LC-ESI$^+$-MS/MS is chosen over GC-MS methods for OPs is the ability to analyze OPs and OP sulfones, sulfoxides, and oxons simultaneously with often comparable sensitivities to their parent OPs [6, 11, 26, 28, 29, 32, 35]. Molecular weight confirmation is available as the protonated molecular ion is high in abundance and generally selected for the precursor ion

for LC-MS/MS (**Table 3**). Similar to the OPs, mobile phase containing methanol (and gradient elution) is often preferred for optimal sensitivity of OP degradation products. However, when OPs (or their degradation products) are included in multiclass methods, acetonitrile may be selected due to the sensitivity needs of other target chemical classes of pesticides and to reduce run times. Other degradation products including hydroxyl degrades of OPs and IMP can also be analyzed in positive ion mode by LC-ESI$^+$(or APCI$^+$)-MS/MS or LC-QTOF [11, 22, 27, 33, 40, 42].

Alkylphosphates and alkylthiophosphates can also be analyzed by LC-MS/MS but to achieve the required sensitivity LC-ESI$^-$-MS/MS is selected such that they are typically analyzed in a separate method from OPs (see **Table 4**) [11, 24, 27, 31, 33, 34, 39]. To provide the best sensitivity, acetonitrile rather than methanol is selected as the organic modifier in the mobile phase with either acetic or formic acid as a mobile phase additive. Chlorpyrifos degradation product 3,5,6-trichloro-2-pyridinol has been widely studied and can be included in LC-ESI$^+$-MS/MS methods with approximately a 50 times higher detection limit than OPoxons [11]. LC-ESI$^-$-MS/MS has also been widely used, however, collision-induced dissociation only produces the Cl^- fragment ion such that it is more common to monitor the ^{35}Cl and ^{37}Cl isotopes peaks of the deprotonated molecular ion at 196→196 or 198→198 if included in SRM methods when concentrations are lower [23, 29, 30, 32, 40, 41].

OP	Parent	Organic modifier, additives; column	SRM (quantitative, confirmation)	Ref
Azinphos methyl oxon	Azinphos methyl	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	302→160, 302→132	[11]
		ACN, 0.1% HCOOH; C18	302→132, 302→245	[28]
Chlorpyrifos-methyl oxon	Chlorpyrifos-methyl	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	308→109, 306→109	[11]
Chlorpyrifos-ethyl oxon	Chlorpyrifos-ethyl	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	336→280, 336→200	[11]
		ACN, 0.1% HCOOH; C18	336→280, 336→308	[28]
		ACN, 0.025% HCOOH; Zorbax Extended C8	336→280	[29]
		ACN, 0.025% HCOOH; XDB-C8	336→280	[32]
Coumaphos oxon	coumaphos	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	347→291, 347→211	[11]
Demeton-S-methyl sulfone	Demeton-S-methyl	MeOH, 0.1% HCOOH; Acquity UPLC™BEH C18	263→169, 263→121	[6]
		MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	263→169, 263→108	[35]
Dibutylphosphate (IS)		ACN, 20 mM CH_3COOH (pH 6.45-7.45); mixed mode RP/WAX	209→79, 209→153^{ESI-}	[24]
Diethyl phosphate	OP	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	155→99, 155→127	[11]

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OP	Parent	Organic modifier, additives; column	SRM (quantitative, confirmation)	Ref
		ACN, 20 mM CH_3COOH (pH 6.45-7.45); mixed mode RP/WAX	153→79, 153→125^{ESI-}	[24]
		ACN, 0.1% HCOOH; MAXRP, RP12	153→125, 153→79^{ESI-}	[31]
		ACN, 1 mM tetrabutylammonium acetate; C18	153→79, 153→125, 153→63^{ESI-}	[34]
		MeOH, 0.1% HCOOH; X-Terra C18	153.0317→125.0004, 153.0317→78.9585^{ESI-*}	[27]
		MeOH, 0.1% CH_3COOH; XSELECT™ CSH™C18	153→79, 153→125^{ESI-}	[33]
Diethyldithiophosphate	OP	ACN, 1 mM tetrabutylammonium acetate; C18	185→111^{ESI-}	[31]
		ACN, 20 mM CH_3COONH_4, RP18	155→127, 155→99	[39]
Diethylthiophosphate	OP	ACN, 20 mM CH_3COOH (pH 6.45-7.45); RP/WAX	169→95, 169→141^{ESI-}	[24]
		ACN, 1 mM tetrabutylammonium acetate; C18	169→97, 169→141^{ESI-}	[31]
		MeOH, 0.1% CH_3COOH; XSELECT™ CSH™C18	169→95, 169→141^{ESI-}	[33]
		ACN, 0.1% HCOOH; MAXRP, C-12	169→95, 169→141, 169→63^{ESI-}	[34]
		MeOH, 0.1% HCOOH; X-Terra C18	169.0977→140.9775, 169.0977→94.9357^{ESI-*}	[27]
		ACN, 20 mM CH_3COONH_4, RP18	171→143, 171→115	[39]
Dimethylphosphate	OP	ACN, 1 mM tetrabutylammonium acetate; C18	125→63, 125→79^{ESI-}	[31]
		MeOH, 0.1% CH_3COOH; XSELECT™ CSH™C18	125→79, 125→63^{ESI-}	[33]
		ACN, 20 mM CH_3COONH_4, RP18	127→109, 129→95	[39]
Dimethylthiophoshate	OP	ACN, 1 mM tetrabutylammonium acetate; C18	141→126, 141→95^{ESI-}	[31]
		MeOH, 0.1% CH_3COOH; XSELECT™ CSH™C18	141→79, 141→63, 141→95^{ESI-}	[33]
		ACN, 20 mM CH_3COONH_4, RP18	143→125, 143→111	[39]

OP	Parent	Organic modifier, additives; column	SRM (quantitative, confirmation)	Ref
dimethyldithiophosphate	OP	ACN, 20 mM CH_3COONH_4, RP18	157→142, 157→112	[39]
Diazinon-oxon	diazinon	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	289→153, 289→93	[11]
		MeOH, 0.1% HCOOH; X-Terra C18	289.1317→153.1028, 289.1317→261.1004*	[27]
Disulfoton sulfone	disulfoton	MeOH, 0.1% HCOOH; Acquity UPLC™BEH C18	307→97, 307→153	[6]
		MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	307→153, 307→171	[35]
Disulfoton sulfoxide	disulfoton	MeOH, 0.1% HCOOH; Acquity UPLC™BEH C18	291→185, 291→97	[6]
		MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	291→213, 291→185	[35]
Fenamiphos sulfone	fenamiphos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	336→266, 336→308	[35]
Fenamiphos sulfoxide	fenamiphos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	320→171, 320→251	[35]
Fenchlorphos oxon	fenchlorphos	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	307→109, 305→109	[11]
Fenthion sulfone	fenthion	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	311→125, 311→279	[35]
Fenthion sulfoxide	fenthion	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	295→280, 295→127	[35]
5-hydroxydiazinon	diazinon	MeOH, 0.1% HCOOH; X-Terra C18	321.1038→293.0725, 321.1038→185.0749*	[27]
			319.0882→291.0568, 319.0882→229.0412^{ESI-*}	
7(1-hydroxy isopropyl diazinon	diazinon	MeOH, 0.1% HCOOH; X-Terra C18	321.1038→303.0932, 321.1038→275.0619*	[27]
4(1-hydroxyisopropyl diazoxon	diazinon	MeOH, 0.1% HCOOH; X-Terra C18	305.1266→287.1161, 305.1266→277.0953*	[27]
2-(1-hydroxy-1-methylethyl)-6-methyl-4(1H)-pyrimidinone	diazinon	MeOH, 0.1% HCOOH; Zorbax SB-CN	169→84	[19]
2-isopropyl-6-methyl-4-pyrimidinol	diazinon	ACN, 0.1% HCOOH; XDB-C18	153.1022, 84.0444, 70.0651*	[22]
		MeOH, 0.1% HCOOH; X-Terra C18	153.1028→137.0715, 153.1028→84.0575*, 151.0872→135.0558, 151.0872→123.0558^{ESI-*}	[27]
isomalathion	malathion	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	331→99, 331→127	[11]

OP	Parent	Organic modifier, additives; column	SRM (quantitative, confirmation)	Ref
2-isopropyl-6-methyl-4-pyrimidinol (IMP)	diazinon	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	153→84, 153→70	[11]
		MeOH, 0.1% CH_3COOH; XSELECT™ CSH™C18	153→84, 153→70	[33]
		MeOH, 1% CH_3COOH; C18	153→84, 153→70	[40]
		ACN, 0.1% HCOOH; XDB-C18	153.1022, 84.0444, 70.0651*	[22]
Malathion monocarboxylic acid	malathion	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	303→127, 303→99	[11]
		MeOH, 0.1% CH_3COOH; XSELECT™ CSH™C18	301→142, 301→157	[33]
			301→126, 301→141	
Malathion dicarboxylic acid	malathion	MeOH, 0.1% CH_3COOH; XSELECT™ CSH™C18	273→141, 273→157	[33]
Malathion-oxon	malathion	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	315→127, 315→99	[11]
o-methoate	dimethoate	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	214→183, 214→125	[11]
		MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	214→125, 214→109	[35]
		MeOH, 5 mM $HCOONH_4$; ODS-4	214→125, 214→183	[37]
			214→183	[4]
6-methyl-2-(1-methylethyl)4(1H)-pyrimidinone	diazinon	MeOH, 0.1% HCOOH; Zorbax SB-CN	153→84	[19]
3-methyl4-nitrophenol	fenitrothion	MeOH, 10mM CH_3COONH_4; XTerra MS C18	152	[25]
Parathion methyl oxon	Parathion methyl	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	248→202, 248→109	[35]
Phorate oxon	phorate	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	245→75, 245→47	[11]
Phorate sulfone	phorate	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	293→171, 293→97	[35]
Phorate sulfoxide	phorate	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	277→199, 277→143	[35]
3,5,6-trichloro-2-pyridinol	chlorpyrifos	MeOH, 0.1% HCOOH and 2 mM CH_3COONH_4; C_6phenyl	198→107, 198→134	[11]
		ACN, 0.1% CH_3COOH; XDB-C18	$198→198, 196→196^{ESI-}$	[23]
		ACN, 20 mM CH3COOH (pH 6.45-7.45); RP/WAX	$196→35, 198→35^{ESI-}$	[24]

OP	Parent	Organic modifier, additives; column	SRM (quantitative, confirmation)	Ref
		ACN, 0.025% HCOOH; Zorbax Extended C8	198^{ESI-}	[29]
		ACN, 0.1% HCOOH; C18	196→196, 198→198, $200\rightarrow200^{ESI-}$	[30]
		ACN, 0.025% HCOOH; XDB-C8	198→198	[32]
		MeOH, 0.1% CH_3COOH; XSELECT™ CSH™C18	198→37, 198→35, $196\rightarrow35^{ESI-}$	[33]
		ACN, 0.1% HCOOH; MAXRP, RP12	196→35, 198→37, $198\rightarrow35,^{ESI-}$	[34]
		MeOH, 1% CH_3COOH; C18	$196\rightarrow196, 198\rightarrow198^{ESI-}$	[40]
		MeOH, 1% CH_3COOH; PhenylC6	$196\rightarrow196, 198\rightarrow198^{ESI-}$	[41]
Temephos oxon	temephos	ACN, CH_3COONH_4; C18	468	[26]
Temephos sulfoxide	temephos	ACN, CH_3COONH_4; C18	482, 483, 500, 523	[26]
Terbufos sulfone	terbufos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	321→115, 321→171	[35]
Terbufos sulfoxide	terbufos	MeOH, 5 mM CH_3COONH_4; MAX RP, C-12	305→131, 305→159	[35]

Table 4. Selected ion monitoring (SIM) or selected reaction monitoring (SRM) transitions for organophosphorus pesticides (OPs) metabolites or degradation products by LC-ESI^+-MS/MS methods.

3. Carbamates and phenylureas

LC-ESI^+-MS/MS can be used for the simultaneous analysis of carbamates (general structure $R_1OCONR_2R_3$), phenylureas, and selected degradation products (see **Table 5** for target list). Few carbamates are still analyzed directly by GC-EI-MS or GC-EI-MS/MS in multiclass methods (primarily carbaryl, carbofuran, carbosulfan, EPTC, isoprocarb, pirimicarb) [3, 9, 42, 43]. To improve sensitivity and extend the range of carbamates amenable to GC-EI-MS methods derivatized prior to analysis with 9-xanthydol, trimethylphenylammonium hydroxide and trimethylsulfonium hydroxide or sodium hydride has been used [43–45]. Metabolites of carbofuran and carbaryl have been analyzed after derivatization using trifluoroacetic acid with trimethylamine to produce volatile derivatives that can be analyzed by GC-EI-MS [46]. Photodegradation products (phenols and para-hydroxybenzamides) of carbamates were analyzed directly by GC-EI-MS/MS method [47].

LC-ESI^+-MS/MS is more frequently chosen than GC-MS methods for the analysis of carbamates and phenylureas in chemical class-specific or multiclass methods [39, 48–58]. OPs, carbamates, and phenylureas have a wide range of polarities so they can elute over similar

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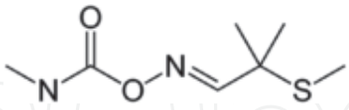
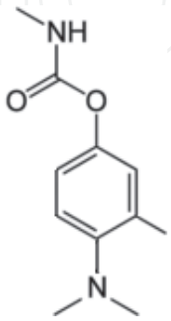
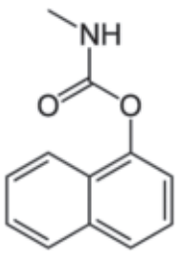
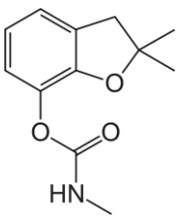
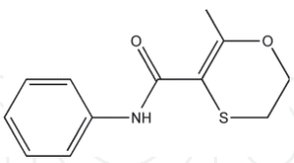
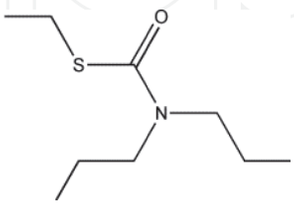
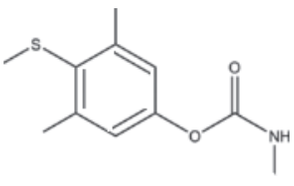
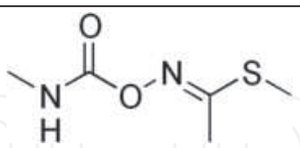
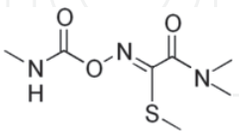
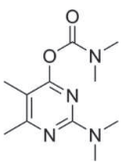
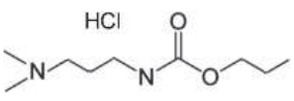
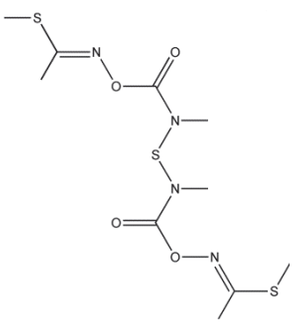
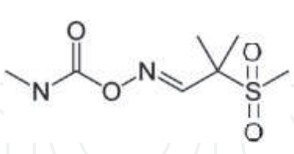
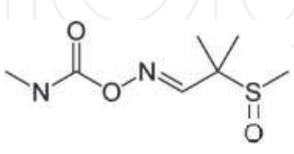
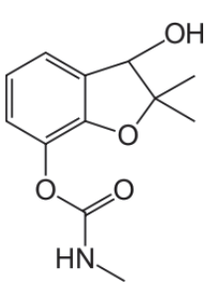
Carbamates

Compound (Parent compound) Molecular formula Molecular weight (g/mol)	**Structure**
Aldicarb $C_7H_{14}N_2O_2S$ 190.27	
Aminocarb $C_{11}H_{16}N_2O_2$ 208.26	
Carbaryl $C_{12}H_{11}NO_2$ 201.22	
Carbofuran $C_{12}H_{15}NO_3$ 221.25	
Carboxin $C_{12}H_{13}NO_2S$ 235.31	
EPTC $C_9H_{19}NOS$ 189.32	
Methiocarb $C_{11}H_{15}NO_2S$ 225.31	

Carbamates	
Compound (Parent compound) Molecular formula Molecular weight (g/mol)	**Structure**
Methomyl $C_5H_{10}N_2O_2S$ 162.21	
Oxamyl $C_7H_{13}N_3O_3S$ 219.36	
Pirimicarb $C_{11}H_{18}N_4O_2$ 238.29	
Propamocarb HCl $C_9H_{21}ClN_2O_2$ 224.73	
Thiodicarb $C_{10}H_{18}N_4O_4S_3$ 354.47	
Degradation products	
Aldicarb sulfone (aldicarb) $C_7H_{14}N_2O_4S$ 222.26	
Aldicarb sulfoxide (aldicarb) $C_7H_{14}N_2O_3S$ 206.26	
3-Hydroxycarbofuran (carbofuran) $C_{12}H_{15}NO_4$ 237.25	

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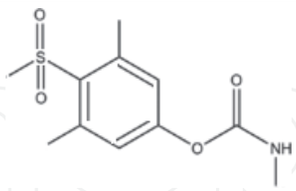
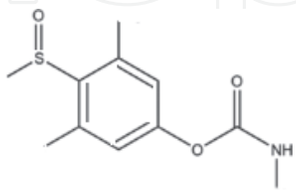
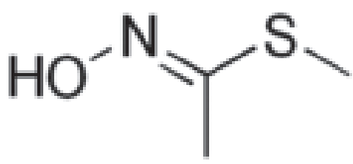
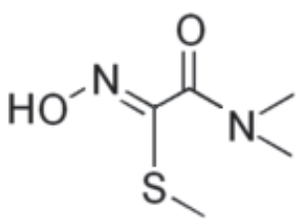
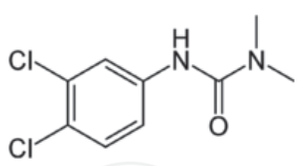
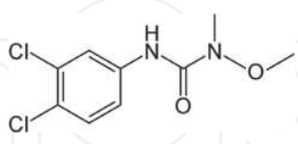
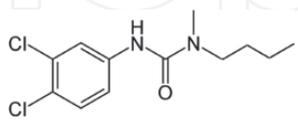
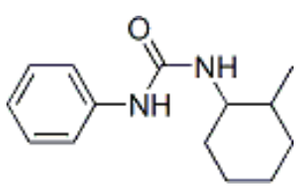
Carbamates	
Compound **(Parent compound)** **Molecular formula** **Molecular weight (g/mol)**	**Structure**
Methiocarb sulfone (methiocarb) $C_{11}H_{15}NO_4S$ 257.31	
Methiocarb sulfoxide (methiocarb) $C_{11}H_{15}NO_3S$ 241.31	
Methomyl-oxime (methomyl) C_3H_7NOS 105.16	
Oxamyl-oxime (oxamyl) $C_5H_{10}N_2O_2S$ 162.21	
Phenylureas	
Diuron $C_9H_{10}Cl_2N_2O$ 233.10	
Linuron $C_9H_{10}Cl_2N_2O_2$ 249.09	
Neburon $C_{12}H_{16}Cl_2N_2O$ 275.18	
Siduron $C_{14}H_{20}N_2O$ 232.32	

Table 5. Carbamates, selected degradation products, and phenylureas.

time periods when typical reversed-phase stationary phases are used; however, in general, phenylureas elute later than carbamates and within the time range for OPs and pyrethroid insecticides.

For LC-ESI$^+$-MS/MS the precursor ion is generally selected as the protonated molecular ion $[M+H]^+$ (see **Table 6**). Both methanol and acetonitrile have been used as the organic modifier in the mobile phase for the separation of carbamates and when both chemical classes are analyzed together; however, acetonitrile provides the best overall sensitivity. Sodium adducts of carbamates can also be observed with ESI$^+$ and have been attributed to impurities in methanolic mobile phases or sodium from metal tubing [51]. Both 0.1% formic acid and 5 mM ammonium acetate should be added to the mobile phase to improve sensitivity and to provide for ammonium adduct $[M+NH_4]^+$ formation for aldicarb, methiocarb sulfone, and oxamyl (see **Table 6**) [51, 53]. Ammonium acetate can also improve the peak shapes observed in the separation. Aldicarb sulfone and methiocarb sulfone observed both the protonated molecular ion and ammonium adduct under these conditions [53]. The addition of ammonium acetate to the mobile phase also minimizes sodium adduct formation which was observed in this work and others for aldicarb, aldicarb sulfone, aldicarb sulfoxide, 3-hydroxycarbofuran, siduron, and diuron [51]. The common, group-specific fragmentation pathway for *N*-methylcarbamates is the neutral loss of methyl isocyanate (CH_3-N=C=O), while for phenylureas, loss of the substituted aniline ring is common. For methomyl-oxime only one significant fragment ion was formed. The RSD of the ratio of areas SRM1/SRM2 was less than 20% for the majority of the compounds (see **Table 6**) and method detection limits are generally 1–5 μg/L. Methomyl-oxime and methiocarb sulfone are not as sensitive as other carbamates, with detection limits of 10 μg/L for the quantitative SRM transition. Siduron has two isomers which are partially resolved on the Fusion-RP column. Other carbamates and phenylureas that have been analyzed by LC-ESI$^+$-MS/MS include bendiocarb (224→167, 224→109 or 224→81 and 202→145), ethiofencarb (226→164, 253→126), ethiofencarb sulfone (258→107, 258→201), fenobucarb (208→152, 404→372), isoprocarb (194→137, 222→165), propoxur (210→110, 210→168), and other phenylureas include chlorotoluron (213→168, 213→140), desmethylisoproturon (193→151, 193→94), diflubenzuron (311→158, 311→141), isoproturon (207→165, 207→72), forchlorfenuron (248→129, 248→155), lufenuron (512→158, 512→141), metobromuron (259→148, 259→170), pencyuron (329→125, 329→218), teflubenzuron (381→158, 381→141), and triflumuron (359→156, 359→139) [6, 39, 49, 50, 53, 56].

Atmospheric pressure chemical ionization in positive and negative modes (APCI$^+$ or APCI$^-$) can give similar range of sensitivity and structural information as ESI$^+$ and can provide added selectivity for the LC-MS/MS analysis of carbamates [51]. Sodium adducts of the molecular ion do not form with APCI$^+$ and sensitivity is better in positive ion mode than in negative ion mode, partially due to greater fragmentation with to $[M\text{-}CONHCH_3]^-$ in the APCI$^-$ ion source [52, 59]. LC-APCI$^+$-MS has also been found to be more sensitive for some phenylureas [60].

Some of the main degradation products analyzed by LC-ESI$^+$-MS/MS are shown in **Table 6** and include carbamate sulfone or sulfoxides and hydroxyl derivative. Metabolites of carbofuran and carbosulfan have also been analyzed using LC-turboIonSpray-MS/MS, LC-APCI$^+$-MS and LC-QqTOF-MS/MS [61–66]. Other degradation products identified include 3-ketocarbofuran, 3-hydroxy-7-phenolcarbofuran, 3-keto-7-phenolcarbofuran, 7-phenolcarbofuran, and dibutyl amine.

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Compound (molecular weight)	Transitions	Cone voltage (V)	Collision energy (eV)	Ratio SRM1/ SRM2 areas ± RSD	Retention time (min)
Aldicarb (190.27)	**208→89**	10	15	2.66 ± 12.5%	12.46
	208→116	10	15		
Aldicarb sulfone (222.26)	**223→76**	15	10	2.83 ± 35.9%	4.60
	240→86	15	20		
Aldicarb sulfoxide (206.26)	**207→89**	15	15	1.13 ± 17.7%	3.29
	207→132	10	5		
Aminocarb (208.26)	**209→152**	20	15	1.39 ± 4.72%	2.85
	209→137	20	20		
Carbaryl (201.22)	**202→145**	22	10	3.32 ± 14.2%	16.35
	202→127	20	25		
Carbofuran (221.25)	**222→123**	20	20	2.73 ± 34.5%	15.27
	222→165	20	20		
Carboxin (235.31)	**236→143**	25	15	3.08 ± 11.3%	16.35
	236→86	20	25		
EPTC (189.32)	**190→128**	20	10	1.70 ± 20.5%	19.99
	190→86	20	10		
3-Hydroxycarbofuran (237.25)	**238→163**	20	10	3.03 ± 10.6%	8.92
	238→220	20	10		
Methiocarb (225.31)	**226→121**	15	20	1.40 ± 11.4%	18.31
	226→169	15	10		
Methiocarb sulfone (257.31)	**275→122**	15	20	1.01 ± 2.10%	12.61
	258→122	25	15		
Methiocarb sulfoxide (241.31)	**242→122**	20	25	1.24 ± 9.46%	9.35
	242→170	20	25		
Methomyl (162.21)	**163→88**	10	10	1.63 ± 4.24%	5.48
	163→106	10	10		
Methomyl-oxime (105.16)	**106→58**	15	10	1.00 ± 7.02%	3.23
	106→106	20	0.010		
Oxamyl (219.36)	**237→72**	20	10	2.45 ± 35.9%	4.66
	237→90	20	10		
Oxamyl-oxime (162.21)	**163→72**	15	10	7.03 ± 27.7%	2.68
	163→90	15	20		
Pirimicarb (238.29)	**239→72**	25	20	2.51 ± 7.80%	8.35
	239→182	30	15		

Compound (molecular weight)	Transitions	Cone voltage (V)	Collision energy (eV)	Ratio SRM1/ SRM2 areas ± RSD	Retention time (min)
Propamocarb HCl (224.73)	**189→102**	30	10	7.49 ± 21.4%	2.90
	189→74	35	15		
Thiodicarb (354.47)	**355→163**	15	10	2.06 ± 29.5%	15.63
	355→108	15	15		
Diuron (233.10)	**233→72**	25	15	1.98 ± 23.1%	16.83
	235→72	25	15		
Linuron (249.09)	**251→162**	15	20	2.20 ± 30.5%	18.68
	251→184	20	15		
Neburon (275.18)	**276→88**	30	15	4.86 ± 15.0%	20.27
	276→114	35	15		
Siduron (232.32)	**233→94**	30	20	1.12 ± 6.70%	18.22
	233→137	30	17		
EPTC-d_{14} (203.4)	**204→50**	20	20	N/A	19.99
Diuron-d_6 (239.13)	**239→52**	20	20	N/A	16.83

Quantitative transitions, where applicable, are shown in bold.

LC-ESI$^+$-MS/MS conditions: Synergi™ Fusion-RP, 60 mm × 2.0 mm i.d., 2.5 μm column; mobile phase of water/acetonitrile with 5 mM ammonium acetate and 0.1% formic acid in aqueous and 0.1% formic acid in organic modifier at a flow rate of 0.15 mL/min with organic modifier starting at 25% v/v and undergoing a gradient to 35% v/v over 4 min, followed by a series of gradient steps as follows: to 80% v/v from 4 to 14.5 min, held for 8 min, to 100% v/v from 22.5 to 23.5 min, and held for 25 min with column temperature at 22°C.

Table 6. Selected reaction monitoring transitions, cone voltage, collision energy, and retention times for the selected carbamates, their degradation products, phenylureas.

LC-APCI $^+$-MS and LC-atmospheric pressure photoionization (APPI$^+$)-MS have also been used to analyze these metabolites as well as sulfoxides and sulfones of carbamates with the protonated molecular ion, ammonium adduct, and [M+H-CH_3NCO]$^+$ observed in the ion source [67–69].

4. Pyrethroid insecticides and their metabolites

Figure 3 shows the structures of the pyrethroid insecticides. They have been routinely analyzed with GC-EI/MS, GC-EI-MS/MS, or GC-NCI-MS methods (see **Table 7**) [3, 5, 6, 9, 10, 14, 42, 70–81]. For the diverse range of pyrethroids these methods are preferred over LC-MS/MS methods. Pyrethroid insecticides are also often analyzed simultaneously with OCs and OPs (either EI or NCI) and generally elute latter in the separation than OCs and OPs. Detection limits with GC-EI-MS for pyrethroids are often more than sufficient for routine analysis in the μg/L range [10].

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Negative chemical ionization can provide higher MS selectivity for halogenated pyrethroids compared to GC-EI-MS [7, 10]. Some studies have shown that ammonia, rather than methane, as the reagent gas yields lower detection limits for pyrethroids analyzed by GC-NCI-MS [74], however, methane is still preferred for analysis of OCs and OPs [7, 10]. Pyrethroids also easily fragment in the EI source such that the molecular ion has low abundance and fragment ions are selected for quantitation and confirmation as shown in **Table 7**. For GC-EI-MS/MS the precursor ion is selected as a fragment ion in order to obtain sufficient sensitivity and used over GC-EI-MS when added selectivity is required for more difficult sample matrices.

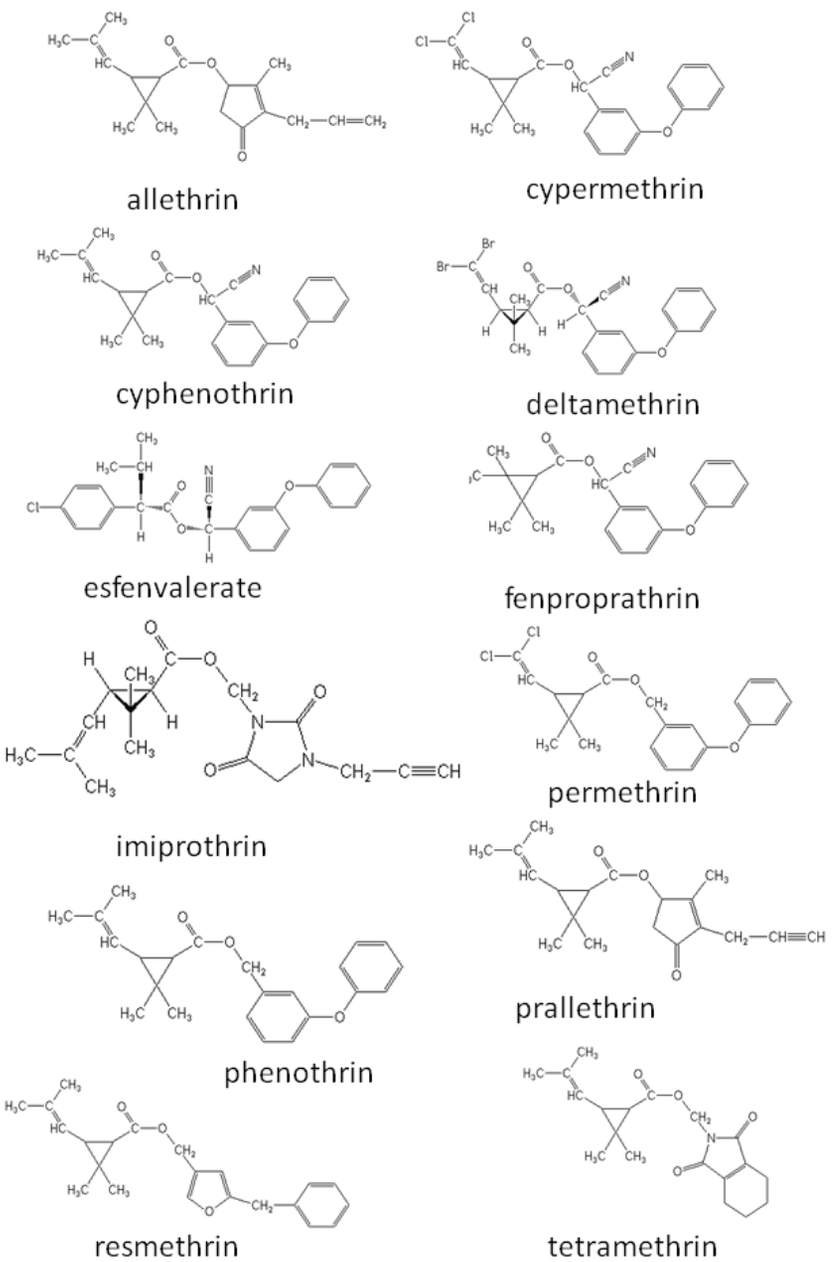

Figure 3: Structures of pyrethroid insecticides.

Analyte	SIM or SRM (*m/z*)	Ref
Pyrethroid insecticides		
Allethrin $C_{19}H_{26}O_3$	123, 136, 202	[70]
	167, 68$^{NCI, CH4}$	This work
Bifenthrin $C_{22}H_{22}ClF_3O_2$	181, 165	[5, 6]
	181, 105	[9]
	181→ 115, 181→165	[3]
	181, 165, 166	[79, 10]
	181→166, 181→165	[76]
	205, 241$^{NCI, CH4}$	[77], this work
	386, 387, 388$^{NCI, CH4}$	[10]
Cyfluthrin (4 peaks) $C_{22}H_{18}Cl_2FNO_3$	163, 226	[70]
	163, 127	[5]
	206, 150	[6]
	163→127, 226→206	[3]
	207, 209$^{NCI, CH4 or NH3}$	This work
λ-Cyhalothrin $C_{23}H_{19}ClF_3NO_3$	209, 181	[70]
	181, 127	[5]
	181, 152	[6]
	205→121, 241→205	[76]
	197→141, 197→161	[14]
	181→127, 197→161	[3]
	181→152, 197→141, 197→161	[80]
	205, 241$^{NCI, NH3 or CH4}$	[77], this work
Cypermethrin (4 peaks) $C_{22}H_{19}Cl_2NO_3$	163, 181	[70]
	181, 163, 209	[79]
	181, 127	[5]
	163, 127	[6]
	91, 163, 181	[42]
	163, 165, 181	[10]
	207, 171$^{NCI, NH3}$	[77]
	207, 209$^{NCI, CH4}$	This work
	207, 209, 171	[10]
	207→35, 209→35	[14]
	163→127, 181→127	[3]

http://dx.doi.org/10.5772/68074

Analyte	SIM or SRM (*m/z*)	Ref
	163→127, 165→127, 165→129	[80]
Deltamethrin (2 peaks)	253, 255	[70]
$C_{22}H_{19}Br_2NO_3$	253, 172	[14]
	93, 181, 253	[42]
	253, 172+174	[6]
	181, 253, 163, 165	[81]
	181, 253, 251	[10]
	172→93, 253→93	[3]
	253→172, 253→174	[80]
	79, $137^{NCI, NH3}$	[77]
	$79,81^{NCI, CH4}$	This work
	297, 299, $79^{NCI, CH4}$	[10]
Esfenvalerate (2 peaks) $C_{25}H_{22}ClNO_3$	419, 167, 181	[70]
	$211, 167^{NCI}$	[77]
	$211, 213^{NCI}$	This work
	225→119, 225→147	[3]
Fenpropathrin $C_{22}H_{23}NO_3$	181, 265	[70]
	141^{NCI}	[77], this work
Fenvalerate (2 peaks) $C_{22}H_{22}ClNO_3$	167, 125	[5]
	109, 127, 244	[42]
	$211, 167^{NCI}$	[77]
	211→167, 213→169	[14]
	225→119, 225→147	[3]
	167→125, 125→89, 125→99	[80]
τ-fluvalinate $C_{26}H_{22}ClF_3N_2O_3$	250, 55	[5]
	250, 206, 252	[79]
	250, 200+214	[6]
	$294, 258^{NCI}$	[77]
	$294, 296^{NCI}$	This work
	250→55, 250→200	[3]
Flucythrinate (2 peaks) $C_{26}H_{23}F_2NO_4$	199, 157	[5]
Imiprothrin	123, 318, 151	[70]
Cis/trans-permethrin (2 peaks) $C_{21}H_{20}Cl_2O_3$	183, 165	[6, 70, 78]
	183, 163	[5, 9]

Analyte	SIM or SRM (*m/z*)	Ref
	207, 171^{NCI}	[77]
	207, 209^{NCI}	This work
	207→35, 209→35	[14]
	163→127, 183→128	[3]
	163→127, 165→127	[80]
	165→129	
Phenothrin $C_{23}H_{26}O_3$	183, 163	[70]
	331, 167^{NCI}	[77]
Prallethrin $C_{19}H_{24}O_3$	123, 300	[70]
	167, 132, 168	This work
Resmethrin (two peak) $C_{22}H_{26}O_3$	171, 123, 338	[70]
	337, 167^{NCI}	[77]
Tefluthrin $C_{17}H_{14}ClF_7O_2$	205, 241^{NCI}	This work
Tetramethrin (two peak) $C_{19}H_{25}NO_4$	164, 123	[70]
	164, 107	[5]
	349, 167^{NCI}	[77]
Tralomethrin $C_{22}H_{19}Br_4NO_3$	181, 253, 163, 165	[81]
	79, 137^{NCI}	[77]
Transfluthrin $C_{15}H_{12}C_{12}F_4O_2$	163→121, 163→117	[3]
Metabolites (derivatization reagent)		
CA (diazomethane)	182, 167, 123	[70]
CA (PFBBr)	295→79, 297→79	[14]
DBCA(diazomethane)	231, 233	[70]
DBCA (PFBBr)	312, 253, 231	[71]
DBCA (PFBBr)	295→79, 297→79	[14]
DBCA (MTBSTA)	355, 353, 357, 172	[73, 75]
DBCA (HFIP)	369	[74]
DCCA (diazomethane)	187, 189, 163	[70]
DCCA (PFBBr)	222, 187, 163	[71]
DCCA (PFBBr)	207→35, 209→35	[14]
DCCA (MTBSTA)	265, 267	[72, 75]
DCCA (MTBSTA)	265, 267, 128, 307	[73]
DCCA (HFIP)	323	[74]
3PBA (diazomethane)	197, 228	[70]
3PBA (PFBBr)	228, 197	[71]

Analyte	SIM or SRM (*m/z*)	Ref
3PBA (MTBSTFA)	271, 227, 197	[73, 75]
3PBA (HFIP)	364	[74]
4F3PBA (diazomethane)	246, 215	[70]
4F3PBA (PFBBr)	246, 215	[71]
4F3BA (MTBSTFA)	289, 245, 214	[73, 75]
FBAc(TMSI-TMCS)	251, 252	[72]
MCA(TMSI-TMCS)	211, 212	[72]
CH_3FBAc(TMSI-TMCS)	265, 266	[72]
FB-Al (TMSI-TMCS)	237, 238	[72]
CH3-FB-Al (TMSI-TMCS)	251, 252	[72]
CH_3OCH_2-FB-Al	281, 282	[72]
$HOCH_2$-FB-Al	339, 340	[72]

Electron ionization unless noted. Pentafluorobenzyl bromide, PFBBr; tert-butyldimethylsilyl derivatives of MTBSTFA; 1,1,1,3,3,3-hexafluoroisopropanol (HFIP); and N-trimethlsilylimidazole (TMSI)-trimethylchlorosilane (TMCS) for alcoholic metabolites.

Table 7. GC-MS or GC-MS/MS methods for pyrethroids and metabolites.

Metabolites of pyrethroids include the following: 3-(2,2-dimethylvinyl)-2,2-dimethylcyclopropane-1-carboxylic acid, CA (metabolite of allethrin, imiprothrin, phenothrin, prallethrin, resmethrin, and tetramethrin); 4-fluoro-3-phenoxybenzoic acid, 4-fluoro-3-phenoxybenzoic acid, 4FPBA (metabolite of cyfluthrin), cis- and trans-2,2-dichlorvinyl-2,2-dimethylcyclopropane-1-carboxylic acid, DCCA (metabolite of cyfluthrin, cypermethrin, and permethrin); and 3-phenoxybenzoic acid, 3-PBA (metabolite of cyhalothrin, cypermethrin, deltamethrin, esfenvalerate, fenpropathrin, phenothrin, and permethrin), cis-2,2-dibromovinyl-2,2-dimethyl-2,2-dimethylcyclopropane-1-carboxylic acid, DBCA (metabolite of deltamethrin). Additionally, both carboxylic acid and alcoholic derivatives can form fluoro-containing pyrethroids including the following: 2,3,5,6-tetrafluorobenzyl alcohol (FB-Al) and 2,3,5,6-tetraflurobenzoic acid (FB-Ac) (metabolites of transfluthrin); 2,3,5,6-tetrafluorobenzoic acid (CH_3-FB-Ac) and 4-methyl-2,3,5,6-tetrafluorobenzyl alcohol (CH_3-FB-Al) (metabolites of profluthrin); 4-methoxymethyl-2,3,5,6-tetrafluoro benzyl alcohol (CH_3OCH_2-FB-Al) (metabolite of metofluthrin); and 4-hydroxymethyl-2,3,5,6-tetrafluorobenzyl alcohol ($HOCH_2$-FB-Al) (metabolite of metofluthrin and profluthrin) [72]. Most studies include cis/trans-DCCA, DBCA, 4F3PBA, and 3PBA in their analysis of metabolites of pyrethroids (see **Table 7**). Analysis of metabolites by GC-EI-MS requires derivatization of the metabolites prior to analysis with pentafluorobenzyl bromide (PFBBr), tert-butyldimethylsilyl-N-methyltrifluoroacetamide (MTMSTFA). or 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), and N-trimethlsilylimidazole (TMSI)-trimethylchlorosilane (TMCS) for alcoholic metabolites [14, 70–75]. GC-EI-MS/MS has not been widely used for analysis of the metabolites. Derivatization extends the range of metabolites that are amenable to GC-EI-MS above those commonly analyzed by LC-MS/MS. Some metabolites of pyrethroids including DBCA, DCCA, 4FPBA, and 3PBA can

be analyzed by LC-ESI$^-$-MS/MS (see **Table 8**) [33, 41, 82–84]. Pyrethroids that ionize in an electrospray ion source are more sensitive in positive ion mode with the ammonium adduct formed such that ammonium acetate at ~5 mM should be added to the mobile phase. For those pyrethroids that are more sensitive with LC-ESI$^-$-MS/MS (cyfluthrin and cyhalothrin), the deprotonated molecular ion forms in the ion source. The metabolites form the deprotonated molecular ion in the ESI ion source. In general, only a few pyrethroids have been included in LC-ESI$^+$-MS/MS multiclass methods.

Analyte (monoisotopic mass)	SIM or SRM (*m/z*)	Reference
Pyrethroids		
Bifenthrin (422.1)	440→182	[82]
Cyfluthrin (433.1)	451→191, 451→434	[39]
	435→191, 435→127	[84]
	432→405	[82]
Cyhalothrin (449.1)	448.2→402.8^{ESI-}	[82]
Cypermethrin (415.1)	433→191, 433→416	[35, 39, 84]
	433→191	[82]
Deltamethrin (502.0)	523→506, 523→281	[39]
	506→281, 506→253	[84]
	521→279	[82]
Permethrin (390.1)	408→355, 408→183	[84]
	408→183	[82]
Esfenvalerate (419)	437→167	[82]
Metabolites		
DBCA	343→81, 297→81^{ESI-}	[83]
	295→79^{ESI-}	[82]
	299→299	[84]
DCCA	207→207, 209→209^{ESI-}	[41, 84]
	207→207, 207→35^{ESI-}	[39]
	207→35, 209→35, 209→37^{ESI-}	[33]
	209→37, 207→35^{ESI-}	[83]
	207→35^{ESI-}	[82]
4-FPBA	231→93, 231→65^{ESI-}	[83]
	231→93^{ESI-}	[82]
3-PBA	213→93, 213→169^{ESI-}	[33, 41]
	213→93, 213→65^{ESI-}	[83]
	213→93^{ESI-}	[82]

Table 8. Pyrethroid insecticides and their metabolites by LC-MS/MS. Electrospray ionization in positive ion mode unless noted.

5. Other considerations

Generally, there is a larger diversity of azole fungicides and strobilurin fungicides that can be analyzed with LC-ESI$^+$-MS/MS methods as compared to those amenable to GC-MS methods [76, 79, 80, 85, 86]. For pesticides that are halogenated, GC-NCI-MS should be considered as an option to improve the sensitivity or selectivity of the analysis. Dissociative electron capture is often observed in negative chemical ionization for OPs, OCs, pyrethroids, azole fungicides, and strobilurin fungicides. GC-EI-MS/MS methods may also provide added selectivity; however, as many pesticides from these chemical classes fragment easily in an EI ion source, the precursor ion may need to be selected as a fragment ion which is capable of undergoing further collision-induced dissociation to achieve the required sensitivity. OP metabolites (OP oxons, sulfones, sulfoxides, and selected others) can be analyzed by LC-ESI$^+$-MS/MS, while alkylphosphates or alkylthiophosphates should be analyzed by LC-ESI $^-$-MS/MS or following derivatization by GC-MS. Pyrethroid metabolites are still commonly analyzed following derivatization with GC-EI-MS methods with a small selection of common pyrethroid metabolites also frequently analyzed by LC-MS/MS.

6. Conclusions

A larger number of OPs including organophosphates and organothiophosphates have been analyzed by GC-MS or GC-MS/MS methods as compared to LC-ESI$^+$-MS/MS. GC-EI-MS or GC-EI-MS/MS is most commonly selected for analysis of OPs, and GC-EI-MS provides excellent confirmation of identity of the OP through spectral library matches. When added selectivity is required, such as when matrix remains after sample clean-up, analysis of OPs by GC-NCI-MS or GC-EI-MS/MS should be selected. GC-NCI-MS analysis of halogenated (or nitro substituted) OPs generally provides better sensitivity than GC-EI-MS/MS, particularly when the precursor ion selected for CID is the molecular ion. Although NCI is a softer ionization process than EI, fragment ions are still often observed as a result of dissociative electron capture. Sensitivity of GC-EI-MS/MS can be improved by selection of an abundant fragment ion for the precursor ion rather than the molecular ion which may be too low in abundance. The number of applications using LC-ESI$^+$-MS/MS for the analysis of OPs has increased in the past ten years and for those OPs that can be ionized efficiently by ESI, the sensitivity may be better than with GC-MS methods (particularly for OPs that elute later in the GC separations). Another advantage of LC-ESI$^+$-MS/MS is that it is feasible to analyze OP degradation products (OP oxons, OP sulfones, or OP sulfoxides) simultaneously with parent OPs. Derivatization of alkylphosphates and alkylthiophosphates metabolites of OPs is required to achieve the desired sensitivity when analyzed by GC-MS or GC-MS/MS methods. Alkylphosphate metabolites can also be analyzed by LC-ESI$^-$-MS/MS.

Pyrethroids can be analyzed simultaneously with OCs and OPs using GC-EI-MS or GC-EI-MS/MS. A number of pyrethroids are halogenated and consequently they can be analyzed by GC-NCI-MS for added selectivity and sensitivity. Metabolites of pyrethroids are derivatized prior to the analysis by GC-EI-MS or GC-EI-MS/MS and this approach remains the method

of choice for their analysis. Analysis of pyrethroids by LC-MS/MS is more limited; however, metabolites of pyrethroids can be analyzed using LC-ESI$^-$-MS/MS.

Carbamates and phenylureas are commonly analyzed by LC-ESI$^+$-MS/MS. Selected carbamates can be analyzed by GC-MS methods, but a derivatization step is required prior to analysis. The main degradation products of carbamates including carbamate sulfone or sulfoxides can be analyzed by LC-ESI$^+$-MS/MS simultaneously with carbamates and phenylureas. APCI and APPI in positive ion mode have also been used to ionize metabolites of carbamates to achieve better sensitivity than ESI. APCI$^+$ is also not prone to sodium adduct formation. Mobile phase additives used for the LC-ESI$^+$-MS/MS separation of both OPs, carbamates and phenylureas include 0.1% formic acid and 5 mM ammonium acetate. Better sensitivity for OPs is obtained when methanol is used as the organic modifier for gradient elution, while acetonitrile is more commonly used for the separation of carbamates to obtain optimal sensitivity. Carbamates are prone to adduct formation (reduce sensitivity) in mobile phases containing methanol, and ammonium formate or ammonium acetate is generally used to reduce sodium adduct formation. Other pesticides that can be analyzed by LC-ESI$^+$-MS/MS include azole fungicides, neonicotinoid insecticides, and strobilurin fungicides. Pending the target list of pesticides, it is feasible to obtain simultaneous analysis of all these chemical classes; however, if optimal sensitivity is required then class-specific methods will achieve better results.

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Author details

Renata Raina-Fulton*, Nicole Dunn and Zhen Xie

*Address all correspondence to: renata.raina@uregina.ca

Department of Chemistry & Biochemistry, Trace Analysis Facility, The University of Regina, Regina, SK, Canada

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