

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Advances in Analytical Methods for Organophosphorus Pesticide Detection

Tova A. Samuels and Sherine O. Obare

*Department of Chemistry, Western Michigan University, Kalamazoo, Michigan
United States of America*

1. Introduction

Environmental pollution by organic chemicals continues to be one of the world's leading challenges to sustainable development. Modern developed and developing countries utilize millions of synthetic organic compounds in their civilian, commercial, and defense sectors for an ever-expanding diversity of uses (Ariese et al., 2001). Common applications include plastics, lubricants, refrigerants, fuels, solvents, preservatives, surfactants, dispersants and pesticides. As a result of widespread global usage coupled with improper handling practices, many of these organic compounds enter the environment and cause air, water, and soil pollution. For example, pesticides and herbicides are applied directly to plants and soils, while accidental releases originate from spills, leaking pipes, underground storage tanks, waste dumps, and waste repositories. Many pesticides are sprayed in large amounts with only 1% reaching the intended target. Some of these contaminants have long half-lives and thus persist to varying degrees in the environment. They migrate through large regions of soil until they reach water resources, where they may present an ecological or human-health threat (Karr & Dudley, 1981). Organisms, vegetation, animals and humans are affected by various chemicals through absorption, inhalation or ingestion. These contaminants pose serious to fatal health hazards, such as asthma, birth defects and deaths. Therefore, environmental monitoring is required to protect the public and the environment from possible organic toxins released into the air, soil, and water.

The United States Environmental Protection Agency (U.S. EPA) has imposed strict regulations on the concentrations of many environmental contaminants in air and water (U.S. EPA, 2010). However, current monitoring methods for most organic contaminants are costly and time-intensive, and limitations in sampling and analytical techniques exist (United States Geological Survey, U.S.G. S., 2010). Thus, there is a great demand for development of quick, simple and reliable methods for the detection of organic-based agricultural pesticides. In this chapter, advancements in methods to detect organophosphorus (OP) pesticides are discussed.

1.1 Structure of OP Compounds

OP pesticides are synthetic esters, amides, or thiol derivatives of phosphoric, phosphonic, phosphorothioic, or phosphonothioic acids. Table 1 lists the names of the most commonly used OP pesticides (International Programme on Chemical Safety, INCHEM, 2010; Pesticide Action Network, PAN, 2010; Ullmann's Agrochemicals, 2007). The chemical structure of all

OP pesticides consists of a central phosphorus atom, with either a double bonded oxygen ($P = O$), which are termed oxon pesticides, or a double bonded sulfur atom ($P = S$), which are termed thion pesticides, as shown in Figure 1. Structurally, both oxons and thions vary in the single-bonded R_1 , R_2 and X groups attached to the central pentavalent phosphorus atom. However, R_1 and R_2 generally tend to be alkoxy, aryloxy and thioalkoxy groups, while X is a labile leaving group.

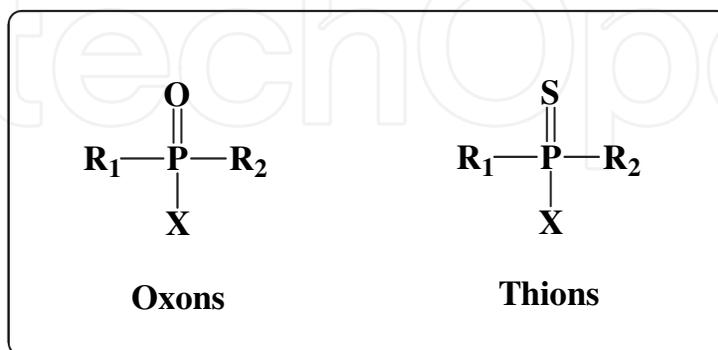


Fig. 1. General chemical structure of oxon and thion OP compounds.

1.2 OP Compounds and their toxicity

Pesticides are described as chemicals that kill or slow down the growth of undesirable organisms. Pesticides include herbicides, insecticides, fungicides, and nematocides (Celik et al., 1995). OP pesticides constitute the most widely used insecticides available today. This class of compounds has achieved enormous commercial success as a key component in the arsenal of agrichemicals, and is currently an integral element of modern agriculture across the globe. According to the U.S. EPA, about 70% of the insecticides in current use in the US are OP pesticides (U.S. EPA, 2010). Although OP compounds are considered safer than organohalides, they are still highly neurotoxic to humans and in some cases their degradation products have the potential to be more toxic with chronic exposure. OP pesticides are efficiently absorbed by inhalation, ingestion, and skin penetration. They are strong inhibitors of cholinesterase enzymes that function as neurotransmitters, including acetylcholinesterase, butylcholinesterase, and pseudocholinesterase. These enzymes are inhibited by binding to the OP compound. Upon binding, the OP compound undergoes hydrolysis leading to a stable phosphorylated and a largely unreacted enzyme. This inhibition results in the accumulation of acetylcholine at the neuron/neuron and neuron/muscle junctions or synapses.

Each year OPs poison thousands of humans across the world. In fact, in 1994, an estimated 74,000 children were involved in common household pesticide related poisoning or exposures in the United States (U.S. EPA, 2010). In a more recent study, it was found that children exposed to OP pesticides were more likely to be diagnosed with attention deficit hyperactivity disorder (ADHD) (Bouchard et al., 2010). Exposure has been attributed to frequent use of OPs in agricultural lands and their presence as residues in fruits, vegetables, livestock, poultry products and municipal aquifers (G. L. Liu & Lin, 1995). For example, typical pesticide concentrations that flow into aqueous waste range from 10,000 to 1 ppm (Gilliom et al., 1999; U.S.G.S., 2010). Pesticides are influenced by a number of biological, chemical and physical processes once they enter the environment. Figure 2 shows the

possible routes of environmental exposure of OP pesticides to humans and wildlife (Vermeire et al., 2003). While many OP pesticides can degrade via microbial or environmental processes, some of the pesticides are consumed by organisms, or they could leach into ground water. Once a pesticide enters ground water it can remain there for considerable periods of time. In ground water, there is little sunlight exposure, which slows down the degradation of OP pesticides and increases their potential risks to the environment and human health.

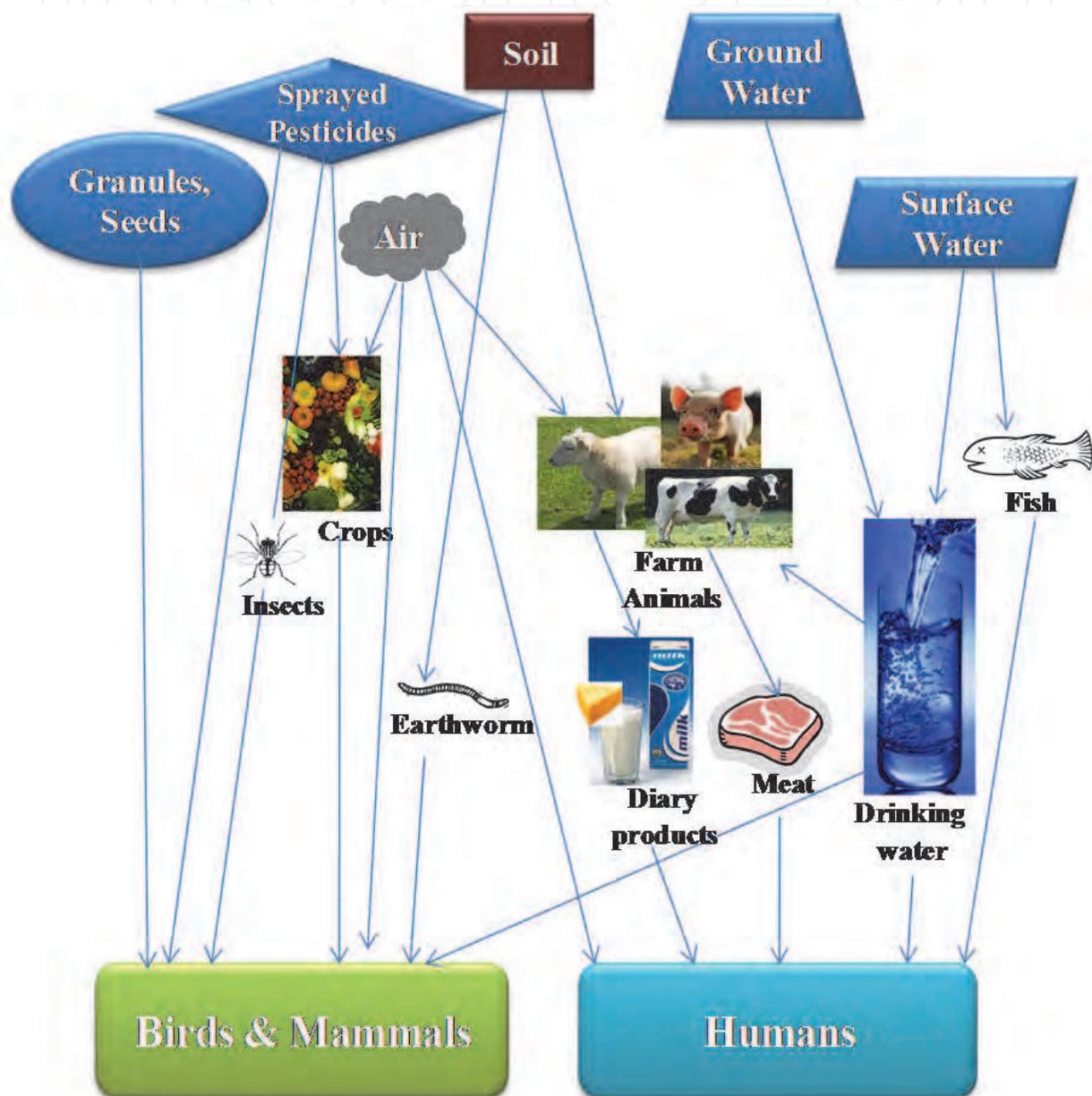


Fig. 2. Schematic representation of the possible routes of environmental exposure of OP pesticides to humans and wildlife. Adopted from Reference Vermeire et al., 2003.

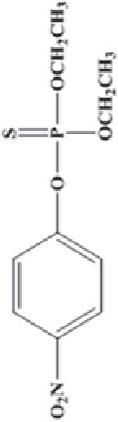
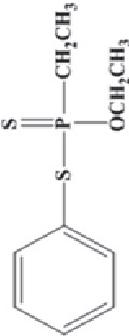
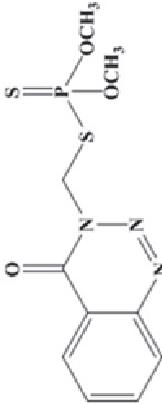
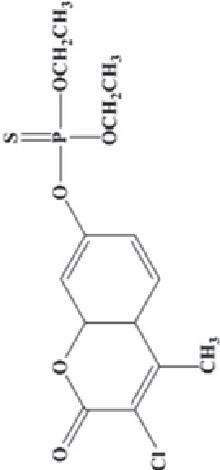
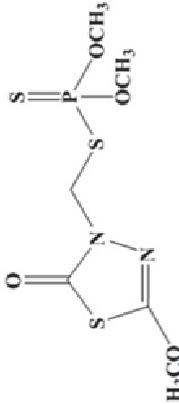
No	OP Name	Structure (Thions: 1–17; Oxons: 18 – 29)	LD ₅₀ , mg/kg *		WHO Acute Hazard [§]	IARC Carcinogens [†]	U.S. EPA Carcinogens [†]
			Oral	Dermal			
1	Parathion		1	21	Ia	3, Unclassifiable	C, Possible
2	Fonofos		8–17	147	Ia	N/A	E, Unlikely
3	Azinphos-methyl		11–13	220	Ib	N/A	Not Likely
4	Coumaphos		16–41	1,000	Ib	N/A	Not Likely
5	Methidathion		25–48	1,546	Ib	N/A	C, Possible

Table 1.

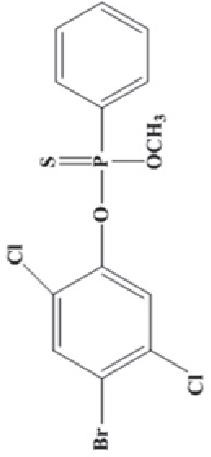
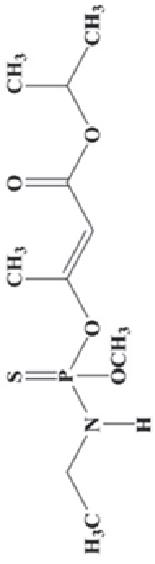
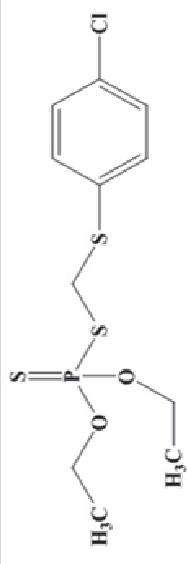
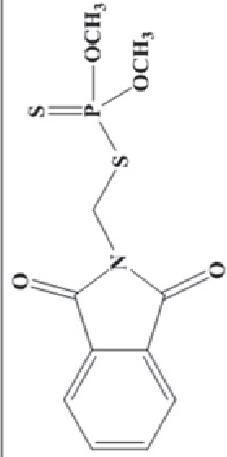
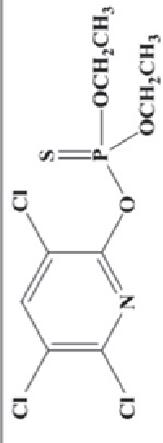
6	Leptophos 	45-53	>800	N/A	N/A	N/A
7	Propetamphos 	75-82	2,300	Ib	N/A	Not Likely
8	Carbophenothion 	98-120	190-215	N/A	N/A	N/A
9	Phosmet 	113-160	>1,500	II	N/A	Suggestive
10	Chlorpyrifos 	135-165	2,000	II	N/A	E, Unlikely

Table 1. Cont.

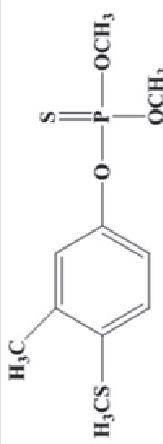
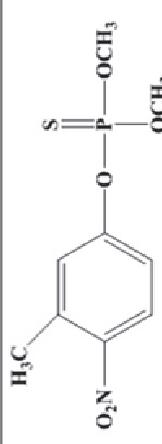
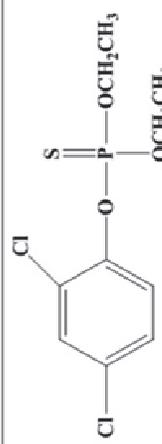
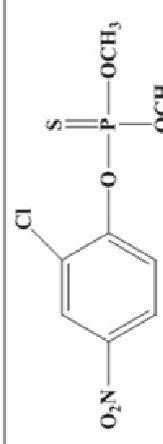
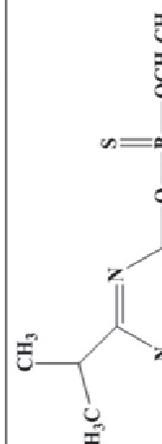
11	Fenthion		214–245	330	II	N/A	E, unlikely
12	Fenitrothion		250	>3,000	II	N/A	E, unlikely
13	Dichlofenthion		270	6,000	N/A	N/A	N/A
14	Dicapthion		330–400	790–1,250	N/A	N/A	N/A
15	Diazinon		300–850	2,150	II	N/A	Not Likely

Table 1. *Cont.*

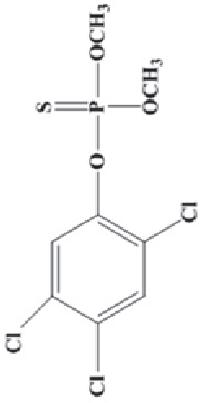
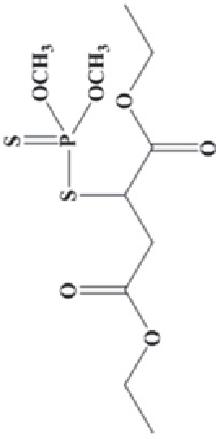
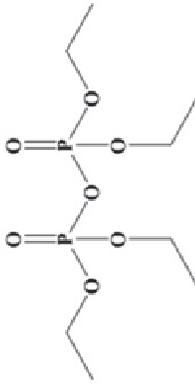
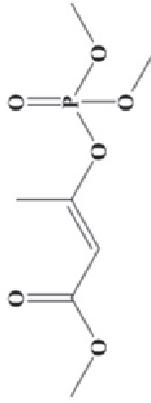
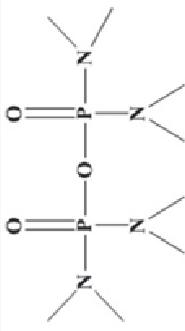
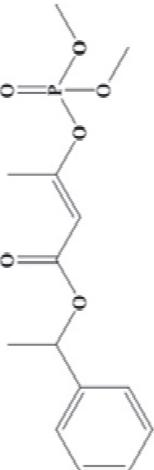
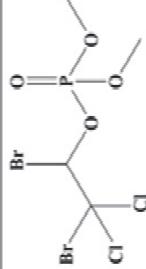
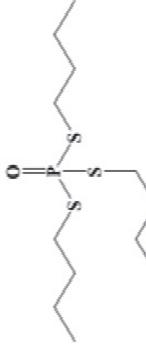
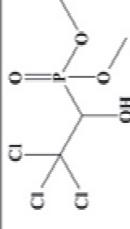
16	Ronnel		1,250–2,630	2,000	N/A	N/A	N/A
17	Malathion		5,400–5,700	>2,000	III	3 _p Unclassifiable	Suggestive
18	Tetraethyl pyrophosphate (TEPP)		0.5	2.4	N/A	N/A	N/A
19	Mevinphos		3.7–6.1	4.2–2.7	Ia	N/A	N/A
20	Schradan		10	15	N/A	N/A	N/A

Table 1. *Cont.*

21	Monocrotophos		18-20	112-126	Ib	N/A	N/A
22	Phosphamidon		24	107-143	Ia	N/A	C, Possible
23	Oxydemeton methyl		47-52	158-173	Ib	N/A	Not Likely
24	Ethoprophos		61	26	Ia	N/A	Likely
25	Dichlorvos		56-80	75-107	Ib	2b, Possible	Suggestive

Table 1. *Cont.*

26	Crotoxyphos		74-110	202-375	N/A	N/A	N/A
27	Naled		250	800	II	N/A	E, Unlikely
28	Tribufos		560-630	>2,000	N/A	N/A	Likely (high doses), Not likely (low doses)
29	Trichlorfon		400-800	>2,000	II	3, Unclassifiable	Likely (high doses), Not likely (low doses)

- Toxic interactions of organophosphorus compounds with any given biological system are dose-related. Their toxicity is expressed in terms of the lethal dose (LD) which will kill 50% of the animal species (LD₅₀). LD₅₀ values are generally expressed as amount per unit weight (e.g., mg·kg⁻¹).
- Toxic interactions of organophosphorus compounds with any given biological system are dose-related. Their toxicity is expressed in terms of the lethal dose (LD) which will kill 50% of the animal species (LD₅₀). ^sWHO = World Health Organization, acute hazard classify: Ia = extremely hazardous to human health; Ib = highly hazardous; II = moderately hazardous; III = slightly hazardous. [#] IARC = International Agency for Research on Cancer. [†] EPA = Environmental Protection Agency.

Table 1. Common OP pesticides classified by oxon/thion structure and oral LD₅₀ toxicities (Gilliom et al., 1999; Vermeire et al., 2003; Walker, 1972) .

2. Advances in the detection of OP pesticides

Significant advances toward the development of detection methods for OP compounds have been reported in the literature (Jenkins et al., 1997a, 1999b; Jenkins et al., 2001; Rudzinski et al., 2002; Russell et al., 2003; Sohn et al., 2000; Steiner et al., 2005). Analysis of OPs in environmental and biological samples is routinely conducted using various analytical techniques, including nuclear magnetic resonance (NMR) spectroscopy (Ross & Biros, 1970), gas, liquid or thin layer chromatography, and mass spectrometry (Steiner et al., 2005). A variety of approaches have been investigated for new sensors, including enzymatic assays (Russell et al., 2003), molecular imprinting coupled with luminescence (using lanthanides) (Jenkins et al., 1997a, 1999b; Jenkins et al., 2001; Rudzinski et al., 2002), colorimetric methods (Michel et al., 1973; Novak et al., 1979; Wallace et al., 2005), surface acoustic waves (Ngehngwainbi et al., 1986; Nieuwenhuizen & Harteveld, 1997), fluorescent organic molecules (Van Houten et al., 1998; Yamaguchi et al., 2005; S. W. Zhang & Swager, 2003), and interferometry (Sohn et al., 2000). The most common ways for detecting OP pesticides are chromatographic methods coupled with different detectors and different types of spectroscopy, immunoassays, and enzyme biosensors based on inhibition of cholinesterase activity (Evtugyn et al., 1996; Sherma, 1995; Trojanowicz, 2002). Recently, advances have risen toward designing and developing optical sensors, *i.e.*, colorimetric or fluorimetric chemosensors or reagents. One of the most convenient and simple means of chemical detection is the generation of an optical signal, for example, changes in absorption or emission bands of the chemosensor in the presence of the target analyte. Optical outputs have been used extensively in recent years for the development of chemosensors for ion or neutral molecule recognition and sensing based on supramolecular concepts (Martínez-Mañez & Sancenón, 2003). Unfortunately, although the utility of optical detection is becoming increasingly appreciated in terms of both qualitative and quantitative analysis, the number of optical sensors currently available for OP compound detection is quite limited. We review recent advances in (1) mass spectrometric techniques, and (2) enzymatic assays and chemosensors for detection of OP pesticides.

3. Determining OP pesticides using mass spectrometric techniques

Mass spectrometry (MS) techniques have been utilized for the detection and quantification of various OP pesticides due to their low detection limits in the part per billion (ppb) and part per trillion (ppt) range, as well as the selective detection of analytes in multi-residue samples. The mass spectrometry techniques are often coupled with separation methods like gas chromatography (GC) or liquid chromatography (LC), and other analyte introduction methods such as inductively coupled plasma (ICP), or fiber introduction (FI). The following sections describe extraction methods, sources of ionization, analyzers, and data acquisition modes generally chosen for GC-MS, LC-MS, and other MS configurations specifically for the detection of OP pesticides.

3.1 Gas chromatography

GC-MS has been a widely practiced OP detection method of choice over the last decade for various sample types; biological (Barr et al., 2002; Tsatsakis et al., 2008), environmental (Castro et al., 2001; Goncalves & Alpendurada, 2005; Hildebrandt et al., 2007; Kristenson et al., 2004; Miranda et al., 2008; Riederer et al., 2010; Sabik et al., 2003; Tahboub et al., 2005;

Toledano et al., 2010; Villaverde et al., 2008;), agricultural (Berrada et al., 2010; Kirchner et al., 2008; Kristenson et al., 2001; Mastovska et al., 2004), and food products (Fontana et al., 2010; Sasamoto et al., 2007; Schellin et al., 2004; Zheng et al., 2007). GC-MS offers sensitive and selective determination of OP analytes. Optimization of instrument limits of detection (LODs) and quantification (LOQs), and analysis time has been investigated by adapting various combinations of extraction methods, ionization sources, and analyzers for the determination of OP pesticides.

3.1.1 Extraction methods

Sample types vary for OP pesticide analysis from fruits and vegetable sources to biological specimen and environmental samples; thus extraction and clean-up methods used for sample pretreatment play an important role, and influence the results provided by the instrument technique. Solid phase extraction (SPE) is a frequently used technique for various sample matrix types, including aqueous samples (Aguilar et al., 1997; Baugros et al., 2008; El-Kabbany et al., 2000; Gupta et al., 2008), biological specimen (Adachi et al., 2008; Park et al., 2009; Raposo et al., 2010), and clean-up of solid samples (Diaz-Cruz & Barcelo, 2006; Shuling et al., 2007a). SPE is an efficient method for isolating and concentrating solutes from relatively large volumes of liquid. The technique can be very effective, even when the solutes are present at extremely dilute concentrations (e.g. ppb). Limits of the technique include extensive time and labor expense, and requirement of large quantities of high-quality solvents. As there is a trend to simplify and miniaturize sample preparation, and to minimize organic solvents used, solid phase microextraction (SPME) and matrix solid-phase dispersion (MSPD) reduce the effect of the aforementioned disadvantages. MSPD extraction is a microscale preparation technique used with solid sample matrices, such as soil (Shen et al., 2006) and fruit (Ramos et al., 2008) matrices that reduce the required amount of sample and solvent to efficiently extract analytes of interest. SPME is a sorptive extraction method in which analyte enrichment occurs through partitioning between the polymer and the aqueous phase according to the distribution constant. A silica fiber coated with a stationary phase is immersed in an aqueous sample, followed by injection and desorption by temperature in the GC injector. The quantity of analyte extracted by the fiber is proportional to its concentration in the sample as long as equilibrium is reached. The attraction of SPME for OP pesticide detection is that the extraction is fast and simple and can be done without solvents, and detection limits can reach parts per trillion (ppt) levels for certain compounds. SPME has been applied to aqueous samples (Bagheri et al., 2010; Berceiro-Gonzales et al., 2007; Garcia-Rodriguez et al., 2008; Menezes Filho et al., 2010; Natangelo et al., 1999), biological specimen (Beltran et al., 2001; Hernandez et al., 2002), food samples (Lambropoulou & Albanis, 2002; Zambonin et al.; 2004), textiles (Zhu et al., 2009), soil (Zambonin et al., 2002), and sewage samples (Basheer et al., 2006). Polydimethylsiloxane (PDMS) fibers are shown to have good extraction efficiency and are thus often used (Berceiro-Gonzales et al., 2007; Garcia-Rodriguez et al., 2008; Lambropoulou & Albanis, 2002). However, Natangelo *et al.* were able to use a small 10 mL sample aliquot for extraction by a divinylbenzene-based carbowax, followed by thermal desorption at 250°C for 15 min for a total extraction time of 70 min (Natangelo et al., 1999). Shorter extraction times have been reported as low as 30 min (Menezes Filho et al., 2010; Beltran et al., 2001; Zhu et al., 2009). Restricted application of SPME may be due to the coated material on the fiber, as well as expense and fragility of the fibers during the extraction process. Alternatively, Basheer *et al.* packed multi-walled carbon nanotubes (MWCNT) inside a sheet

of porous polypropylene membrane for supported micro-solid-phase extraction (μ -SPE) (Basheer et al., 2006). Adsorption of the analytes occurred through π - π electrostatic interactions between the analytes and the large surface area of the MWCNT, yielding good repeatability of the extractions (RSD 2-8%) and low LODs (1-7 pg/g).

Stir bar sorption extraction (SBSE) is another popular extraction technique that is based on equilibrium sorption opposed to adsorption. Extraction by this method is performed by adding a suitable sample amount to an extraction vessel, then adding a polydimethylsiloxane (PDMS) coated magnetic stir bar, and stirring for a period of time, followed by relocation of the stir bar to a glass desorption tube in a thermal desorption unit (Benanou et al., 2011). Application of this extraction technique has been mainly applied to aqueous samples (Leon et al., 2003; Leon et al., 2006; Ochiai et al., 2006; Ochiai et al., 2008; Perez-Carrera et al., 2007; Serodio & Nogueira, 2004), a few specific liquid food types (Lavagnini et al., 2011; Zuin et al., 2006), and even a solid food sample that required extraction of 85 pesticides in vegetable, fruit, followed by green tea by an alcohol and dilution with water (Ochiai et al., 2005). For the sorptive enrichment techniques, SPME and SBSE, extraction is significantly influenced by aqueous volume, extraction and desorption time, desorption solvent and ionic strength. For instance, addition of a NaCl solution aids to target solutes with low partition coefficients and improves sensitivity (Leon et al., 2003; Ochiai et al., 2008). Alternatively, addition of methanol favors the extraction of apolar compounds, thus making the analytes more available for partitioning (Lavagnini et al., 2011; Ochiai et al., 2005).

As an alternative to SPE methods, liquid-phase microextraction (LPME) is cheap, rapid, and easily automated, in which only microliters of solvents are required to concentrate analytes from aqueous samples. LPME involves the distribution of a solute between two immiscible liquid phases. Therefore, the extraction solvent must be stable during extraction time, its polarity should be compatible with that of the fiber, and it should be water immiscible. Longer exposure time results in higher extraction efficiency. Furthermore, other parameters such as rate of agitation can enhance extraction efficiency, and the addition of salt can increase extraction yields for compounds with low octane-water partition coefficients. Examples utilizing LPME include the determination of ethoprop, diazinon, disulfoton and fenthion from lake water samples (P. Chen & Huang, 2006), and other OP pesticides from wastewater (Basheer et al., 2007). The optimal LPME parameters adopted by Chen et al. were as follows: 20 mL aqueous sample, 15% w/v NaCl, cyclohexane extraction solvent, 50 min extraction time, a stirring rate of 700 rpm, and a polypropylene hollow fiber was incorporated (P. Chen & Huang, 2006). Polypropylene is highly compatible with a broad range of organic solvents, and it strongly immobilizes the solvents, thus preventing leakage of the organic phase during extraction. Another miniature liquid-phase extraction technique recently investigated for OP pesticide detection in natural water samples is single-drop microextraction (SDME) (H. Chen et al., 2009). 1.5 μ L of toluene was exposed via the tip of a microsyringe directly immersed in a 5 mL aqueous sample, followed by stirring at 800 rpm at a pH of 5, for extraction of OP analytes before transferring the single drop to a GC-MS detection system. Inter- and intra-day RSD values were below 5.4 and 6.1%, respectively.

Supercritical fluid extraction (SFE) is an alternative to the solvent-intensive isolation procedures, like SPE or LLE, especially for environmental samples (Goncalves et al., 2006; S. R. Rissato, M. S. Galhiane, B. M. Apon, et al., 2005) and complex food matrices (Norman & Panton, 2001; Rissato et al., 2004; S. R. Rissato, M. S. Galhiane, A.G. de Souza, et al., 2005). Advantages of SFE that have been discussed in the literature include: rapidity, simplicity,

great analyte selectivity, good extraction efficiency, no need of a clean-up step, suitability for thermally labile compounds, automation, solventless or near solvent free character and reduced environmental hazard (Goncalves et al., 2006; Norman & Panton, 2001; Rissato et al., 2004; S. R. Rissato, M. S. Galhiane, B. M. Apon, et al., 2005; S. R. Rissato, M. S. Galhiane, A. G. de Souza, et al., 2005). The greatest advantage of supercritical fluids, however, is the fact that they have densities and solvating powers comparable to the density of liquids, which can be continuously varied by one order of magnitude by varying the temperature and pressure of the extraction vessel. CO₂ is frequently used as a supercritical fluid due to its suitable critical temperature (31.2 °C) and pressure (72.8 atm), since it can be easily removed by reducing its pressure (S. R. Rissato, M. S. Galhiane, B. M. Apon, et al., 2005; Norman & Panton, 2001; Rissato et al., 2004; S. R. Rissato, M. S. Galhiane, A. G. de Souza, et al., 2005). Analysis of a honey and soil sample prepared by SFE required 400 bar CO₂ pressure and a CO₂ modifier, acetonitrile and methanol, respectively (S. R. Rissato, M. S. Galhiane, B. M. Apon, et al., 2005; Rissato et al., 2004).

Recently, Morgan's group at the University of South Carolina adapted disposable pipette extraction (DPX), a dispersive SPE method that uses loosely contained sorbent that is mixed with sample solutions in a pipette tip, for the extraction of OP pesticides from high fat content food (H. Guan et al., 2009), as well as fruit and vegetable samples (H. Guan et al., 2010). The method involved dynamic mixing of DPX sorbent with solutions that provide rapid equilibration, partitioning, and enhanced contact between analytes and solid-phase sorbent for more rapid performance and sensitivity (H. Guan et al., 2009). Guan et al. studied the effectiveness of weak anion exchange mechanisms to remove fatty acid matrix interferences from cocoa beans (50% fat) prior to multiresidue pesticide analysis (H. Guan et al., 2009). Average recoveries reached 100% for most targeted pesticides studied, with relative standard deviations below 10%.

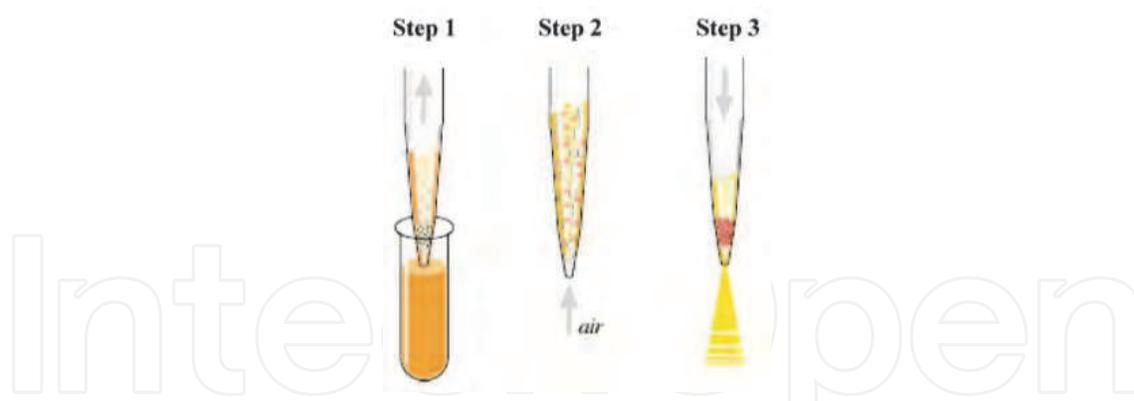


Fig. 3. Schematic representation of DPX cleanup extraction method. After blending and filtering, the sample solution is aspirated into the DPX tip (step 1), and then air bubbles are created by aspirating air into the tip causing mixing (step 2); the solution is then dispensed to a GC vial after a short exposure time (step 3). (Taken with permission from Reference H. Guan et al., 2009)

Microwave-assisted extraction (MAE), a rapid heating process that yields an accelerated kinetic dissolution of the matrix when a microwave field is applied to the sample, has been explored through, hydrological samples (Gfrerer et al., 2003), working air quality samples (Esteve-Turrillas et al., 2008), and olive oil (Fuentes, E.; Báez, M. E. & Quiñones, A., 2008). Scientists at the University of Chile incorporated atmospheric pressure microwave-assisted

liquid-liquid extraction (APMAE) for the determination of OP pesticides in olive and avocado oil and where LOQs ranged from 0.004 to 0.015 $\mu\text{g/g}$ (Fuentes, E.; Báez, M. E. & Diaz, J., 2009). The APMAE glass system employed for this extraction consisted of an Erlenmeyer flask, with 5 g of oil in 5 mL diluted *n*-hexane, attached to an air-cooled condenser where 15 mL of acetonitrile was added. The system was put into a microwave oven and heated for 13 min at 150 W. After cooling, the upper layer of the solution was transferred to a test tube before GC-MS/MS analysis. Power, time of extraction, volume of extracting solvent, and the step of dilution of oil with *n*-hexanes were assessed to optimize the extraction efficiency of the aforementioned extraction set-up.

3.1.2 Ionization sources

There are various pathways to provide the ionization energy required to generate the fragment and /or molecular ion for an OP analyte of interest during GC-MS detection, namely electron impact (EI), chemical ionization (CI), and atmospheric pressure chemical ionization (APCI). Electron impact is a widely used hard impact ionization source implemented in MS detection of OP compounds. It is robust and generates standard mass spectra that can be compared with those in established MS libraries. EI-MS detection is also rapid, sensitive, and accurate, minimizing the possibility of releasing false positive and false negative results (Araoud et al., 2007; Albero et al., 2003; Aybar-Munoz et al., 2003; Aybar-Munoz et al., 2005; Elfein et al., 2003; Frenich et al., 2007; Haib et al., 2003; Ling et al., 2006; Tarbah et al., 2001;). To accurately determine toxic OP pesticide exposure, for malathion in pregnant women in the Philippines, researchers employed electron impact (EI) ionization (+70 eV), which led to OP pesticide detection limits of low ppm in umbilical cord blood (Corrion et al., 2005) and hair samples (Posecion et al., 2006).

Mass spectrometry techniques have successfully been applied to determine OP pesticides in food samples. To greatly optimize the sensitivity and selectivity of the EI-MS system, selective ion monitoring (SIM) mode was utilized to monitor 3 particular ion analytes of interest in various OP pesticides containing samples, including textiles (Zhou et al., 2007), biological samples (Lacassie et al., 2001), environmental samples (Berger-Preiss & Elflein, 2006; Patsias & Papadopoulou-Mourkidou, 1996; Stiles et al., 2008; Wang et al., 2007), agricultural (Aguera et al., 2002a; Nguyen et al., 2008; Stajnbaher & Zupancic-Kralj, 2003; Wong et al., 2007), and different food matrices (Albero, B.; Sanchez-Brunete, C. & Tadeo, J. L., 2004; Wong et al., 2004). For example, Rissato *et al.* showed that GC-EI-MS detection in the SIM mode was used to detect high concentrations of malathion residues in original honey samples inundated by mosquito control methods during a three year time period prior to the year of study (Rissato et al., 2007).

Low probability of obtaining molecular ion (M^+) in EI spectra, due to extensive fragmentation, is a drawback of EI screening reliability (Portoles et al., 2010). Soft ionization techniques such as chemical ionization (CI) would overcome this issue. CI results in a significant increase in selectivity, while allowing the simultaneous confirmation and quantification of trace levels, e.g. ppb, of pesticides in complex matrices (Hernando et al., 2001; R. Húšková, E. Matisová, L. Švorc, et al., 2009; Jover & Bayona, 2002; Kolberg et al., 2010; Li et al., 2010; Russo et al., 2002;). Due to OP pesticides having electronegative elements and being capable of producing a negative ion, chemical ionization is mostly utilized under negative ion (NI) mode. Negative chemical ionization (NCI) offers several advantages of EI including limited fragmentation, simple mass spectra with reduced interferences from ions derived from the sample matrix, better signal-to-noise ratio, and

higher sensitivity and selectivity at ultratrace concentrations (ppt) (R. Húšková, E. Matisová, S. Hrouzková, et al. 2009). Húšková *et al.*, confirmed the advantages of GC-NCI-MS through the determination of dimethoate, chlorpyrifos-methyl, malathion, and diazinon in non-fatty food matrices, fruits and vegetables (R. Húšková, E. Matisová, S. Hrouzková, et al. 2009). The instrument's LODs and LOQs were up to 3 orders of magnitude lower for NCI compared to EI ionization, with analyte levels in the ppt range.

Portoles *et al.* applied atmospheric pressure chemical ionization (APCI) to GC quadrupole time-of-flight (QTOF) MS, operating in NI mode, and found that using water as a modifier, and investigating the highly abundant MH^+ ions yielded optimum parameters to perform wide-scope screening of OP pesticides in agricultural products (Portoles et al., 2010). They suggested that the corona discharge needle, using N_2 as an auxiliary gas, generates $N_2^{+\bullet}$ and $N_4^{+\bullet}$ ions that react with water or any proton source to indirectly transfer protons to the analyte of interest as shown in Figure 4.

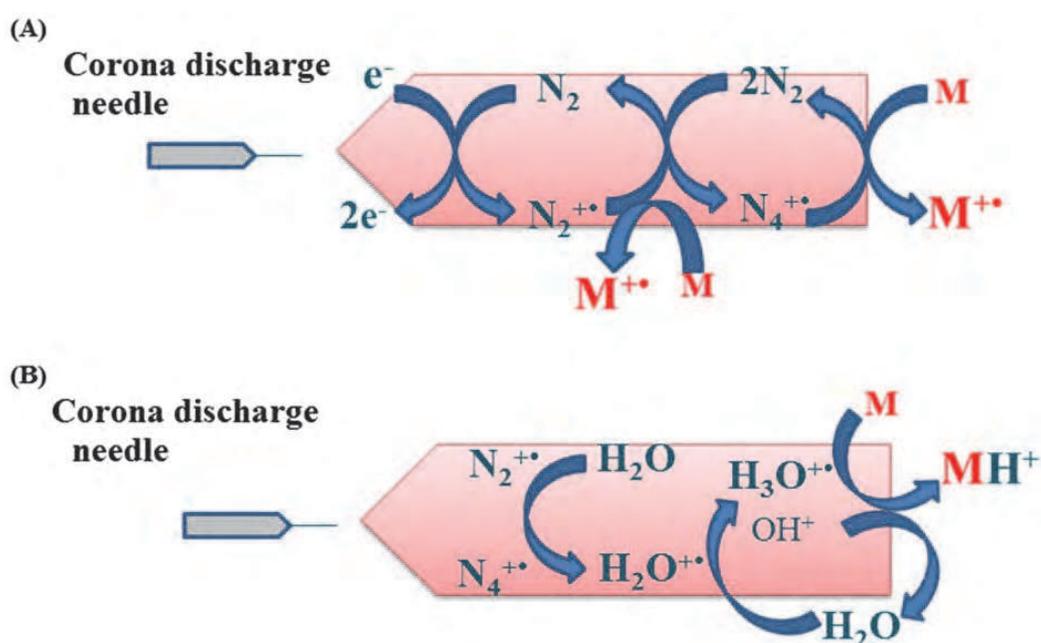


Fig. 4. Molecule reactions when using APCI source: (A) N_2 transfer conditions; (B) proton transfer conditions. (Modified and Taken with permission from reference Portoles et al., 2010).

Amendola *et al.* aimed to optimize the ionization conditions for detecting 19 OP pesticides by investigating effects of source temperature, influence of electron energy, emission intensity, and gas pressure of the ionizing gases isobutane, methane, ammonia in methane, and pure ammonia (Amendola et al., 2002). They found that the different ionizing gases generate significant differences in the mass spectra of several of pesticides investigated. Additionally, it was determined that the use of pure ammonia reduces the background noise thereby improving the overall sensitivity of the method to reach low LODs ($< 1 \mu\text{g/L}$).

In determining OP pesticide content of various matrices, both hard (e.g. EI) and soft (e.g. CI) ionization methods have been primarily used to generate analyte ions of interest. EI is a robust source, which produces standardized mass spectra that can be compared with those from commercially available MS libraries. However extensive fragmentation is a drawback for some applications when multiresidue screening is necessary. Alternatively, CI overcomes these limitations and provides better sensitivity and selectivity. Furthermore a

combination of EI and CI in GC tandem mass spectrometry has also proven useful in agricultural samples (Aguera et al., 2002b; Sanchez et al., 2006).

3.1.3 Mass analyzers

The impact of analyte ionization is realized through the choice of analyzer available. Ion trap (IT) and triple quadrupole (QqQ) detectors have been coupled with gas chromatography for the determination of OP pesticides in assorted sample matrices. Ion trap (IT) mass spectrometry is a low cost and easy to operate analyzer, which is based on a selected parent ion and whole mass spectrum of the daughter ions that result in high sensitivity and selectivity of target analytes (Boy-Bolan et al., 1996; Ma et al., 2001; Na et al., 2006; Shuling et al., 2007b; Tao et al., 2009). While there is the possibility of obtaining higher order MS spectra from the large amounts of fragments generated in IT-MS, there is also a limit to low scan speeds that result in longer analysis time (Frenich et al., 2008). Frenich et al. demonstrated the robustness of IT-MS in comparison to QqQ-MS through intra-day and inter-day precision; it was found that the RSD values obtained by IT-MS were two times lower than the RSD values obtained by QqQ as shown in Figure 5. In addition to the low scan speeds, IT analysis suffers from sample matrix limitations, where for example, high fat content matrices result in low signal to noise ratios and require additional sample clean-up stages (Frenich et al., 2008).

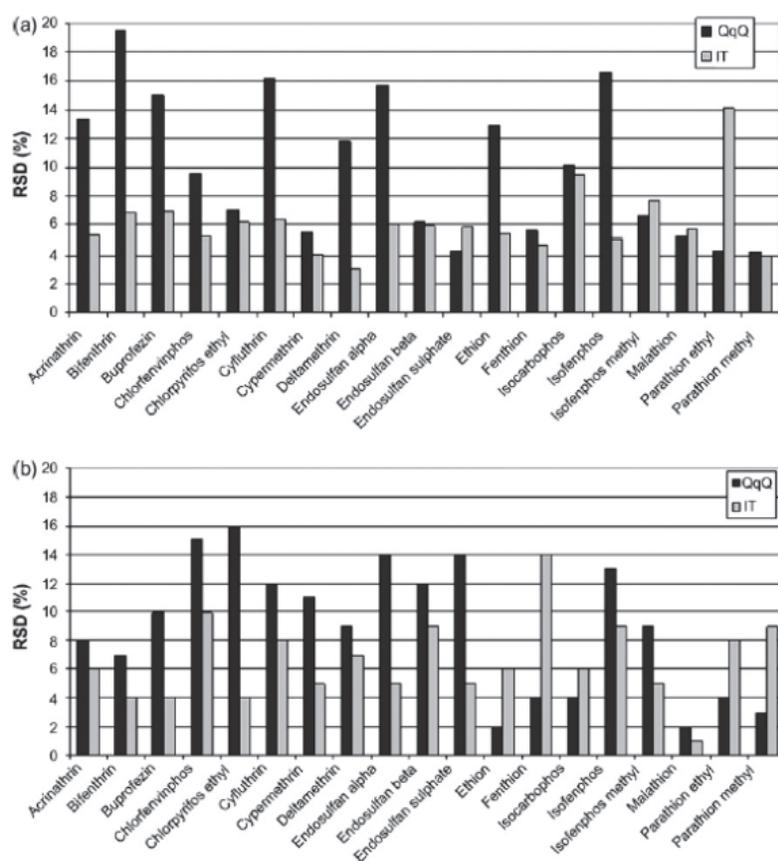


Fig. 5. Inter-day (a) and intra-day (b) precision values, expressed as relative standard deviation (RSD), obtained with the QqQ and the IT analyzer for solvent standards at 50 µg/L. (Taken with permission from Reference Frenich et al., 2008).

Tandem mass spectrometry (MS/MS) incorporates two or more analyzer stages to better resolve and select analytes of interest. The first stage selects the precursor ion after ionization, and in the latter stage fragment ions obtained from collision-induced dissociation (CID) of the precursor ion with an inert gas (e.g. helium or argon) are analyzed. MS/MS methods can be carried out in either tandem-in-time, performance of a sequence of events recorded in an ion storage device; or tandem-in-space, where two different instruments are coupled together for the analysis. Low ppb LODs in aqueous (Esteve-Turrillas et al., 2007; Rubio et al., 2006), fruit and vegetable samples (Gonzalez-Cubelo et al., 2011; Martinez Salvador et al., 2006; Moreno et al., 2006; Rawn et al., 2006; Schachterle & Feigel, 1996; Wong et al., 2010), and food products (Guardia-Rubio et al., 2006; Mezcua et al., 2007; S. N. Sinha, V. K. Bhatnagar, et al., 2011; Yague et al., 2005) were established by GC-MS/MS; still LODs in ppt have also been established utilizing this method (Garcia-Rodriguez et al., 2010; Goncalves & Alpendurada, 2004). Triple quadrupole (QqQ) analyzers represent 3-stage tandem-in-space detectors that are commonly used in pesticide residue analysis. The system offers the advantages of high scan speed that allows for simultaneous determination of roughly 25-30 target compounds at a time, thereby reducing analysis time and enhancing selectivity such that false positive results are minimized. (A. Garrido Frenich, J.L. Martínez Vidal et al., 2006; A. Garrido-Frenich, R. Romero-González, et al., 2006; Pitarch et al., 2007; P. Plaza Bolaños, J. L. Fernández Moreno, et al., 2007; P. Plaza Bolaños, A. Garrido Frenich, et al., 2007; Qu et al., 2010). Qu *et al.* incorporated QqQ-MS to examine leeks, representing complex matrices of pigments and sulfur, for OP pesticide contamination (Qu et al., 2010). Time-of-flight (TOF) mass spectrometry detects OP pesticides by way of recording the ion m/z ratio as a result of the time it takes the particles to reach a microchannel plate detector. TOF-MS can have higher spectral acquisition rates with accurate mass information, yet suffer limited dynamic ranges as compared to quadrupole instruments (Hayward & Wong, 2009). Nevertheless, more recently TOF-MS instruments have been employed for the determination of OP pesticides in agriculture (Banerjee et al., 2008; Cochran, 2008; Hayward & Wong, 2009), food (Patil et al., 2009), and surface waters (Matamoros et al., 2010).

3.1.4 Data acquisition modes

Data acquisition modes are another important process for the GC-MS detection system and can enhance detection sensitivity and selectivity. For an extensive range of ion spectra, MS systems typically run in full scan mode. However, that could be time consuming, especially for routine analysis of various commodities and environmental samples. Data acquisition modes that limit particular analyte m/z ratios that are transmitted and/or detected by the instrument include selective ion monitoring (SIM), selective ion storage (SIS), and selective reaction monitoring (SRM). SIM significantly increases sensitivity of OP pesticides detection examined in a range of agricultural (Albero, B.; Sanchez-Brunete, C.; Donoso, A. et al., 2004; Gelsomino et al., 1997; Lambropoulou & Albanis, 2003; W. Zhang et al., 2006), food products (Jeong et al., 2008; Jiang et al., 2009; Mastovska et al., 2001; Wong et al., 2006), biological (S. Liu & Pleil, 2002; Simonelli et al., 2007), and environmental (S. Liu & Pleil, 2002) matrices (Berhanu et al., 2008; Lambropoulou et al., 2004). EI generates large quantities of ion fragments, thus SIM is often operated during the analysis of specific analytes in attempts to increase the sensitivity and selectivity of OP pesticide detection (Albero et al., 2004; Berger-Preiss & Elflein, 2006; Nguyen et al., 2008; Rissato et al., 2007; Stajnbaher & Zupancic-Kralj, 2003; Wong et al., 2004; Wong et al., 2007; Zhou et al., 2007). SIM has also led to ppb LODs in other GC-MS instrument configurations (Hayward & Wong, 2009; Russo et al., 2002).

Through special control of an ion trap during its ionization phase, only preselected ions of analytical interest may be stored in selective ion storage mode (SIS) for detection even during the co-elution of multi components, or complex matrices (Ma et al., 2001; Shuling et al., 2007b). Shuling *et al.* were able to determine 100 pesticides (ppm) in vegetables within 35 min upon employing GC-IT-MS in the SIS mode (Shuling et al., 2007b). Selected reaction monitoring is a highly specific analysis method that when performed with tandem MS, permits simultaneous measurement of a high number of MS/MS transitions, thus providing chromatographic peaks with an adequate number of scans (Frenich et al., 2008; Pitarch et al., 2007; P. Plaza Bolaños, A. Garrido Frenich, et al., 2007; Qu et al., 2010). In this type of experiment a specific fragment ion of a particular parent ion is detected, thus reducing the SRM chromatogram to represent only ions of interest. Frenich *et al.* noted that sensitivity in SRM depends on the efficiency of the isolation of the precursor ions, the CID fragmentation yield and the specificity of the selected transitions when choosing the ionization source and analyzer combination (Frenich et al., 2008).

3.2 Liquid chromatography

Often times, pesticide analysis via GC-MS experimental conditions may not be most effective. An alternative method is the application of liquid chromatography mass spectrometry (LC-MS), a rapid and efficient alternative (Alder et al., 2006; Sharma et al., 2010). LC-MS is gaining popularity with the advancing of soft ionization techniques that generate molecular ions that can be more easily monitored (John et al., 2008). For more detailed information, we refer the readers to the references (John et al., 2008) and on the specific application of LC-MS for OP determination for food safety (Pico et al., 2006) and biological exposure monitoring (Hernandez et al., 2005).

3.2.1 Extraction methods

The range of OP pesticide polarities precludes the establishment of a universal procedure for efficient sample preparation. Compounding that issue is the complexity of sample matrices, for example, biological specimen contain lipids, proteins, and salts; or food samples, which include sugars, amino acids, and pigments. Several extraction techniques have been studied for spectral optimization. Precipitation extraction is a simple and frequently used method for clinical specimen with rapid performance with a low cost (Inoue et al., 2007). Inoue *et al.* deproteinated serum samples by acetonitrile precipitation to analyze 10 OP pesticides (Inoue et al., 2007). The supernatant was directly injected for LC-APCI-MS measurements, yielding recoveries over 60%. Ultrasonic solvent extraction (USE) is another low cost and effective preparation method for multi-residue OP pesticides at ppb levels (Garcia-Valcarcel & Tadeo, 2009; Pan et al., 2008). USE provides efficient contact between sample matrix and solvent by increasing analyte-extractant interface contact, with acoustic cavitation, mechanical function and thermal function having direct effects on the extraction efficiency. The procedure proposed by Pan *et al.* allowed extraction of 6 pesticides in a single step with a small volume of ethyl acetate for a short 35 min sonication time (Pan et al., 2008). This optimized extraction method provided analyte recovery rates over 83% and low ppb LOQs. Determining trace levels of pesticides in fruits by pressurized liquid extraction (PLE) offers low solvent use and short extraction times, with recoveries ranging from 58% to 97% (Blasco et al., 2005). Prior to analysis by a combined IT/QqQ LC-MS, samples were extracted at 75 °C and 1500 psi, using ethyl acetate as the extraction solvent and acidic alumina as they drying agent (Blasco et al., 2005). Another liquid extraction method used

ethyl acetate to extract 57 multi-residues in one single determination step at 0.01 mg/kg (Jansson et al., 2004).

SPE is a widely used technique for sample preparation, mainly due to optimization of extraction efficiency by appropriate choice of SPE sorbent material (John et al., 2008). On-line SPE-LC mass spectrometers fitted with turbulent-flow columns allowed complete OP extraction from surface and drinking water with good recoveries in less than 14 min (Asperger et al., 2002; Koal et al., 2003). OP pesticides extracted from fruits and vegetable samples with acetonitrile and dispersive SPE, with primary or secondary amines as the sorbent, rendered simultaneous determination, with recoveries in the range of 70-100% and RSD values less than 8% (M. Liu et al., 2005). Blasco *et al.* applied SPME and SBSE extraction methods to determine OP contamination in honey samples (Blasco et al., 2004; Blasco et al., 2008.). They optimized parameters affecting the sorption process, such as sample volume (25 mL), sorption and desorption times (120 min total extraction time), ionic strength (30% w/w NaCl), elution solvent (methanol), and dilution, and found that SBSE exhibited higher concentration capability, and accuracy (5-20 times) and sensitivity (10-50 times) greater than that of SPME (Blasco et al., 2004). It has been demonstrated that both self-contained working separation steps, and on-line multistep separation techniques prove viable in OP pesticide determination in various matrices. If further recommendation is needed, Niessen *et al.* provide a review on matrix effects in quantitative pesticide analysis using LC-MS (Niessen et al., 2006). Here, we have highlighted selective and efficient extraction techniques.

3.2.2 Ionization sources

Efficient ionization of OP analytes is necessary for reliable and sensitive measurement. Hard ionization impact, e.g. EI, generate a full range of fragment ions that offer detailed information. On the other hand, soft ionization impact, e.g. APCI and ESI, produce molecular ions that can be more easily monitored for specific analytes. Here we discuss the ionization sources used to detect trace levels of OP toxicants.

Thermospray ionization is generally carried out by filament activation, whereby emission of the electron beam from the heated filament supports ionization of the vaporized mobile phase and analytes. Analysis takes place in either positive (PI) or in negative (NI) ionization mode (Barcelo et al., 1993; Lacorte & Barcelo, 1995). Upon monitoring two main ions, for example, $[M+H]^+$ and $[M + NH_4]^+$ for PI detection mode, and $[M-H]^-$ and $[M+HCOO]^-$ for NI detection mode, it is possible to obtain LODs in the ppb range (Barcelo et al., 1993; Lacorte & Barcelo, 1995). LC-MS instruments with APCI have been widely utilized for trace detection of OP levels in a range of samples from the environment (Ingelse et al., 2001; Schreiber et al., 2000; Slobodnik et al., 1996) to agriculture (Mol et al., 2003; Titato et al., 2007) and biological specimen (Inoue et al., 2009), due to APCI's lack of signal suppression from matrix components. Ingelse *et al.* demonstrated APCI usefulness for detecting very polar OP pesticides in water (Ingelse et al., 2001). APCI-MS was performed in PI mode, with the nebulizer heated to 400°C and 50 psi held for curtain, nebulizer, and auxiliary gases. They found that solvent mixtures of methanol/water (50/50 v/v) improved analyte response by a factor of 2, and the addition of 0.1% acetic acid also improved the signal-to-noise ratio for the polar compounds. Fernández and collaborators used APCI LC-MS to detect trace levels of OP pesticides in honeybees as a means to assess pesticide exposure in agricultural fields (Blasco et al., 2003; Fernández et al., 2001a, 2002b, 2003c; Ghini et al., 2004). Optimized to achieve better sensitivity and specificity for a range of OP pesticides,

APCI parameters were established as having a 350°C vaporizing temperature with nitrogen as the nebulization gas and drying gas, and a corona current of 4 μA and 25 μA for PI and NI mode, respectively (Blasco et al., 2003; Fernandez et al., 2001; Fernandez et al., 2002; Fernandez et al., 2003; Ghini et al., 2004).

Electrospray ionization (ESI) is another commonly incorporated ionization technique in LC-MS that is used for rapid and sensitive OP detection. For optimal OP detection in clinical samples, for example, urine and serum, ESI has been integrated in LC tandem mass spectrometry (Araoud et al., 2010; John et al., 2010; Olsson et al., 2003). The LC-ESI-MS/MS detection system exploited by John *et al.* proved robust and highly selective for simultaneous quantification of pesticides in porcine urine and plasma, with established intra- and inter-day RSD precision values between 1-14% and accuracy values ranging between 90-115% (John et al., 2010). Kmellar *et al.* used an acetonitrile-based QuEChERS preparation method and ESI in PI mode for high water, high sugar, and high acidic content produce commodities (Kmellar et al., 2008). Mixed soft, medium, and strong matrix effects were observed for the compounds studied, yet more than 90% of the investigated compounds had LODs in the ppb range, thus supporting ESI robustness. ESI has also demonstrated efficacy for polar OP pesticide detection in aqueous samples (Kuster et al., 2008; Molina et al., 1994). While not utilized as often as the aforementioned soft impact ionization techniques, direct-EI provided sensitive detection of OP pesticides commonly distributed in local sugar beet cultivation water. The direct-EI interface mechanism is based on the formation of aerosols in high vacuum conditions followed by a quick droplet desolvation and final vaporization of the solute prior to ionization (Cappiello et al., 1996). Azinphos-methyl, parathion-methyl, azinphos-ethyl, and parathion-ethyl were detected at a concentration level of ~ 3 ng/L in real sugar beet water cultivation samples.

compound	positive mode			negative mode		
	SIM ion (<i>m/z</i>)	LOD ($\mu\text{g kg}^{-1}$)	LOQ ($\mu\text{g kg}^{-1}$)	SIM ion (<i>m/z</i>)	LOD ($\mu\text{g kg}^{-1}$)	LOQ ($\mu\text{g kg}^{-1}$)
azinphos-ethyl	346	10	32	185	8	25
bromophos		nd	nd	349	5	15
chlorpyrifos-methyl	322	10	32	302	7	21
coumaphos	363	6	18	361	4	12
diazinon	305	2	6	275	17	51
dimethoate	230	4	12	214	5	15
fonofos	247	2	6	153	15	45
heptenophos	251	4	12	235	30	90
malathion	285	6	18	157	13	42
methidathion	145	90	200	287	8	24
paraoxon	248	25	75	232	8	25
parathion-ethyl		nd	nd	262	2	7
parathion-methyl		nd	nd	138	1	4
phenthoate	321	60	180	319	8	24
phosalone	368	12	36	338	4	13
phosmet	160	15	45	157	20	60
pirimiphos-ethyl	334	1	4	304	5	15
pirimiphos-methyl	306	2	7	290	7	21
pyrazophos	374	3	9	372	1	3
quinalphos	299	4	12	169	10	30
triazophos	314	5	15		nd	nd
vamidothion	288	4	12	272	5	17

Table 2. Limits of detection (LOD) and quantification (LOQ) in both ionization modes of APCI and the ion used for quantification in LC-MS to assess OP levels in honeybees. (Taken with permission from Reference Fernandez et al., 2001)

3.2.3 Mass analyzers

Optimized accuracy for measurement of analyte mass results in more reliable and precise data. Tandem mass detectors enhance the selectivity and sensitivity of analytes studied in

complex matrices, especially when coupled to various column chromatography separation techniques; liquid-liquid (Sancho et al., 2000), hydrophilic interaction liquid chromatography (Hayama et al., 2008), high pressure liquid chromatography (Salm et al., 2009), and ultra performance liquid chromatography (G. Chen et al., 2011). G. Chen *et al.* developed optimum tandem analyzer parameters, including ion transition, collision energy, and cone voltage for analysis of OP pesticides in multi-residues of tea matrices, which also contain pigments, organic acids, and caffeine interferents (G. Chen et al., 2011). LOQs were measured at 0.01 mg/kg across all pesticides, and reproducibility for OP pesticides analyzed was less than 29% RSD. More recently, triple quadrupole tandem mass spectrometry (QqQ), operating with ESI, has been exploited as a highly accurate and precise method to analyze OP constituents of environmental (Barco-Bonilla et al., 2010; Rodrigues et al., 2007) and food samples (Chung & Chan, 2010; S. Guan et al., 2011). S. Guan *et al.* optimized performance and sensitivity of the QqQ-MS/MS by using high-purity nitrogen as the collision gas, and operating quadrupoles Q1 and Q3 at unit resolution to produce the highest intensity for the main fragment (S. Guan et al., 2011). A good linear relationship between response and concentration over a selected range was established, with LODs as low as 0.06-0.15 µg/kg and LOQs of 0.2-0.5 µg/kg for 9 OP pesticides.

Other tandem MS/MS hybrid systems, namely between ion trap and quadrupole analyzers, are also utilized for trace level pesticide detection in food (C. Ferrer et al., 2005), human blood (Salm et al., 2009), and drinking water (S. N. Sinha, K. Vasudev, et al., 2011). Salm *et al.* established compound dependent parameters of the HPLC-IT/Q-MS/MS that led to reduced sample preparation and low LODs (Salm et al., 2009). Parameters were set for dwell times between 50-100 ms, declustering potentials between 20-50 V, and collision energies between 30-35 eV, depending on the type of OP pesticide. Excellent chromatographic separation using time-of-flight LC-MS was provided in a 30 min interval by using narrow accurate mass windows (0.05 Da) in the determination of food and water OP pesticide contaminants (I. Ferrer & Thurman, 2007).

3.2.4 Data acquisition modes

Applying an appropriate MS scan mode helps to optimize selectivity and limits of detection. When matrices are less complex, full-scan or simple SIM mode are sufficient. However, there are other data acquisition modes that may be more appropriate to use, as is the case with tandem MS. Multiple reaction monitoring (MRM) is a highly specific monitoring mode that improves signal-to-noise ratios and maximizes sensitivity as a result of only data on the analyte of interest is collected. This in turn allows for faster flow rates into the ion source and quicker analysis. Typically two MRM transitions (parent ion → daughter ion) and the corresponding MS conditions are chosen for each pesticide under analysis, as demonstrated for 9 OP pesticides determined in fruit and vegetable samples by LC-ESI-QqQ-MS/MS as shown in Table 3 (S. Guan et al., 2011). MRM is frequently exploited for APCI (Ingelse et al., 2001; Mol et al., 2003) and ESI (Araoud et al., 2010; Chung & Chan, 2010; S. Guan et al., 2011; John et al., 2010) ionization techniques as more abundant molecular parent ions are generated. Additionally, other selective data acquisition modes have been used alongside APCI and ESI, including selected ion-recording (SIR) (Titato et al., 2007) and selected reaction monitoring (SRS) (Hayama et al., 2008; Raina & Sun, 2008).

3.3 Other types of MS

While coupled GC and LC mass spectrometry systems are the primary choice for OP determination, other mass spectrometry methods have also been investigated. For instance,

Retention time (min)	Analyte	Parent ion	Daughter ion (p1/p2)	Fragmentor potential (V)	Collision energy (V)
1.24	Methamidophos	142.0	94.0 125.1	80 80	15 10
2.98	Monocrotophos	224.0	127.1 192.6	100 100	20 5
3.35	Mevinphos	225.2	193.3 127.1	80 80	10 15
4.97	Methidathion	303.2	85.0 145.1	80 80	10 5
5.44	Parathion-methyl	264.2	232.1 125.2	120 120	15 20
5.95	Malathion	331.3	127.1 285.2	80 80	10 5
6.95	Parathion-ethyl	292.2	236.0 264.0	120 120	10 5
7.51	Diazinon	305.2	169.0 153.2	160 160	20 20
8.50	Ethion	385.0	171.2 199.0	80 80	15 5

Table 3. Parent/ daughter ions and conditions used for MRM mode of LC-ESI-QqQ-MS/MS analysis. (Taken with permission from Reference S. Guan et al., 2011).

fiber introduction mass spectrometry (FIMS) is a relatively new technique which directly couples SPME and MS without chromatographic separation. In this technique, the SPME fiber containing the sorbed analytes is directly introduced into the ionization chamber of a mass spectrometer and placed between two EI filaments, which cause desorption of the extracted species directly in the region of maximum ionization power (Cesar da Silva et al., 2007). Cesar da Silva *et al.* have shown FIMS to be an effective alternative to determine OP pesticides, offering simplicity, speed, selectivity, and robustness with low LOD and LOQ values. Fiber coating was important as the PDMS/PVA composite coated fiber has been shown to provide fast detection and better signal resolution than PDMS/DVB coating.

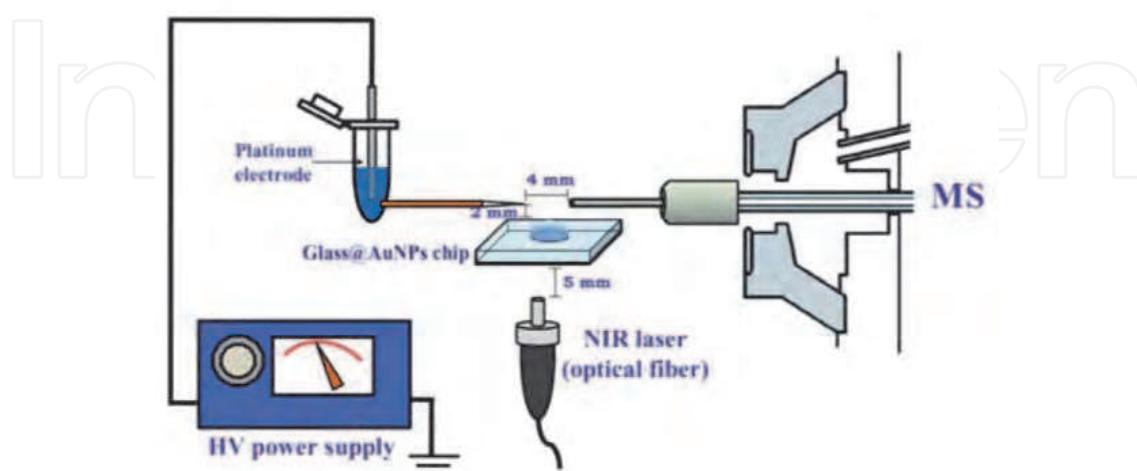


Fig. 6. Representation of the TDAMS system used to detect small OP analytes. (Taken with permission from Reference (Lin et al., 2010))

Lin *et al.* studied multilayered gold nanoparticles (Au NPs) as an NIR energy absorber and sample holder for sample deposition at ambient conditions during a thermal desorption-based ambient mass spectrometry (TDAMS) analysis of small OP compounds, e.g. methamidophos (Lin *et al.*, 2010). A NIR laser diode (808 nm) was employed as the thermal desorption source to liberate molecules from the self-assembled Au NP layers prior to ESI and IT analysis. Because the analysis was carried out under ambient conditions, direct analysis at atmospheric pressure with minimal sample preparation offered advantages of speed and easy use. Figure 6 represents the setup of the TDAMS system (Lin *et al.*, 2010). While this MS detection system offers speed and simplicity, it is only suitable for small organics, and one must be mindful to the configuration of the laser focusing beam which is critical.

Inductively coupled plasma mass spectrometry (ICP-MS), coupled to capillary electrophoresis (CE) (Wuilloud *et al.*, 2005; Yang *et al.*, 2009) or GC (Fidalgo-Used *et al.*, 2005a, 2006b; Profrock *et al.*, 2004; Vonderheide *et al.*, 2003), is another approach used for OP analysis. For OP detection, ICP-MS monitors ^{31}P levels as a means to identify OP analytes in a given matrix. Argon sustained plasma ICP-MS methods suffer from low ionization efficiency and interference from polyatomic ions $^{14}\text{N}^{16}\text{O}^+\text{H}^+$ and $^{15}\text{N}^{16}\text{O}^+$, which overlap phosphorus's only isotope peak at $m/z = 31$; thus different experimental conditions have been exploited as a means to overcome these limitations. The addition of small percentages of nitrogen in the carrier flow has proven to enhance the sensitivity for GC coupled ICP-MS (Fidalgo-Used *et al.*, 2005a; Vonderheide *et al.*, 2003); for example, a N_2 flow rate between 8-8.5% permitted ruelene detection in the ppt level (Fidalgo-Used *et al.*, 2006b). Using He as a collision gas in a collision cell was found to further reduce background noise without affecting analyte signal (Profrock *et al.*, 2004; Vonderheide *et al.*, 2003). Wuilloud *et al.* also noted that selection of a proper make-up electrolyte solution helps to eliminate polyatomic interferences, as is the case when using a sodium borate solution (Wuilloud *et al.*, 2005). Yang *et al.* employed a collective sample introduction technique that allowed for the simultaneous determination and quantification of OP pesticides in vegetable samples (Figure 7) (Yang *et al.*, 2009). The collective sample-introduction technique reduced the dilution of analyte and makeup volume, and narrowed the peak width, which resulted in higher sensitivity, lower LOD, and better electrophoretic resolution as compared to continuous sample-introduction.

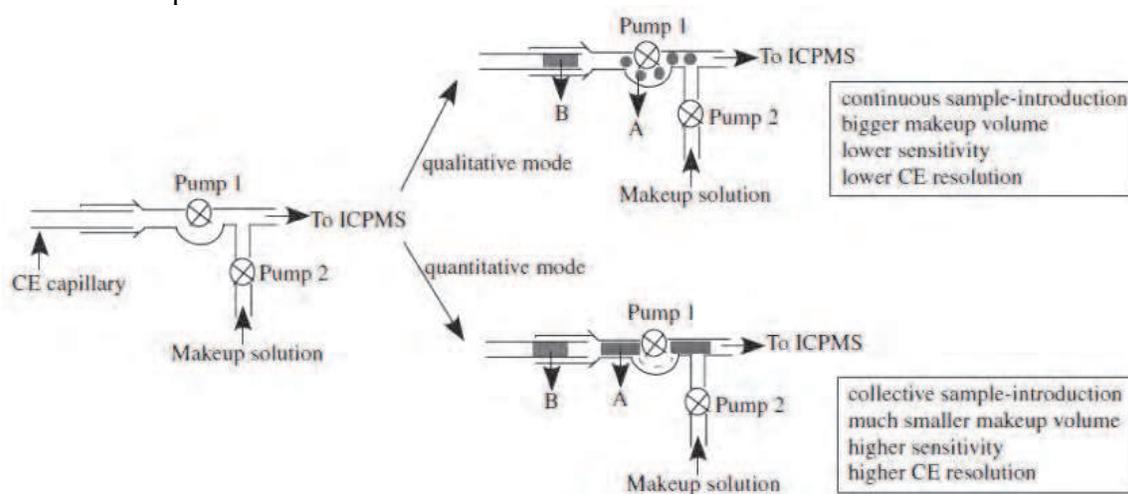


Fig. 7. Schematic of continuous sample-introduction (qualitative mode) and collective sample-introduction (quantitative mode). (Taken with permission from Reference Yang *et al.*, 2009).

Herein, mass spectrometry and experimental design based on extraction methods, ionization, detectors, and data acquisition modes have been discussed. Gas and liquid chromatography remain the most prevalently used detection systems for regular analysis of trace levels of OP pesticides in environmental, clinical, and food product samples. MS methods involving ICP or direct fiber introduction, although highly useful, have not been employed as frequently. Given these considerations and the recent advances it is clear that MS analysis offers high sensitivity and selectivity for accurate determination of OP pesticides.

4. Optical sensors

The past decade has shown several advancements in the development of selective biosensors and chemosensors for the detection of OP pesticides via optical and fluorescence spectroscopy. Below we highlight some of the most notable work reported recently in the literature. Additional information is also available in a review article published by Obare and coworkers (Obare et al., 2010).

4.1 Fluorescence-based biosensors for OP compounds

Fluorescence-based sensors, both biosensors and chemosensors, offer significant advantages over other conventional methods for detection of OP compounds. The principal advantages of fluorescence are its high single-molecule sensitivity and in most cases almost an instantaneous response. Fluorescence methods are capable of measuring concentrations of analytes 10^6 times smaller than absorbance techniques (Brufani et al., 1986). Thus, fluorescence techniques have been widely used in molecular biology and analytical chemistry but not extensively in the detection of OP pesticides. To date, a number of sensitive biosensors based on acetylcholinesterase (AChE) or butyryl cholinesterase (BChE) inhibition have been developed and used for OP compound detection (Cao et al., 2004; Brufani et al., 1986; Burnworth et al., 2007; Evtugyn et al., 1996; Lei et al., 2005; Mionetto et al., 1994; Palleschi et al., 1992; Rogers et al., 1991; Russell et al., 2003). In general, enzyme-based sensors for the detection of OP compounds can be broadly categorized into two major classes based on the enzyme employed-(1) AChE or (2) hydrolase (OPH).

Hydrolysis of acetylcholine by AChE produces one proton per substrate molecule resulting in an increase in the acidity of the solution. This forms the basis for AChE-based sensors. Rogers *et al.* used a pH-sensitive fluorescent dye, consisting of AChE linked to the pH-sensitive compound fluorescein isothiocyanate (FITC) (Rogers et al., 1991). The enzyme-dye adduct was immobilized on a quartz fiber which was attached to a fluorescence spectrophotometer. In the absence of an OP compound, the labeled AChE was able to hydrolyze acetylcholine leading to a decrease in pH which resulted in the reduction of the FITC fluorescence intensity due to interruption of the fluorophore's conjugation upon protonation. However, in the presence of diisopropylfluorophosphate (DFP) and subsequently acetylcholine, it was observed that 90% of the enzyme activity was lost, which was quantified by a less pronounced reduction of the fluorescence intensity. This biosensor was found to be very sensitive (capable of detecting nanomolar (nM) concentrations of paraoxon when exposed to the solution containing the analyte for ten minutes), and it demonstrated some selectivity toward different OP pesticides.

The second family of biosensors utilizes OPH as the enzymatic sensor for the detection of OP compounds. The mode of action of OPH is different from AChE; it catalytically

hydrolyses the OP compound, as illustrated in Figure 8, instead of covalently binding to it. Thus, instead of measuring the enzyme inhibition, detection methods involving OPH allow for a more direct measurement of OP compounds. Nowadays, OPH is widely used as a biosensor because of its ability to hydrolyze a wide range of compounds containing P-O, P-F, P-S, or P-CN bonds (Burnworth et al., 2007; H. Cao et al., 2007). Hydrolysis of the OP compounds led to the stoichiometric production of two protons which can be monitored and directly correlated to the amount of OP substrate (Dave et al., 1993). For instance, X. Cao *et al.* labeled OPH with FITC and deposited the resulting material onto silanized quartz slides in the form of Langmuir-Blodgett films thus creating organized monolayers of the enzyme-based sensors (X. Cao et al., 2004). It was demonstrated that this OPH based enzyme sensor showed enhanced sensitivity and could detect the analyte at nM concentrations.

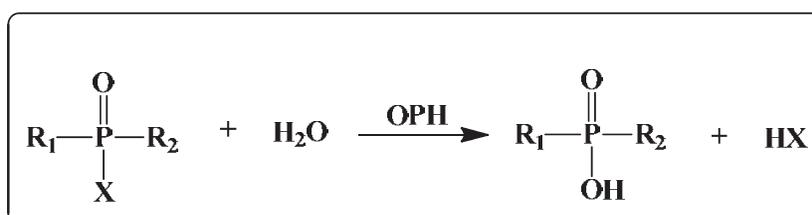


Fig. 8. Mechanism for the hydrolysis of OP compounds by OPH.

A number of biosensors have been developed based on fluorescence polarization immunoassays (FPIA) (Lee et al., 2005; Kim et al., 2003; Kolosova et al., 2003; Kolosova et al., 2004; Tang et al., 2008). One example reported by Kolosova *et al.* showed the use of a monoclonal antibody for the detection of parathion-methyl using FPIA (Kolosova et al., 2003). The sensing unit comprised a parathion-methyl derivative linked to fluorescein. Binding to parathion methyl or other closely related compounds was confirmed by measuring the intensity of emitted polarized light which indicated antibody binding. Despite the susceptibility of interference with different components existing in some matrices and the wide determinative range, the FPIA method is highly specific and reproducible and without complicated cleanup the method meets the performance criteria for detecting parathion-methyl.

In summary, enzyme based sensors are both very sensitive and selective in their approach to detect OP compounds. Furthermore, OPH based enzyme sensors offer distinct advantages over AChE-based systems. While these approaches towards OP detection have been significant, the inhibition-based biosensors suffer from three drawbacks: (1) the enzymes easily lose activity in the event of environmental or handling factors, therefore these enzymes may provide false positive signals, (2) the sensors require baseline testing prior to sample application and lengthy incubation times to allow enzyme-analyte interaction, and (3) due to the irreversible nature of cholinesterase enzyme inhibition, inhibition-based sensors cannot be reused without regeneration of enzyme activity. In addition, the lifetime of these sensors is limited by enzyme degradation.

4.2 Fluorescence-based chemosensor detection methods

Recently, a number of innovative methods for the detection of OP compounds based on optical chemosensors have been reported in the literature. Delattre and co-workers reported a cyclodextrin (CD) based fluorescent sensor for the detection of pesticides in water (Delattre

et al., 2009). D-Glucopyranose units in CDs form truncated cone-shaped molecules with a hydrophobic cavity, which can induce the inclusion phenomena of a guest, as shown in Figure 9. The dipole of the macromolecular system varies with the entry of a guest molecule. A modified β -cyclodextrin, pyridinoindolizin- β -cyclodextrin, was used to detect pesticides and herbicides, linadane, parathion, malathion, imidacloprid, atrazine, and simazine, through an inclusion complex between the pesticide or herbicide and the hydrophobic cavity of the macrocycle. This interaction leads to fluorescence quenching of the fluorophore. An advantage of this fluorescence sensor is the ability to quantify concentration data via fluorescence intensity concentration-dependence.

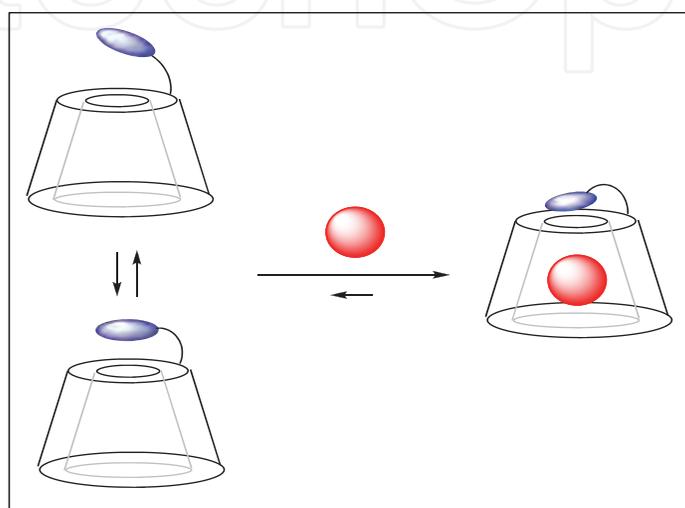


Fig. 9. Inclusion phenomena of a guest in CDs molecules. Reproduced with permission from Reference (Delattre et al., 2009), published by Bentham Science, 2009.

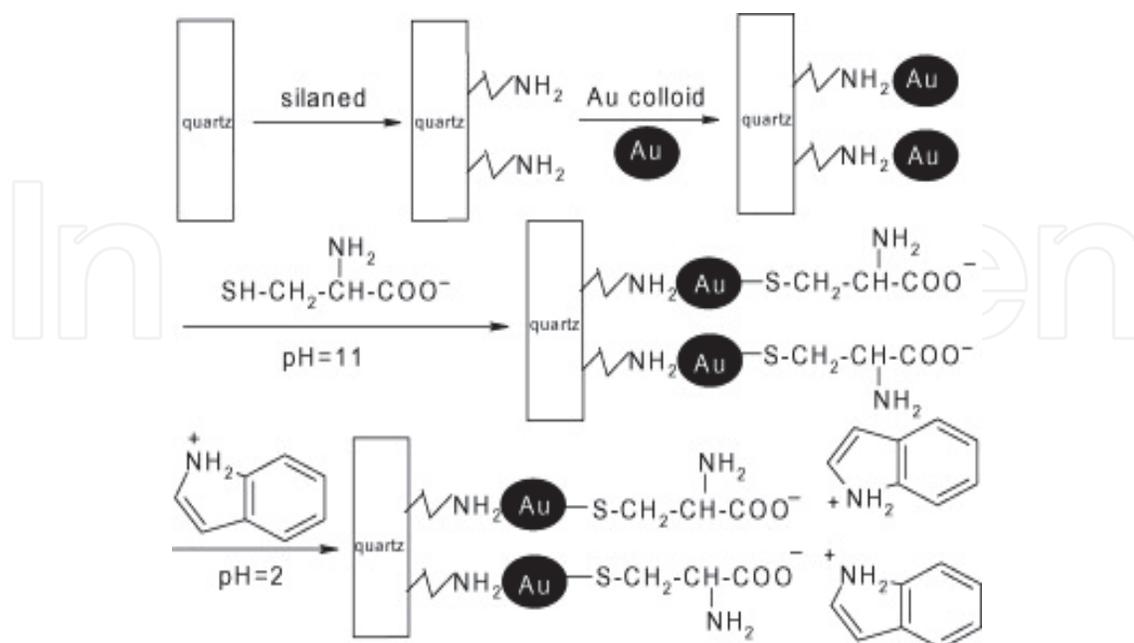


Fig. 10. Representation of the formation of the indole-based SAM sensor. (Reproduced with permission from Reference Sun et al., 2008)

A self-assembled multilayer (SAM) consisting of amino-silanized quartz functionalized with gold nanoparticles and coated with indole via a L-cysteine linker was fabricated as shown in Figure 10 (Sun et al., 2008). When the SAM sensor was exposed to the pesticide, the indole group of the sensor on the modified film was oxidized to a fluorescent indoxyl group. The oxidation process depended on the pesticide concentration and was reflected by changes in intensity. The sensor was capable of detecting methylparathion and monocrotophos in the ppm and ppb range, respectively. An advantage of the indole-based SAM sensor is that it could detect OP pesticides in ionic and other environmental species, but it was subject to interference at 20 equivalents of Fe^{3+} ions.

4.3 Sensors with multiple modes of signal transduction

There is a growing awareness and trend toward the development of multimodal systems reminiscent of living organisms that utilize multiple senses to intelligently respond to multiple stimuli in real-world environments. A major advantage of multimodal sensors is the minimization of false positives. With this in mind, we have recently developed and reported new chemosensors with multimodal sensing capabilities for analytes such as saccharides (Beaudoin & Obare, 2008) and toxic OP compounds (De et al., 2010). Our design strategy, shown in Figure 11, utilizes and couples the electrophilic reactivity of the pentavalent phosphorus atom of the phosphoryl and thiophosphoryl groups of toxic OPs to a nucleophilic fluorophore capable of recognizing and reporting sensor-analyte interactions. We have shown that the azastilbene, dimethyl-[4-(2-quinolin-2-yl-vinyl)-phenyl]-amine (DQA), Figure 12, recognizes, reacts with and responds to the pesticides: ethion, malathion, parathion, and fenthion. DQA binding to either of the above mentioned pesticides resulted in changes of the UV-visible and cyclic voltammogram of DQA (De et al., 2010) indicating the selective binding.

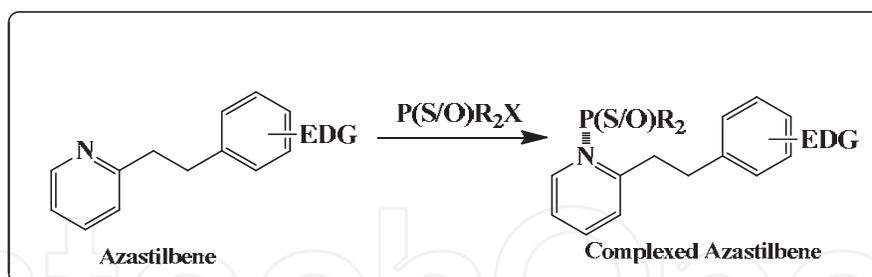


Fig. 11. Schematic representation of uncomplexed (*left*) and complexed (*right*) azastilbene (De et al., 2010). (EDG = electron donating group).

DQA was titrated with the pesticides, with ethion, malathion, parathion and fenthion and changes in the UV-visible absorbance spectrum of DQA were measured. As shown in Figure 13a, increase in ethion concentration to a solution of DQA in acetonitrile resulted in the decrease in the UV-visible absorbance intensity at 385 nm, and was accompanied by formation of two new peaks at 325 nm and at 500 nm. Similar behavior was observed in the case of malathion, except two new peaks arise at 330 nm and 505 nm, as shown in Figure 13b. In both cases two isosbestic points were observed at 340 nm and 425 nm for ethion, and at 335 nm and 430 nm for malathion. Furthermore, we observed that titration of parathion to a solution of DQA in acetonitrile did not result in the quenching of the 325 nm peak,

however, a new peak at 505 nm formed and increased in intensity with an increase in parathion concentration as shown in Figure 13c. On the other hand, addition of fenthion to the DQA solution did not show any notable changes in the original absorbance of DQA as shown in Figure 13d. Changes in the UV-visible absorbance spectrum show that DQA is efficient in distinguishing between the four OP pesticides and results in different colored solutions with different λ_{\max} values. The method of continuous variation was used to determine the stoichiometry of DQA with ethion, malathion and parathion. In each case, it was found that a 1:1 DQA-OP complex formed. Based on the 1:1 stoichiometry, binding constants were calculated to be $6.5 \times 10^4 \text{ M}^{-1}$, $1.1 \times 10^4 \text{ M}^{-1}$, and $0.2 \times 10^4 \text{ M}^{-1}$ for ethion, malathion, and parathion, respectively. At the end of the DQA titrations with ethion, malathion and parathion, the solution color had changed from yellow to red-orange, orange and peach-orange, respectively. The same color changes in DQA were also observed when saturation concentrations of OP pesticides were added. No color change was observed when fenthion was added to DQA.

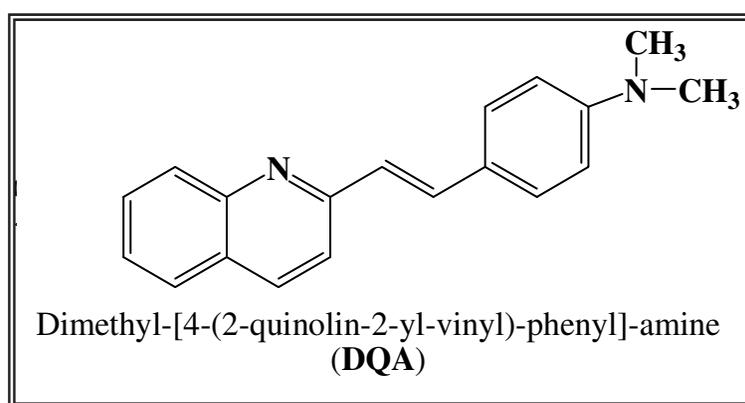


Fig. 12. Chemical Structure of DQA.

Molecules that provide optical and electrochemical signals are ideal for developing sensors that offer dual signal transductions (Ko & Park, 2006). Cyclic voltammograms were acquired using a BAS CV50 electrochemical workstation using glassy carbon as the working electrode, a platinum wire as the counter electrode, and Ag/AgCl as the reference electrode. The electrolyte was a 0.1 M solution of tetrabutyl ammonium hexafluorophosphate (TBAPF₆). DQA was found to have a formal potential (E^0) at 860 mV *vs.* Ag/AgCl. Changes in the electrochemical waves of DQA with 1 equivalent of the pesticides ethion, malathion, parathion and fenthion were measured. In the case of ethion, malathion and parathion, the DQA-OP complex formed had significantly different redox characteristics relative to DQA, Figure 14. The DQA/ethion complex showed three redox waves at $E_{1/2} = -875 \text{ mV vs. Ag/AgCl}$, $E_{1/2} = -500 \text{ mV vs. Ag/AgCl}$ and $E_{1/2} = +500 \text{ mV vs. Ag/AgCl}$. The cyclic voltammogram of the DQA/malathion complex was also different relative to that of DQA; in this case two waves at $E_{1/2} = -1,498 \text{ mV vs. Ag/AgCl}$ and $E_{1/2} = -870 \text{ mV vs. Ag/AgCl}$ corresponding to DQA-malathion complex were observed.

The formation of a DQA/parathion complex also demonstrated significant changes in the redox behavior ($E_{1/2} = -1,072 \text{ mV vs. Ag/AgCl}$, $E_{1/2} = -773 \text{ mV vs. Ag/AgCl}$) in comparison to DQA. As expected, there were no changes in the redox behavior of DQA with the addition of fenthion. The observed DQA-OP reactions can be explained by Lewis acid-base or nucleophile-electrophile interactions between the quinolinyl nitrogen and the OP

phosphorus atoms. Reactions of electrophiles (for example, proton, metal cations, and carbon-based) with 4-dimethylamino styrylazaaromatics occurs exclusively at the 'ring' (pyridyl, quinoliny) nitrogen (Allen & Dunaway-Mariano, 2004). This generally results in the formation of the corresponding quaternary pyridinium and quinolinium salts. It is thus reasonable to assume that electrophilic phosphorus reactants will also react preferentially at the azaaromatic 'ring' nitrogen. Furthermore, our computational calculations done by GAUSSIAN 03 program suite (Frisch et al., 2004) reveals, as expected, that the electrostatic potential at the quinoline nitrogen is higher relative to the dimethylamino nitrogen. One common mechanistic pathway for phosphoryl transfer reactions is *via* concerted $S_N2(P)$ processes in which a nucleophilic attack on phosphorus leads to expulsion of the leaving group. In these S_N2 scenarios, the reaction rate for the thiophosphoryl transfer is expected to be highly dependent on the leaving group. This in turn will affect the binding constant of the incoming nucleophile. This interpretation is consistent with our results since, for example, it is known that the *p*-nitrophenolate anion of parathion is a much better, more stable leaving group than the phenolate anion of fenthion. Thus, parathion has a stronger binding constant than fenthion to DQA. The interaction of DQA with each OP pesticide relies on the stability of the leaving group - the more stable the OP leaving group, the more likely it will dissociate upon interaction with the nucleophilic DQA quinoliny nitrogen.

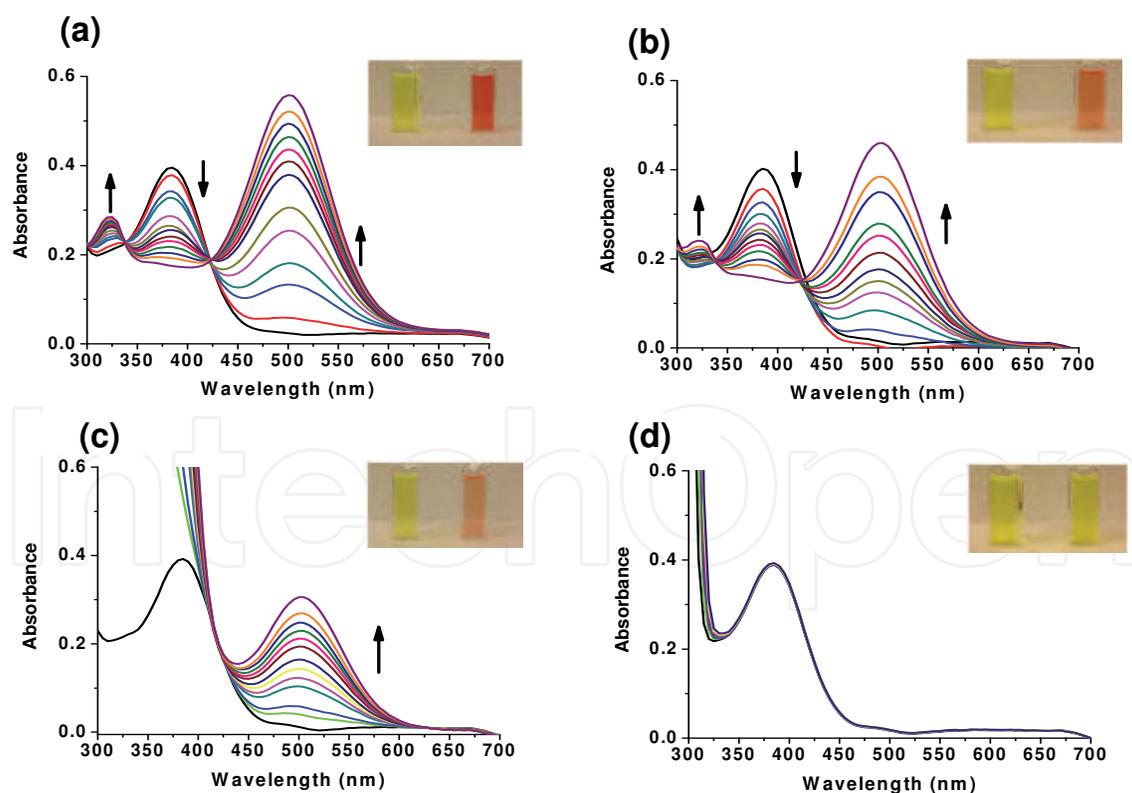


Fig. 13. Changes in UV-visible absorbance of DQA upon binding to OP pesticides: (a) titration with ethion; (b) titration with malathion; (c) titration with parathion; and (d) titration with fenthion. In each case the direction of the arrow indicates concentration of 0, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24 μM .

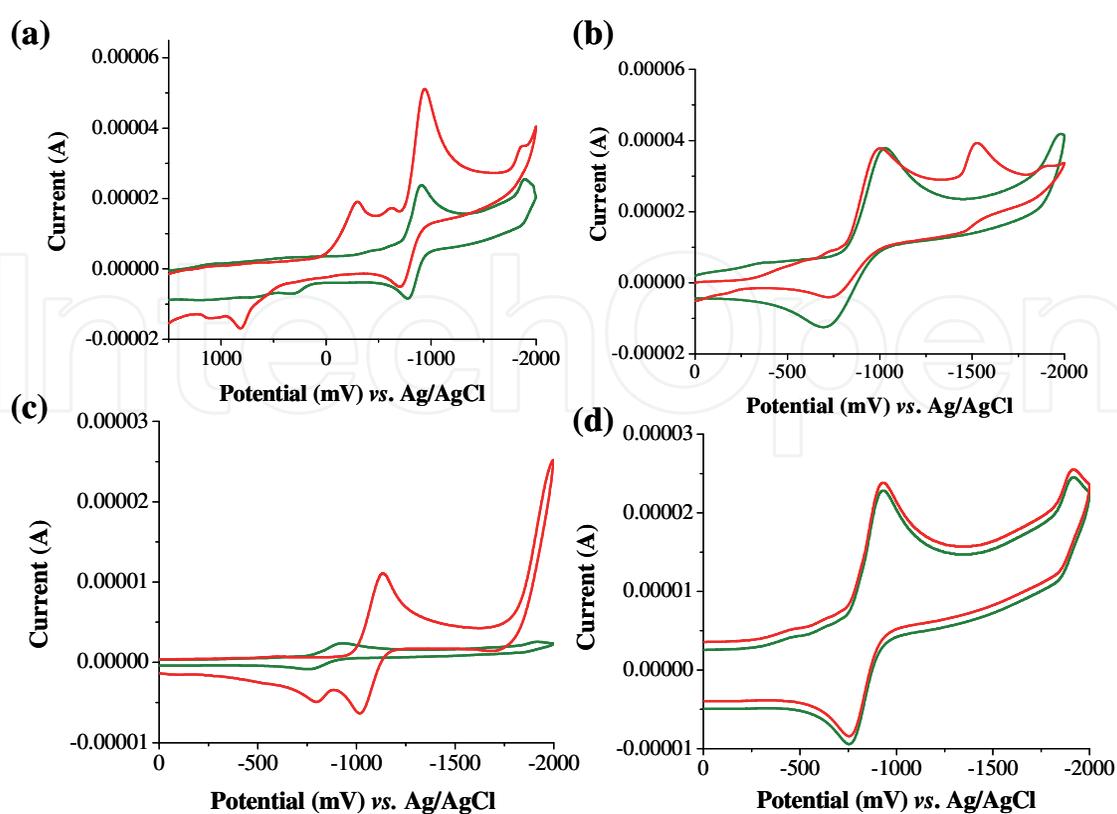


Fig. 14. Cyclic voltammograms of DQA before and after addition of (a) ethion, (b) malathion, (c) parathion, and (d) fenthion.

The optical and electrochemical changes of the azastilbene DQA when exposed to ethion, malathion, parathion and fenthion shows the potential of azastilbenes as viable structural motifs for development of multimodal chemosensors. Azastilbenes have demonstrated the capability of distinguishing between various pesticides, which is important for both environmental as well as homeland security applications. Future work on this project to further develop our azastilbene-based multimodal chemosensors for toxic organophosphates and other important toxic analytes is continuing.

5. Future perspectives

Significant progress has been achieved toward the development of detection methods for toxic OP pesticides. The most common and effective developments have been in mass spectrometric techniques as well as in the development of optical biosensors and chemosensors. While the mass spectrometric methods offer high sensitivity and specificity, they require well trained technicians and experts to run the analysis. In recent years there have been advancements in the development of miniaturized devices that are expected to be portable and operable *in situ*. Such advancements will enable the rapid detection of OP pesticides and in turn lead to improved quality of life. Biosensors and chemosensors are easier to develop for *in situ* analysis. Biosensors offer improved selectivity relative to chemosensors, however, biosensors require careful control of environmental conditions, for example, temperature and pH, otherwise the biosensor could degrade. Chemosensors are expected to have much more robustness and there continue to be increasing research developments in this area. It is clear that future improvements in this area will require the

design of new chemosensors with additional modes for signal transduction. Such sensors will play an important role in minimization or elimination of false-positives. Due to the structural similarity of OP compounds, it is also paramount that the designed sensors are fabricated such that they are highly selective toward specific OP compounds.

6. Acknowledgements

This work was partially supported by the National Science Foundation Grant CHE-1005456 and DMR-0963678 and partially by U.S. Army Grant No. W911QY-07-1-0003. T.A.S. thanks Western Michigan University for the AGEF fellowship and the Kodak Eastman Foundation for the Sorrell Theophilus Fellowship administered by NOBCChE.

7. References

- Adachi, N.; Kinoshita, H.; Nishiguchi, M.; Takahashi, M.; Ouchi, H.; Minami, T.; Matsui, K.; Yamamura, T.; Motomura, H.; Ohtsu, N.; Yoshida, S. & Hishida, S. (2008). Simultaneous analysis of acephate and methamidophos in human serum by improved extraction and GC-MS. *Forensic Toxicol.*, Vol.26, pp. 76-79
- Agüera, A.; Piedra, L.; Hernando, M. D.; Fernández-Alba, A. R. & Contreras, M.(2002a). Splitless large-volume GC-MS injection for the analysis of organophosphorus and organochlorine pesticides in vegetables using a miniaturised ethyl acetate extraction. *Analyst*, Vol.125, pp. 1397-1402
- Agüera, A.; Contreras, M.; Crespo, J. & Fernandez-Alba, A. R. (2002b). Multiresidue method for the analysis of multiclass pesticides in agricultural products by gas chromatography-tandem mass spectrometry. *Analyst*, Vol.127, pp. 347-354
- Aguilar, C.; Borruil, F. & Marce, R. M. (1997). Determination of pesticides in environmental waters by solid-phase extraction and gas chromatography with electron-capture and mass spectrometry detection. *J. Chromatogr. A*, Vol.771, pp. 221-231
- Albero, B.; Sánchez-Brunete, C. & Tadeo, J. L. (2003). Determination of Organophosphorus Pesticides in Fruit Juices by Matrix Solid-Phase Dispersion and Gas Chromatography. *J. Agric. Food Chem.*, Vol.51, pp. 6915-6921
- Albero, B.; Sanchez-Brunete, C. & Tadeo, J. L. (2004). Determination of herbicide residues in juice by matrix solid-phase dispersion and gas chromatography-mass spectrometry. *J. Agric. Food Chem.*, Vol.52, pp. 5825-5835
- Albero, B.; Sanchez-Brunete, C.; Donoso, A. & Tadeo, J. L. (2004). Determination of herbicide residues in juice by matrix solid-phase dispersion and gas chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.1043, pp. 127-133
- Alder, L.; Greulich, K.; Kempe, G. & Vieth, B. (2006). Residue analysis of 500 high priority pesticides: Better by GC-MS or LC-MS/MS? *Mass Spectrom. Rev.*, Vol.25, pp. 838-865
- Allen, K.N. & Dunaway-Mariano, D. (2004). Phosphoryl group transfer: Evolution of a catalytic scaffold Trends. *Biochem. Sci.*, Vol.29, pp. 495-503
- Amendola, L.; Botrè, F.; Carollo, A. S.; Longo, D. & Zoccolillo, L. (2002). Analysis of organophosphorus pesticides by gas chromatography-mass spectrometry with negative chemical ionization: a study on the ionization conditions. *Anal. Chim. Acta.*, Vol.461, pp. 97-108

- Araoud, M.; Douki, W.; Najjar, M. F. & Kenani, A. (2010). Simple analytical method for determination of pesticide residues in human serum by liquid chromatography tandem mass spectrometry. *J. Environ. Sci. Heal. B*, Vol.45, pp. 242-248
- Araoud, M.; Douki, W.; Rhim, A.; Najjar, M. F. & Gazzah, N. (2007). Multiresidue analysis of pesticides in fruits and vegetables by gas chromatography-mass spectrometry. *J. Environ. Sci. Health. B*, Vol.42, pp. 179 - 187
- Ariese, F.; Ernst, W.H.O. & Sijm, D.T.H.M. (2001). Natural and synthetic organic compounds in the environment – A symposium report. *Environ. Toxicol. Pharmacol.* Vol.10, pp. 65-80
- Asperger, A.; Efer, J.; Koal, T. & Engewald, W. (2002). Trace determination of priority pesticides in water by means of high-speed on-line solid-phase extraction-liquid chromatography-tandem mass spectrometry using turbulent-flow chromatography columns for enrichment and a short monolithic column for fast liquid chromatographic separation. *J. Chromatogr. A*, Vol.960, pp. 109-119
- Aybar-Muñoz, J.; Fernández González, E.; García-Ayuso, L. E.; González Casado, A. & Cuadros-Rodríguez, L. (2003). A new approach to qualitative analysis of organophosphorus pesticide residues in cucumber using a double gas chromatographic system: GC-pulsed-flame photometry and retention time locking GC-mass spectrometry. *Talanta*, Vol.60, pp. 433-447
- Aybar-Muñoz, J.; Fernández-González, E.; García-Ayuso, L. E.; González-Casado, A. & Cuadros-Rodríguez, L. (2005). Semiquantitative Method for Detection of Pesticide Residues Over Established Limits in Vegetables by Use of GC- μ ECD and GC-(EI)MS. *Chromatographia*, Vol.61, pp. 505-513
- Bagheri, H.; Ayazi, Z. & Babanezhad, E. (2010). A sol-gel-based amino functionalized fiber for immersed solid-phase microextraction of organophosphorus pesticides from environmental samples. *Microchem. J.*, Vol.94, pp. 1-6
- Banerjee, K.; Patil, S. H.; Dasgupta, S.; Oulkar, D. P.; Patil, S. B.; Savant, R. & Adsule, P. G. (2008). Optimization of separation and detection conditions for the multiresidue analysis of pesticides in grapes by comprehensive two-dimensional gas chromatography-time-of-flight mass spectrometry. *J. Chromatogr. A*, Vol.1190, pp. 350-357
- Barcelo, D.; Durand, G.; Bouvot, V. & Nielen, M. (1993). Use of Extraction Disks for Trace Enrichment of Various Pesticides from River Water and Simulated Seawater Samples Followed by Liquid Chromatography-Rapid-Scanning UV-Visible and Thermospray-Mass Spectrometry Detection. *Environ. Sci. Technol.*, Vol.27, pp. 271-277
- Barco-Bonilla, N.; Romero-Gonzalez, R.; Plaza-Bolanos, P.; Frenich, A. G. & Vidal, J. (2010). Analysis and study of the distribution of polar and non-polar pesticides in wastewater effluents from modern and conventional treatments. *J. Chromatogr. A*, Vol.1217, pp. 7817-7858
- Barr, D. B.; Barr, J. R.; Maggio, V. L.; Whitehead, Jr., R. D.; Sadowski, M. A.; Whyatt, R. M. & Needham, L. L. (2002). A multi-analyte method for the quantification of contemporary pesticides in human serum and plasma using high-resolution mass spectrometry. *J. Chromatogr. B*, Vol.778, pp. 99-111
- Basheer, C.; Alnedhary, A. A.; Rao, B. S. M.; Valliyaveetil, S. & Lee, H. K. (2006). Development and Application of Porous Membrane-Protected Carbon Nanotube

- Micro-Solid-Phase Extraction Combined with Gas Chromatography/Mass Spectrometry. *Anal. Chem.*, Vol.78, pp. 2853-2858
- Basheer, C.; Alnedhary, A.; Rao, B. S. M. & Lee, H. K. (2007). Determination of organophosphorous pesticides in wastewater samples using binary-solvent liquid-phase microextraction and solid-phase microextraction: A comparative study. *Anal. Chim. Acta*, Vol.605, pp. 147-152
- Baugros, J. B.; Giroud, B.; Dessalces, G.; Grenier-Loustalot, M.F. & Cren-Olivé, C. (2008). Multiresidue analytical methods for the ultra-trace quantification of 33 priority substances present in the list of REACH in real water samples. *Anal. Chim. Acta.*, Vol.607, pp. 191-203
- Beaudoin, D.S. & Obare, S.O. (2008). Dual optical and electrochemical saccharide detection based on a dipyrrodo[3,2-a:2'3'-c]phenazine (DPPZ) ligand. *Tetrahedron Lett.*, Vol.49, pp. 6054-6057
- Beceiro-González, E.; Concha-Graña, E.; Guimaraes, A.; Gonçalves, C.; Muniategui-Lorenzo, S. & Alpendurada, M. F. (2007). Optimisation and validation of a solid-phase microextraction method for simultaneous determination of different types of pesticides in water by gas chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.1141, pp. 165-173
- Beltran, J.; Pitarch, E.; Egea, S.; López, F. J. & Hernández, F. (2001). Gas chromatographic determination of selected pesticides in human serum by head-space solid-phase microextraction. *Chromatographia*, Vol.54, pp. 757-763
- Benanou, D.; Acobas, F.; De Roubin, M. R. & Wylie, P. L. (n.d.) Stir Bar Sorptive Extractions: A New Way to Extract Off-Flavor Compounds in the Aquatic Environment. In, Agilent [Online] Applications Library, (last accessed Feb 28, 2011), <http://chem.agilent.com/library/applications/5988-8900EN.pdf>
- Berger-Preiss, E. & Elflein, L. (2006). Determination of Household Insecticides in Indoor Air by Gas Chromatography-Mass Spectrometry. *Method. Biotechnol.*, Vol.19, pp. 179-190
- Berhanu, T.; Megersa, N.; Solomon, T. & Jounlnsson, J. A. (2008). A novel equilibrium extraction technique employing hollow fibre liquid phase microextraction for trace enrichment of freely dissolved organophosphorus pesticides in environmental waters. *Int. J. Environ. Anal. Chem.*, Vol.88, pp. 933-945
- Berrada, H.; Fernández, M.; Ruiz, M. J.; Moltó, J. C.; Mañes, J. & Font, G. (2010). Surveillance of pesticide residues in fruits from Valencia during twenty months (2004/05). *Food Control*, Vol.21, pp. 36-44
- Blasco, C.; Fernández, M.; Picó, Y. & Font, G. (2004). Comparison of solid-phase microextraction and stir bar sorptive extraction for determining six organophosphorus insecticides in honey by liquid chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.1030, pp. 77-85
- Blasco, C.; Fernández, M.; Pena, A.; Lino, C.; Silveira, M. I.; Font, G. & Picó, Y. (2003). Assessment of Pesticide Residues in Honey Samples from Portugal and Spain. *J. Agric. Food Chem.*, Vol.51, pp. 8132-8138
- Blasco, C.; Font, G. & Picó, Y. (2005). Analysis of pesticides in fruits by pressurized liquid extraction and liquid chromatography-ion trap-triple stage mass spectrometry. *J. Chromatogr. A*, Vol.1098, pp. 37-43

- Blasco, C.; Font, G. & Picoacute, Y. (2008). Solid-phase microextraction-liquid chromatography-mass spectrometry applied to the analysis of insecticides in honey. *Food Addit. Contam. A*, Vol.25, pp. 59-69
- Bouchard, M.F.; Bellinger, D.C.; Wright, R.O. & Weisskopf, M.G. (2010). Attention-deficit/hyperactivity disorder and urinary metabolites of organophosphate pesticides. *Pediatrics*, Vol.125, pp. 1216-1226
- Boy-Boland, A. A.; Magdic, S. & Pawliszyn, J. B. (1996). Simultaneous Determination of 60 Pesticides in Water Using Solid-phase Microextraction and Gas Chromatography-Mass Spectrometry. *Analyst*, Vol.121, pp. 929-938
- Brufani, M.; Marta, M. & Pomponi, M. (1986). Anticholinesterase activity of a new carbamate, heptylphysostigmine, in view of its use in patients with Alzheimer-type dementia. *Eur. J. Biochem.*, Vol.157, pp. 115-120
- Burnworth, M.; Rowan, S.J. & Weder, C. (2007). Fluorescent Sensors for the detection of chemical warfare agents. *Chem. Eur. J.*, Vol.13, pp. 7828-7836
- Cao, H.; Nam, J.; Harmon, H.J. & Branson, D.H. (2007). Spectrophotometric detection of organophosphate diazinon by porphyrin solution and porphyrin-dyed cotton fabric. *Dyes Pigments*, Vol.74, pp. 176-180
- Cao, X.; Mello, S.V.; Leblanc, R.M.; Rastogi, V.K.; Cheng, T.C. & DeFrank, J.J. (2004). Detection of paraoxon by immobilized organophosphorus hydrolase in a langmuir-blodgett film. *Colloids Surf. A*, Vol.250, pp. 349-356
- Cappiello, A.; Famiglini, G.; Palma, P. & Mangani, F. (1996). Trace Level Determination of Organophosphorus Pesticides in Water with the New Direct-Electron Ionization LC/MS Interface. *Anal. Chem.*, Vol.68, pp. 2464-2470
- Castro, J.; Sánchez-Brunete, C. & Tadeo, J. L. (2001). Multiresidue analysis of insecticides in soil by gas chromatography with electron-capture detection and confirmation by gas chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.918, pp. 371-380
- Celik, S.; Kunc, S. & Asan, T. (1995). Degradation of some pesticides in the field and effect of processing. *Analyst*, Vol.120, pp. 1739-1743
- Cesar da Silva, R.; Zuin, V. G.; Yariwake, J. H.; Eberlin, M. N. & Augusto, F. (2007). Fiber introduction mass spectrometry: determination of pesticides in herbal infusions using a novel sol-gel PDMS/PVA fiber for solid-phase microextraction. *J. Mass Spectrom.*, Vol.42, No.6, pp. 825-829
- Chen, G.; Cao, P. & Liu, R. (2011). A multi-residue method for fast determination of pesticides in tea by ultra performance liquid chromatography-electrospray tandem mass spectrometry combined with modified QuEChERS sample preparation procedure. *Food Chem.*, Vol.125, pp. 1406-1411
- Chen, H.; Chen, R.; Feng, R. & Li, S. (2009). Simultaneous Analysis of Carbamate and Organophosphorus Pesticides in Water by Single-Drop Microextraction Coupled with GC-MS. *Chromatographia*, Vol.70, pp. 165-172
- Chen, P. & Huang, S. (2006). Determination of ethoprop, diazinon, disulfoton and fenthion using dynamic hollow fiber-protected liquid-phase microextraction coupled with gas chromatography-mass spectrometry. *Talanta*, Vol.69, pp. 669-675
- Chung, S. & Chan, B. (2010). Validation and use of fast sample preparation method and liquid-chromatography-tandem mass spectrometry in analysis of ultra-trace levels of 98 organophosphorus pesticide and carbamate residues in a total diet study involving diversified food types. *J. Chromatogr. A*, Vol.1217, pp. 4815-4824

- Cochran, J. (2008). Evaluation of comprehensive two-dimensional gas chromatography – time-of-flight mass spectrometry for the determination of pesticides in tobacco. *J. Chromatogr. A*, Vol.1186, pp. 202-210
- Corrion, M. L.; Ostrea Jr., E. M.; Bielawski, D. M.; Posecion, Jr., N. C. & Seagraves, J. J. (2005). Detection of prenatal exposure to several classes of environmental toxicants and their metabolites by gas chromatography–mass spectrometry in maternal and umbilical cord blood. *J Chromatogr. B*, Vol.822, pp. 221-229
- Dave, K.I.; Miller, C.E. & Wild, J.R. (1993). Characterization of organophosphorus hydrolases and the genetic manipulation of the phosphotriesterase from *Pseudomonas diminuta*. *Chem-Biol. Interact.*, Vol.87, pp. 55-68
- De, C.; Samuels, T.A.; Haywood, T.L.; Anderson, G.A.; Campbell, K.; Fletcher, K.; Murray, D.H. & Obare, S.O. (2010). Dual colorimetric and electrochemical sensing of organothiophosphorus pesticides by an azastilbene derivative *Tetrahedron Lett.*, Vol.51, pp. 1754-1757
- Delattre, F.; Cazier, F.; Cazier, F. & Tine, A. (2009). Use a fluorescent molecular sensor for the detection of pesticides and herbicides in water. *Curr. Anal. Chem.*, Vol.5, pp. 48-52
- Díaz-Cruz, M. S. & Barceló, D. (2006). Highly selective sample preparation and gas chromatographic–mass spectrometric analysis of chlorpyrifos, diazinon and their major metabolites in sludge and sludge-fertilized agricultural soils. *J. Chromatogr. A*, Vol.1132, pp. 21-27
- Elflein, L.; Berger-Preiss, E.; Levsen, K. & Wünsch, G. (2003). Development of a gas chromatography–mass spectrometry method for the determination of household insecticides in indoor air. *J. Chromatogr. A*, Vol.985, pp. 147-157
- El-Kabbany, S.; Rashed, M. M. & Zayed, M. A. (2000). Monitoring of the pesticide levels in some water supplies and agricultural land, in El-Haram, Giza (A.R.E.). *J. Hazard. Mater.*, Vol.72, pp. 11-21
- Esteve-Turrillas, F. A.; Pastor, A. & de la Guardia, M. (2007). Behaviour of semipermeable membrane devices in neutral pesticide uptake from waters. *Anal. Bionanal. Chem.*, Vol.387, pp. 2153-2162
- Esteve-Turrillas, F. A.; Pastor, A. & de la Guardia, M. (2008). Evaluation of working air quality by using semipermeable membrane devices: Analysis of organophosphorus pesticides. *Anal. Chim. Acta.*, Vol.626, pp. 8859-8866
- Evtugyn, G.A.; Budnikov, H.C. & Nikolskaya, E.B. (1996). Influence of surface-active compounds on the response and sensitivity of cholinesterase biosensors for inhibitor determination. *Analyst*, Vol.121, pp. 1911-1915
- Fernández, M.; Picó, Y.; Girotti, S. & Mañes, J. (2001). Analysis of Organophosphorus Pesticides in Honeybee by Liquid Chromatography–Atmospheric Pressure Chemical Ionization–Mass Spectrometry. *J. Agric. Food Chem.*, Vol.49, pp. 3540-3547
- Fernández, M.; Picó, Y. & Mañes, J. (2002). Rapid screening of organophosphorus pesticides in honey and bees by liquid chromatography–Mass spectrometry. *Chromatographia*, Vol.56, pp. 577-583
- Fernández, M.; Picó, Y. & Mañes, J. (2003). Simultaneous Determination of Carbamate and Organophosphorus Pesticides in Honeybees by Liquid Chromatography–Mass Spectrometry. *Chromatographia*, Vol.58, pp. 151-158

- Ferrer, C.; Gomez, J.; Garcia-Reyes, J.; Ferrer, I.; Thurman, M. & Fernandez-Alba, A. (2005). Determination of pesticide residues in olives and olive oil by matrix solid-phase dispersion followed by gas chromatography/mass spectrometry and liquid chromatography/tandem mass spectrometry. *J. Chromatogr. A*, Vol.1069, pp. 183-194
- Ferrer, I. & Thurman, E. M. (2007). Multi-residue method for the analysis of 101 pesticides and their degradates in food and water samples by liquid chromatography/time-of-flight mass spectrometry. *J. Chromatogr. A*, Vol.1175, pp. 24-37
- Fidalgo-Used, N.; Montes-Bayón, M.; Blanco-González, E. & Sanz-Medel, A. (2005a). Determination of organophosphorus pesticides in spiked river water samples using solid phase microextraction coupled to gas chromatography with EI-MS and ICP-MS detection. *J. Anal. At. Spectrom.*, Vol.20, pp. 876-882 234
- Fidalgo-Used, N.; Montes-Bayón, M.; Blanco-González, E. & Sanz-Medel, A. (2006b). SPME-enantioselective gas chromatography with ECD and ICP-MS detection for the chiral speciation of the pesticide ruelene in environmental samples. *J. Anal. At. Spectrom.*, Vol.21, pp. 876-883 235
- Fontana, A. R.; Camargo, A. B. & Altamirano, J. C. (2010). Coacervative microextraction ultrasound-assisted back-extraction technique for determination of organophosphates pesticides in honey samples by gas chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.1217, pp. 6334-6341
- Frenich, A. G.; Bolaños, P. P. & Vidal, J. L. M. (2007). Multiresidue analysis of pesticides in animal liver by gas chromatography using triple quadrupole tandem mass spectrometry. *J. Chromatogr. A* 2007, Vol.1153, pp. 194-202
- Frenich, A. G.; Plaza-Bolaños, P. & Martínez Vidal, J. L. (2008). Comparison of tandem-in-space and tandem-in-time mass spectrometry in gas chromatography determination of pesticides: Application to simple and complex food samples. *J. Chromatogr. A*, Vol.1203, pp. 229-238
- Frisch, M.J.; Trucks, G.W.; Schlegel, H.B.; Scuseria, G.E.; Robb, M.A.; Cheeseman, J.R.; Montgomery, J.A., Jr.; Vreven, T.V.; Kudin, K.N.; Burant, J.C.; Millam, J.M.; Iyengar, S.S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G.A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H.P.; Cross, J.B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R.E.; Yazyev, O.; Austin, A.J.; Cammi, R.; Pomelli, C.; Ochterski, J.W.; Ayala, P.Y.; Morokuma, K.; Voth, G.A.; Salvador, P.; Dannenberg, J.J.; Zakrzewski, V.G.; Dapprich, S.; Daniels, A.D.; Strain, M.C.; Farkas, O.; Malick, D.K.; Rabuck, A.D.; Raghavachari, K.; Foresman, J.B.; Ortiz, J.V.; Cui, Q.; Baboul, A.G.; Clifford, S.; Cioslowski, J.; Stefanov, B.B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R.L.; Fox, D.J.; Keith, T.; Al-Laham, M.A.; Peng, C.Y.; Nanayakkara, A.; Challacombe, M.; Gill, P.M.W.; Johnson, B.; Chen, W.; Wong, M.W.; Gonzalez, C. & Pople, J.A. Gaussian 03, Gaussian, Inc.: Wallingford CT, USA, 2004
- Fuentes, E.; Báez, M. E. & Diaz, J. (2009). Microwave-assisted extraction at atmospheric pressure coupled to different clean-up methods for the determination of organophosphorus pesticides in olive and avocado oil. *J. Chromatogr. A*, Vol.1216, pp. 8859-8866

- Fuentes, E.; Báez, M. E. & Quiñones, A. (2008). Suitability of microwave-assisted extraction coupled with solid-phase extraction for organophosphorus pesticide determination in olive oil. *J. Chromatogr. A*, Vol.1207, pp. 38-45
- García-Rodríguez, D.; Carro, A. M.; Lorenzo, R. A.; Fernández, F. & Cela, R. (2008). Determination of trace levels of aquaculture chemotherapeutants in seawater samples by SPME-GC-MS/MS. *J. Sep. Sci.*, Vol.31, pp. 2882-2890
- García-Rodríguez, D.; Carro-Díaz, A.M.; Lorenzo-Ferreira, R.A. & Cela-Torrijos, R. (2010). Determination of pesticides in seaweeds by pressurized liquid extraction and programmed temperature vaporization-based large volume injection-gas chromatography-tandem mass spectrometry. *J. Chromatogr. A*, Vol.1217, pp. 2940-2949
- García-Valcárcel, A. I. & Tadeo, J. L. (2009). A combination of ultrasonic assisted extraction with LC-MS/MS for the determination of organophosphorus pesticides in sludge. *Anal. Chim. Acta.*, Vol.641, pp. 117-123
- Garrido Frenich, A.; Martínez Vidal, J.L.; Cruz Sicilia, A.D.; González Rodríguez, M.J. & Plaza Bolaños, P. (2006). Multiresidue analysis of organochlorine and organophosphorus pesticides in muscle of chicken, pork and lamb by gas chromatography-triple quadrupole mass spectrometry. *Anal. Chim. Acta.*, Vol.558, pp.42-52
- Garrido-Frenich, A.; Romero-González, R.; Martínez-Vidal, J.L.; Plaza-Bolaños, P.; Cuadros-Rodríguez, L. & Herrera-Abdo, M. A. (2006). Characterization of recovery profiles using gas chromatography-triple quadrupole mass spectrometry for the determination of pesticide residues in meat samples. *J. Chromatogr. A*, Vol.1133, pp. 315-321
- Gelsomino, A.; PetroviImage ová, B.; Tiburtini, S.; Magnani, E. & Felici, M. (1997). Multiresidue analysis of pesticides in fruits and vegetables by gel permeation chromatography followed by gas chromatography with electron-capture and mass spectrometric detection. *J. Chromatogr. A*, Vol.782, pp. 105-122
- Gfrerer, M.; Wenzl, T. & Lankmayr, E. (2003). Multi-residue Analysis of 66 Biocides in River Water, River Sediment and Suspended Solids Samples by Gas Chromatography-Mass Spectrometry. *Int. J. Environ. Anal. Chem.*, Vol.83, pp. 111-125
- Ghini, S.; Fernández, M.; Picó, Y.; Marín, R.; Fini, F.; Mañes, J. & Girotti, S. (2004). Occurrence and Distribution of Pesticides in the Province of Bologna, Italy, Using Honeybees as Bioindicators. *Arch. Environ. Con. Tox.*, Vol.47, pp. 479-488
- Gilliom, R.J.B.; Barbash, J.E.; Kolpin, D.W. & Larson, S.J. (1999). Testing water quality for pesticide pollution. *Environ. Sci. Technol.*, Vol.33, pp. 164A-169A
- Goncalves, C. & Alpendurada, M. F. (2004). Solid-phase micro-extraction-gas chromatography-(tandem) mass spectrometry as a tool for pesticide residue analysis in water samples at high sensitivity and selectivity with confirmation capabilities. *J. Chromatogr. A*, Vol.1026, pp. 239-250
- Gonçalves, C. & Alpendurada, M. F. (2005). Assessment of pesticide contamination in soil samples from an intensive horticulture area, using ultrasonic extraction and gas chromatography-mass spectrometry. *Talanta*, Vol.65, pp. 1179-1189
- Gonçalves, C.; Carvalho, J. J.; Azenha, M. A. & Alpendurada, M. F. (2006). Optimization of supercritical fluid extraction of pesticide residues in soil by means of central

- composite design and analysis by gas chromatography–tandem mass spectrometry. *J. Chromatogr. A*, Vol.1110, pp. 6-14
- Gonzalez-Cubelo, M.; Hernandez-Borges, J.; Ravelo-Perez, L. & Rodriguez-Delgado, M. (2011). Insecticides extraction from banana leaves using a modified QuEChERS method. *Food Chem.*, Vol.125, pp. 1083-1090
- Guan, H.; Brewer, W. E. & Morgan, S. L. (2009). New Approach to Multiresidue Pesticide Determination in Foods with High Fat Content Using Disposable Pipette Extraction (DPX) and Gas Chromatography–Mass spectrometry (GC-MS). *J. Agric. Food Chem.*, Vol.57, pp. 10531–10538
- Guan, H.; Brewer, W. E.; Garris, S. T. & Morgan, S. L. (2010). Disposable pipette extraction for the analysis of pesticides in fruit and vegetables using gas chromatography/mass spectrometry. *J. Chromatogr. A*, Vol.1217, pp. 1867-1875
- Guan, S.; Yu, Z.; Y, H.; Song, C.; Song, Z. & Qin, Z. (2011). Multi-Walled Carbon Nanotubes as Matrix Solid-Phase Dispersion Extraction Adsorbent for Simultaneous Analysis of Residues of Nine Organophosphorus Pesticides in Fruit and Vegetables by Rapid Resolution LC-MS-MS. *Chromatographia*, Vol.73, pp. 33-41
- Guardia-Rubio, M.; Fernández-De Córdoba, M. L.; Ayora-Cañada, M. J. & Ruiz-Medina, A. (2006) Simplified pesticide multiresidue analysis in virgin olive oil by gas chromatography with thermoionic specific, electron-capture and mass spectrometric detection. *J. Chromatogr. A*, Vol.1108, pp. 231-239
- Gupta, M.; Pillai, A. K. K. V.; Jain, A. & Verma, K. K. (2008). Coupled in-tube and on-fibre solid-phase microextractions for cleanup and preconcentration of organic micropollutants from aqueous samples and analysis by gas chromatography–mass spectrometry. *Anal. Chim. Acta.*, Vol.618, pp. 61-69
- Haib, J.; Hofer, I. & Renaud, J. M. (2003). Analysis of multiple pesticide residues in tobacco using pressurized liquid extraction, automated solid-phase extraction clean-up and gas chromatography–tandem mass spectrometry. *J. Chromatogr. A*, Vol.1020, pp. 173-187
- Hayama, T.; Yoshida, H.; Todoroki, K.; Nohta, H. & Yamaguchi, M. (2008). Determination of polar organophosphorus pesticides in water samples by hydrophilic interaction liquid chromatography with tandem mass spectrometry. *Rapid Commun. Mass Sp.*, Vol.22, pp. 2203-2210
- Hayward, D. G. & Wong, J. W. (2009). Organohalogen and Organophosphorous Pesticide Method for Ginseng Root – A Comparison of Gas Chromatography-Single Quadrupole Mass Spectrometry with High Resolution Time-of-Flight Mass Spectrometry. *Anal. Chem.*, Vol.81. No.14, pp. 5716–5723
- Hernández, F.; Pitarch, E.; Beltran, J. & López, F. J. (2002). Headspace solid-phase microextraction in combination with gas chromatography and tandem mass spectrometry for the determination of organochlorine and organophosphorus pesticides in whole human blood. *J. Chromatogr. A*, Vol.769, pp. 65-77
- Hernandez, F.; Sancho, J. V. & Pozo, O. J. (2005). Critical review of the application of liquid chromatography /mass spectrometry to the determination of pesticide residues in biological samples. *Anal Bioanal. Chem.*, Vol.382, pp. 934-946
- Hernando, M.D.; Agüera, A.; Fernández-Alba, A. R.; Piedra, L. & Contreras, M. (2001). Gas chromatographic determination of pesticides in vegetable samples by sequential

- positive and negative chemical ionization and tandem mass spectrometric fragmentation using an ion trap analyser. *Analyst*, Vol.126, pp. 46-51
- Hildebrandt, A.; Lacorte, S. & Barceló, D. (2007). Assessment of priority pesticides, degradation products, and pesticide adjuvants in groundwaters and top soils from agricultural areas of the Ebro river basin. *Anal. Bioanal. Chem.*, Vol.387, pp. 1459-1468
- Húšková, R.; Matisová, E.; Hrouzková, S. & Švorc, L. (2009). Analysis of pesticide residues by fast gas chromatography in combination with negative chemical ionization mass spectrometry. *J. Chromatogr. A*, Vol.1216, pp. 6326-6334
- Húšková, R.; Matisová, E.; Švorc, L.; Mocák, J. & Kirchner, M. (2009). Comparison of negative chemical ionization and electron impact ionization in gas chromatography-mass spectrometry of endocrine disrupting pesticides. *J. Chromatogr. A*, Vol.1216, pp. 4927-4932
- Ingelse, B. A.; van Dam, R.; Vreeken, R. J.; Mol, H. & Steijger, O. M. (2001). Determination of polar organophosphorus pesticides in aqueous samples by direct injection using liquid chromatography-tandem mass spectrometry. *J. Chromatogr. A*, Vol.918, pp. 67-78
- Inoue, S.; Saito, T.; Mase, H.; Suzuki, Y.; Takazawa, K.; Yamamoto, I. & Inokucha, S. (2007). Rapid simultaneous determination for organophosphorus pesticides in human serum by LC-MS. *J. Pharmaceut. Biomed.*, Vol.44, pp. 258-264
- Inoue, S.; Saito, T.; Miyazawa, T.; Mase, H. & Inokuchi, S. (2009). A simple method for detecting fenitrothion, its metabolite 3-methyl-4-nitrophenol, and other organophosphorus pesticides in human urine by LC-MS. *Forensic Toxicol.*, Vol.27, pp. 32-36
- International Programme on Chemical Safety (INCHEM). International Programme on Chemical Safety INCHEM Database. (last accessed on 26 February 2010), Available online: <http://www.inchem.org>
- Jansson, C.; Pihlström, T.; Österdahl, B. & Markides, K. E. (2004). A new multi-residue method for analysis of pesticide residues in fruit and vegetables using liquid chromatography with tandem mass spectrometric detection. *J. Chromatogr. A*, Vol.1023, pp. 93-104
- Jenkins, A.L.; Uy, O.M. & Murray, G.M. (1997a). Polymer based lanthanide luminescent sensors for the detection of nerve agents. *Anal. Commun.*, Vol.34, pp. 221-224
- Jenkins, A.L.; Uy, O.M. & Murray, G.M. (1999b). Polymer-based lanthanide luminescent sensor for detection of the hydrolysis product of the nerve agent Soman in water. *Anal. Chem.*, Vol.71, pp. 373-378
- Jenkins, A.L.; Yin, R. & Jensen, J.L. (2001). Molecularly imprinted polymer sensors for pesticide and insecticide detection in water. *Analyst*, Vol.26, pp. 798-802
- Jeong, M. L.; Zahn, M.; Trinh, T.; Brooke, F. A. & Ma, W. (2008). Pesticide residue analysis of a dietary ingredient by gas chromatography/selected-ion monitoring mass spectrometry using neutral alumina solid-phase extraction cleanup.(RESIDUES AND TRACE ELEMENTS)(Report). *J. AOAC Int.*, Vol.91, pp. 630-637
- Jiang, Y.; Li, X.; Xu, J.; Pan, C.; Zhang, J. & Niu, W. (2009). Multiresidue method for the determination of 77 pesticides in wine using QuEChERS sample preparation and gas chromatography with mass spectrometry. *Food Addit. Contam. A*, Vol.26, pp. 859-866

- John, H.; Eddleston, M.; Clutton, R. E.; Worek, F. & Thiermann, H. (2010). Simultaneous quantification of the organophosphorus pesticides dimethoate and omethoate in porcine plasma and urine by LC-ESI-MS/MS and flow-injection-ESI-MS/MS. *J. Chromatogr. B*, Vol.878, pp. 1234-1245
- John, H.; Worek, F. & Thiermann, H. (2008). LC-MS-based procedures for monitoring of toxic organophosphorus compounds and verification of pesticide and nerve agent poisoning. *Anal. Bioanal. Chem.*, Vol.391, pp. 97-116
- Jover, E. & Bayona, J. M. (2002). Trace level determination of organochlorine, organophosphorus and pyrethroid pesticides in lanolin using gel permeation chromatography followed by dual gas chromatography and gas chromatography-negative chemical ionization mass spectrometric confirmation. *J. Chromatogr. A*, Vol.950, pp. 213-220
- Karr, J.R. & Dudley, D.R. (1981). Ecological perspective on water quality goals. *Environ. Manage.* Vol.5, pp. 55-68
- Kim, M. J.; Lee, H. S.; Chung, D. H. & Lee, Y. T. (2003). Synthesis of haptens of organophosphorus pesticides and development of enzyme-linked immunoabsorbent assay for parathion-methyl, *Analytica Chim. Acta*, Vol.493, pp. 47-62
- Kirchner, M.; Húšková, R.; Matisová, E. & Mocák, J. (2008). Fast gas chromatography for pesticide residues analysis using analyte protectants. *J. Chromatogr. A*, Vol.1186, pp.271-280
- Kmellar, B.; Fodor, P.; Pareja, L.; Ferrer, C.; Martinez-Uroz, M. A.; Valverde, A. & Fernandez-Alba, A. R. (2008). Validation and uncertainty study of a comprehensive list of 160 pesticide residues in multi-class vegetables by liquid chromatography-tandem mass spectrometry. *J. Chromatogr. A*, Vol.1215, pp. 37-50
- Ko, H.J. & Park, T.H. (2006). Dual signal transduction mediated by a single type of olfactory receptor expressed in a heterologous system. *Biol. Chem.*, Vol.387, pp. 59-68
- Koal, T.; Asperger, A.; Efer, J. & Engewald, W. (2003). Simultaneous determination of a wide spectrum of pesticides in water by means of fast on-line SPE-HPLC-MS-MS—a novel approach. *Chromatographia*, Vol.57, pp. S93-S101 190
- Kolberg, D. I.; Prestes, O. D.; Adaime, M. B. & Zanella, R. (2010). A new gas chromatography/mass spectrometry (GC-MS) method for the multiresidue analysis of pesticides in bread. *J. Braz. Chem. Soc.*, Vol.21, pp. 1065-1070
- Kolosova, A.Y.; Park, J.H.; Eremin, S.A.; Kang, S.J. & Chung, D. (2003). Fluorescence polarization immunoassay based on a monoclonal antibody for the detection of the organophosphorus pesticide parathion-methyl. *J. Agric. Food Chem.*, Vol.51, pp.1107-1114
- Kolosova, A.Y.; Park, J.H.; Eremin, S.A.; Park, S.J.; Kang, S.J.; Lee, H.S. & Chung, D.H. (2004). Comparative study of three immunoassays based on monoclonal antibodies for detection of the pesticide parathion-methyl in real samples. *Anal. Chim. Acta*, Vol.511, pp. 323-331
- Kristenson, E. M.; Haverkate, E. G. J.; Slooten, C. J.; Ramos, L.; Vreuls, R. J. J. & Brinkman, U. A. (2001). Miniaturized automated matrix solid-phase dispersion extraction of pesticides in fruit followed by gas chromatographic-mass spectrometric analysis. *J. Chromatogr. A*, Vol.917, pp. 277-286

- Kristenson, E. M.; Shahmiri, S.; Slooten, C. J.; Vreuls, R. J. J. & Brinkman, U. A. (2004). Matrix Solid-Phase Dispersion Micro-Extraction of Pesticides from Single Insects with Subsequent GC-MS Analysis. *Chromatographia*, Vol.59, pp. 3156-320
- Kuster, M.; López de Alda, M. J.; Barata, C.; Raldúa, D. & Barceló, D. (2008). Analysis of 17 polar to semi-polar pesticides in the Ebro river delta during the main growing season of rice by automated on-line solid-phase extraction-liquid chromatography-tandem mass spectrometry. *Talanta*, Vol.75, pp. 390-401
- Lacassie, E.; Dreyfuss, M. F.; Gaulier, J. M.; Marquet, P.; Daguet, J. L. & Lachâtre, G. (2001). Multiresidue determination method for organophosphorus pesticides in serum and whole blood by gas chromatography-mass-selective detection. *J. Chromatogr. B*, Vol.759, pp. 109-116
- Lacorte, S. & Barcelo, D. (1995). Determination of organophosphorus pesticides and their transformation products in river waters by automated on-line solid-phase extraction followed by thermospray liquid chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.712, pp. 103-112
- Lambropoulou, D. A. & Albanis, T. A. (2002). Headspace Solid Phase Microextraction Applied to the Analysis of Organophosphorus Insecticides in Strawberry and Cherry Juices. *J. Agric. Food Chem.*, Vol.50, pp. 3359-3365
- Lambropoulou, D. A. & Albanis, T. A. (2003). Headspace solid-phase microextraction in combination with gas chromatography-mass spectrometry for the rapid screening of organophosphorus insecticide residues in strawberries and cherries. *J. Chromatogr. A*, Vol.993, pp. 197-203
- Lambropoulou, D. A.; Psillakis, E.; Albanis, T. A. & Kalogerakis, N. (2004). Single-drop microextraction for the analysis of organophosphorous insecticides in water. *Anal. Chim. Acta*, Vol.516, pp. 205-211
- Lavagnini, I.; Urbani, A. & Magno, F. (2011). Overall calibration procedure via a statistically based matrix-comprehensive approach in the stir bar sorptive extraction-thermal desorption-gas chromatography-mass spectrometry analysis of pesticide residues in fruit-based soft drinks. *Talanta*, Vol.83, pp. 1754-1762
- Lee, E.K.; Kim, Y.J.; Park, W.C.; Chung, T.W. & Lee, Y.T. (2005). Monoclonal antibody-based enzyme-linked immunosorbent assays for the detection of the organophosphorus insecticide diazinon. *Anal. Chim. Acta.*, Vol.530, pp. 143-153
- Lei, Y.; Mulchandani, P.; Wang, J.; Chen, W. & Mulchandani, A. (2005). Highly sensitive and selective amperometric microbial biosensor for direct determination of p-nitrophenyl-substituted organophosphate nerve agents. *Environ. Sci. Technol.*, Vol.39, pp. 8853-8857
- León, V. M.; Álvarez, B.; Cobollo, M. A.; Muñoz, S. & Valor, I. (2003). Analysis of 35 priority semivolatile compounds in water by stir bar sorptive extraction-thermal desorption-gas chromatography-mass spectrometry: I. Method optimization. *J. Chromatogr. A*, Vol.999, pp. 91-101
- León, V. M.; Llorca-Pórcel, J.; Álvarez, B.; Cobollo, M. A.; Muñoz, S. & Valor, I. (2006). Analysis of 35 priority semivolatile compounds in water by stir bar sorptive extraction-thermal desorption-gas chromatography-mass spectrometry: Part II: Method validation. *Anal. Chim. Acta.*, Vol.558, pp. 261-266

- Li, H.; Wei, Y.; You, J. & Lydy, M. J. (2010). Analysis of sediment-associated insecticides using ultrasound assisted microwave extraction and gas chromatography-mass spectrometry. *Talanta*, Vol.83, pp. 171-177
- Lin, J.; Chen, T.; Chen, J. & Chen, Y. (2010). Multilayer gold nanoparticle-assisted thermal desorption ambient mass spectrometry for the analysis of small organics. *Analyst*, Vol.135, pp. 2668-2675
- Ling, T.; Xiaodong, M. & Chongjiu, L. (2006). Application of Gas Chromatography-Tandem Mass Spectrometry (GC-MS-MS) with Pulsed Splitless Injection for the Determination of Multiclass Pesticides in Vegetables. *Anal. Lett.*, Vol.39, pp. 985-996
- Liu, G.L. & Lin, Y. (1995). Electrochemical sensor for organophosphate pesticides and nerve agents using Zirconia nanoparticles as selective Sorbents. *Anal. Chem.*, Vo.77, pp. 5894-5901
- Liu, M.; Hashi, Y.; Song, Y. & Lin, J. (2005). Simultaneous determination of carbamate and organophosphorus pesticides in fruits and vegetables by liquid chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.1097, pp. 183-187
- Liu, S. & Pleil, J. D. (2002). Human blood and environmental media screening method for pesticides and polychlorinated biphenyl compounds using liquid extraction and gas chromatography-mass spectrometry analysis. *J. Chromatogr. B*, Vol.769, pp. 155-167
- Ma, X.; Li, C.; Tao, C.; Liu, W. & Zheng, S. (2001). Multi-residue determination of 41 insecticides in garlic by gas chromatography and ion trap mass spectrometry using the selective ion storage technique. *Rapid Comm. Mass Spec.*, Vol.15, pp. 15-19
- Martinez Salvador, I.; Garrido Frenich, A.; Egea González, F. J. & Martínez Vidal, J. L. (2006). Determination of Organophosphorus Pesticides in Vegetables by GC with Pulsed Flame-Photometric Detection, and Confirmation by MS. *Chromatographia*, Vol.64, No.11-12, pp. 667-672
- Martínez-Mañez, R. & Sancenón, F. (2003). Fluorogenic and chromogenic chemosensors and reagents for anions. *Chem. Rev.*, Vol.103, pp. 4419-4476
- Mastovská, K.; Hajslova, J. & Lehotay, S. J. (2004). Ruggedness and other performance characteristics of low-pressure gas chromatography-mass spectrometry for the fast analysis of multiple pesticide residues in food crops. *J. Chromatogr. A*, Vol.1054, pp. 335-
- Mastovská, K.; Lehotay, S. J. & Lová, J. H. (2001). Optimization and evaluation of low-pressure gas chromatography-mass spectrometry for the fast analysis of multiple pesticide residues in a food commodity. *J. Chromatogr. A*, Vol.926, pp. 291-308
- Matamoros, V.; Jover, E. & Bayona, J. M. (2010). Part-per-Trillion Determination of Pharmaceuticals, Pesticides, and Related Organic Contaminants in River Water by Solid-Phase Extraction Followed by Comprehensive Two-Dimensional Gas Chromatography Time-of-Flight Mass Spectrometry. *Anal. Chem.*, Vol.82, pp. 699-706
- Menezes Filho, A.; Neves dos Santos, F. & Pereira, P. A. (2010). Development, validation and application of a method based on DI-SPME and GC-MS for determination of pesticides of different chemical groups in surface and groundwater samples. *Microchem. J.*, Vol.96, pp. 139-145
- Mezcua, M.; Repetti, M. R.; Agüera, A.; Ferrer, C.; García-Reyes, J. F. & Fernández-Alba, A. R. (2007). Determination of pesticides in milk-based infant formulas by pressurized

- liquid extraction followed by gas chromatography tandem mass spectrometry. *Anal. Bioanal. Chem.*, Vol.389, pp. 1833-1840
- Michel, H.O.; Gordon, E.C. & Epstein, J. (1973). Detection and estimation of isopropyl methylphosphonofluoridate and O-ethyl S-diisopropylaminoethyl methylphosphonothioate in seawater in parts-per-trillion level. *Environ. Sci. Technol.*, Vol.7, pp. 1045-1049
- Mionetto, N.; Marty, J.L. & Karube, I. (1994). Acetylcholinesterase in organic-solvents for the detection of pesticides – Biosensor application. *Biosens. Bioelectr.*, Vol.9, pp. 463-470
- Miranda, K.; Cunha, M. L.; Dores, E. F. & Calheiros, D. F. (2008). Pesticide residues in river sediments from the Pantanal Wetland, Brazil. *J. Environ. Sci. Heal. B*, Vol.43, pp. 717-722
- Mol, H.; van Dam, R. & Steijger, O. (2003). Determination of polar organophosphorus pesticides in vegetables and fruits using liquid chromatography with tandem mass spectrometry: selection of extraction solvent. *J. Chromatogr. A*, Vol.1015, pp. 119-127
- Molina, C.; Honing, M. & Barcelo, D. (1994). Determination of Organophosphorus Pesticides in Water by Solid-Phase Extraction Followed by Liquid-Chromatography/High-Flow Pneumatically Assisted Electrospray Mass Spectrometry. *Anal. Chem.*, Vol.66, pp. 4444-4449
- Moreno, J. L. F.; Liebanas, F. J. A.; Frenich, A. G. & Vidal, J. L. M. (2006). Evaluation of different sample treatments for determining pesticide residues in fat vegetable matrices like avocado by low-pressure gas chromatography-tandem mass spectrometry. *J. Chromatogr. A*, Vol.1111, pp. 97-105
- Na, T.; Fang, Z.; Zhanqi, G.; Ming, Z. & Cheng, S. (2006). The Status of Pesticide Residues in the Drinking Water Sources in Meiliangwan Bay, Taihu Lake of China. *Environ. Monitor. Assess.*, Vol.123, pp. 351-370
- Natangelo, M.; Tavazzi, S.; Fanelli, R. & Benfenati, E. (1999). Analysis of some pesticides in water samples using solid-phase microextraction-gas chromatography with different mass spectrometric techniques. *J. Chromatogr. A*, Vol.859, pp. 193-201
- Ngehngwainbi, J.; Foley, P.H.; Kuan, S.S. & Guilbault, G.G. (1986). Parathion antibodies on piezoelectric crystals. *J. Am. Chem. Soc.*, Vol.108, pp. 5444-5447
- Nguyen, T. D.; Yu, J. E.; Lee, D. M. & Lee, G. H. (2008). A multiresidue method for the determination of 107 pesticides in cabbage and radish using QuEChERS sample preparation method and gas chromatography mass spectrometry. *Food Chem.*, Vol.110, pp. 207-213
- Niessen, W.M.A.; Manini, P. & Andreoli, R. (2006). Matrix effects in quantitative pesticide analysis using liquid chromatography-mass spectrometry. *Mass Spectrom. Rev.*, Vol.25, No.6, pp. 881-899
- Nieuwenhuizen, M.S. & Harteveld, J.L.N. (1997). Studies on a surface acoustic wave (SAW) dosimeter sensor for organophosphorous nerve agents. *Sens. Actuat. B*, Vol.40, pp. 167-173
- Norman, K. N. T. & Panton, S. H. W. (2001). Supercritical fluid extraction and quantitative determination of organophosphorus pesticide residues in wheat and maize using gas chromatography with flame photometric and mass spectrometric detection. *J. Chromatogr. A*, Vol.907, pp. 247-255

- Novak, T.J.; Daasch, L.W. & Epstein, J. (1979). Decomposition at 90 degrees celcius of the cholinesterase substrate indoxyl acetate impregnated on paper supports. *Anal. Chem.*, Vol.51, pp. 1271-1275
- Obare, S. O.; De, C.; Guo, W.; T. A.; Haywood, T. L.; Samuels, T. A.; Adams, C. P.; Masika, N. O.; Murray, D. H.; Anderson, G. A.; Campbell, K. & Fletcher, K. (2010). Fluorescent Chemosensors for Toxic Organophosphorus Pesticides: A Review, *Sensors*, Vol.10, pp. 7018 - 7043
- Ochiai, N.; Sasamoto, K.; Kanda, H. & Nakamura, S. (2006). Fast screening of pesticide multiresidues in aqueous samples by dual stir bar sorptive extraction-thermal desorption-low thermal mass gas chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.1130, pp. 83-90
- Ochiai, N.; Sasamoto, K.; Kanda, H. & Pfannkoch, E. (2008). Sequential stir bar sorptive extraction for uniform enrichment of trace amounts of organic pollutants in water samples. *J. Chromatogr. A*, Vol.1200, pp. 72-79
- Ochiai, N.; Sasamoto, K.; Kanda, H.; Yamagami, T.; David, F.; Tienpont, B. & Sandra, P. (2005). Optimization of a multi-residue screening method for the determination of 85 pesticides in selected food matrices by stir bar sorptive extraction and thermal desorption GC-MS. *J. Sep. Sci.*, Vol.28, pp. 1083-1092
- Olsson, A. O.; Nguyen, J. V.; Sadowski, M. A. & Barr, D. B. (2003). A liquid chromatography/electrospray ionization-tandem mass spectrometry method for quantification of specific organophosphorus pesticide biomarkers in human urine. *Anal. Bioanal. Chem.*, Vol.376, pp. 808-815
- Palleschi, G.; Bernabei, M.; Cremisini, C. & Mascini, N. (1992). Determination of organophosphorus insecticides with a choline electrochemical biosensor. *Sens. Actuat. B*, Vol.7, pp. 513-517
- Pan, J.; Xi, X. & Liang, J. (2008). Analysis of pesticide multi-residues in leafy vegetables by ultrasonic solvent extraction and liquid chromatography-tandem mass spectrometry. *Ultrason. Sonochem.*, Vol.15, pp. 25-32
- Park, M. J.; In, S. W.; Lee, S. K.; Choi, W. K.; Park, Y. S. & Chung, H. S. (2009) Postmortem blood concentrations of organophosphorus pesticides. *Forensic Sci. Int.*, Vol.184, pp. 28-31
- Patil, S. H.; Banerjee, K.; Dasgupta, S.; Oulkar, D. P.; Patil, S. B.; Jadhav, M. R.; Savant, R. H.; Adsule, P. G. & Deshmukh, M. B. (2009). Multiresidue analysis of 83 pesticides and 12 dioxin-like polychlorinated biphenyls in wine by gas chromatography-time-of-flight mass spectrometry. *J. Chromatogr. A*, Vol.1216, pp. 2307-2319
- Patsias, J. & Papadopoulou-Mourkidou, E. (1996). Rapid method for the analysis of a variety of chemical classes of pesticides in surface and ground waters by off-line solid-phase extraction and gas chromatography ion trap mass spectrometry. *J. Chromatogr. A*, Vol.740, pp. 83-98
- Pérez-Carrera, E.; León, V. M. L.; Parra, A. G. & González-Mazo, E. (2007). Simultaneous determination of pesticides, polycyclic aromatic hydrocarbons and polychlorinated biphenyls in seawater and interstitial marine water samples, using stir bar sorptive extraction-thermal desorption-gas chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.1170, pp. 82-90
- Pesticide Action Network (PAN). (n.d.) Pesticide Action Network (PAN) pesticide database. (last accessed on 26 February 2010). Available online:

- <http://www.pesticideinfo.org> 5
- Picó, Y.; Font, G.; Ruiz, M. J. & Fernández, M. (2006). Control of pesticide residues by liquid chromatography-mass spectrometry to ensure food safety. *Mass Spectrom. Rev.*, Vol.25, pp. 917-960
- Pitarch, E.; Medina, C.; Portolés, T.; López, F.J. & Hernández, F. (2007). Determination of priority organic micro-pollutants in water by gas chromatography coupled to triple quadrupole mass spectrometry. *Anal. Chim. Acta*, Vol.583, pp. 246-258
- Plaza Bolaños, P.; Fernández Moreno, J. L.; Shtereva, D. D.; Garrido Frenich, A. & Martínez Vidal, J. L. (2007). Development and validation of a multiresidue method for the analysis of 151 pesticide residues in strawberry by gas chromatography coupled to a triple quadrupole mass analyzer. *Rapid Commun. Mass Sp.*, Vol.21, No.14, pp. 2282-2294
- Plaza Bolaños, P.; Garrido Frenich, A. & Martínez Vidal, J. L. (2007). Application of gas chromatography-triple quadrupole mass spectrometry in the quantification-confirmation of pesticides and polychlorinated biphenyls in eggs at trace levels. *J. Chromatogr. A*, Vol.1167, pp. 9-17
- Portolés, T.; Sancho, J. V.; Hernández, F.; Newton, A. & Hancock, P. (2010). Potential of atmospheric pressure chemical ionization source in GC-QTOF MS for pesticide residue analysis. *J. Mass. Spectrom.*, Vol.45, No.8, pp. 926-936
- Posecion, N.; Ostrea, E.; Bielawski, D.; Corrion, M.; Seagraves, J. & Jin, Y. (2006). Detection of Exposure to Environmental Pesticides During Pregnancy by the Analysis of Maternal Hair Using GC-MS. *Chromatographia*, Vol.64, pp. 681-687
- Profrock, D.; Leonhard, P.; Wilbur, S. & Prange, A. (2004). Sensitive, simultaneous determination of P, S, Cl, Br, and I containing pesticides in environmental samples by FC hyphenated with collision-cell ICP-MS. *J. Anal. At. Spectrom.*, Vol.19, pp. 623-631
- Qu, L.; Zhang, H.; Zhu, J.; Yang, G. & Aboul-Enein, H. (2010). Rapid determination of organophosphorus pesticides in leeks by gas chromatography-triple quadrupole mass spectrometry. *Food Chem.*, Vol.122, pp. 327-332
- Raina, R. & Sun, L. (2008). Trace level determination of selected organophosphorus pesticides and their degradation products in environmental air samples by liquid chromatography-positive ion electrospray tandem mass spectrometry. *J. Environ. Sci. Heal. B*, Vol.43, pp. 323-332
- Ramos, J. J.; Rial-Otero, R.; Ramos, L. & Capelo, J. L. (2008). Ultrasonic-assisted matrix solid-phase dispersion as an improved methodology for the determination of pesticides in fruits. *J. Chromatogr. A*, Vol.1212, pp. 145-149
- Raposo, R.; Barroso, M.; Fonseca, S.; Costa, S.; Queiroz, J. A.; Gallardo, E. & Dias, M. (2010). Determination of eight selected organophosphorus insecticides in postmortem blood samples using solid-phase extraction and gas chromatography/mass spectrometry. *Rapid Commun. Mass Spectrom.*, Vol.24, pp. 3187-3194
- Rawn, D.; Quade, S.; Shields, J.; Conca, G.; Sun, W.; Lacroix, G.; Smith, M.; Fouquet, A. & Bélanger, A. (2006). Organophosphate Levels in Apple Composites and Individual Apples from a Treated Canadian Orchard. *J. Agric. Food Chem.*, Vol.54, No.5, pp. 1943-1948

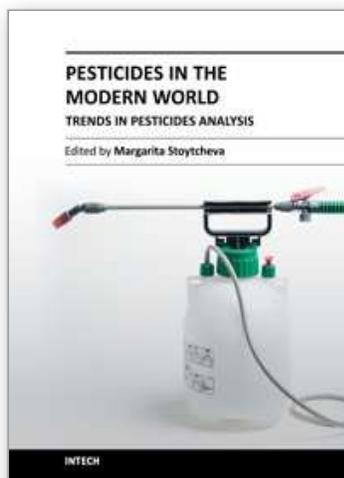
- Riederer, A. M.; Smith, K. D.; Barr, D. B.; Hayden, S. W.; Hunter, R. E. & Ryan, P. B. (2010). Current and Historically Used Pesticides in Residential Soil from 11 Homes in Atlanta, Georgia, USA. *Arch. Environ. Con. Tox.*, Vol.58, pp. 908-917
- Rissato, S. R.; Galhiane, M. S.; Apon, B. M. & Arruda, M. S. P. (2005). Multiresidue Analysis of Pesticides in Soil by Supercritical Fluid Extraction/Gas Chromatography with Electron-Capture Detection and Confirmation by Gas Chromatography–Mass Spectrometry. *J. Agric. Food Chem.*, Vol.53, pp. 62-69
- Rissato, S. R.; Galhiane, M. S.; de Almeida, M. V.; Gerenutti, M. & Apon, B. M. (2007). Multiresidue determination of pesticides in honey samples by gas chromatography–mass spectrometry and application in environmental contamination. *Food Chem.*, Vol.101, pp. 1719-1726
- Rissato, S. R.; Galhiane; M. S.; de Souza, A. G. & Apon, B. M. (2005). Development of a Supercritical Fluid Extraction method for simultaneous determination of organophosphorus, organohalogen, organonitrogen and pyrethroids pesticides in fruit and vegetables and its comparison with a conventional method by GC-ECD and GC-MS. *J. Braz. Chem. Soc.*, Vol.16, pp. 1038-1047
- Rissato, S. R.; Galhiane, M. S.; Knoll, F. R. N. & Apon, B. M. (2004). Supercritical fluid extraction for pesticide multiresidue analysis in honey: determination by gas chromatography with electron-capture and mass spectrometry detection. *J. Chromatogr. A*, Vol.1048, pp. 153-159
- Rodrigues, A. M.; Ferreira V. ; Cardoso, V.V.; Ferreira, E. & Benoliel, M. J. (2007). Determination of several pesticides in water by solid-phase extraction, liquid chromatography and electrospray tandem mass spectrometry. *J. Chromatogr. A*, Vol.1150, pp. 267-278
- Rogers, K.R.; Cao, C.J.; Valdes, J.J.; Elderfrawi, A.T. & Eldefrai, M.E. (1991) Acetylcholinesterase fiber-optic biosensor for detection of anticholinesterases. *Appl. Toxicol.*, Vol.16, pp. 810-820
- Ross, R.T. & Biros, F.J. (1970). Correlations between ³¹P NMR chemical shifts and structures of some organophosphorus pesticides. *Anal. Chim. Acta.*, Vol.52, pp. 139-141
- Rubio, M. G.; Medina, A. R.; Díaz, A. M. & Fernández de Córdoba, M. L. (2006). Determination of pesticides in washing waters of olive processing by gas chromatography-tandem mass spectrometry. *J. Sep. Sci.*, Vol.29, pp. 1578-1586
- Rudzinski, C.M.; Young, A.M. & Nocera, D.G. (2002). A supramolecular microfluidic optical chemosensor. *J. Am. Chem. Soc.*, Vol.124, pp. 1723-1727
- Russell, A.J.; Berberich, J.A.; Drevon, G.E. & Koepsel, R.R. (2003). Biomaterials for mediation of chemical and biological warfare agents. *Annu. Rev. Biomed. Eng.*, Vol.5, pp. 1-27
- Russo, M.V.; Campanella, L. (2002). Avino, P. Determination of organophosphorus pesticide residues in human tissues by capillary gas chromatography–negative chemical ionization mass spectrometry analysis. *J. Chromatogr. B*, Vol.780, pp. 431-441
- Sabik, H.; Rondeau B.; Gagnon, P.; Jeannot, R. & Dohrendorf, K. (2003). Simultaneous Filtration and Solid-Phase Extraction Combined with Large-Volume Injection in GC/MS for Ultra-Trace Analysis of Polar Pesticides in Surface Water. *Int. J. Environ. An. Ch.*, Vol.86, pp. 457-468
- Salm, P.; Taylor, P. J.; Roberts, D. & de Silva, J. (2009). Liquid chromatography–tandem mass spectrometry method for the simultaneous quantitative determination of the

- organophosphorus pesticides dimethoate, fenthion, diazinon and chlorpyrifos in human blood. *J. Chromatogr. B*, Vol.877, No.5-6, pp. 568-574
- Sanchez, A. G.; Martos, N. R. & Ballesteros, E. (2006). Multiresidue analysis of pesticides in olive oil by gel permeation chromatography followed by gas chromatography-tandem mass-spectrometric determination. *Anal. Chim. Acta.*, Vol.558, pp. 53-61
- Sancho, J. V.; Pozo, O. J.; López, F. J. & Hernández, F. (2000). Different quantitation approaches for xenobiotics in human urine samples by liquid chromatography/electrospray tandem mass spectrometry. *Rapid Commun. Mass Spec.*, Vol.14, pp. 1485-1490
- Sasamoto, K.; Ochiai, N. & Kanda, H.(2007). Dual low thermal mass gas chromatography-mass spectrometry for fast dual-column separation of pesticides in complex sample. *Talanta*, Vol.72, pp. 1637-1643
- Schachterle, S. & Feigel, C. (1996). Pesticide residue analysis in fresh produce by gas chromatography-tandem mass spectrometry. *J. Chromatogr. A*, Vol.754, pp. 411-422
- Schellin, M.; Hauser, B. & Popp, P. (2004). Determination of organophosphorus pesticides using membrane-assisted solvent extraction combined with large volume injection-gas chromatography-mass spectrometric detection. *J. Chromatogr. A*, Vol.1040, pp. 251-258
- Schreiber, A.; Efer, J. & Engewald, W. (2000). Application of spectral libraries for high-performance liquid chromatography-atmospheric pressure ionisation mass spectrometry to the analysis of pesticide and explosive residues in environmental samples. *J. Chromatogr. A*, Vol.869, pp. 411-425
- Serôdio, P. & Nogueira, J. M. F. (2004). Multi-residue screening of endocrine disrupters chemicals in water samples by stir bar sorptive extraction-liquid desorption-capillary gas chromatography-mass spectrometry detection. *Anal. Chim. Acta.*, Vol.517, pp. 21-32
- Sharma, D.; Nagpal, A.; Pakade, Y. B. & Kanoria, J. K. (2010). Analytical methods for estimation of organophosphorus pesticide residues in fruits and vegetables: A review. *Talanta*, Vol.82, pp. 1077-1089
- Shen, X.; Cai, J.; Gao, Y. & Su, Q. (2006). Determination of Organophosphorus Pesticides in Soil by MMSPD-GC-NPD and Confirmation by GC-MS. *Chromatographia*, Vol.64, pp. 71-77
- Sherma, J. (1995). Pesticides. *Anal. Chem.*, Vol.67, pp. R1-R20
- Shuling, S.; Xiaodong, M. & Chongjiu, L. (2007a). Multi-residue determination method of pesticides in leek by gel permeation chromatography and solid phase extraction followed by gas chromatography with mass spectrometric detector. *Food Control*, Vol.18, No.5, pp. 448-453
- Shuling, S.; Xiaodong, M. & Chongjiu, L. (2007b). Rapid Multiresidue Determination Method for 100 Pesticides in Vegetables by One Injection Using Gas Chromatography/Mass Spectrometry with Selective Ion Storage Technology. *Anal. Lett.*, Vol.40, pp. 183 - 197
- Simonelli, A.; Basilicata, P.; Miraglia, N.; Castiglia, L.; Guadagni, R.; Acampora, A. & Sannolo, N. (2007). Analytical method validation for the evaluation of cutaneous occupational exposure to different chemical classes of pesticides. *J. Chromatogr. B*, Vol.860, pp. 26-33

- Sinha, S. N.; Bhatnagar, V. K.; Doctor, P.; Toteja, G. S.; Agnihotri, N. P. & Kalra, R. L. (2011). A novel method for pesticide analysis in refined sugar samples using a gas chromatography-mass spectrometer (GC-MS/MS) and simple solvent extraction method. *Food Chem.*, Vol.126, pp. 379-386
- Sinha, S. N.; Vasudev, K.; Rao, M. V. & Odetokun, M. (2011). Quantification of organophosphate insecticides in drinking water in urban areas using lyophilization and high-performance liquid chromatography-electrospray ionization-mass spectrometry techniques. *Int. J. Mass. Spectrom.*, Vol.300, pp. 12-20
- Slobodník, J.; Hogenboom, A. C.; Vreuls, J. J.; Rontree, J. A.; van Baar, B. L. M.; Niessen, W. M. A. & Brinkman, U. A. Th. (1996). Trace-level determination of pesticide residues using on-line solid-phase extraction-column liquid chromatography with atmospheric pressure ionization mass spectrometric and tandem mass spectrometric detection. *J. Chromatogr. A*, Vol.741, pp. 59-74
- Sohn, H.; Letant, S.; Sailor, M.J. & Trogler, W.C. (2000). Detection of fluorophosphonate chemical warfare agents by catalytic hydrolysis with a porous silicon interferometer. *J. Am. Chem. Soc.*, Vol.122, pp. 5399-5400
- Stajnbaher, D. & Zupancic-Kralj, L. (2003). Multiresidue method for determination of 90 pesticides in fresh fruits and vegetables using solid-phase extraction and gas chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.1015, pp. 185-198
- Steiner, W.E.; Klopsch, S.J.; English, W.A.; Clowers, B.H. & Hill, H.H. (2005). Detection of a chemical warfare agent simulant in various aerosol matrixes by ion mobility time-of-flight mass spectrometry. *Anal. Chem.*, Vol.77, pp. 4792-4799
- Stiles, R.; Yang, I.; Lippincott, R. L.; Murphy, E. & Buckley, B. (2008). Measurement of Drinking Water Contaminants by Solid Phase Microextraction Initially Quantified in Source Water Samples by the USGS. *Environ. Sci. Technol.*, Vol.42, pp. 2976-2981
- Sun, X.Y.; Xia, K.H. & Liu, B. (2008). Design of fluorescent self-assembled multilayers and interfacial sensing for organophosphorus pesticides. *Talanta*, Vol.76, pp. 747-751
- Tahboub, Y. R.; Zaater, M. F. & Al-Talla, Z. A. (2005). Determination of the limits of identification and quantitation of selected organochlorine and organophosphorous pesticide residues in surface water by full-scan gas chromatography/mass spectrometry. *J. Chromatogr. A*, Vol.1098, pp. 150-155
- Tang, S.J.; Zhang, M.; Cheng, C.G. & Lu, Y.T. (2008). Development of fluorescence polarization immunoassay for the detection of the organophosphorus pesticides parathion and azinophos-methyl. *J. Immuno. Immunochem.*, Vol.29, pp. 356-369
- Tao, C.; Hu, J.; Li, J.; Zheng, S.; Liu, W. & Li, C. (2009). Multi-Residue Determination of Pesticides in Vegetables by Gas Chromatography/Ion Trap Mass Spectrometry. *B. Environ. Contam. Tox.*, Vol.82, pp. 111-115
- Tarbah, F. A.; Mahler, H.; Temme, O. & Daldrup, T. (2001). An analytical method for the rapid screening of organophosphate pesticides in human biological samples and foodstuffs. *Forensic Sci. Int.*, Vol.121, pp. 126-133
- Titato, G. M.; Bicudo, R. C. & Lanças, F. M. (2007). Optimization of the ESI and APCI experimental variables for the LC/MS determination of s-triazines, methylcarbamates, organophosphorous, benzimidazoles, carboxamide and phenylurea compounds in orange samples. *J. Mass Spectrom.*, Vol.42, pp. 1348-1357
- Toledano, R. M.; Cortés, J. M.; Andini, J. C.; Villén, J. & Vázquez, A. (2010). Large volume injection of water in gas chromatography-mass spectrometry using the Through

- Oven Transfer Adsorption Desorption interface: Application to multiresidue analysis of pesticides. *J. Chromatogr. A*, Vol.1217, pp. 4738-4742
- Trojanowicz, M. (2002). Determination of pesticides using electrochemical enzymatic biosensors. *Electroanalysis*, Vol.14, pp. 1311-1328
- Tsatsakis, A. M.; Tzatzarakis, M. N. & Tutudaki, M. (2008). Pesticide levels in head hair samples of Cretan population as an indicator of present and past exposure. *Forensic. Sci. Int.*, Vol.176, pp. 67-71
- Ullmann's Agrochemicals. Wiley-VCH: Weinheim, Germany, 26 March 2007; Volume 7
- United States Environmental Protection Agency (U.S. EPA). Pesticides and food: Why children may be especially sensitive to pesticides. (n.d.) Available online: <http://www.epa.gov/pesticides/food/pest.htm> (last accessed on February 26, 2010). 3
- United States Geological Survey (U.S.G.S.) Organophosphorus pesticides occurrence and distribution in surface and ground water of the United States. (last accessed on 26 February 2010) Available online: <http://ga.water.usgs.gov/publications/ofr00-187.pdf> 4
- Van Houten, K.A.; Heath, D.C. & Pilato, R.S. (1998). Rapid luminescent detection of phosphate esters in solution and the gas phase using (dppe)Pt{S2C2(2-pyridyl)(CH2CH2OH)}. *J. Am. Chem. Soc.*, Vol.120, pp. 12359-12360
- Vermeire, T.; MacPhail, R. & Waters, M. (2003). Integrated human and ecological assessment: A case study of organophosphorus pesticides in the environment. *Hum. Ecol. Risk Assessment*, Vol.9, pp. 343-357
- Villaverde, J.; Hildebrandt, A.; Martínez, E.; Lacorte, S.; Morillo, E.; Maqueda, C.; Viana, P. & Barceló, D. (2008) Priority pesticides and their degradation products in river sediments from Portugal. *Sci. Total Environ.*, Vol.390, pp. 507-513
- Vonderheide, A. P.; Meija, J.; Montes-Bayón, M. & Caruso, J. A. (2003). Use of optional gas and collision cell for enhanced sensitivity of the organophosphorus pesticides by GC-ICP-MS. *J. Anal. At. Spectrom.*, Vol.18, pp. 1097-1102
- Walker, B.J. (1972). Organophosphorus Chemistry. Penguin, ISBN 0140806474, London, UK
- Wallace, K.J.; Morey, J.; Lynch, V.M. & Anslyn, E.V. (2005). Colorimetric detection of chemical warfare simulants. *New J. Chem.*, Vol.29, pp. 1469-1474
- Wang, S.; Zhao, P.; Min, G. & Fang, G. (2007). Multi-residue determination of pesticides in water using multi-walled carbon nanotubes solid-phase extraction and gas chromatography-mass spectrometry. *J. Chromatogr. A*, Vol.1165, pp. 166-171
- Wong, J. W.; Hennessy, M. K.; Hayward, D. G.; Krynitsky, A. J.; Cassias, I. & Schenck, F. J. (2007). Analysis of Organophosphorus Pesticides in Dried Ground Ginseng Root by Capillary Gas Chromatography–Mass Spectrometry and –Flame Photometric Detection. *J. Agric. Food Chem.*, Vol.55, pp. 1117–1128
- Wong, J. W.; Webster, M. G.; Bezabeh, D. Z.; Hengel, M. J.; Ngim, K. K.; Krynitsky, A. J. & Ebeler, S. E. (2004). Multiresidue Determination of Pesticides in Malt Beverages by Capillary Gas Chromatography with Mass Spectrometry and Selected Ion Monitoring. *J. Agric. Food Chem.*, Vol.52, pp. 6361–6372
- Wong, J. W.; Wirtz, M. S.; Hennessy, M. K. & Schenck, F. J. (2006). Pesticides in Botanical Dietary Supplements. *Acta Hort.*, Vol.720, pp. 113-128
- Wong, J. W.; Zhang, K.; Tech, K.; Hayward, D. G.; Makovi, C. M.; JKrynitsky, A.; Schenck, F. J.; Banerjee, K.; Dasgupta, S. & Brown, D. (2010). Multiresidue Pesticide Analysis in

- Fresh Produce by Capillary Gas Chromatography–Mass Spectrometry/Selective Ion Monitoring (GC-MS/SIM) and –Tandem Mass Spectrometry (GC-MS/MS). *J. Agric. Food Chem.*, Vol.58, pp. 5868–5883
- Wuilloud, R. G.; Shah, M.; Kannamkumarath, S. S. & Altamirano, J. C. (2005). The potential of inductively coupled plasma-mass spectrometric detection for capillary electrophoretic analysis of pesticides. *Electrophoresis*, Vol.26, pp. 1598-1605
- Yagüe, C.; Bayarri, S.; Conchello, P.; Lázaro, R.; Pérez-Arquillué, C.; Herrera, A. & Ariño, A. (2005). Determination of Pesticides and PCBs in Virgin Olive Oil by Multicolumn Solid-Phase Extraction Cleanup Followed by GC-NPD/ECD and Confirmation by Ion-Trap GC–MS. *J. Agric. Food Chem.*, Vol.53, pp. 5105–5109
- Yamaguchi, S.; Yoshimura, L.; Kohira, T.; Tamaru, S. & Hamachi, I. (2005). Cooperation between artificial receptors and supramolecular hydrogels for sensing and discriminating phosphate derivatives. *J. Am. Chem. Soc.*, Vol.127, pp. 11835-11841
- Yang, G.; Xu, X.; Shen, M.; Wang, W.; Xu, L.; Chen, G. & Fu, F. (2009). Determination of organophosphorus pesticides by capillary electrophoresis-inductively coupled plasma mass spectrometry with collective sample-introduction technique. *Electrophoresis*, Vol.30, pp. 1718-1723
- Zambonin, C. G.; Losito, I.; Cilenti, A. & Palmisano, F. (2002). Solid-phase microextraction coupled to gas chromatography-mass spectrometry for the study of soil adsorption coefficients of organophosphorus pesticides. *J. Environ. Monitor.*, Vol.4, pp. 477-481
- Zambonin, C. G.; Quinto, M.; De Vietro, N. & Palmisano, F. (2004). Solid-phase microextraction – gas chromatography mass spectrometry: A fast and simple screening method for the assessment of organophosphorus pesticides residues in wine and fruit juices. *Food Chem.*, Vol.86, pp. 269-274
- Zhang, S.W. & Swager, T.M. (2003). Fluorescent detection of chemical warfare agents: Functional group specific ratiometric chemosensors. *J. Am. Chem. Soc.*, Vol.125, pp. 3420-3421
- Zhang, W.; Chu, X.; Cai, H.; An, J. & Li, C. (2006). Simultaneous determination of 109 pesticides in unpolished rice by a combination of gel permeation chromatography and Florisil column purification, and gas chromatography/mass spectrometry. *Rapid Commun. Mass Sp.*, Vol.20, pp. 609–617
- Zheng, P.; Hu, Y.; Sheng, X.; Zhang, L.; Sun, H. & Sheng, G. (2007). Multiresidue determination of thermolabile insecticides in cereal products by gas chromatography–mass spectrometry: Evaluation with on-column injection and conventional hot splitless injection. *J. Sep. Sci.*, Vol.30, pp. 2719-2726
- Zhou, X.; Wang, M.; Sun, Z.; Li, A.; Xu, L.; Mu, J. & Lu, L. (2007). Multiresidue determination of 77 Pesticides in Textiles by Gas Chromatography-Mass Spectrometry. *J. Chromatogr. Sci.*, Vol.45, pp. 375-399
- Zhu, F.; Ruan, W.; He, M.; Zeng, F.; Luan, T.; Tong, Y.; Lu, T. & Ouyang, G. (2009). Application of solid-phase microextraction for the determination of organophosphorus pesticides in textiles by gas chromatography with mass spectrometry. *Anal. Chim. Acta.*, Vol.650, pp. 202-206
- Zuin, V. G.; Schellin, M.; Montero, L.; Yariwake, J. H.; Augusto, F. & Popp, P. (2006). Comparison of stir bar sorptive extraction and membrane-assisted solvent extraction as enrichment techniques for the determination of pesticide and benzo[a]pyrene residues in Brazilian sugarcane juice. *J. Chromatogr. A*, Vol.1114, No.2, pp. 180-187



Pesticides in the Modern World - Trends in Pesticides Analysis

Edited by Dr. Margarita Stoytcheva

ISBN 978-953-307-437-5

Hard cover, 514 pages

Publisher InTech

Published online 21, October, 2011

Published in print edition October, 2011

The book offers a professional look on the recent achievements and emerging trends in pesticides analysis, including pesticides identification and characterization. The 20 chapters are organized in three sections. The first book section addresses issues associated with pesticides classification, pesticides properties and environmental risks, and pesticides safe management, and provides a general overview on the advanced chromatographic and sensors- and biosensors-based methods for pesticides determination. The second book section is specially devoted to the chromatographic pesticides quantification, including sample preparation. The basic principles of the modern extraction techniques, such as: accelerated solvent extraction, supercritical fluid extraction, microwave assisted extraction, solid phase extraction, solid phase microextraction, matrix solid phase dispersion extraction, cloud point extraction, and QuEChERS are comprehensively described and critically evaluated. The third book section describes some alternative analytical approaches to the conventional methods of pesticides determination. These include voltammetric techniques making use of electrochemical sensors and biosensors, and solid-phase spectrometry combined with flow-injection analysis applying flow-based optosensors.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Tova A. Samuels and Sherine O. Obare (2011). Advances in Analytical Methods for Organophosphorus Pesticide Detection, Pesticides in the Modern World - Trends in Pesticides Analysis, Dr. Margarita Stoytcheva (Ed.), ISBN: 978-953-307-437-5, InTech, Available from: <http://www.intechopen.com/books/pesticides-in-the-modern-world-trends-in-pesticides-analysis/advances-in-analytical-methods-for-organophosphorus-pesticide-detection>

INTECH
open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2011 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen