Chromatographia (2019) 82:1121–1138
https://doi.org/10.1007/s10337-019-03748-3

REVIEW

Solid-Phase Extraction of Glyphosate in the Analyses of Environmental, Plant, and Food Samples

Marilda Rigobello-Masini[1] · Erico A. Oliveira Pereira[1] · Gilberto Abate[2] · Jorge C. Masini[1]

Received: 27 November 2018 / Revised: 16 May 2019 / Accepted: 24 May 2019 / Published online: 5 June 2019

Abstract

This review presents the state of the art concerning the strategies of solid-phase extraction of glyphosate and some of its metabolites in the analysis of environmental (water and soil), plant, and food samples. Glyphosate is the most used broad-spectrum herbicide around the world. As a consequence of this intense use, worries have arisen because of controversial questions regarding the risks glyphosate may pose to human health through dietary exposure, as well as to the equilibrium of ecosystems. Answers to these questions depend on efficient and reliable analytical methodologies that are applicable to monitoring programs. As a result of the complexity of sample matrices (especially soil and vegetable extracts) or the low concentrations of target analytes in natural water samples, solid-phase extraction has been used for either cleaning the extracts or enrichment of the analyte from highly diluted samples. The first part of this review introduces the current issues and controversies surrounding glyphosate, followed by systematic approaches used for its solid-phase extraction. Underivatized glyphosate can be extracted by strong anion exchange, immobilized metal affinity, and sorbents affording molecular recognition properties such as those of immunosorbents and molecular imprinted polymers. The use of new sorbents based on nanostructured materials for extraction of underivatized glyphosate is also addressed. Another approach describes the derivatization of glyphosate with 9-fluorenylmethyloxycarbonyl chloroformate which enables the retention of the product on hydrophobic sorbent phases, again aiming either at cleanup or analyte enrichment. Extraction strategies and the figures of merit of methods used in relevant applications are summarized in tables.

Keywords Glyphosate · Glyphosate metabolites · Liquid chromatography · Extraction · Environmental analysis · Food analysis

Introduction: The Glyphosate Issue

The herbicide glyphosate was introduced in 1974 for weed control in agriculture. It is also used in orchards, as a weed killer in walkways, management of roadside vegetation, in streams to kill aquatic weeds, as a desiccant, and as a ripener for speeding up the maturation of seeds [1]. Glyphosate acts by inhibiting the enzyme 5-enolpyruvylshikimate 3-phosphate synthase (EC 2.5.1.19) in the aromatic amino acid synthesis pathway, present in plants and in some bacteria, thus disrupting the flow of carbon in photosynthesis and several other biochemical routes [1, 2].

Glyphosate was used as a pre-emergence herbicide in traditional agriculture techniques, but after the onset of genetically modified organisms (GMO), it also started to be used in post-emergence control. In 1996, genetically modified plants such as soybean, maize, and cotton, named Roundup Ready plants, were introduced on the market. A gene, isolated from *Agrobacterium* sp., which confers resistance to glyphosate, was inserted in the genome of these plants. Since then, other plants have been modified to resist glyphosate, and owing to the easiness of management, the use of GMO and glyphosate grew at an unprecedented rate in several

Published in the topical collection *Recent Trends in Solid-Phase Extraction for Environmental, Food and Biological Sample Preparation* with guest editors Anna Laura Capriotti, Giorgia La Barbera, and Susy Piovesana.

✉ Jorge C. Masini
jcmasini@iq.usp.br

[1] Departamento de Química Fundamental, Instituto de Química, Universidade de São Paulo, Av. Prof. Lineu Prestes 748, São Paulo, SP 05508-000, Brazil

[2] Departamento de Química, Universidade Federal do Paraná, Centro Politécnico, CP 19032, Curitiba, PR CEP 81531-980, Brazil

countries [3]. The annual global production of glyphosate is about 825,800,000 kg [4].

The onset of weeds tolerant to glyphosate is forcing more intensive herbicide application [5]. Therefore, biotechnology companies are planning to market genetically modified plants tolerant to more than one herbicide. Among them are 2,4-D and Dicamba which can be potentially more dangerous than glyphosate to health and ecosystems [6–8]. Thus, there are risks of turning integrated weed management based on solid ecological principles [9] almost impracticable and of having more and more resistant weeds, with the increase of non-target effects [10].

The risks that glyphosate pose to human health are still the subject of intense debate [11–13]. Because the biochemical pathway inhibited by glyphosate occurs only in plants, there was little concern about the effects of glyphosate on animals. Moreover, initial studies about the effects of glyphosate on health showed almost no harm to animals. Some epidemiological data showed very few statistical correlations between health problems and glyphosate exposure [14, 15]. However, as the use of glyphosate became more widespread, health problems such as cardiovascular abnormalities began to be reported in residents of farm areas where glyphosate was applied to crops [16]. Other studies demonstrated that animals exposed to glyphosate showed increased evidence of carcinogenicity [17, 18]. Currently, there are several data about deleterious effects caused by feeds manufactured with GMOs, and also data reporting problems in aquatic vertebrates, among others [8, 19, 20].

A review by Mesnage et al. [21] showed that glyphosate and its metabolites can be toxic at levels below the regulatory limits. Another complication arises from the impact that simultaneous application of several other herbicides can pose to health and environment [6–8]. Therefore, from the chemical analysis point of view, there are multiple challenges to be overcome when determining the causes of impacts on health and the environment.

Different points of view about glyphosate use and toxicity are causing arguments among researchers and regulatory agencies. Whereas some authors postulate that glyphosate may be the cause of most of the modern western maladies [11, 12], other authors argue that some environmentally directed points of view are also ideologically biased [22].

Regulatory agencies diverge about how glyphosate should be classified in terms of its potential toxicological effects. Since 1974, it has been stated that glyphosate poses no potential harm to mammals. In 1993, the United States Environmental Protection Agency (US EPA) classified glyphosate as a group E carcinogen, meaning no evidence of carcinogenicity [15, 23]. In a recent communication, EPA proposed new herbicide management measures, stating that a final decision on glyphosate registration will be released by the end of 2020 [24, 25]. In 2015, the International Agency for Research on Cancer, by its turn, had classified glyphosate as category 2A, which means that it is probably carcinogenic [26, 27]. Reports from the World Health Organization/Food and Agricultural Organization (WHO/FAO) and European Union (EU) claim that different methodologies in the evaluation of toxicity and possible carcinogenicity may lead to different points of view about glyphosate classification [13, 28, 29].

The maximum concentration levels (MCL) allowed in drinking water also diverge from one regulatory agency to another. For instance, MCL values of 0.10, 65, and 700 μg L^{-1} are the current limits established by the EU, the Brazilian National Environment Council (CONAMA) [30], and US EPA [31], respectively.

As the regulations about glyphosate safety are based on assessment studies performed 30 years ago, these classifications and MCL values must be reviewed because they are failing to protect public health [32]. The technical assessments should be based on the risks posed by each component of commercial glyphosate formulas, as well as all the metabolites that can be released into the environment or accumulated in plants and animal organs, under the application of the herbicide.

The main metabolite of glyphosate metabolism is aminomethylphosphonic acid (AMPA), but other metabolites can be found [26, 27] (Fig. 1). The relative levels of glyphosate (**1**) and AMPA (**2**) can change with the second generation of GMOs. These plants may have genes that code for the enzymes glyphosate oxidase and glyphosate *N*-acetyl transferase (GAT). The first enzyme can convert glyphosate into AMPA and glyoxylate (**3**), thus raising the levels of AMPA and lowering glyphosate levels. The GAT enzyme converts glyphosate into *N*-acetyl glyphosate (**4**) and then to *N*-acetyl AMPA (**5**). Thus, additionally to glyphosate and AMPA, the chemical determination of all these and other potential metabolites (Fig. 1) must be considered in studies about glyphosate toxicity to assess health and environmental risks [28, 33].

Besides, the formulation used influences the absorption of glyphosate by leaves and the adsorption on soils [33, 34]. Several adjuvants (Fig. 2) have been used in glyphosate formulations since the herbicide became commercial. Compounds such as polyoxyethylene amine (POEA, **11**), which is used as a surfactant in Roundup, should also be included in studies of environment and health impacts [4, 36]. Other commercial forms include glyphosate as the isopropylamine (**12**), ammonium, and trimesium salts (**13**). Besides, some impurities such as *N*-(phosphonomethyl)iminodiacetic acid (**14**) and bis(phosphonomethyl)amine (**15**) are likely to be found in formulations. All compounds, metabolites, and adjuvants, once released into the environment, can accumulate and be even more toxic than glyphosate itself to nontarget organisms [37].

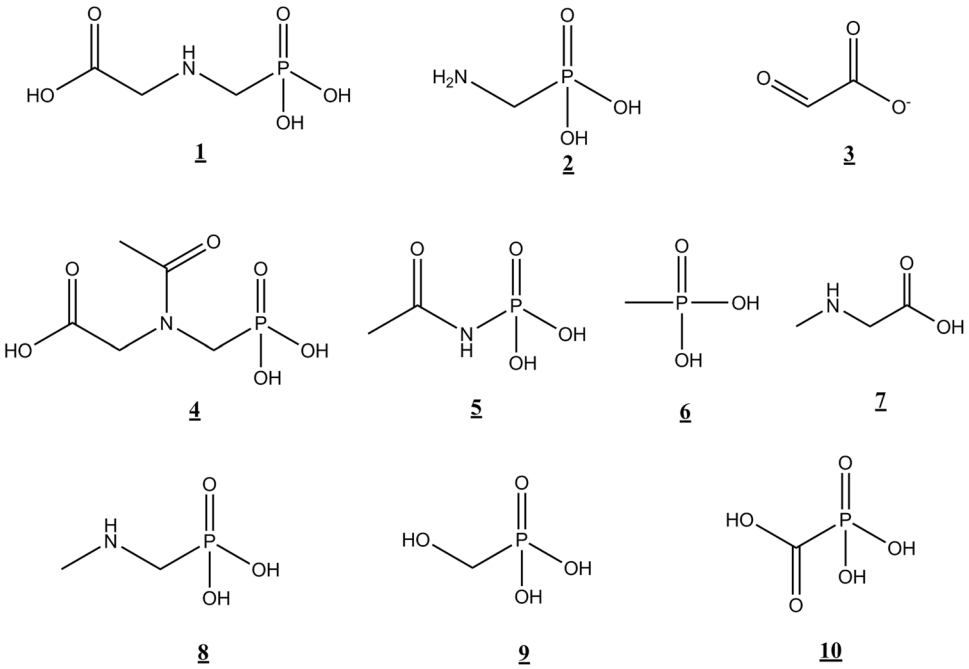

Fig. 1 Structures of glyphosate (**1**) and its metabolites AMPA (**2**), glyoxylate (**3**), *N*-acetyl glyphosate (**4**), *N*-acetyl-AMPA (**5**), methylphosphonic acid (**6**), sarcosine (**7**), *N*-methyl-aminomethyl phosphonic acid (MAMPA) (**8**), hydroxymethyl phosphonic acid (**9**), and phosphonoformic acid (**10**)

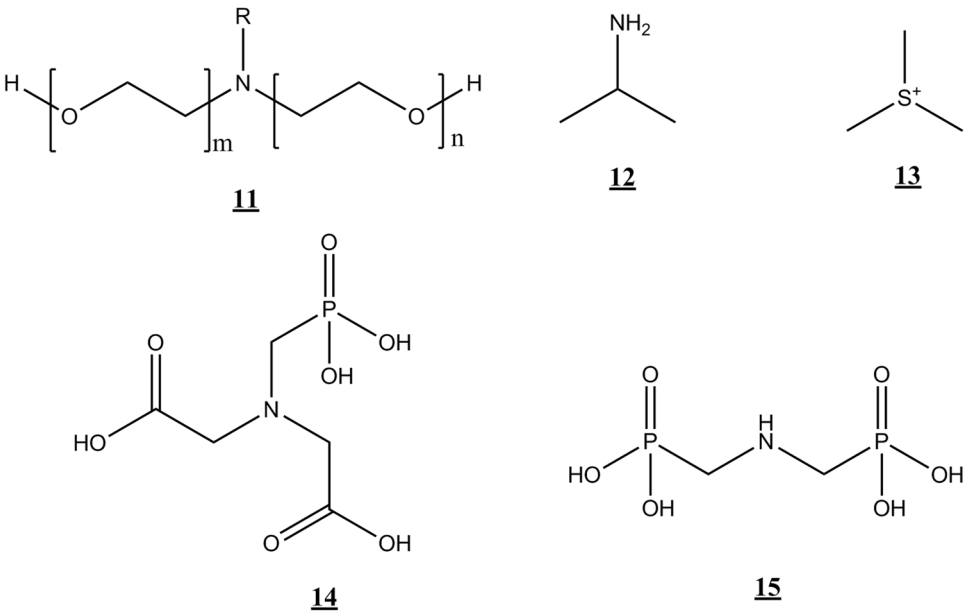

Fig. 2 Some common adjuvants in glyphosate formulations: POEA (**11**), isopropyl amine (**12**), trimethyl sulfonium (**13**), and some contaminants *N*-(phosphonomethyl) iminodiacetic acid (**14**) and bis(phosphonomethyl)amine (**15**)

The 5-year re-approval of glyphosate by the State Members of the EU in 2017 was preceded by intense discussions that arose as a consequence of the poorly understood fate of glyphosate and its metabolites and adjuvants in the environment, as well as their impact on ecosystems and human health [38, 39]. Analytical chemistry plays an important role in answering these questions by providing simple and efficient methodologies for the quantification of glyphosate in environmental samples, food, and biological fluids [38]. This review highlights the challenges imposed by the physicochemical properties of glyphosate on the development of standardized protocols for quantification of glyphosate in the presence of its metabolites, adjuvants, humic substances (co-extracted from soils), metal cations, etc.

Analytical Methods for Quantification of Glyphosate

As a result of the presence of phosphonic, amino, and carboxylic groups in its structure (Fig. 3), glyphosate is an ionic compound (log $K_{OW} = -3.40$), highly soluble in water

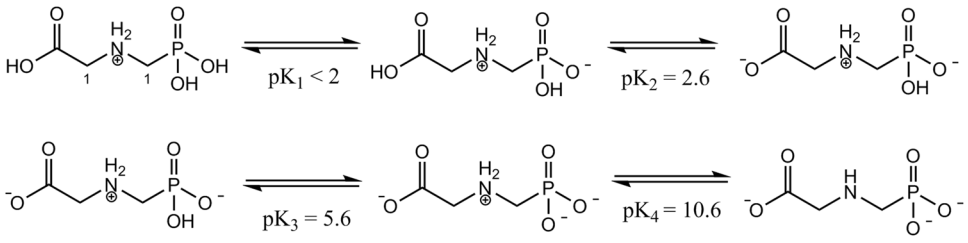

Fig. 3 Ionic forms of glyphosate and the approximate pK_a

(10.5 g L^{-1} at pH 1.9 and 20 °C) [40]. Despite its retention on soils, and its biodegradation into aminomethyl phosphonic acid (AMPA, **2**), glyphosate has been detected in soils and water long after its application, and sometimes far from the application site [41].

Glyphosate is not volatile and lacks chromophore and fluorophore groups, so its detection may require derivatization, as reviewed by Arkan and Molnár-Perl [42]. Gas chromatography methods coupled with mass spectrometers are used after derivatization by simultaneous acylation and esterification or trialkylsilylation to convert the analytes into volatile compounds [43]. Liquid chromatography demands pre- or post-column derivatization to produce fluorescent derivatives and to enhance their retention in hydrophobic stationary phases prior to detection by fluorescence or tandem mass spectrometry. Two more common liquid chromatography methods are based on (1) separation of glyphosate and AMPA by ion-exchange, post-column derivatization with hypochlorite to convert glyphosate into glycine, and downstream reaction of glycine with *o*-phthaldialdehyde (OPA) in 2-mercaptoethanol to produce a detectable indole fluorescent derivative (Fig. 4) [44–48]; and (2) pre-column derivatization with 9-fluorenylmethyloxycarbonyl chloroformate (FMOC-Cl) followed by reversed-phase chromatography and detection by fluorescence or tandem mass spectrometry [49–58] (Fig. 5). The use of either hydrophilic/weak exchange or reversed-phase/weak exchange mixed-mode chromatography without any derivatization, followed by diverse detection techniques including tandem mass spectrometry detection is gaining interest [59–65]. Capillary electrophoresis methods have been reported in recent years using detection systems as varied as contactless conductivity, electrochemiluminescence [60, 61], and laser-induced fluorescence [61, 66], as reviewed by Gauglitz et al. [67].

Solid-Phase Extraction of Glyphosate

Since the first publication describing the use of solid-phase extraction (SPE) for preconcentration purposes [68], many developments were described, and the first extraction cartridges became commercially available in 1978. During the last four decades, extensive progress has been achieved thanks to the impressive developments in materials sciences and nanotechnology, as demonstrated by excellent recent reviews [69–73]. The concentrations of glyphosate

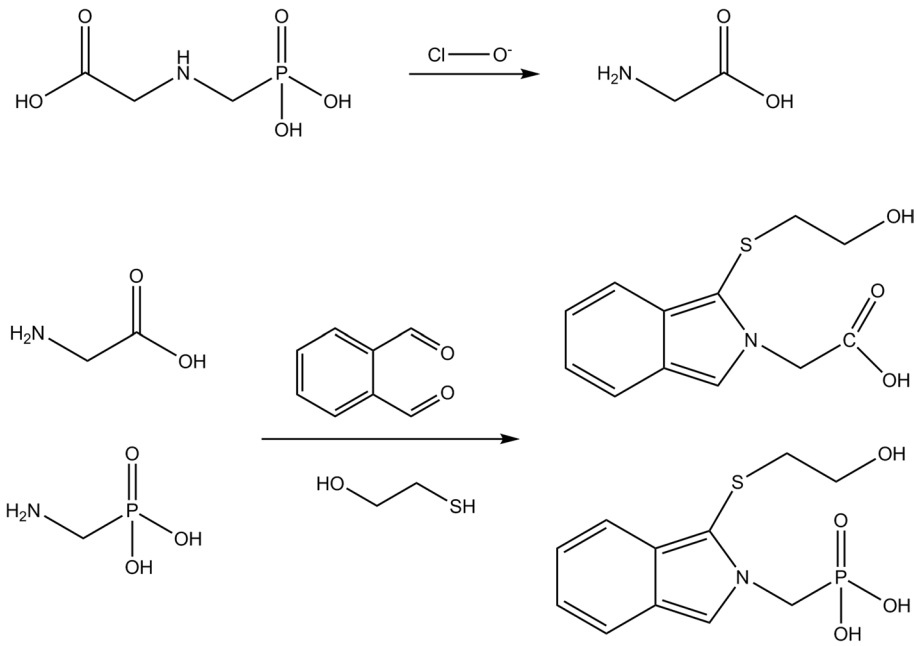

Fig. 4 Derivatization of glyphosate with hypochlorite and OPA in the presence *o*-2-mercaptoethanol

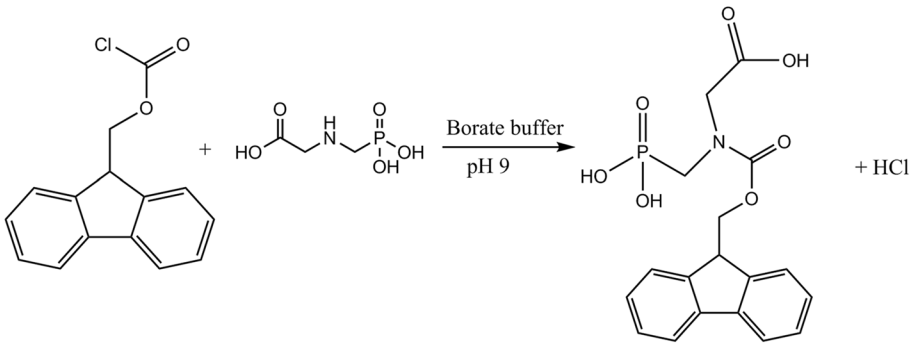

Fig. 5 Reaction of glyphosate with FMOC-Cl

in environmental water is usually low (nanograms per liter) so that preconcentration by either off- or online SPE is mandatory prior to detection.

In the case of soil analysis, the extraction of glyphosate is hampered by the strong interactions of the phosphonate, carboxyl, and amino groups with iron oxides, silica, alumina, and organic matter [74]. The strength of these interactions depends on factors such as pH, metal cations, phosphate from fertilizers, etc. [38]. Extraction is usually performed with either alkaline solutions (KOH or NaOH, aqueous NH_3, triethylamine, sodium tetraborate) [55, 75] or weak acids [65, 76]. Mixed solutions of NH_3 and KH_2PO_4 were proposed by Huang et al. [40]. A difficulty imposed by extraction with strong bases is the co-extraction of humic acids which interfere with the derivatization and suppress the ionization in ESI–MS/MS detectors [55]. Therefore, the extract cleanup in SPE cartridges has been essential for the determination of glyphosate in soils [65].

Another important application of SPE systems is in the determination of glyphosate in foods and plants. Most methods described in the literature adopted water as the extracting solvent [65, 77–81]. However, there are methods that used monosodium phosphate [82], borate buffer [83], and even a mixture of water and dichloromethane [80]. Chamkasem [84] used a mixture of an acidic solution with EDTA for the extraction of glyphosate in grapes. Liao et al. [85] applied mixtures of solvents, deionized water, acidified water, methanol, and dichloromethane for extracting glyphosate and glufosinate from different food samples. The composition of the extracting solutions depended on the water content of the food. Solid-phase extraction in reversed-phase [65, 77, 83, 85], ion-exchange [78, 82], and mixed-mode sorbents [80, 84] has been described. In the case of plant-based materials, the predominant goal is the cleanup of the extract. For instance, Ding et al. proposed a combination of C_{18} and strong anion exchange (SAX) cartridges in which the protein and nonpolar substances, such as lipids, were retained in the C_{18} phase. The solution that passed through the C_{18} was applied to the SAX cartridge which retained glyphosate, thereby separating the analyte from neutral and alkaline substances [81].

To the best of our knowledge, there is no specific review on the applications of SPE for quantification of glyphosate and related compounds in matrices such as environmental water samples, soils, and vegetables. The chemical properties of glyphosate that are exploited for suitable retention and separation in liquid chromatography were used for SPE as well [75]. In some methods, glyphosate is retained by weak or strong anion exchange for enrichment and matrix exchange. In other cases, hydrophobic sorbents (predominantly C_{18}) are used after derivatization of glyphosate (and AMPA) with FMOC-Cl. The presence of phosphonate, amine, and carboxylic groups makes glyphosate and AMPA strong complexing agents [86] so that the principles of immobilized metal affinity chromatography (IMAC) were explored to develop SPE methods using chelating sorbents. Some studies demonstrated the applicability of metal oxides for the selective extraction of glyphosate in soil-like interactions [87]. A special case of SPE is based on hydrophobic-hydrophilic sorbents to retain nonpolar interferences, but not glyphosate, thus performing a sample cleanup prior to the derivatization or chromatographic analysis. Sample cleanup was also performed by using chelating, strong cation exchangers to retain metal ions and mixtures of strong cation and anion exchangers [61, 66, 88].

The current review describes the diverse materials and strategies of SPE with emphasis on ion-exchange or reversed-phase sorbents, IMAC, interactions with metal oxides, and sorbents affording molecular recognition mechanisms, particularly the recent development of molecularly imprinted polymers (MIPs). Some strategies using SPE for the development of sensors is also addressed. Examples of applications to the analysis of environmental samples and vegetables are given in Table 1 (water samples) and 2 (plants and food).

Solid-Phase Extraction on Anion Exchangers

Glyphosate can exist as a zwitterionic molecule (Fig. 3) which can be retained in cation or anion exchangers depending on the pH. Retention in cation exchangers, however,

Table 1 SPE materials and figures of merit for some methods for determination of glyphosate in water samples, denoting if the derivatization was performed before or after the SPE step

Sorbent phase	Matrix	Separation technique	Derivatization	Linearity ($\mu g\ L^{-1}$)	LOD ($\mu g\ L^{-1}$)	LOQ ($\mu g\ L^{-1}$)	RSD (%)	Recovery (%)	References
Amberlite®IR-120[a]	Drinking water	LC–FLD	FMOC-Cl (after)	0.01–0.20	0.012	–	3.3–8.7	98–100	[88]
(Purolite A-510S + Purolite C-100H)[a] Bio-Rad AG1-X8[b]	River water	CE–LIF	Naphthalene-2,3-dicarboxaldehyde/NaCN (after)	0.169–16.9	0.27	–	6.3	103	[66]
LiChrolut EN[a]/Amberlite IRA 410[b]	River water Groundwater	LC–FLD	Hypochlorite/OPA (after)	5.0–200	2.0	–	5–18	83–90	[45]
Amberlite®IRA-900[b] Isolute-NH_2®[b]	River water	LC–FLD	FMOC-Cl (after)	1–200	< 0.1	–	< 12	90–100	[89]
Dowex AG1X8-100[b]	Tap water Filtered water River water	LC–DAD	*p*-Toluenesulfonyl chloride (after)	200–10,000	90	200	13–34	67.1–104	[90]
Gemini-NX C18[b]	Groundwater River water Wastewater	LC–MS/MS	FMOC-Cl (before)	0.01–2.00	–	0.005	< 3.2	91–100	[98]
Strata™-X[b]	Surface water	LC–ESI–MS/MS	FMOC-Cl (before)	–	0.2	–	8.2	79	[54]
Oasis HLB[b]	Runoff water	LC–MS/MS	FMOC-Cl (before)	0.1–500	0.2	0.6	< 6	89–102	[56]
Oasis HLB[b]	Surface water Groundwater	LC–ESI–MS/MS	FMOC-Cl (before)	0.025–5.00	0.005	0.05	< 12	89–106	[50]
IC RP[a]	River water	LC–MS/MS	–	2–200	3.04	–	–	99–103	[65]
Spheron Oxine 1000-Pd(II)[b]	River water Groundwater	LC–UV	FMOC-Cl (before)	–	0.2	–	< 15	80–92	[105]
Magnetic SPE[b]	River water	CE–UV	FMOC-Cl (before)	5.0–1000	4.0	–	1.3–3.2	81.2–106	[107]
Carbon dot magnetic particles[b]	River water	Fluorescence	–	10–80,000	8.0	–	1.22–3.84	94–98.3	[113]
MIPs[b]	Mineral water Groundwater	UPLC–MS/MS	FMOC-Cl (before)	–	–	0.05	12	96	[119]
MIP-SBSE[b]	River water Soil extracts	LC–FLD	FMOC-Cl (before)	0.25–1000	0.140	0.468	< 5	93.3–97.3 90.6–96.7	[121]
(MIP) AFFINIMIP®[b]	Mineral water	UPLC–MS/MS	FMOC-Cl (before)	0.1–0.75	0.01	0.1	–	68	[62]

[a]Cleanup

[b]Enrichment of glyphosate or the derivatized glyphosate

requires an extremely acidic medium, which is not compatible with chemically bonded silica-based materials. Consequently, the majority of SPE methods using ion exchange are based on strong and weak anion exchangers supported on poly(styrene-*co*-divinylbenzene), P(ST-*co*-DVB), or silica [45, 89, 90]. For instance, Corbera et al. [89] compared two strong polymeric anion exchangers based on P(ST-*co*-DVB) (Amberlite® IRA-416 and Amberlite® IRA-900) with a

silica-based weak anion exchanger (Isolute-$NH_2^{®}$) for extraction of glyphosate and AMPA from water samples. All sorbents extracted glyphosate quantitatively, but only Amberlite® IRA-900 also extracted AMPA quantitatively. Enrichment factors of glyphosate in Isolute-NH_2 and Amberlite® IRA-900 were 125 and 17, respectively.

The first paper describing the use of anion exchange to pre-concentrate glyphosate and AMPA was published in 1998 by Mallat and Barceló [45]. The developed methodology was aimed at the determination of trace concentrations of glyphosate and AMPA in water samples and degradation studies. In that method, the filtered samples were first passed through a cleanup polymeric column (LiChrolut EN) to retain polar organic compounds, but not glyphosate and AMPA. In a second SPE step, glyphosate and AMPA were retained in a strong anion exchange sorbent in the hydroxide form (Amberlite IRA 410) and eluted using a 0.40 mol L^{-1} sodium citrate buffer. Since the pH of this solution is around 9.5, glyphosate is in its anionic form (Fig. 3) so that the elution mechanism is the exchange of the retained glyphosate (and AMPA) by citrate. Chromatographic separation was performed by strong cation exchange (SCX) with post-column derivatization with hypochlorite and OPA (Fig. 4), followed by fluorescence detection (Table 1).

Patsias et al. [46] proposed an automated online SPE extraction of glyphosate and AMPA from water samples prior to SCX and fluorescence detection after derivatization with OPA. Ionic components in environmental water samples reduced the recoveries to values as low as 3.2% for glyphosate and 0.5% for AMPA. The issue of low recoveries was circumvented by coupling a cleanup column filled with a 60:40 (w/w) mixture of strong anion and cation exchangers. Glyphosate was completely unretained, whereas 14% of AMPA was retained on this cleanup column. The SPE material contained trimethylammonium immobilized on a P(ST-*co*-DVB) support. Elution was performed with 5 mmol L^{-1} KH_2PO_4 mobile phase acidified to pH 1.9 with H_3PO_4. The cleanup and the SPE increased the recoveries to 83% and 26% for glyphosate and AMPA, respectively.

Immobilized quaternary ammonium functional groups were used for retention of glyphosate and AMPA from several matrixes [66, 79, 91–93]. For instance, the AG1-X8 resins were used by Delmonico et al. [90] and by Jiang and Lucy [66] for off-line preconcentration of glyphosate and AMPA (see Table 1 for figures of merit). Sample loading, especially in the cases of water samples, is performed without any buffering since in these samples the pH range is between 5 and 9, a condition in which glyphosate is anionic (Fig. 3). Elution is performed using mixtures of methanol with HCl [79, 90], HNO_3 [82], or formic acid [92], the last of these attending the volatility requirement of MS detectors.

Strong anion exchangers were also used in passive samplers in aquatic environments and exhibited quantitative retention. However, no release was observed by immersing the membrane in alkaline solutions (NaOH, pH 12) [64], a fact that may be explained by the low specificity of the resin by OH^-, and its low concentration, which probably prevented the exchange of the anionic glyphosate by the OH^-.

Weak anion exchange cartridges were used for retention of glyphosate and AMPA from water samples using trimethylaminopropyl and diethylaminopropyl groups on silica or P(ST-*co*-DVB) supports. The retention of the analytes on these weak exchangers suffered from competition with the ionic contents of the samples so that cleanup in a mixed ion exchanger prior to the SPE was necessary [46]. The choice of the composition of the loading and elution solutions is critical. For instance, loading of glyphosate and AMPA in phosphate buffer at pH 7 may lead to poor recoveries due to the competition for phosphate anions by the protonated amine sites of the sorbent [82].

Strong anion exchangers were used, for instance, by García De Llasera et al. [82] for analysis of tomatoes, by Nagatomi et al. [79] in beer and barley tea, and by Ding et al. [81] in aqueous extracts of corn, carrot, and spicy cabbage (Table 2). The main goal in these cases was the cleanup of the extract and the retention of glyphosate and glyphosate-related compounds on SAX cartridges. These analyses may be preceded by another cleanup in C_{18} or mixed phases containing C_{18} and strong cation exchangers to retain proteins and neutral and basic compounds.

Reversed-Phase Solid-Phase Extraction

Solid-phase extraction in the reversed-phase mode may be used for either sample cleanup or analyte enrichment (Table 1). For sample cleanup, the underivatized sample is passed through the sorbent to retain the nonpolar compounds that can interfere with the derivatization and/or detection [80, 94–96]. If used for preconcentration, derivatization is crucial to enable the retention of the derivatized analyte on the sorbent and elimination of the matrix, as demonstrated by Wang et al. for analysis of seawater [53]. A commonly used protocol for SPE of glyphosate in the reversed-phase mode is illustrated in Fig. 6.

Derivatizations

The reaction of glyphosate with FMOC-Cl (Fig. 5) is the most used pre-column derivatization for SPE on nonpolar sorbents [97] containing either C_{18} functionalities [52, 54, 92, 95, 98, 99] or the hydrophilic/hydrophobic copolymer of divinylbenzene with *N*-vinylpyrrolidone commercialized by Waters Company as OASIS HLB [50, 51, 56, 100]. An innovative approach was proposed by Ghanem et al., exploiting

Table 2 SPE materials and figures of merit for some methods for determination of glyphosate in plants and food samples denoting if the derivatization was performed before or after the SPE step

Sorbent phase	Cereal, fruit, or vegetable	Separation technique	Derivatization	Spike levels	LOD	LOQ	RSD (%)	Recovery (%)	References
C18 bonded silica[b]	Flour	LC–FLD	FMOC-Cl	1–10 mg kg^{-1}	–	0.5 mg kg^{-1}	5.3–17	61.3–99	[77]
C18 bonded silica[b] + SAX[a]	Soybean, corn, carrot, etc.	HILIC–MS/MS	–	0.05, 0.1, and 1.0 mg kg^{-1}	0.005 mg kg^{-1} (corn)	0.02 mg kg^{-1} (all matrices)	< 7	83.1–100.6	[81]
SAX-Cl[b]	Tomato	LC–FLD	FMOC-Cl (after)	0.4–40 µg g^{-1}	0.05 µg g^{-1}	0.08 µg g^{-1}	2–10	87–94	[82]
AG 50 W-X8 (CAX)[b]	Food (various)	LC–MS/MS	FMOC-Cl (after)	0.05–0.5 µg kg^{-1}	–	0.05 mg kg^{-1}	6.7–18.2	80.0–104	[78]
C18[b]	Apple	LC–UV	CNBF[c] (before)	0.1–50 µg g^{-1}	0.01 µg g^{-1}	–	1.43–6.32	86–99.55	[94]
Oasis MCX[b]/InertSep SAX[b]	Malt and corn	LC–MS/MS	–	5–500 µg kg^{-1}	–	10 µg kg^{-1}	3.8–10.2	89.2–97.5	[79]
Oasis HLB[b]	Rice, maize, and soybean	UPLC–MS/MS	–	0.1–20 µg kg^{-1}	≤ 0.12 mg kg^{-1}	≤ 0.4 mg kg^{-1}	1–17	77–100	[80]
Grace Maxi-Clean™ (IC-RP)[b]	Diverse sources	LC–MS/MS	–	0.05–0.5 µg g^{-1}	–	0.05 mg kg^{-1}	2–19	80–86	[65]
C18[b]/SAX[b]	Soybean, corn, carrot, apple, spicy cabbage	LC–MS/MS	–	0.1–1 mg kg^{-1}	≤ 0.008 mg kg^{-1}	≤ 0.026 mg kg^{-1}	1.7–6.1	83.1–100.8	[112]
Oasis HLB[b]	Grape	LC–MS/MS	–	100–2000 ng g^{-1}	6 ng g^{-1}	19 ng g^{-1}	≤6	83−100	[84]
C18[a,b]	Food (various)	LC–MS/MS	FMOC-Cl (before)	5–20 µg kg^{-1}	≤ 2 µg kg^{-1}	5 µg kg^{-1}	3.8–6.1	91−114	[85]
Strata-X[b]/Strata-XA[a]	Beer	UPLC–MS/MS	–	0.2–25 µg kg^{-1}	0.2 µg kg^{-1}	0.5 µg kg^{-1}	1.6–4.1	87–119	[123]

[a]Enrichment glyphosate or derivatized glyphosate

[b]Cleanup

[c]4-Chloro-3,5-dinitrobenzotrifluoride

the retention of glyphosate on strong anion exchange sorbent which was used as solid support for derivatization with FMOC-Cl [101]. The excess of reagent was eluted from the SPE column with a mixture of 0.025 mmol L^{-1} borate buffer (pH 9.2) and acetonitrile (ACN) (50:50), while the derivatized analytes were eluted with a mixture of 1 mol L^{-1} NaCl and ACN (70:30, v/v) to an OASIS HLB cartridge for concentration. This method was applied for the determination of glyphosate and AMPA in sewage sludge by LC–ESI–MS/MS, affording average recoveries of 70 ± 7% for glyphosate at 100 mg kg^{-1} (dry weight) and limit of detection (LOD) 20 µg kg^{-1} (also in dry weight).

The first article reporting the derivatization of glyphosate, aminomethylphosphonic acid, and glufosinate with FMOC-Cl prior to the SPE in an OASIS HLB sorbent was published by Ibáñez et al. in 2005 [50]. Analyses of water and soil samples were performed by SPE coupled online to an LC–ESI–MS/MS system using isotope-labeled glyphosate as the internal standard for quantification. After the unretained compounds were washed out, the FMOC derivatives were eluted from the SPE to the analytical column by a gradient of ACN in 5.0 mmol L^{-1} acetic acid/ammonium acetate buffer (pH 4.8) (Table 1). Recoveries of glyphosate were 89% and 90% for water and soil samples spiked with

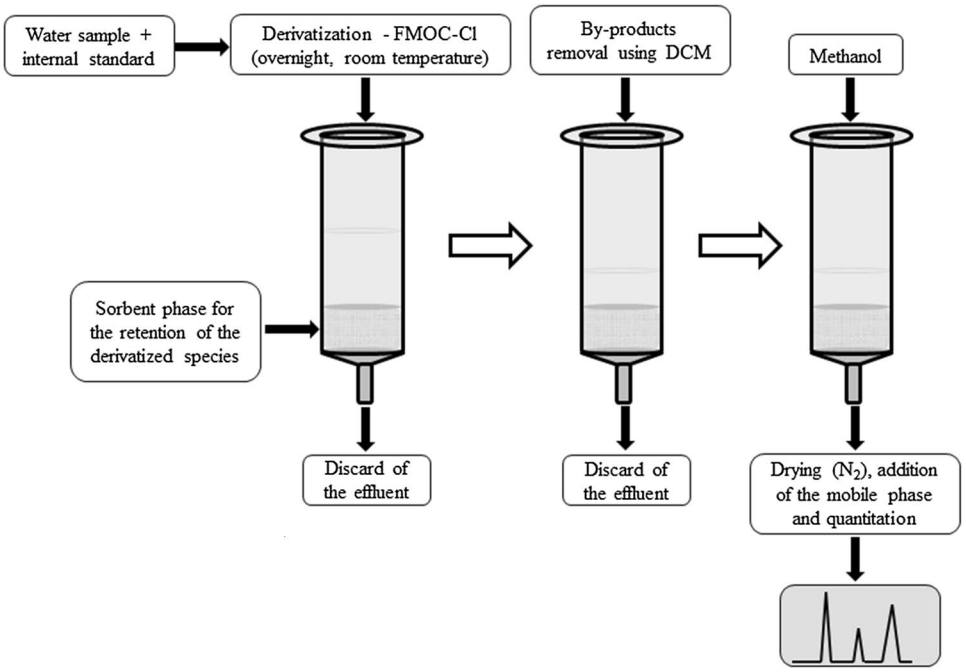

Fig. 6 Procedure commonly adopted for reversed-phase SPE of glyphosate and glyphosate-related compounds

50 ng L^{-1} and 0.05 mg kg^{-1}, respectively. The same research group improved the methodology in 2006 [51], extending its application to ground water samples for which poor recoveries (15%) were observed. This poor recovery was assigned to the formation of strong chelates between glyphosate and metal cations such as Fe^{2+}, Fe^{3+}, Cu^{2+}, and Ca^{2+}, leading to poor yields in the derivatization with FMOC-Cl, as further confirmed by Freuze et al. [86]. To circumvent the chelation effect, the samples were first acidified to pH 1.5 with 6.0 mol L^{-1} HCl and then neutralized to pH 6–7 with 6 mol L^{-1} KOH, buffered with borate, and immediately derivatized with FMOC-Cl. After this procedure, and the online SPE using OASIS-HLB sorbent, the recoveries in groundwater were near 100%. The results suggested that the kinetic of re-complexation is slow, allowing the derivatization with FMOC-Cl to be performed without the interference of glyphosate complexes.

Hanke et al. [52] studied in detail the derivatization of glyphosate with FMOC-Cl and developed a method for the determination of ultra-trace concentrations of glyphosate, AMPA, and glufosinate in natural water samples. Systematic studies on the concentrations of ACN and FMOC-Cl were undertaken since the reagent must be in stoichiometric excess over the amines in the sample. The concentration of ACN used to dissolve the FMOC-Cl reagent should be kept at a minimum to avoid the elution of the FMOC derivatives of the analytes from the C_{18} sorbent (Strata-X from Phenomenex, in this case). The excess of FMOC-Cl and the reaction time may be problematic because the FMOC-OH formed by hydrolysis and decarboxylation of the parent reagent is less water soluble than the derivatized analytes and potentially impairs the chromatographic column as a result of precipitation. Besides, this by-product may decrease the ionization efficiency in the ESI–MS/MS detection. To circumvent this issue, prior to the elution of the target analytes to the analytical column, the FMOC-OH was washed from the SPE column with dichloromethane, which among the studied solvents (hexane, ACN) was the one capable of removing considerable amounts of the by-products without eluting the analytes. The LOD for glyphosate was between 0.2 and 0.5 ng L^{-1} (ground and surface water samples, respectively) with recoveries close to 100%. In this work the authors verified a low recovery in the presence of cations, even performing the acidification of the sample [51, 86]. As the derivatization with FMOC-Cl is performed at pH 9.5 and the reaction times lasts from 30 min to 2 h (overnight in some cases) it is likely that complexes may be formed again. This problem was resolved by adding EDTA after 2 h of derivatization, leading to recoveries of 85% for glyphosate. The method reported by Hanke et al. [52] was further developed and validated for analysis of soils [55, 99].

In water samples rich in natural organic matter, Toss et al. [54] found systematic low recoveries using the original method reported by Hanke et al. [52]. When SPE is used to concentrate glyphosate, undesirable compounds can be concentrated as well, causing matrix effects in the LC–ESI–MS/MS analysis, especially if the stationary phases in both SPE and chromatographic columns are of similar chemical nature. To reach recoveries around 80% using C_{18} stationary phase for SPE (Strata X) and chromatographic separation (Phenomenex Synergi 4u Hydro-RP column), Toss et al. [54] optimized the sample volume loaded in SPE,

the liquid chromatography mobile phase buffer concentration, and pH and the gradient speed. The conditions of pre-column derivatization were systematically studied. It was demonstrated that excess of borate partially decomposes the glyphosate-FMOC derivative so that borate concentration should be kept at a minimum and the SPE cartridge should be properly washed before elution of the analytes and evaporation of the solvent. Optimization of the MS parameters allowed the authors to use isotope-labeled internal standard with just one ^{13}C atom.

In recent work, Poiger et al. [98] investigated the occurrence of glyphosate and AMPA in surface water samples from Switzerland using a miniaturized online SPE method. The samples were first spiked with [$^{13}C_2^{15}N$]glyphosate and [$^{13}C^{15}ND_2$]AMPA (internal standards) and derivatized with FMOC-Cl in borate buffer overnight at room temperature. The excess of reagent, as well as side products (FMOC-OH) and some ACN, was extracted with 2 mL of dichloromethane. The aqueous phase was then injected into two stacked Gemini-NX C18 cartridge columns (4 × 3.0 mm i.d., 5 µm) for the enrichment of the analytes and cleanup of the sample from highly polar components such as the borate buffer. After the enrichment step, the derivatized analytes were eluted back to a Gemini C_{18} column for separation with a linear gradient of methanol. Detection was performed by tandem mass spectrometry and the main figures of merit appear in Table 1.

As previously mentioned, analysis of soils may involve a solid–liquid extraction with strong bases which co-extract humic substances with glyphosate and glyphosate-related compounds. Botero-Coy et al. [96] employed SPE on Oasis HLB cartridges for cleanup of 0.6 mol L^{-1} KOH soil extracts spiked with the isotopically labeled internal standard. For this, the pH was adjusted to 9 with HCl and the solution was passed through the preconditioned SPE cartridge. The eluate was derivatized with FMOC-Cl and the filtered extract was acidified to pH 1.5 and injected (20 µL) into the LC–ESI–MS/MS system. The linearity was between 0.05 and 25 mg kg^{-1}. The LOD and LOQ values were estimated as 0.02 and 0.05 mg kg^{-1}, respectively. Recoveries from soils spiked with 0.5 and 5.0 mg kg^{-1} were between 92% and 107% (5.0 mg kg^{-1}) and between 79% and 117% (0.5 mg kg^{-1}).

To minimize the extraction of humic substances, Todorovic et al. [55] proposed the use of sodium tetraborate. Analysis of the extract was based on the method reported by Hanke et al. [52], adapted for soil, that is, the extract spiked with ^{13}C and ^{15}N isotopically labeled glyphosate and AMPA was derivatized with FMOC-Cl and concentrated on a reversed-phase cartridge before analysis by LC–ESI–MS/MS. The LOD was between 6.8 and 46.5 µg kg^{-1} (for three kinds of soil) with recoveries between 69.9% and 95.7% at the 200 µg kg^{-1} spiking level. De Gerónimo et al. [102] compared the extraction of glyphosate and AMPA from Argentinian soils using phosphate buffer and potassium hydroxide as extractant solutions. To minimize the ionic suppression effects in the tandem mass spectrometry, the most efficient strategy was the treatment of the phosphate extract with dichloromethane to decrease the organic content. The alkaline extract was acidified to pH 9.0 and cleaned up in an OASIS HLB cartridge [96]. Next, the extract was spiked with isotopically labeled glyphosate and derivatized with FMOC-Cl prior to the UPLC–MS/MS analysis. The authors stated that the SPE cleanup was insufficient to remove the interferences, whereas the dilution and the cleanup with dichloromethane were more effective in minimizing the ionic suppression. The insufficient cleanup may be explained by the fact that at pH 9.0 the humic substances are predominantly anionic, as well as glyphosate and AMPA, being thus poorly retained in the OASIS HLB cartridges.

Schrübbers et al. [95] developed a method for determination of glyphosate and AMPA in leaves of *Coffea arabica* based on two-step SPE using Strata X cartridges. In the first step, the SPE was used to retain the nonpolar interferences from the aqueous supernatant obtained after the liquid–liquid extraction step carried out with a mixture of 18 mL H_2O, 2 mL of 1 mol L^{-1} HCl, and 10 mL dichloromethane. The unretained analytes were derivatized with FMOC-Cl and concentrated in another Strata X cartridge. Intriguingly, the sorbent was washed with ACN, and the derivatized analytes were eluted only with methanol in an off-line approach, prior to the LC–MS analysis. The conventional procedure is the washing of the C_{18} cartridge containing the retained FMOC derivatives with acidified water (0.1% formic acid) followed by dichloromethane. The elution is performed usually with methanol, or with 50% methanol adjusted to pH 9.0 with aqueous ammonia [85].

Sample Cleanup Without Derivatization

New stationary phases in LC operating in ion-exchange/reversed-phase or hydrophilic interaction/reversed-phase mixed modes enable the retention and the separation of polar compounds such as glyphosate, AMPA, and glufosinate using mobile phases compatible with ESI–MS/MS, thus avoiding the need for tedious and time-consuming derivatization steps [80, 103]. In this case, the most common procedure is SPE for retention of nonpolar compounds. The unretained compounds are then injected into the LC–ESI–MS/MS system for analysis. This approach was used for the analysis of soybean and corn samples extracted with aqueous Na_2EDTA and acetic acid. The extracts were cleaned up in an OASIS-HLB cartridge and directly injected into a cation/anion exchange mixed-mode column using ammonium formate as the mobile phase [104] (Table 2). A similar

method was applied for the analysis of grapes [84]. In other work, plant-derived foods (soybean, carrot, apple, and spicy cabbage) were extracted with water, and the extracts were loaded into C_{18} cartridges for removal of proteins and weak polar interferences. The unretained compounds were directed to a SAX column for the enrichment of the analytes and removal of basic and neutral substances. After the washing step, the cartridges were eluted with 0.1% (v/v) formic acid in water. The solvent was evaporated, the residue was dissolved in 0.1% formic acid in 10% (v/v) ACN/ water and analyzed by LC–MS/MS using a HILIC/WAX column [81].

Marek and Koskinen [65] proposed a simplified method for the determination of glyphosate and AMPA in water, vegetable, and soils. Extractions with H_3PO_4 prevented the formation of complexes and exploited the competition of phosphate with phosphonate for the adsorption sites of the matrixes, enhancing extraction efficiency, without extracting humic substances in the case of soils and water samples. The extracts were cleaned up in reversed-phase and cation exchange sorbents and directly injected into a tandem mass spectrometer using only a BioRad Cation H guard column to separate glyphosate and AMPA.

Immobilized Metal Affinity Extraction (IMAE)

Sorbent materials relying on the affinity of phosphate and phosphonate groups for metal cations and metal oxides were investigated as potential sorbents for glyphosate. Rios et al. [105] described the first method relying on IMAE for determination of glyphosate and AMPA using a Spheron Oxime 1000 macropore chelating resin onto which Pd(II) was immobilized on the 8-hydroxyquinoline functional groups. Elution was performed with a mixture of 1 mol L^{-1} HCl and 1 mol L^{-1} NaCl. The eluate was analyzed by HPLC with fluorescence detection using FMOC-Cl as a derivatizing reagent.

Inspired in the field of proteomics, where there is a great demand for methods that selectively enrich phosphopeptides and phosphoproteins, Hsu and Whang [60] investigated the use of alumina-coated iron oxide nanoparticles (Fe_3O_4@Al_2O_3 NPs) to develop a microscale method for determination of glyphosate and AMPA in water and guava fruit extracts. The aqueous samples (5 mL) were dispersed in 1 mg of NP and extracted for 5 min by sonication. The NPs were isolated by an external magnet and extracted with 5 µL of 20 mmol L^{-1} $Na_2P_2O_7$ (5 min). The extract was analyzed by CE-electroluminescence. Enrichment factors were 460 and 64 for glyphosate and AMPA, respectively, whereas the LOD values were 0.30 ng mL^{-1} (glyphosate) and 30 (AMPA) ng mL^{-1}. Watanabe et al. [106] used zirconia-based hybrid SPE-phospholipid SPE cartridges to extract glyphosate and other phosphorus-containing amino acid herbicides from serum and urine. The retention is explained by the interactions between Lewis acids and bases, thus being dependent on the pH. In a neutral or acidic medium, the vacant *d*-orbitals of the zirconium atoms act as Lewis acid, coordinating to the electron pairs of the phosphonate Lewis bases. In the SPE protocol, glyphosate is retained at pH around 6.0 and eluted with 0.3% aqueous ammonia.

Magnetic solid-phase extraction with iron oxide nanoparticles immobilized with Ti(IV) having polydopamine (PDA) as bridging molecules [Fe_3O_4@PDA-Ti(VI) NPs] was used for the analysis of water samples [107]. After extraction from 10 mL of sample (5 min) with 2 mg of NPs and elution with 50 µL of Na_3PO_4 (5 min), the analytes were derivatized with FMOC-Cl and quantified by capillary electrophoresis with diode array UV detection, reaching a LOD of 0.4 ng mL^{-1}. In another interesting study, the affinity of glyphosate and AMPA for TiO_2 was exploited in the development of a passive sampler device for a diffusive gradient thin-film technique. This technique enabled the accumulation of the freely dissolved fraction of glyphosate and AMPA in water samples, thus providing potentially useful information to predict their ecotoxicology [108].

Solid-Phase Extraction on Nanostructured Materials

Metal organic frameworks (MOF) are crystalline structures consisting of clusters of metal ions connected by organic linkers. These materials have surface areas that can reach thousands of square meters per gram, making them potentially useful adsorbents. Besides, the chemical nature of the metallic centers and of the organic ligands enables the development of materials highly selective towards the target analyte. For instance, Yang et al. explored the high affinity of phosphate and phosphonates for Zr-OH groups of the MOF known as UiO-67 prepared on graphene oxide for adsorption of glyphosate [109]. In further work, Yang et al. [110] prepared a magnetic UiO-67 for simultaneous adsorption and detection of glyphosate. The authors prepared a material containing a magnetic core of Fe_3O_4 recovered by a SiO_2 shell, wherein the UiO-67 was incorporated via a layer by layer assembly strategy, denoting the final product as Fe_3O_4@SiO_2@UiO-67. In this case, the magnetic core facilitated the separation of the adsorbent from the aqueous phase via application of a magnetic field, whereas the SiO_2 shell impeded the electron transfer between UiO-67 and the magnetic core. The luminescence on the MOF surface was enhanced by glyphosate and the LOD of the proposed method was 0.093 mg L^{-1}. Other compounds with phosphate and phosphonate groups such as dipterex, paraoxon, dichlorvos, malathion, and phoxim did not interfere. The simultaneous extraction and detection approach is quite

interesting and further studies should be undertaken for method validation, which would include the effect of other structurally related compounds such as glufosinate and the glyphosate metabolites AMPA and sarcosine (**7**), as well as the adjuvants of commercial formulations (Fig. 2). Additionally, the effects of major cations (Ca^{2+}, Mg^{2+}, $Fe^{2+/3+}$, Al^{3+}) and naturally occurring organic matter (humic and fulvic acids) are yet to be studied.

New sorbent materials have been developed for the removal of glyphosate and AMPA from wastewater and runoff water. For instance, a polyaniline composite with zeolite ZSM-5 was demonstrated to be an efficient adsorbent for glyphosate, owing to the molecular conformation of both adsorbate and adsorbent, favoring hydrogen bonding between the N and O atoms of glyphosate and the N atoms in polyaniline [111]. Despite the high adsorption capacity of the material (98.5 mg g^{-1}), the reversibility of the adsorption (essential for SPE) was not investigated. Three-dimensional carboxymethyl chitosan (CM-CS)–graphene aerogels (CM-CS@GA) were prepared by Ding et al. [112] through an integration strategy of carboxylation and freeze-drying technology for efficient removal of glyphosate from water. The impressive adsorption capacity of this new material was 578 mg g^{-1}, and the adsorption was reversible, allowing about 30 cycles of adsorption and desorption without a decrease in efficiency. This new material was designed for wastewater treatment, but materials like this, exhibiting high adsorption capacities and recyclability, have potential use as efficient sorbents in SPE.

Solid-Phase Extraction Based on Molecular Recognition

The major drawback of SPE sorbents based on either ion exchange or partition of FMOC derivatives on nonpolar sorbents is the poor selectivity towards glyphosate in the presence of compounds of similar chemical nature (Fig. 1). These compounds can be extracted and eluted together with glyphosate, thus causing interference in the derivatization and detection steps. In some cases, the cleanup is not so efficient, and, in case of preconcentration, despite the large concentration factors, some potential interferences are co-concentrated as well, interfering in either the derivatization or detection. New materials are being developed to afford molecular recognition properties with the aim to increase the specificity towards glyphosate.

Although not yet explored in SPE, highly specific interactions between antibodies and the target analyte (antigens) were used by Wang et al. to develop an immunosorbent for glyphosate antibodies [113]. In this work, carbon dot magnetic particles were used to immobilize the glyphosate antibody for fluorescent visualization of the herbicide distribution in plant tissues. Immunoassays for glyphosate using magnetic particles were used for detection ultra-trace levels of glyphosate in 140 samples of groundwater from Catalonia and the results were confirmed by the online SPE-LC–MS/MS method based on derivatization with FMOC-Cl [52, 114].

Molecularly imprinted polymers (MIPs) are synthetic materials that contain artificially generated recognition sites able to bind a target analyte in preference to other compounds of similar chemical nature [115, 116]. Preparation of MIP involves copolymerization of a complex formed between the template and the functional monomer with a high percentage of cross-linker responsible for the formation of a three-dimensional structure [117, 118]. The polymerization can be initiated by thermal or photoinduced reactions using initiators such as azobisisobutyronitrile (AIBN) and benzophenone, respectively. After the polymerization is completed, the porogenic solvents, unreacted monomers, and the template are washed out, leaving behind a polymer containing cavities with an arrangement of functional groups that can re-bind the template molecule.

The first MIP for glyphosate and AMPA was designed by Puzio et al. [119]. Owing to the high polarity and water solubility of the analytes, the preparation of the MIP was based on templates and functional monomers which favored electrostatic interactions and hydrogen bonds. Thus, phenyl phosphonic acid and diethyl(2-aminobenzyl) phosphonic acid were tested as templates, and 1-allyl-2-thiourea and methacrylic acid were tested as functional monomers in the presence of ethylene glycol dimethacrylate as a cross-linker. Mixtures of ACN or ACN/MeOH were tested as the porogenic solvents. The MIP prepared with 1-allyl-2-thiourea as functional monomer and phenyl phosphonic acid as template displayed a capacity of 0.033 μmol of glyphosate per mg of sorbent (5.6 mg g^{-1}). The cartridges containing 250 mg of MIP were conditioned with deionized water (3 mL), loaded with the sample (15 mL), and eluted with 0.010 mol L^{-1} aqueous ammonia or 0.10 mol L^{-1} HCl. Recoveries from a 5 mg L^{-1} spiked deionized water were greater than 80% for both glyphosate and AMPA in deionized water, but when the matrix was substituted with mineral water the recoveries decreased to roughly 30% for glyphosate and 5% for AMPA. This drawback was partially circumvented by treating the samples with a strong cation exchanger to retain major divalent cations (Ca^{2+} and Mg^{2+}) which are known to form strong complexes with glyphosate and AMPA. Further treatment with anion exchanger or mixed cation/anion exchangers decreased the recovery of glyphosate. Using both cation exchange and the MIP resulted in higher recoveries than using the MIP alone. UPLC–MS/MS analysis of groundwater spiked with 0.50 μg L^{-1} of glyphosate and AMPA revealed quantitative retention of glyphosate, while AMPA was not retained.

Another MIP was prepared by da Mata et al. [120] by using glyphosate as the template, acrylamide as functional monomer, and ethylene glycol dimethacrylate as the cross-linker in a 1:1 mixture of chloroform and DMSO (porogenic solvent) and AIBN as the free radical initiator. The adsorption capacity of the MIP was 3.37 and 4.74 mg g^{-1} glyphosate and AMPA, respectively. The adsorption kinetics was also determined, but the applicability to real samples is still to be proven because selectivity tests towards glyphosate in the presence of chemical species that are likely to occur in environmental samples were not evaluated. Application to real samples and enrichment factors is yet to be demonstrated.

Gomez-Caballero et al. [121] prepared a MIP selective for glyphosate over a stir bar to perform stir bar sorptive extraction (SBSE). The coating was performed by radical polymerization initiated by UV (benzophenone as initiator), using glyphosate as the template, *N*-allylthiourea, and 2-dimethyl aminoethyl methacrylate as functional monomers, and ethylene glycol dimethacrylate as the cross-linker. The mechanical stability of the coating was improved by adding 1,3-divinyltetramethyldisiloxane in the polymerization mixture. SBSE was carried out by immersing the MIP-stir bar in 10 mL of a 10 mmol L^{-1} acetate buffer solution (pH 5) and stirring at 600 rpm for 120 min. The bars were rinsed with deionized water and methanol. Glyphosate was desorbed in 1 mL of 10 mmol L^{-1} NaH_2PO_4, under stirring for 1 h (room temperature). The desorbed compounds were then derivatized with FMOC-Cl and analyzed by HPLC with a fluorescence detector. Excellent selectivity was observed towards glyphosate in the presence of gluphosinate, AMPA, glycine, and sarcosine. The protocol was applied for quantification of glyphosate in river water samples and in 0.6 mol L^{-1} KOH soil extracts. The LOD and LOQ were 0.140 and 0.468 µg L^{-1}, respectively. The recoveries in spiked river water samples (from 1.5 to 600 µg L^{-1}) were between 93.3% and 97.3%. Soils were spiked with 1.5–75 µg g^{-1} glyphosate and the recoveries were between 90.6% and 96.7%. This is an interesting finding since the treatment of soils with 0.6 mol L^{-1} KOH extracts large amounts of humic and humic-like substances. These extracts are often dark and require extensive treatment to isolate the humic substances prior to injecting the sample into the LC system. The high affinity and selectivity of MIP-coated stir bar toward glyphosate provided a simple and efficient approach to circumvent this issue.

MIP technology is becoming mature so that commercial MIPs are currently available for several analytes, including one for both glyphosate and AMPA, marketed as AFFINIMIP® SPE Glyphosate and AMPA by AFFINISEP. According to a paper by Claude et al. [62], in comparison with the MIP prepared by Puzio et al. [119], the commercial MIP was prepared by substituting thiourea with another functional monomer to enhance the electrostatic interactions with the phosphonate groups of both glyphosate and AMPA. The cross-linker ethylene glycol dimethacrylate was substituted with an ionic/hydrophilic monomer to strengthen the interaction with AMPA and to decrease the nonspecific interactions of non-ionic and less polar compounds with the polymer. After the sample was loaded, glyphosate and AMPA were eluted with 0.10 mol L^{-1} HCl. The solution was evaporated, and the residue dissolved in mineral water, derivatized with FMOC-Cl, and analyzed by UPLC–MS/MS. When a 50–100 times concentration factor was adopted, the LODs of glyphosate and AMPA in mineral and ground water samples were 10 ng L^{-1}. The presence of Pb, Cd, and Zn metal ions in the sample matrix did not significantly modify the performance, and mean recoveries of 68% for glyphosate and 82% for AMPA were obtained. This MIP was further favorably evaluated for use in polar organic chemical integrative sampler (POCIS) [122]. This is an interesting finding because the commonly used hydrophilic-lipophilic balanced sorbents used in POCIS have failed to trap glyphosate and AMPA.

Conclusions and Outlook

In this review, we demonstrated that the amphoteric properties of glyphosate and AMPA impose difficulties for their efficient extraction, especially regarding the selectivity. On the other hand, the same amphoteric characteristics offer diverse alternatives to handle the retention/release mechanisms and extraction efficiency. Although the strategies of SPE in either commercial anion exchangers (post-extraction derivatization) or reversed-phase sorbents (pre-extraction derivatization) seem to be well established, some issues related to low recoveries are still observed, demanding the use of matrix-matching strategies and isotopically labeled glyphosate in the case of detection by tandem mass spectrometry. These issues may be explained by the poor selectivity of the commercially available sorbents so that it is difficult to recommend a general protocol which is independent of the sample. Thus, validation for different kinds of samples is required. For instance, water samples with high or low salinities, high or low contents of organic matter, usually require some method development and validation, even using generally recommended protocols. Thus, in recent years we notice a research trend focused on the development of sorbents with molecular recognition abilities for glyphosate and AMPA. In this sense the current and future research will be focused on the development of nanomaterials, metal oxides, immunosorbents, and molecularly imprinted polymers with high specificity to selectively probe glyphosate and its metabolites in the presence of several other compounds with similar properties. Because of the increase in glyphosate-resistant crops, the demand for

monitoring metabolites such as *N*-acetyl glyphosate (**4**) and *N*-acetyl AMPA (**5**) in food and environmental samples will increase. With the currently available methodologies, these compounds are as yet underevaluated.

Acknowledgements The authors are grateful to the National Council for Scientific and Technological Development (Grant # 303940/2017-4).

Compliance with Ethical Standards

Conflict of interest The authors declare that there is no conflict of interest.

Ethical approval This article does not contain any studies performed with humans or animals.

References

1. Boocock MR, Coggins JR (1983) Kinetics of 5-enolpyruvylshikimate-3-phosphate synthase inhibition by glyphosate. FEBS Lett 154:127–133. https://doi.org/10.1016/0014-5793(83)80888-6
2. Haslam E (1993) Shikimate acid: metabolism and metabolites. Wiley, Chichester
3. Duke SO, Powles SB (2008) Glyphosate: a once-in-a-century herbicide. Pest Manag Sci 64:319–325. https://doi.org/10.1002/ps.1518
4. Benbrook CM (2016) Trends in glyphosate herbicide use in the United States and globally. Environ Sci Eur 28:1–15. https://doi.org/10.1186/s12302-016-0070-0
5. Wright TR, Shan G, Walsh TA et al (2010) Robust crop resistance to broadleaf and grass herbicides provided by aryloxyalkanoate dioxygenase transgenes. PNAS 23:20240–20245. https://doi.org/10.1073/pnas.1013154107
6. Mortensen DA, Egan JF, Maxwell BD et al (2012) Navigating a critical juncture for sustainable weed management. Bioscience 62:75–84. https://doi.org/10.1525/bio.2012.62.1.12
7. Cuhra M, Traavik T, Bøhn T (2013) Clone- and age-dependent toxicity of a glyphosate commercial formulation and its active ingredient in *Daphnia magna*. Ecotoxicology 22:251–262. https://doi.org/10.1007/s10646-012-1021-1
8. Cuhra M, Traavik T, Dando M et al (2015) Glyphosate-residues in roundup-ready soybean impair *Daphnia magna* life-cycle. J Agric Chem Environ 4:24–36. https://doi.org/10.4236/jacen.2015.41003
9. Liebman M (2001) Ecological management of agricultural weeds. Cambridge University Press, Cambridge
10. Heap I, Duke SO (2018) Overview of glyphosate-resistant weeds worldwide. Pest Manag Sci 74:1040–1049. https://doi.org/10.1002/ps.4760
11. Samsel A, Seneff S (2013) Glyphosate, pathways to modern diseases II: celiac sprue and gluten intolerance. Interdiscip Toxicol 6:159–184. https://doi.org/10.2478/intox-2013-0026
12. Samsel A, Seneff S (2013) Glyphosate's suppression of cytochrome P450 enzymes and amino acid biosynthesis by the gut microbiome: pathways to modern diseases. Entropy 15:1416–1463. https://doi.org/10.3390/e15041416
13. Tarazona JV, Court-Marques D, Tiramani M et al (2017) Glyphosate toxicity and carcinogenicity: a review of the scientific basis of the European Union assessment and its differences with IARC. Arch Toxicol 91:2723–2743. https://doi.org/10.1007/s00204-017-1962-5
14. Mink PJ, Mandel JS, Sceurman BK, Lundin JI (2012) Epidemiologic studies of glyphosate and cancer: a review. Regul Toxicol Pharmacol 63:440–452. https://doi.org/10.1016/j.yrtph.2012.05.012
15. Greim H, Saltmiras D, Mostert V, Strupp C (2015) Evaluation of carcinogenic potential of the herbicide glyphosate, drawing on tumor incidence data from fourteen chronic/carcinogenicity rodent studies. Crit Rev Toxicol 45:185–208. https://doi.org/10.3109/10408444.2014.1003423
16. Gress S, Lemoine S, Séralini GE, Puddu PE (2015) Glyphosate-based herbicides potently affect cardiovascular system in mammals: review of the literature. Cardiovasc Toxicol 15:117–126. https://doi.org/10.1007/s12012-014-9282-y
17. Guerrero Schimpf M, Milesi MM, Ingaramo PI et al (2017) Neonatal exposure to a glyphosate based herbicide alters the development of the rat uterus. Toxicology 376:2–14. https://doi.org/10.1016/j.tox.2016.06.004
18. Mesnage R, Antoniou MN (2018) Ignoring adjuvant toxicity falsifies the safety profile of commercial pesticides. Front Public Heal 5:1–8. https://doi.org/10.3389/fpubh.2017.00361
19. Cuhra M, Traavik T, Bøhn T (2015) Life cycle fitness differences in *Daphnia magna* fed Roundup-Ready soybean or conventional soybean or organic soybean. Aquac Nutr 21:702–713. https://doi.org/10.1111/anu.12199
20. Bøhn T, Cuhra M, Traavik T et al (2014) Compositional differences in soybeans on the market: glyphosate accumulates in Roundup Ready GM soybeans. Food Chem 153:207–215. https://doi.org/10.1016/j.foodchem.2013.12.054
21. Mesnage R, Defarge N, Spiroux de Vendômois J, Séralini GE (2015) Potential toxic effects of glyphosate and its commercial formulations below regulatory limits. Food Chem Toxicol 84:133–153. https://doi.org/10.1016/j.fct.2015.08.012
22. Faria M (2015) Glyphosate, neurological diseases—and the scientific method. Surg Neurol Int 6:132. https://doi.org/10.4103/2152-7806.162550
23. Williams GM, Aardema M, Acquavella J et al (2016) A review of the carcinogenic potential of glyphosate by four independent expert panels and comparison to the IARC assessment. Crit Rev Toxicol 46:3–20. https://doi.org/10.1080/10408444.2016.1214677
24. United States Environmental Protection Agency (2019) Glyphosate. https://www.epa.gov/ingredients-used-pesticide-products/glyphosate. Accessed May 2019
25. US EPA (2016) Glyphosate issue paper: evaluation of carcinogenic potential EPA's Office of Pesticide Programs. https://www.epa.gov/sites/production/files/2016-09/documents/glyphosate_issue_paper_evaluation_of_carcincogenic_potential.pdf. Accessed May 2019
26. IARC monographs (2015). Evaluation of five organophosphate insecticides and herbicides IARC Monographs Volume 112. https://www.iarc.fr/wp-content/uploads/2018/07/MonographVolume112-1.pdf. Accessed May 2019
27. Davoren MJ, Schiestl RH (2018) Glyphosate-based herbicides and cancer risk: a post-IARC decision review of potential mechanisms, policy and avenues of research. Carcinogenesis 39:1207–1215. https://doi.org/10.1093/carcin/bgy105
28. FAO/WHO (2016) Pesticide residues in food 2016. Issn 2070-2515 2016. Geneva. http://www.fao.org/3/a-i5693e.pdf. Accessed May 2019
29. van Straalen NM, Legler J (2018) Decision-making in a storm of discontent. Science 360:958–960. https://doi.org/10.1126/science.aat0567
30. http://www2.mma.gov.br/port/conama/res/res05/res35705.pdf. Accessed May 2019

31. US EPA (2019) National Primary Drinking Water Regulations. https://www.epa.gov/ground-water-and-drinking-water/national-primary-drinking-water-regulations. Accessed May 2019
32. Vandenberg LN, Blumberg B, Antoniou MN et al (2017) Is it time to reassess current safety standards for glyphosate-based herbicides? J Epidemiol Community Health 71:613–618. https://doi.org/10.1136/jech-2016-208463
33. Van Bruggen AHC, He MM, Shin K et al (2018) Environmental and health effects of the herbicide glyphosate. Sci Total Environ 616–617:255–268. https://doi.org/10.1016/j.scitotenv.2017.10.309
34. Bai SH, Ogbourne SM (2016) Glyphosate: environmental contamination, toxicity and potential risks to human health via food contamination. Environ Sci Pollut Res 23:18988–19001. https://doi.org/10.1007/s11356-016-7425-3
35. Li J, Smeda RJ, Sellers BA, Johnson WG (2005) Influence of formulation and glyphosate salt on absorption and translocation in three annual weeds. Weed Sci 53:153–159. https://doi.org/10.1614/WS-03-075R1
36. Cuhra M, Bohn T, Petr C (2016) Too much of a good thing? Front Environ Sci 4:1–14. https://doi.org/10.3389/fenvs.2016.00028
37. Mesnage R, Bernay B, Séralini GE (2013) Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity. Toxicology 313:122–128. https://doi.org/10.1016/j.tox.2012.09.006
38. Huhn C (2018) More and enhanced glyphosate analysis is needed. Anal Bioanal Chem 410:3041–3045. https://doi.org/10.1007/s00216-018-1000-3
39. Myers JP, Antoniou MN, Blumberg B et al (2016) Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement. Environ Heal A Glob Access Sci Source 15:1–13. https://doi.org/10.1186/s12940-016-0117-0
40. Huang X, Pedersen T, Fischer M et al (2004) Herbicide runoff along highways. 1. Field observations. Environ Sci Technol 38:3263–3271. https://doi.org/10.1021/es034847h
41. Saunders L, Pezeshki R (2015) Glyphosate in runoff waters and in the root-zone: a review. Toxics 3:462–480. https://doi.org/10.3390/toxics3040462
42. Arkan T, Molnár-Perl I (2015) The role of derivatization techniques in the analysis of glyphosate and aminomethyl-phosphonic acid by chromatography. Microchem J 121:99–106. https://doi.org/10.1016/j.microc.2015.02.007
43. Saito T, Miura N, Namera A et al (2012) Mixed-mode C-C18monolithic spin-column extraction and GC-MS for simultaneous assay of organophosphorus compounds, glyphosate, and glufosinate in human serum and urine. Forensic Toxicol 30:1–10. https://doi.org/10.1007/s11419-011-0120-7
44. Abdullah MP, Daud J, Hong KS, Yew CH (1995) Improved method for the determination of glyphosate in water. J Chromatogr A 697:363–369. https://doi.org/10.1016/0021-9673(94)01161-7
45. Mallat E, Barceló D (1998) Analysis and degradation study of glyphosate and of aminomethylphosphonic acid in natural waters by means of polymeric and ion-exchange solid-phase extraction columns followed by ion chromatography-post-column derivatization with fluorescence detection. J Chromatogr A 823:129–136. https://doi.org/10.1016/S0021-9673(98)00362-8
46. Patsias J, Papadopoulou A, Papadopoulou-Mourkidou E (2001) Automated trace level determination of glyphosate and aminomethyl phosphonic acid in water by on-line anion-exchange solid-phase extraction followed by cation-exchange liquid chromatography and post-column derivatization. J Chromatogr A 932:83–90. https://doi.org/10.1016/S0021-9673(01)01253-5
47. de Miranda Colombo S, Masini JC (2014) A sequential-injection reversed-phase chromatography method for fluorimetric determination of glyphosate and aminomethylphosphonic acid. Anal Methods 6:490–496. https://doi.org/10.1039/C3AY41594E
48. Oliveira Pereira EA, Freitas Melo V, Abate G, Masini JC (2019) Determination of glyphosate and aminomethylphosphonic acid by sequential-injection reversed-phase chromatography: method improvements and application in adsorption studies. Anal Bioanal Chem 411:2317–2326. https://doi.org/10.1007/s00216-019-01672-x
49. Druart C, Delhomme O, De Vaufleury A et al (2011) Optimization of extraction procedure and chromatographic separation of glyphosate, glufosinate and aminomethylphosphonic acid in soil. Anal Bioanal Chem 399:1725–1732. https://doi.org/10.1007/s00216-010-4468-z
50. Ibáñez M, Pozo ÓJ, Sancho JV et al (2005) Residue determination of glyphosate, glufosinate and aminomethylphosphonic acid in water and soil samples by liquid chromatography coupled to electrospray tandem mass spectrometry. J Chromatogr A 1081:145–155. https://doi.org/10.1016/j.chroma.2005.05.041
51. Ibáñez M, Pozo ÓJ, Sancho JV et al (2006) Re-evaluation of glyphosate determination in water by liquid chromatography coupled to electrospray tandem mass spectrometry. J Chromatogr A 1134:51–55. https://doi.org/10.1016/j.chroma.2006.07.093
52. Hanke I, Singer H, Hollender J (2008) Ultratrace-level determination of glyphosate, aminomethylphosphonic acid and glufosinate in natural waters by solid-phase extraction followed by liquid chromatography-tandem mass spectrometry: performance tuning of derivatization, enrichment and detection. Anal Bioanal Chem 391:2265–2276. https://doi.org/10.1007/s00216-008-2134-5
53. Wang S, Liu B, Yuan D, Ma J (2016) A simple method for the determination of glyphosate and aminomethylphosphonic acid in seawater matrix with high performance liquid chromatography and fluorescence detection. Talanta 161:700–706. https://doi.org/10.1016/j.talanta.2016.09.023
54. Toss V, Leito I, Yurchenko S et al (2017) Determination of glyphosate in surface water with high organic matter content. Environ Sci Pollut Res 24:7880–7888. https://doi.org/10.1007/s11356-017-8522-7
55. Todorovic GR, Mentler A, Popp M et al (2013) Determination of glyphosate and AMPA in three representative agricultural Austrian soils with a HPLC–MS/MS method. Soil Sediment Contam 22:332–350. https://doi.org/10.1080/15320383.2013.726296
56. Sasal MC, Demonte L, Cislaghi A et al (2015) Glyphosate loss by runoff and its relationship with phosphorus fertilization. J Agric Food Chem 63:4444–4448. https://doi.org/10.1021/jf505533r
57. Fauvelle V, Montero N, Mueller JF et al (2017) Glyphosate and AMPA passive sampling in freshwater using a microporous polyethylene diffusion sampler. Chemosphere 188:241–248. https://doi.org/10.1016/j.chemosphere.2017.08.013
58. Demonte LD, Michlig N, Gaggiotti M et al (2018) Determination of glyphosate, AMPA and glufosinate in dairy farm water from Argentina using a simplified UHPLC–MS/MS method. Sci Total Environ 645:34–43. https://doi.org/10.1016/j.scitotenv.2018.06.340
59. Yoshioka N, Asano M, Kuse A et al (2011) Rapid determination of glyphosate, glufosinate, bialaphos, and their major metabolites in serum by liquid chromatography-tandem mass spectrometry using hydrophilic interaction chromatography. J Chromatogr A 1218:3675–3680. https://doi.org/10.1016/j.chroma.2011.04.021
60. Hsu CC, Whang CW (2009) Microscale solid phase extraction of glyphosate and aminomethylphosphonic acid in water and guava fruit extract using alumina-coated iron oxide nanoparticles followed by capillary electrophoresis and electrochemiluminescence detection. J Chromatogr A 1216:8575–8580. https://doi.org/10.1016/j.chroma.2009.10.023
61. Chuang HY, Hong TP, Whang CW (2013) A simple and rapid screening method for glyphosate in water using flow-injection

with electrochemiluminescence detection. Anal Methods 5:6186–6191. https://doi.org/10.1039/c3ay41059e
62. Claude B, Berho C, Bayoudh S et al (2017) Preliminary recovery study of a commercial molecularly imprinted polymer for the extraction of glyphosate and AMPA in different environmental waters using MS. Environ Sci Pollut Res 24:12293–12300. https://doi.org/10.1007/s11356-017-8844-5
63. Wuilloud RG, Shah M, Kannamkumarath SS, Altamirano JC (2005) The potential of inductively coupled plasma-mass spectrometric detection for capillary electrophoretic analysis of pesticides. Electrophoresis 26:1598–1605. https://doi.org/10.1002/elps.200410098
64. Sánchez-Bayo F, Hyne RV, Desseille KL (2010) An amperometric method for the detection of amitrole, glyphosate and its aminomethyl-phosphonic acid metabolite in environmental waters using passive samplers. Anal Chim Acta 675:125–131. https://doi.org/10.1016/j.aca.2010.07.013
65. Marek LJ, Koskinen WC (2014) Simplified analysis of glyphosate and aminomethylphosphonic acid in water, vegetation and soil by liquid chromatography-tandem mass spectrometry. Pest Manag Sci 70:1158–1164. https://doi.org/10.1002/ps.3684
66. Jiang J, Lucy CA (2007) Determination of glyphosate using off-line ion exchange preconcentration and capillary electrophoresis-laser induced fluorescence detection. Talanta 72:113–118. https://doi.org/10.1016/j.talanta.2006.10.001
67. Gauglitz G, Wimmer B, Melzer T, Huhn C (2018) Glyphosate analysis using sensors and electromigration separation techniques as alternatives to gas or liquid chromatography. Anal Bioanal Chem 410:725–746. https://doi.org/10.1007/s00216-017-0679-x
68. Braus H, Middleton FM, Walton G (1951) Organic chemical compounds in raw and filtered surface waters. Anal Chem 23:1160–1164. https://doi.org/10.1021/ac60056a031
69. Płotka-Wasylka J, Szczepańska N, de la Guardia M, Namieśnik J (2016) Modern trends in solid phase extraction: new sorbent media. TrAC Trends Anal Chem 77:23–43. https://doi.org/10.1016/j.trac.2015.10.010
70. Andrade-Eiroa A, Canle M, Leroy-Cancellieri V, Cerdà V (2016) Solid-phase extraction of organic compounds: a critical review (Part I). TrAC Trends Anal Chem 80:641–654. https://doi.org/10.1016/j.trac.2015.08.015
71. Khezeli T, Daneshfar A (2017) Development of dispersive micro-solid phase extraction based on micro and nano sorbents. TrAC Trends Anal Chem 89:99–118. https://doi.org/10.1016/j.trac.2017.01.004
72. Ansari S (2017) Application of magnetic molecularly imprinted polymer as a versatile and highly selective tool in food and environmental analysis: recent developments and trends. TrAC Trends Anal Chem 90:89–106. https://doi.org/10.1016/j.trac.2017.03.001
73. Azzouz A, Kailasa SK, Lee SS et al (2018) Review of nanomaterials as sorbents in solid-phase extraction for environmental samples. TrAC Trends Anal Chem. https://doi.org/10.1016/J.TRAC.2018.08.009
74. de Colombo SM, Masini JC (2011) Developing a fluorimetric sequential injection methodology to study adsorption/desorption of glyphosate on soil and sediment samples. Microchem J 98:260–266. https://doi.org/10.1016/j.microc.2011.02.009
75. Koskinen WC, Marek LJ, Hall KE (2016) Analysis of glyphosate and aminomethylphosphonic acid in water, plant materials and soil. Pest Manag Sci 72:423–432. https://doi.org/10.1002/ps.4172
76. De Amarante Júnior OP, Dos Santos TCR, Brito NM, Ribeiro ML (2002) Métodos de extração e determinação do herbicida glifosato: breve revisão. Quim Nova 25:420–428. https://doi.org/10.1590/S0100-40422002000300015
77. Hogendoorn EA, Ossendrijver FM, Dijkman E, Baumann RA (1999) Rapid determination of glyphosate in cereal samples by means of pre-column derivatisation with 9-fluorenylmethyl chloroformate and coupled-column liquid chromatography with fluorescence detection. J Chromatogr A 833:67–73. https://doi.org/10.1016/S0021-9673(98)01055-3
78. Li B, Deng X, Guo D, Jin S (2007) Determination of glyphosate and aminomethylphosphonic acid residues in foods using high performance liquid chromatography-mass spectrometry/mass spectrometry. Chin J Chromatogr 25:486–490. https://doi.org/10.1016/S1872-2059(07)60017-0
79. Nagatomi Y, Yoshioka T, Yanagisawa M et al (2013) Simultaneous LC–MS/MS analysis of glyphosate, glufosinate, and their metabolic products in beer, barley tea, and their ingredients. Biosci Biotechnol Biochem 77:2218–2221. https://doi.org/10.1271/bbb.130433
80. Botero-Coy AM, Ibáñez M, Sancho JV, Hernández F (2013) Direct liquid chromatography-tandem mass spectrometry determination of underivatized glyphosate in rice, maize and soybean. J Chromatogr A 1313:157–165. https://doi.org/10.1016/j.chroma.2013.07.037
81. Ding J, Jin G, Jin G et al (2016) Determination of underivatized glyphosate residues in plant-derived food with low matrix effect by solid phase extraction-liquid chromatography-tandem mass spectrometry. Food Anal Methods 9:2856–2863. https://doi.org/10.1007/s12161-016-0468-8
82. García De Llasera MP, Gómez-Almaraz L, Vera-Avila LE, Peña-Alvarez A (2005) Matrix solid-phase dispersion extraction and determination by high-performance liquid chromatography with fluorescence detection of residues of glyphosate and aminomethylphosphonic acid in tomato fruit. J Chromatogr A 1093:139–146. https://doi.org/10.1016/j.chroma.2005.07.063
83. Qian K, Tang T, Shi T et al (2009) Residue determination of glyphosate in environmental water samples with high-performance liquid chromatography and UV detection after derivatization with 4-chloro-3,5-dinitrobenzotrifluoride. Anal Chim Acta 635:222–226. https://doi.org/10.1016/j.aca.2009.01.022
84. Chamkasem N (2017) Determination of glyphosate, maleic hydrazide, fosetyl aluminum, and ethephon in grapes by liquid chromatography/tandem mass spectrometry. J Agric Food Chem 65:7535–7541. https://doi.org/10.1021/acs.jafc.7b02419
85. Liao Y, Berthion JM, Colet I et al (2018) Validation and application of analytical method for glyphosate and glufosinate in foods by liquid chromatography-tandem mass spectrometry. J Chromatogr A 1549:31–38. https://doi.org/10.1016/j.chroma.2018.03.036
86. Freuze I, Jadas-Hecart A, Royer A, Communal PY (2007) Influence of complexation phenomena with multivalent cations on the analysis of glyphosate and aminomethyl phosphonic acid in water. J Chromatogr A 1175:197–206. https://doi.org/10.1016/j.chroma.2007.10.092
87. Nakashima Y, Yamazaki M, Suzuki S, Inoue Y, Kamichatani W, Yamamoto A (2013) Applicability of metal oxides as selective extractant of glyphosate for ion chromatography with a conductometric detector. Bunseki Kagaku 62:349–354. https://doi.org/10.2116/bunsekikagaku.62.349
88. Küsters M, Gerhartz M (2010) Enrichment and low-level determination of glyphosate, aminomethylphosphonic acid and glufosinate in drinking water after cleanup by cation exchange resin. J Sep Sci 33:1139–1146. https://doi.org/10.1002/jssc.200900556
89. Corbera M, Hidalgo M, Salvadó V (2006) Extraction and preconcentration of the herbicide glyphosate and its metabolite AMPA using anion-exchange solid phases. Microchim Acta 153:203–209. https://doi.org/10.1007/s00604-005-0462-0
90. Delmonico EL, Bertozzi J, de Souza NE, Oliveira CC (2014) Determinação de glifosato e ácido aminometilfosfônico para

verificar a qualidade da água de abastecimento público utilizando EFS e CLAE. Acta Sci Technol 36:513–519. https://doi.org/10.4025/actascitechnol.v36i3.22406
91. Wagner R, Wetzel SJ, Kern J, Kingston HMS (2012) Improved sample preparation of glyphosate and methylphosphonic acid by EPA method 6800A and time-of-flight mass spectrometry using novel solid-phase extraction. J Mass Spectrom 47:147–154. https://doi.org/10.1002/jms.2038
92. Wagner RL, Boggess AJ, Wetzel SJ, Kingston HMS (2015) Sensitive and stable pre-calibrated solid phase extraction columns for environmental and forensic quantification using isotope dilution mass spectrometry. Anal Methods 7:4285–4294. https://doi.org/10.1039/C5AY00443H
93. De Abreu ABG, Da Matta MHDR, Montagner É (2008) Desenvolvimento e validação de método de análise de glifosato em grãos de soja. Quim Nova 31:5–9. https://doi.org/10.1590/S0100-40422008000100002
94. Qian K, Tang T, Shi T et al (2009) Solid-phase extraction and residue determination of glyphosate in apple by ion-pairing reverse-phase liquid chromatography with pre-column derivatization. J Sep Sci 32:2394–2400. https://doi.org/10.1002/jssc.200900118
95. Schrübbers LC, Masís-mora M, Carazo E et al (2015) Analysis of glyphosate and aminomethylphosphonic acid in leaves from *Coffea arabica* using high performance liquid chromatography with quadrupole mass spectrometry detection. Talanta 146:1–12. https://doi.org/10.1016/j.talanta.2015.07.059
96. Botero-Coy AM, Ibáñez M, Sancho JV, Hernández F (2013) Improvements in the analytical methodology for the residue determination of the herbicide glyphosate in soils by liquid chromatography coupled to mass spectrometry. J Chromatogr A 1292:132–141. https://doi.org/10.1016/j.chroma.2012.12.007
97. Catrinck TCPG, Dias A, Aguiar MCS et al (2014) A simple and efficient method for derivatization of glyphosate and AMPA using 9-fluorenylmethyl chloroformate and spectrophotometric analysis. J Braz Chem Soc 25:1194–1199. https://doi.org/10.5935/0103-5053.20140096
98. Poiger T, Buerge IJ, Bächli A et al (2017) Occurrence of the herbicide glyphosate and its metabolite AMPA in surface waters in Switzerland determined with on-line solid phase extraction LC–MS/MS. Environ Sci Pollut Res 24:1588–1596. https://doi.org/10.1007/s11356-016-7835-2
99. Daouk S, Grandjean D, Chevre N et al (2013) The herbicide glyphosate and its metabolite AMPA in the Lavaux vineyard area, western Switzerland: proof of widespread export to surface waters. Part I: Method validation in different water matrices. J Environ Sci Heal B 48:717–724. https://doi.org/10.1080/03601234.2013.780535
100. Han J, Moon H, Hong Y et al (2016) Determination of glyphosate and its metabolite in emergency room in Korea. Forensic Sci Int 265:41–46. https://doi.org/10.1016/j.forsciint.2015.12.049
101. Ghanem A, Bados P, Kerhoas L et al (2007) Glyphosate and AMPA analysis in sewage sludge by LC-ESI-MS/MS after FMOC derivatization on strong anion-exchange resin as solid support. Anal Chem 79:3794–3801. https://doi.org/10.1021/ac062195k
102. De Gerónimo E, Lorenzón C, Iwasita B, Costa JL (2018) Evaluation of two extraction methods to determine glyphosate and aminomethylphosphonic acid in soil. Soil Sci. https://doi.org/10.1097/SS.0000000000000225
103. Chen M, Cao Z, Jiang Y, Zhu Z (2013) Direct determination of glyphosate and its major metabolite, aminomethylphosphonic acid, in fruits and vegetables by mixed-mode hydrophilic interaction/weak anion-exchange liquid chromatography coupled with electrospray tandem mass spectrometry. J Chromatogr A 1272:90–99. https://doi.org/10.1016/j.chroma.2012.11.069
104. Chamkasem N, Harmon T (2016) Direct determination of glyphosate, glufosinate, and AMPA in soybean and corn by liquid chromatography/tandem mass spectrometry. Anal Bioanal Chem 408:4995–5004. https://doi.org/10.1007/s00216-016-9597-6
105. Rios C, Salvadó V, Hidalgo M (2004) Preconcentration of the herbicide glyphosate and its metabolite AMPA by immobilised metal ion affinity chromatography (IMAC). J Sep Sci 27:602–606. https://doi.org/10.1002/jssc.200301657
106. Watanabe D, Ohta H, Yamamuro T (2014) Solid-phase extraction of phosphorous-containing amino acid herbicides from biological specimens with a zirconia-coated silica cartridge. J Chromatogr B Anal Technol Biomed Life Sci 969:69–76. https://doi.org/10.1016/j.jchromb.2014.08.004
107. Dong Y, Guo D, Cui H et al (2015) Magnetic solid phase extraction of glyphosate and aminomethylphosphonic acid in river water using Ti^{4+} -immobilized Fe_3O_4 nanoparticles by capillary electrophoresis. Anal Methods 7:5862–5868. https://doi.org/10.1039/C5AY00109A
108. Fauvelle V, Feret T, Madarassou K, Mazzella N (2015) Evaluation of titanium dioxide as a binding phase for the passive sampling of glyphosate and aminomethyl phosphonic acid in an aquatic environment. Anal Chem 87:6004–6009. https://doi.org/10.1021/acs.analchem.5b00194
109. Yang Q, Wang J, Zhang W et al (2017) Interface engineering of metal organic framework on graphene oxide with enhanced adsorption capacity for organophosphorus pesticide. Chem Eng J 313:19–26. https://doi.org/10.1016/j.cej.2016.12.041
110. Yang Q, Wang J, Chen X et al (2018) The simultaneous detection and removal of organophosphorus pesticides by a novel Zr-MOF based smart adsorbent. J Mater Chem A 6:2184–2192. https://doi.org/10.1039/c7ta08399h
111. Milojević-Rakić M, Janošević A, Krstić J et al (2013) Polyaniline and its composites with zeolite ZSM-5 for efficient removal of glyphosate from aqueous solution. Microporous Mesoporous Mater 180:141–155. https://doi.org/10.1016/j.micromeso.2013.06.025
112. Ding C, Wang AX, Liu AH et al (2018) Glyphosate removal from water by functional three-dimensional graphene aerogels. Environ Chem 15:325–335. https://doi.org/10.1071/EN18087
113. Wang D, Lin B, Cao Y et al (2016) A highly selective and sensitive fluorescence detection method of glyphosate based on an immune reaction strategy of carbon dot labeled antibody and antigen magnetic beads. J Agric Food Chem 64:6042–6050. https://doi.org/10.1021/acs.jafc.6b01088
114. Sanchís J, Kantiani L, Llorca M et al (2012) Determination of glyphosate in groundwater samples using an ultrasensitive immunoassay and confirmation by on-line solid-phase extraction followed by liquid chromatography coupled to tandem mass spectrometry. Anal Bioanal Chem 402:2335–2345. https://doi.org/10.1007/s00216-011-5541-y
115. Ansell RJ, Ramström O, Mosbach K (1996) Towards artificial antibodies prepared by molecular imprinting. Clin Chem 42:1506–1512
116. Kempe M (1996) Antibody-mimicking polymers as chiral stationary phases in HPLC. Anal Chem 68:1948–1953. https://doi.org/10.1021/ac9512160
117. Zheng C, Huang YP, Liu ZS (2013) Synthesis and theoretical study of molecularly imprinted monoliths for HPLC. Anal Bioanal Chem 405:2147–2161. https://doi.org/10.1007/s00216-012-6639-6
118. Saloni J, Walker K, Hill G (2013) Theoretical investigation on monomer and solvent selection for molecular imprinting of nitrocompounds. J Phys Chem A 117:1531–1534. https://doi.org/10.1021/jp2124839
119. Puzio K, Claude B, Amalric L et al (2014) Molecularly imprinted polymer dedicated to the extraction of glyphosate in natural

waters. J Chromatogr A 1361:1–8. https://doi.org/10.1016/j.chroma.2014.07.043
120. Da Mata K, Corazza MZ, De Oliveira FM et al (2014) Synthesis and characterization of cross-linked molecularly imprinted polyacrylamide for the extraction/preconcentration of glyphosate and aminomethylphosphonic acid from water samples. React Funct Polym 83:76–83. https://doi.org/10.1016/j.reactfunctpolym.2014.07.004
121. Gomez-Caballero A, Diaz-Diaz G, Bengoetxea O et al (2016) Water compatible stir-bar devices imprinted with underivatised glyphosate for selective sample clean-up. J Chromatogr A 1451:23–32. https://doi.org/10.1016/j.chroma.2016.05.017
122. Berho C, Claude B, Coisy E et al (2017) Laboratory calibration of a POCIS-like sampler based on molecularly imprinted polymers for glyphosate and AMPA sampling in water. Anal Bioanal Chem 409:2029–2035. https://doi.org/10.1007/s00216-016-0150-4
123. Jansons M, Pugajeva I, Bartkevičs V (2018) Occurrence of glyphosate in beer from the Latvian market. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 35:1767–1775. https://doi.org/10.1080/19440049.2018.1469051