Two novel strategies in food sample preparation for the analysis of dietary polyphenols: micro-extraction techniques and new silica-based sorbent materials

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A B S T R A C T

Background: The multiple health promoting effects associated with the consumption of dietary polyphenols have increased research interest in recent years to develop advanced and environmentally friendly analytical approaches for correctly identify and quantify these compounds in different foodstuffs. However, food samples are highly complex matrices, what hinders determination of these compounds, which additionally, are usually found in food at low concentration levels, therefore a preliminary sample preparation method which provides adequate isolation and enrichment of analytes, as well as effective clean-up from matrices interferences, is often required prior to further analysis.

Scope and approach: Current trends in sample preparation involves moving towards cheaper, cost-effective and more environmentally friendly procedures, by minimizing the number of steps and reducing the consumption of sample and organic solvents, replacing toxic solvents by non-toxic ones, and improving extraction efficiency and selectivity with the application of new advanced sorbents materials and micro-extraction techniques that overcome limitations of conventional sample preparation methods.

Key findings and conclusions: This review provides an overview of the most relevant achievements and improvements in sample preparation and extraction methodologies applied for the determination of dietary polyphenols in food products, regarding the preparation of novel silica-based sorbent materials and the development of new micro-extraction methodologies, giving some recent examples from the last five years. The review gives an updated overview that emphasizes the new developments achieved, providing a broad view of the current trends and the future perspectives in the analysis of dietary polyphenols and expanding knowledge related to food quality.

Keywords: Bi-functionalized mesostructured silicas, reversed-phase/strong anion exchange sorbents, mixed-mode, polyphenols, dispersive solid-phase extraction, Ultra-high performance liquid chromatography coupled to mass spectrometry

Contents

1. Introduction

Over the last years, one of the most important trends that has aroused great interest in the food industry, in order to provide customers with a healthy and balanced diet, has been the extraction and concentration of bioactive compounds obtained from foodstuffs. Bioactive compounds are natural constituents in food that typically occur in small quantities and provide health benefits beyond the basic nutritional value of the product (Biesalski et al., 2009). In this sense, the vegetable kingdom is a primary source of bioactive compounds with potential health benefits, and among them, polyphenols have proven to possess a large number of health-promoting benefits (Scalbert et al., 2005; del Río et al., 2013; Liu 2013). Their probable effect in the prevention of several diseases, the evidences of their antioxidant potential, their great abundance in our diet and their influence on sensory properties of food products, have promoted in recent years the interest in developing analytical approaches that allow identifying and quantifying correctly these compounds in foodstuffs

Nevertheless, food samples are highly complex matrices, since they contain a large number of components of different nature with different chemical properties, which differ in polarity and size. Additionally, polyphenols are usually found at low concentration levels, therefore, the extraction and purification of these compounds from foodstuffs constitutes a tough challenge (La Barbera et al., 2017). Moreover, in most cases, matrix related compounds can be co-extracted and may negatively affect important method parameters, such as linearity, limits of detection (LODs) and quantification (LOQs), accuracy and precision (González-Sálamo et al., 2016). For these reasons, the performance of effective sample preparation techniques which provide high extraction efficiency and offer adequate clean-up of the sample is crucial for food analysis.

Conventional sample preparation procedures, such as liquid-liquid extraction (LLE), solid-phase extraction (SPE), dispersive solid-phase extraction (dSPE) and matrix solid-phase dispersion (MSPD) are often tedious, time-consuming and require large volumes of organic solvents. For these reasons, the current trend in sample preparation involves moving towards the development of cheaper, cost-effective and more environmentally friendly extraction and purification procedures, so they can meet the requirements to be included in the Green Analytical Chemistry (GAC). This can be achieved by minimizing the number of steps (in order to reduce time and sources of error), reducing sample degradation and waste production, avoiding or decreasing consumption of organic solvents, replacing toxic solvents by non-toxic ones, and improving extraction efficiency and selectivity with the application of new advanced sorbents (Filippou et al., 2017; Gilbert-López et al., 2017).

For this purpose, in recent years, micro-extraction techniques have been proposed to meet the GAC requirements and overcome some limitations of conventional sample preparation methods. In this sense, micro-extraction techniques are based on the miniaturization of conventional sample preparation techniques, what involves advantages, such as, minimal solvent and sample consumption, reduction of sample treatment steps and a fewer waste generation (Moreda-Piñeiro & Moreda-Piñeiro, 2015). Additionally, the application of sorbent-based micro-extraction techniques enables to develop more sensible and selective analytical methods, since they provide better sample clean-up and extraction efficiency, as well as good analyte pre-concentration. Up to date, many sorbent-based micro-extraction techniques have been applied to extract bioactive compounds from complex matrices, including miniaturized solid-phase extraction (μ-SPE), dispersive micro-solid-phase extraction (d-MSPE), miniaturized matrix solid-phase dispersion (μ-MSPD), μ-QuEChERS (acronym of "micro-Quick, Easy, Cheap, Effective Rugged and Safe"), micro-

extraction by packed sorbents (MEPS), µSPEed®, pipette-tip solid-phase extraction (PT-SPE), solid-phase micro-extraction (SPME) and stir-bar sorptive extraction (SBSE).

On the other hand, the development and application of new advanced silica-based sorbent materials has achieved a sharp increase in sample preparation, due to their specific characteristics, such as low resistance to diffusion, large adsorptive capability, fast sorption kinetics, etc. Moreover, these new materials have proved to possess several advantages over traditional sorbents, such as amorphous silica and polymeric materials, therefore they can potentially be used as an interesting alternative to them (González-Sálamo et al., 2016; Sanagi et al., 2016; Li et al., 2013; Zhao et al. 2012; Ibarra et al., 2015; Plotka-Wasylka et al., 2016). Furthermore, the integration of these advanced sorbents in micro-extraction technologies can enable the development of high-throughput analytical methods by combining the advantages provided by both concepts, and they can become an interesting alternative to improve conventional extraction and clean-up technologies, as well as making sample preparation methodologies greener.

Therefore, this review aims to provide an overview of the most relevant achievements and improvements in sample preparation methodologies applied for the determination of dietary polyphenols in food products, regarding the development of new micro-extraction methodologies, the preparation of novel silica-based sorbent materials and the integration of both strategies, giving some recent examples from the last five years (from 2013 to 2017).

2. Sorbent-based micro-extraction techniques for isolation of polyphenols from food samples

Miniaturization can be achieved by scaling down conventional sample preparation methods, what involves using fewer solvents and minimal sample amount, reducing sample treatment steps, avoiding hazardous reagents and saving in energy consumption. Additionally, the safety for operators and the environment is maximized, as well as the generation of less waste. On the other hand, in recent years, new formats and configurations have appeared to perform micro-extraction procedures and have also been proposed as an alternative to conventional sample preparation methods, as it has been reviewed by other authors (Pereira et al., 2014; Moein et al., 2015; Yang et al., 2017). In this sense, several micro-extraction techniques based on sorbent-based adsorption process, such as MEPS, µSPEed®, PT-SPE, SPME and SBSE (Fig. 1), have been applied in the last years for the extraction of polyphenols from different food matrices. Table 1 shows the miniaturized and micro-

extraction techniques applied in the last years for the isolation of polyphenols from food samples.
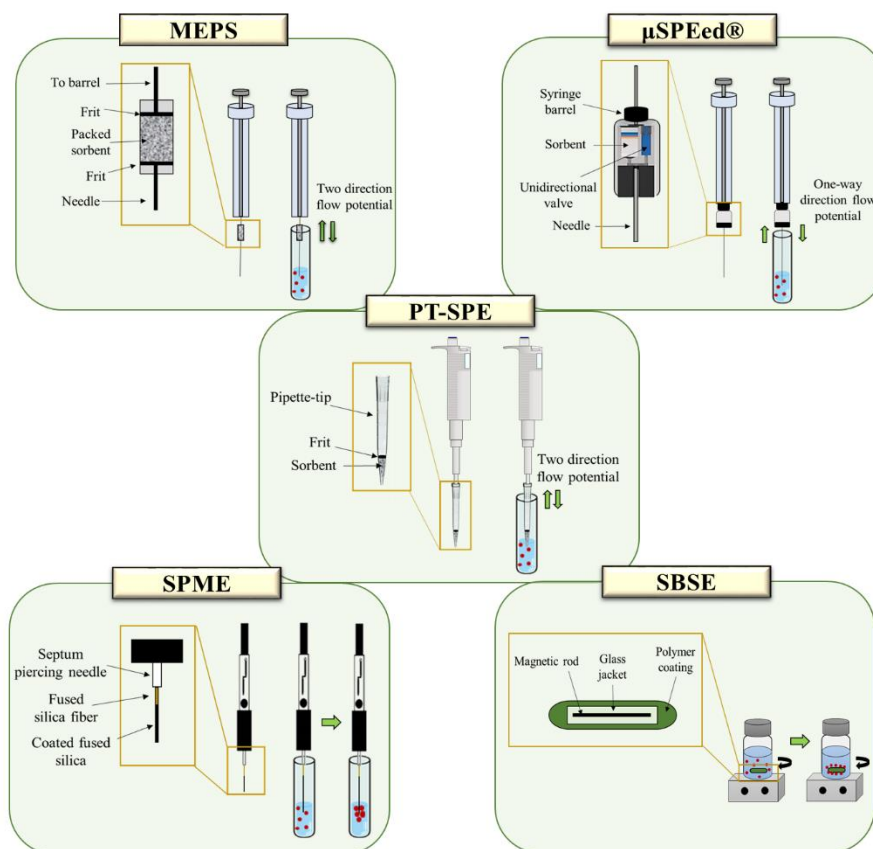

Figure 1. Graphic representation of micro-extractions techniques based on new formats and configurations: MEPS, µSPEed®, PT-SPE, SPME and SBSE.

Table 1. Applications of sorbent-based micro-extraction techniques for isolation of polyphenols from food samples

Micro-extraction technique	Sorbent (amount)	Food matrix	Analytes	Determination	Recoveries (%)	LOD	Additional information*	Ref.
d-MSPE	Ni/Co-NO$_3$-LDH (6 mg)	Fruit juice	*p*-hydroxybenzoic acid, *p*-coumaric acid	HPLC-UV/VIS	82 - 92	0.1 µg L^{-1}	Extraction time: 6 min Analysis time: 13 min	Soltani et al. (2018)
µ-MSPD	Middle-molecular-weight chitosan (25 mg)	Olive fruits	Gallic acid, hydroxytyrosol, methyl gallate, luteolin 7-O-β-d-glucoside, rutin, ellagic acid, oleuropein	UHPLC-Q-TOF-MS/MS	80 - 113	69.6 – 358.4 ng g^{-1}	Extraction time: 1 min Analysis time: 12 min	Peng et al. (2016)
	Florisil (150 mg)	Lime fruit	Neohesperidin, naringin	UHPLC-UV	90 - 96	4.08 – 5.04 µg g^{-1}	Extraction time: 1 min Analysis time: 10 min	Xu et al. (2016)
	Silica-based C18 (200 mg)	Citrus fruit juice	Hesperidin, diosmin, eriocitrin, narirutin, naringin, hesperetin, naringenin	HPLC-UV	86 - 94	23.3 – 46.8 ng mL^{-1}	Extraction time: 10 min Analysis time: 30 min	Barfi et al. (2013)
µ-QuEChERS	MgSO$_4$ and PSA (75 mg and 12.5 mg)	Baby foods	Gallic acid, protocatechuic acid, chlorogenic acid, 4-hydroxibenzoic acid, epicatechin, *p*-coumaric acid, ferulic acid, rutin, *trans*-resveratrol, myricetin, naringenin, kaempferol	UHPLC-PDA	71 - 100	0.03 – 0.56 µg g^{-1}	Extraction time: 15.7 min Analysis time: 14 min	Casado et al. (2018)

Micro-extraction technique	Sorbent (amount)	Food matrix	Analytes	Determination	Recoveries (%)	LOD	Additional information*	Ref.
MEPS	C8 (4 mg)	Wines	Gallic acid, protocatechuic acid, gentisic acid, vanillic acid, syringic acid, *p*-coumaric acid, *m*-coumaric acid, *o*-coumaric acid, ferulic acid, cinnamic acid	UHPLC-PDA	77 - 100	$0.01 – 0.2\ \mu g\ mL^{-1}$	Extraction time: 1 min 5 extraction cycles Sorbent reusability: 100 extraction cycles Analysis time: 11 min	Gonçalves et al. (2013a)
	C18 (4 mg)	Beer	Xanthohumol, isoxanthohumol	UHPLC-PDA	67 – 100	$0.4 – 0.9\ ng\ mL^{-1}$	Extraction time: 5 min 10 extraction cycles Sorbent reusability: 100 extraction cycles Analysis time: 13 min	Gonçalves et al. (2013b)
	CMK-3 nanoporous carbon (2 mg)	Rosemary	Rosmarinic acid	HPLC-UV/VIS	94 - 106	$0.059\ \mu g\ mL^{-1}$	Extraction time: n.p. 14 min extraction cycles Sorbent reusability: 80 extraction cycles Analysis time: 20 min	Rahimi et al. (2013)
µSPEed®	PS/DVB-RP	Baby Foods	Gallic acid, protocatechuic acid, chlorogenic acid, 4-hydroxibenzoic acid, epicatechin, *p*-coumaric acid, ferulic acid, rutin, *trans*-resveratrol, myricetin, naringenin, kaempferol	UHPLC-PDA	67 - 97	$1.4 – 13.6\ \mu g\ Kg^{-1}$	Extraction time: 0.8 min 10 extraction cycles Analysis time: 14 min	Casado et al. (2017a)

Micro-extraction technique	Sorbent (amount)	Food matrix	Analytes	Determination	Recoveries (%)	LOD	Additional information*	Ref.
µSPEed®	PS/DVB-RP	Tea	Rutin, myricetin, quercetin-3-glucoside, *trans*-resveratrol, quercetin, cinnamic acid, naringenin, kaempferol	UHPLC-PDA	89 – 103	3.5 – 16.8 ng mL^{-1}	Extraction time: 1 min 2 extraction cycles Sorbent reusability: 40 extraction cycles Analysis time: 8 min	Porto-Figueira et al. (2015)
SPME	PA fiber	Wines, Spirits, and Grape Juices	Resveratrol	HPLC-DAD	92 – 99	0.5 – 1.1 ng mL^{-1}	Extraction time: 30 min Analysis time: 50 min	Aresta et al. (2017)
	VIED/MMF-SPME	Fruit juice	*p*-hydroxybenzoic acid, syringic acid, *p*-coumaric acid, ferulic acid	HPLC–DAD	70 –118	0.17 – 0.57 µg L^{-1}	Extraction time: 40 min Analysis time: 15 min	Pei & Huang (2016)
	PS-DVB-PAN	Grapes, berries and Wine	Rutin hydrate, quercetin-3-D-galactoside, naringenin, taxifolin, *trans*-resveratrol, catechin hydrate, epicatechin, caffeic acid	HPLC-TQ-MS/MS	69 - 82	0.2 – 3 ng mL^{-1}	Extraction time: 2 h Analysis time: 20 min	Mirnaghi et al. (2013)
SBSE	PDMS	Wine	*Cis*-resveratrol, *cis*-oxyresveratrol, *cis*-piceatannol, *trans*-resveratrol, *trans*-oxyresveratrol, *trans*-piceatannol.	GC-Q-MS	79 -109	14.8 – 49.2 ng L^{-1}	Extraction time: 3 h Analysis time: 16 min	Cacho et al. (2013)

*Extraction time: refers to interaction time between sorbent and sample; Analysis time: refers to chromatographic separation time; n.p.: not provided

2.1. Dispersive micro solid-phase extraction (d-MSPE)

d-MSPE has been developed as a simple and miniaturized modification of dSPE which can be applied to extract and enrich compounds from different matrices by using only few amounts of sorbents and solvents. This method overcomes many of the shortcomings in conventional SPE, since it eludes passing the sample extract through a cartridge, so it avoids channeling and blocking of the sorbent pores and consequently provides a more efficient extraction. Moreover, d-MSPE also offers other advantages, such as less sorbent and solvent consumption, simple operation and short time requirement. In this sense, Soltani et al. (2018) reported a d-MSPE procedure for the extraction of *p*-coumaric acid and *p*-hydroxybenzoic acid from fruit juices using a porous Ni/Co-NO$_3$-based layered double hydroxide nanosheet as sorbent. The extraction procedure was performed adding only 6 mg of sorbent into the sample solution, without using any organic solvent, and ultrasonic irradiation was applied during both extraction and desorption procedures, since ultrasonication leads to faster and more efficient transfer of the analytes to and from the nanosorbent material, respectively. The developed method provided a short extraction time of only 6 min, and the sorbent showed good analytical performance for the extraction of the phenolic compounds, due to its high porosity and ultrathin layered structure, providing recovery values between 82 - 92%, what implies the applicability of the method for real sample analysis.

2.2. Miniaturized matrix solid-phase dispersion (μ-MSPD)

MSPD was first proposed in 1989 by Barker et al. for the extraction of drug residues from animal tissues. Nowadays, this extraction technique has found particular application as an analytical strategy for the preparation, extraction and fractionation of analytes from different types of samples. Miniaturization of MSPD can be achieved by reducing the amount of sample and dispersant sorbent, as well as the volume of solvents used, what leads to save time, cost of analysis and improves the quality and sensitivity of the method in comparison to traditional methods. For example, Peng et al. (2016) developed a μ-MSPD method using chitosan as dispersant sorbent for the extraction of seven polyphenols and their derivatives in olive fruits (Fig. 2). The proposed method used small amounts of sample (50 mg) and dispersant sorbent (25 mg), little extraction time (1 min) and small elution solvent volume (1.5 mL). Compared to other reported conventional MSPD methods, the developed method proved to be more environmentally friendly and to have many practical advantages. Moreover, the extraction method was combined with ultra-high-performance liquid chromatography coupled with quadrupole time-of-flight tandem mass spectrometry (UHPLC-

Q-TOF/MS) what provided low LODs (ranging between 69.6 – 358.4 ng g^{-1}), and recovery values were above 80% for all the target compounds.
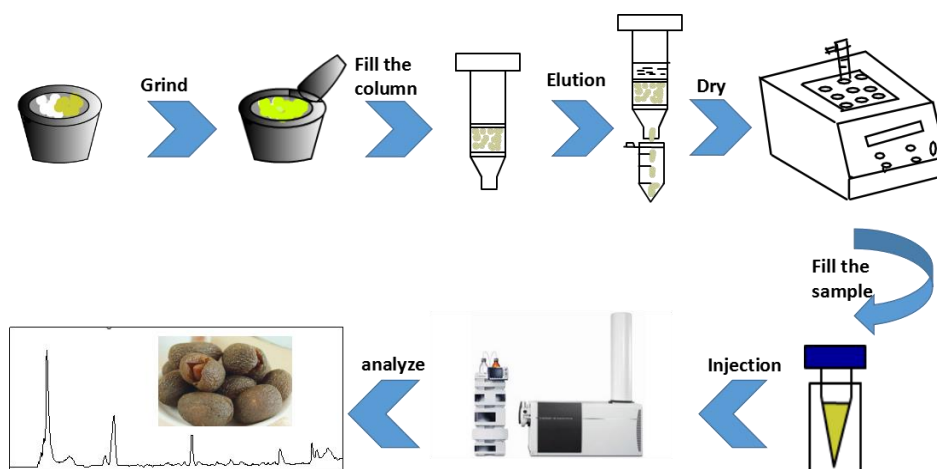

Figure 2. Experimental process of the μ-MSPD method (Peng et al., 2016).

In order to meet the GAC requirements, Xu et al. (2016) developed a μ-MSPD method for the extraction of 2 flavonoids from lime fruit using ionic liquids (ILs) as green elution solvents. The optimum extraction was achieved using 50 mg of lime fruit sample, florisil (150 mg) as dispersant sorbent and 1-butyl-3-methylimidazolium tetrafluoroborate 250 mM (0.4 mL) as elution solvent. The developed method provided good precision and good recovery values for the target compounds (90 – 96%). On the other hand, in order to save time, cost of analysis and improve the quality and sensitivity of the method, Barfi et al. (2013) developed an ultrasound-assisted μ-MSPD method for the extraction of 7 flavonoids from orange, grape and lime fruit juices. The optimum extraction conditions were achieved using 150 μL of sample, 200 mg of silica-based octadecylsilane (C18) as dispersant sorbent, 0.5 mL of methanol (MeOH) as elution solvent and 6 min of sonication during the extraction step. Results showed sonication considerably improved the recovery values of the target analytes, which ranged between 85 – 101%. However, although this methodology uses a small volume of organic solvent, it requires a higher amount of sorbent than its previous counterparts. Nevertheless, it must also be considered that this method extracts a higher number of polyphenols than the other μ-MSPD methods reported.

2.3. Micro-QuEChERS (μ-QuEChERS)

The QuEChERS strategy is an extraction and clean-up technique originally developed by Anastassiades et al. in 2003 as a green, environmentally friendly and cheap strategy to perform multiresidue extraction of more than 200 pesticides from fruits and vegetables. Nevertheless, in the last years the QuEChERS concept has spread beyond its original field of

application to be adapted to other analytes and food matrices. In this sense, due to the high interest in recent years on micro-extraction techniques, the QuEChERS method can also be miniaturized. For example, Casado et al. (2018) developed a µ-QuEChERS strategy combined with UHPLC coupled to photodiode array detection (UHPLC-PDA) for the simultaneous determination of 12 polyphenols in different types of baby food samples (including pureed solids, juices and porridges). The proposed method proved to be highly cost-effective and environmentally friendly, since results showed good extraction efficiency by using few amounts of sample (300 mg), organic solvents (1 mL), clean-up sorbents (87.5 mg) and partitioning salts (200 mg), as well as producing minimal waste disposal in comparison to the original method. Best results were achieved using PSA (primary and secondary amines) and $MgSO_4$ in the clean-up step and the overall average recoveries ranged from 71 – 100% with relative standard deviation (RSD) values lower than 6%.

2.4. Micro-extraction by packed sorbent (MEPS)

MEPS is a miniaturization of conventional SPE, which was developed by Abdel-Rehim et al. in 2004. Compared with SPE, in MEPS the sorbent is directly integrated and packed inside a micro-syringe and not in a separate column. This technique performs sample extraction, pre-concentration and clean-up in a single device, which can be used with different set-ups: the sorbent in syringe set-up and the BIN (barrel insert and needle) set-up. MEPS technique employs very low sorbent amounts (1 – 4 mg) which are able to quickly and efficiently extract a wide range of sample volumes (µL – mL). Unlike SPE, in MEPS the two direction flow potential (up and down) provides repetition of each step, improving method efficiency, since it enhances the sample-sorbent contact, pre-concentration and analyte elution. For all these reasons, MEPS technique present many advantages over other conventional sample preparation techniques, nevertheless, its main drawback is its inability to be applied to viscous or highly concentrated samples, which need to be previously diluted and fully dissolved in the solvent in order to avoid BIN blocking. A critical parameter in MEPS extraction is the choice of the sorbent, in order to achieve acceptable clean-up and extraction yield. In this context, there is a wide range of commercial sorbents with different properties, including reversed-phase, normal phase, ion exchange and mixed-mode.

Gonçalves et al. (2013a) proposed a MEPS strategy combined with UHPLC-PDA for the simultaneous determination of 5 hydroxybenzoic acids and 5 hydroxycinnamic acids in wine samples. The optimal extraction conditions were achieved using 4 mg of octylsilane (C8) phase as sorbent material, extracting 250 µL of sample 5 times in extract-discard mode and using only 50 µL of MeOH:water (95:5, v/v) to elute the target analytes retained in the sorbent material. In order to overcome the negative influence of ethanol on the extraction efficiency,

wine samples were firstly dealcoholize. The proposed method was applied in 30 commercial wines and recovery values obtained ranged from 77 – 100%. In the same research group, a semi-automatic MEPS approach using a digitally controlled syringe (eVol®) was designed for the extraction of 2 prenylated chalcones: xanthohumol and its isomeric flavonone isoxanthohumol, from beer samples (Gonçalves et al., 2013b). So for their extraction, the MEPS procedure was performed with the eVol® hand-held automated analytical syringe (500 µL) fitted with a BIN containing 4 mg of C18 sorbent material. The eVol® was used to draw and discharge the samples through the BIN. Operating in optimal conditions, an aliquot of 500 µL of sample was passed through the C18 sorbent 10 times in extract-discard mode, and elution was achieved with 250 µL of ACN, which were directly analysed in the UHPLC system. In this case, samples were not dealcoholized and recovery values ranged between 74 – 100% for xanthohumol and 67 – 99% for isoxanthohumol, with RSD < 9%.

In recent years, the development of new materials have promoted their application in sample preparation methods as sorbents due to their advantageous properties. In this context, Rahimi and co-workers (2013) synthesized a carbon-based nanoporous material (CMK-3) for its evaluation as MEPS sorbent in the extraction of rosmarinic acid from rosemary samples. For this purpose, 2 mg of CMK-3 were inserted between the barrel and the needle of a syringe as a plug, with propylene frits at both sides. The packed syringe was placed on a laboratory-made apparatus for automation of its plunger up and down movements and programming the number of cycles in each step. Since rosemary is a solid sample, it was first ground and then subjected to a solvent extraction procedure using ethanol:water (30:70, v/v) under sonication for 10 min. The resulting mixture was then centrifuged and the supernatant was purified by the MEPS procedure designed. In this sense, 250 µL of sample extract were drawn through the syringe up and down 14 times in draw-eject mode, and analyte elution was achieved passing 100 µL of ACN 10 times through the packing in draw-eject mode. The recovery values for the target analyte ranged between 94 – 106%, and it was confirmed that the packing bed could be used for at least 80 extractions without significant changes in its properties. Additionally, the extraction efficiency of the sorbent was compared with that one using activate carbon as sorbent, and it was found that CMK-30 was superior for the extraction of rosmarinic acid (about 17 times).

2.5. µSPEed®

µSPEed® is a novel micro-extraction technique, similar to MEPS but using direct flow through the sorbent bed. This is achieved by the existence of a one-way check valve that provides ultra-low dead volume connection. In this sense, the sample can only be aspirate through the cartridge into the syringe barrel under vacuum conditions when the plunger is

pulled back, therefore it not pass the bed but bypasses the sorbent. The sorbent is tightly packed in a disposable needle equipped with the pressure-driven valve to withdraw sample flow in a single direction, therefore, this configuration allows constant and high pressure (up to 1600 psi) single direction flow through the sorbent, achieving more efficient extraction of the target analytes. The high pressure generated by the analytical syringe, push the sample through the sorbent bed focusing the analytes onto the top of the sorbent bed. Then, during elution, the analytes retained in the sorbent are not disturbed by the solvent aspiration, as it occurs with MEPS. Additionally, µSPEed® uses small sorbent particles (≤ 3µm) instead of the 50 – 60 µm particles normally used in SPE or MEPS processes. These smaller particles provide higher surface area and relatively high pressures, achieving more efficient adsorption of analytes.

In this context, Casado et al. (2017a) evaluated and compared both MEPS and µSPEed® techniques, regarding the performance criteria, for the extraction of 12 polyphenols from different baby food samples prior to their determination by UHPLC-PDA. The chromatographic method developed allowed the separation of the target compounds in less than 11 min. Both extraction procedures were performed with the electronic pipette eVOL® by changing the syringe and the sorbents tested. Different commercial silica-based and polymeric sorbents were evaluated in both extraction techniques, and results revealed that both techniques were very similar adsorption-based methods. However, best performance was achieved with µSPEed®, since it provided, in general, higher recovery values of the target analytes and lower LODs and LOQs, since it achieved higher pre-concentration of analytes. The sorbent selected in the µSPEed® procedure was a porous polymeric polystyrene-divinylbenzene reversed phase (PS/DVB-RP) sorbent, since it provided higher extraction efficiency and reproducibility in the optimization step. Additionally, it used fewer amounts of solvents, since only 50 µL of MeOH:water (95:5, v/v) containing 0.1% of formic acid were required to elute the analytes, as well as fewer sample, using only 1 mL of sample extract compared with the 2.5 mL used in the MEPS procedure, consequently the procedure was also less time-consuming.

In other work, µSPEed® was used for the extraction of 8 polyphenols from tea samples (Porto-Figueira et al., 2015). Best performance was also achieved with the PS/DVB-RP sorbent. The extraction was carried out with the electronic pipette eVOL® by loading twice 100 µL of sample extract in extract-discard mode, and elution was performed with 50 µL of acidified MeOH 95%. Method performance provided high recovery values, ranging between 89 – 103% with very good precision (RSD <5%). The proposed strategy was applied to 10 commercial tea samples of different type, including red, black and green teas.

2.6. Solid-phase micro-extraction (SPME)

SPME is a kind of sorptive extraction technique, which was first developed by Arthur and Pawliszyn in 1990 with the aim to solve some drawbacks associated to SPE, such as reducing time extraction and organic solvent consumption. SPME is a solvent free sample preparation technique that uses a fused silica fiber coated with an appropriate stationary phase attached to a modified micro-syringe. It is experimentally simpler than SPE, because the cylindrical surface geometry of the fibers is well defined and less complex than the surface of SPE cartridges. This allows easy access of the analytes, what facilitates efficient extraction and desorption. The method does not require an exhaustive extraction of the analytes from the matrix since it is more an equilibrium technique, and it can be applied to liquid, gas and solid samples. Nevertheless, parameters such as extraction temperature, time and sample agitation must be optimized, and operating conditions must be consistent. Compared with conventional extraction techniques such as LLE or SPE, SPME is simple, sensitive, solvent-less, time-efficient (combines sampling and extraction in one step), and it is easy to couple with analytical separation instruments such as gas chromatography (GC), high-performance liquid chromatography (HPLC) and capillary electrophoresis (CE). However, some drawbacks of this technique include batch to batch variation and fragility of fibers. Other important drawback of SPME is the restricted choice of commercially available stationary phases and fiber coatings used in this preparation technique, as well as the insufficient selectivity of these commercially materials and the possible unsatisfactory extraction capacity as a result of its limited sorbent phase on the silica fiber. SPME can be used for the extraction of volatile and non-volatile compounds from complex sample matrices, and in the last years it has been used for the extraction of different polyphenols from food samples, such as fruits and beverage samples.

In this sense, a SPME of *trans*-resveratrol was optimized and interfaced with HPLC coupled to diode array detection (HPLC-DAD) and was applied in wine, spirits and grape juice samples (Aresta et al., 2017). For this purpose, different fibers, such as polydimethylsiloxane (PDMS), polydimethylsiloxane/divinylbenzene (PDMS/DVB) and polyacrylate (PA), were tested. Results revealed that PA fiber provided the most efficient extraction; therefore, it was selected as the most suitable. The extraction was performed by direct immersion of the fiber in the sample extracts under magnetic stirring during 30 min at 20 ºC in the presence of 6.6% ethanol and 10% of NaCl. Analyte desorption was achieved in static mode by soaking the fiber in the mobile phase into the desorption chamber of the interface for 15 min. The average recoveries varied from 92 to 99%, and *trans*-resveratrol was found in all the analyzed samples at concentration levels ranging from 0.007 – 4.486 µg mL^{-1}.

Pei and Huang (2016) proposed a SPME approach using a self-made multiple monolithic fiber based on a poly(vinylimidazole-co-ethylene dimethacrylate) porous monolith (denoted as VIED/MMF-SPME) to extract and pre-concentrate different phenolic acids (*p*-hydroxybenzoic acid, syringic acid, *p*-coumaric acid and ferulic acid) from fruit juice samples. In this sense, extraction was performed by direct immersion of the VIED/MMF-SPME fiber in the sample solution for 40 min under magnetic stirring. Desorption was performed with 0.4 mL of MeOH:1% acetic acid aqueous (90:10, v/v) during 20 min. Under this optimized extraction conditions, four commercial fruit juice samples were successfully analyzed. Low concentrations of phenolic acids were found in the different analyzed samples, and recovery values were in the range 70 – 118%, with RSD values ranging between 0.9 – 10%, what indicates the reliability and applicability of the proposed method, although sample matrices have some effect that negatively affects the extraction of some of the analytes.

Mirnaghi et al. (2013) also proposed a SPME method using a self-made thin-film polystyrene-divinylbenzene-polyacrylonitrile (PS-DVB-PAN) SPME coating for the extraction 8 polyphenols from wine, berry and grape samples. They evaluated five different self-made stationary phases based on polyacrylonitrile (PAN), including C18 silica-based-PAN, PS-DVB-PAN, phenylboronic acid-PAN (PBA-PAN), mixed-mode-PAN and diol-PAN, since PAN provides high chemical and mechanical stability, making it ideal for use as a binder for stationary phase immobilization. The thin-film PS-DVB-PAN SPME coating provided the best results, with recovery values, ranging from 69 – 82% in the synthetic wine samples. The extraction procedure was performed for 2 h under stirring conditions, and desorption was achieved under stirring conditions during 90 min in 1 mL of ACN:water 1:1 (v/v). The extraction procedure was more time-consuming than the previous ones since it determined a higher number of compounds.

2.7. Stir bar sorptive extraction (SBSE)

SBSE was developed to overcome the limited extraction capacity of SPME fibers. This sorptive technique is a solvent-less sample preparation method based on the same principles as SPME, an equilibrium distribution between the sample matrix and a non-miscible liquid phase. However, in SBSE, the amount of non-miscible liquid phase coated on the stir bar is 50-250 times larger than on SPME fibers, providing higher recovery values and extraction capacity. Nevertheless, the major drawback of SBSE is that commercially available stir bars are generally coated with PDMS, what fails to achieve good performance towards polar and semipolar compounds. To overcome this, derivatization could be used as an additional step in the extraction procedure to improve the recovery of polar analytes. However, derivatization sometimes can be tedious and time-consuming, and in addition it requires

more reagents in the overall process and it cannot always be applied to all analytes. On the other hand, new commercially available thermal desorption units (TDU) enable hyphenation between GC and SBSE, allowing the complete introduction of the sample in the analytical sample providing high sensitivity, however, TDU is expensive and its application is restricted to stable volatile and semivolatile compounds. In this context, a SBSE method coupled to GG equipped with a quadrupole mass spectrometer (GC-Q-MS) by means of a TDU was developed for the determination of both *cis-* and *trans-*isomers of resveratrol, piceatannol and oxyresveratrol (Cacho et al., 2013). *Cis-*isomer standards were generated by irradiation of the corresponding *trans-*isomers once they have been pre-concentrated on the SBSE extracting phase. Acetylation derivatization, SBSE extraction and thermal desorption steps were optimized, and the recoveries of the target analytes obtained from spiked wine samples varied from 79 – 97% at the lowest concentration validation level, and from 99 – 109% at the highest level. Finally, the developed method was applied to 15 different samples of wine (red, rosé and white), and resveratrol was the main analyte found in the analyzed samples.

3. Novel silica-based sorbent materials applied for isolation of dietary polyphenols

In recent years, great efforts have been made on the improvement and investigation of new advanced sorbent materials, which have promoted the development of high-throughput extraction and clean-up technologies. In this concern, different types of new silica-based sorbents, such as mesostructured and magnetic materials, have been evaluated for the extraction of dietary polyphenols from diverse food matrices using different extraction techniques (Table 2).

Table 2. Application of silica-based sorbent materials for isolation of dietary polyphenols from food samples.

Type of sorbent	Sorbent (amount)	Food matrix	Analytes	Extraction technique	Determination	Recoveries (%)	LOD	Additional information*	Ref.
Mesostructured silicas	HMS-C18 (50 mg)	Fruit and vegetables juices and smoothies	Gallic acid, caftaric acid, protocatechuic acid, catechin, chlorogenic acid, epigallocatechin, 4-hydroxybenzoic acid, epigallocatechin gallate, caffeic acid, epicatechin, piceid, *p*-coumaric acid, ferulic acid, naringin, quercetin-3-β-D-glucoside, rutin, *trans*-resveratrol, myricetin, quercetin, naringenin	dSPE	UHPLC-IT-MS/MS	57 – 99	0.01 – 1.7 µg mL^{-1}	Extraction time: 20 min Analysis time: 12 min	Casado et al. (2017c)
	MIMP (1000 mg)	*Artemisia stelleriana* extract	Vanillic acid	SPE	HPLC-UV	98	n.p.*	Extraction time: n.p. Sorbent reusability: 9 extraction cycles Analysis time: 40 min	Li et al. (2015)
	HPMIP (20 mg)	Fruits	Caffeic acid	dSPE	HPLC–DAD	87 - 101	0.2 µg mL^{-1}	Extraction time: 40 min Analysis time: 45 min	Fan et al. (2017)
	HPMIP (20 mg)	Apple and orange juices	Cinnamic acid	dSPE	HPLC–UV	89 - 103	0.006 mg L^{-1}	Extraction time: 40 min Analysis time: 9 min	Xiang et al. (2017)
Magnetic silica-based materials	MMIP (50 mg)	*Calendula officinalis*	Quercetagetin	MSPE	HPLC-DAD	83 - 95	32.66 µg mL^{-1}	Extraction time: 25 min Analysis time: 4 min	Ma & Shi (2015)
	MMIP (20 mg)	Bread, milk powder, biscuit and chocolate	Vanillin	MSPE	HPLC–UV	83 - 96	2.67 µmol L^{-1}	Extraction time: 1 h Analysis time: 4 min	Ning et al. (2014)

Type of sorbent	Sorbent (amount)	Food matrix	Analytes	Extraction technique	Determination	Recoveries (%)	LOD	Additional information*	Ref.
Magnetic silica-based materials	MMIP (10 mg)	Fruit juices	Protocatechuic acid	MSPE	HPLC–UV	92 - 107	0.5 µg mL^{-1}	Extraction time: 40 min Sorbent reusability: 6 extraction cycles Analysis time: 30 min	Xie et al. (2014)
	HMIP (20 mg)	Fruits	Caffeic acid	dSPE	HPLC–DAD	86 - 103	0.2 µg mL^{-1}	Extraction time: 40 min Analysis time: 45 min	Fan et al. (2016)
	DMMIP (40 mg)	Wine	Resveratrol	MSPE	HPLC-DAD	79 - 91	4.42 ng mL^{-1}	Extraction time: 30 min Analysis time: 8 min	Chen et al. (2013)
	MPMIP (10 mg)	Apple juice	Cinnamic acid	MSPE	HPLC–UV	93 - 101	0.006 µg mL^{-1}	Extraction time: 60 min Sorbent reusability: 6 extraction cycles Analysis time: 9 min	Shi et al. (2017)
	MPMIP (10 mg)	Fruit juices	Gallic acid	MSPE	HPLC–UV	92 - 102	0.1 µg mL^{-1}	Extraction time: 100 min Sorbent reusability: 6 extraction cycles Analysis time: 30 min	Hu et al. (2015)
	MPMIP (20 mg)	*Syzygium aromaticum*	Protocatechuic acid	MSPE	HPLC–UV	94 - 101	0.5 µg mL^{-1}	Extraction time: 140 min Sorbent reusability: 6 extraction cycles Analysis time: 40 min	Xie et al. (2015)
	MHPMIP (10 mg)	*Syzygium aromaticum*	Protocatechuic acid	MSPE	HPLC-DAD	94 - 101	0.4 µg mL^{-1}	Extraction time: 25 min Analysis time: 40 min	Li et al. (2015)

* Extraction time: refers to interaction time between sorbent and sample; Analysis time: refers to chromatographic separation time; n.p.: not provided

3.1. Mesostructured silicas

Mesostructured silicas were prepared for the first time in 1992 by researchers of the Mobil Oil Company (Kresge et al., 1992; Beck et al., 1992). They present very high surface area, regularly ordered pore arrangement, well-defined pore size distribution, controllable wall composition and large pore volume. These textural properties, in addition to their morphology and particle size, are highly dependent on the experimental synthesis conditions. Thus, by combining and varying the templates and mineral precursors agents, and using different sol-gel reaction conditions, a wide variety of mesostructured silicas with different structures have been achieved such as, Santa Barbara amorphous, SBA (Zhao et al., 1998), hexagonal mesoporous silica, HMS (Tanev & Pinnavaia, 1995), Fudan University, FDU (Yu et al., 2000), periodic mesoporous organosilicas, PMOs (Inagaki et al., 1999; Melde et al., 1999; Asefa et al., 1999), etc. These materials contain many Si-O-Si and Si-OH groups on their surface, therefore, they can interact by hydrogen bonds with polar hydroxyl groups (-OH) of certain analytes. Moreover, the functionalization of these materials with different organic groups using different modification process offers a further possibility of tailoring their physical and chemical properties, making them potential sorbents to be used for different applications in adsorption processes. In these sense, these materials have proved to be successful sorbents in the extraction and pre-concentration of organic contaminants in food matrices, which has been extensively reviewed (Casado et al., 2017b), and in the extraction of inorganic contaminants (Sierra & Pérez-Quintanilla, 2013). However, there are only a few studies which apply these materials for the extraction of polyphenols from food samples.

In this context, Casado et al. (2017c) evaluated a HMS silica as sorbent material for the simultaneous multicomponent extraction of 20 polyphenols belonging to different structural families (phenolic acids, flavonoids and stilbenes) from juice and smoothie samples, followed by their analysis by UHPLC-MS/MS. HMS is a mesostructured silica with wormhole-like framework and it presents some advantages over other mesostructured silicas such as SBA-15, since its synthesis is more cost-effective and environmentally friendly, and it provides mesostructures with thicker pore walls (which improve stability), small particle size and spherical morphology. The functionalization of the material with C18 groups was necessary to perform a multicomponent analysis, so its extraction efficiency could cover and be effective in a wide range of compounds of different nature. The material was evaluated as sorbent in SPE and dSPE, (Fig. 3). Best performance was achieved with dSPE, since it provided higher recovery values and some advantages over SPE, such as the use of less amounts of sample,

solvents, sorbent and time-consumption. Additionally, the advantages of this material towards commercial C18 amorphous silica were demonstrated under same conditions.
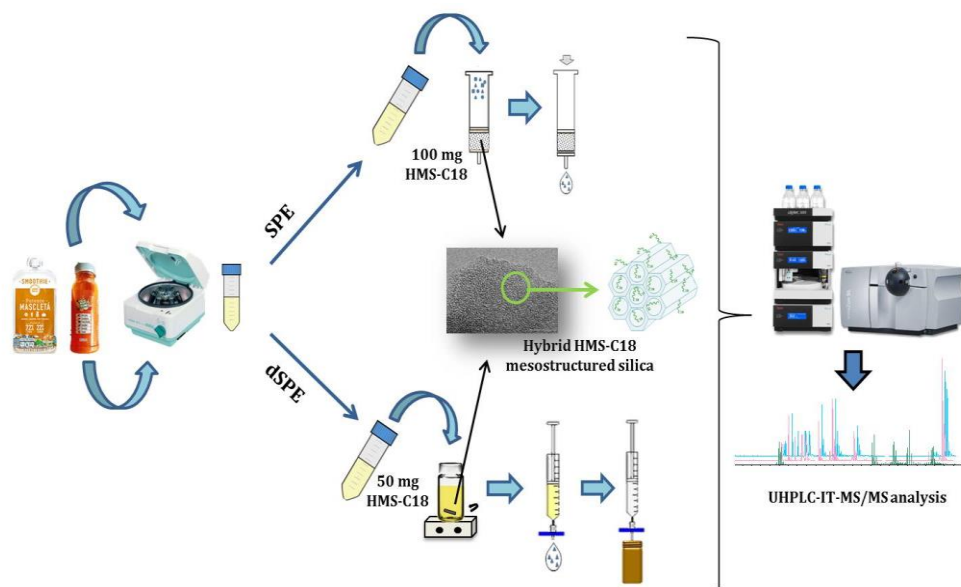

Figure 3. Schematic representation of the application of HMS-C18 mesostructured silica as sorbent in SPE and dSPE for the extraction of polyphenols from juice and smoothie samples.

However, sometimes selectivity and specificity are required when developing an extraction and purification method, thus, a way to achieve this is to use sorbent materials developed by molecular imprinting technology (MIT). Different molecular imprinting methods have been developed, such as surface molecular imprinting (SMIP), which consist of localizing the recognition sites on the surface of a supporter. Mesostructured silicas, due to their specific and advantageous characteristics, can be used as supporter materials because of their good stability and because their channels, instead of closed pores, facilitate the diffusion of solvent and template, what helps to remove easily the template. Moreover, due to their high surface-to-volume ratio, most of the template molecules are situated at the surface or in the vicinity of the material surface, what leads to increase the molecular recognition capacity of the material, and improves the binding capacity, the mass transfer dynamics and the accessibility of the recognition sites. For these reasons, some authors have used the SMIP technique with mesostructured silicas as supporter materials for the preparation of molecularly imprinted mesostructured silica polymers (MIMPs), which have been used as novel sorbents in sample preparation for the selective extraction of polyphenols from food samples. In this sense, Li et al. (2015) prepared a MIMP for vanillic acid by copolymerizing a modified mesostructured silica molecular sieve with the template molecule, 4-vinylpyridine (4-VP) as functional monomer and ethylene glycol dimethacrylate (EGDMA) as cross-linker. Results revealed rapid adsorption dynamics and a high binding capacity, reaching adsorption equilibrium within 230 min and with an improved adsorption capacity of 50.7 mg g^{-1}. It was

observed that the material also showed adsorption capacity for other 4 phenolic acids (caffeic, chlorogenic, protocatechuic and gallic acids) with similar structure to vanillic acid, however, the capacity factor (K_d) of the material for the template molecule was higher than the ones for the structural analogues, with selectivity coefficients ranging from 1.36 to 1.50. The material was also applied as a selective SPE sorbent for the extraction of vanillic acid from *Artemisia stelleriana* extracts showing selective capture capability for the target analyte (recovery 98%), and in addition, good reusability of the material was confirmed during adsorption-desorption recycling use.

Other authors have developed hollow porous molecularly imprinted polymers (HPMIPs) using MCM-48 mesostructured silica as sacrificial support, since its hollow porous structure provides highly recognition sites spread at the surface of the material, what favors mass transfer and improves binding capacity. In this sense, HPMIPs have been developed for the selective extraction of caffeic acid and cinnamic acid from fruit and juice samples, respectively (Fan et al., 2017; Xiang et al., 2017). In both works, HPMIPs were characterized, showing large surface area (563 and 534 m^2 g^{-1}), high binding capacity (27 and 15 mg g^{-1}) and fast kinetic binding (40 min in both cases), respectively. The performance of these materials was compared with the one achieved with solid molecularly imprinted polymers (MIPs) imprinted on nano/micro solid supports but which solid core no presents any recognition site, and it was observed that HPMIPs exerted higher adsorption capacity, faster binding kinetics and higher selectivity than solid MIPs. Additionally, the application of both materials for real sample analysis was successfully performed with good recovery (87-101% and 89-103%) and repeatability (RSD 5-9% and 4-8%) values, respectively.

3.2. Magnetic silica-based materials

In recent years, the development and application of new magnetic sorbents has achieved a sharp interest in sample preparation for extraction of several compounds from food samples (Ibarra et al., 2015), what it is known as magnetic solid-phase extraction (MSPE). MSPE has attracted considerable attention due to its simplicity and advantages over conventional methods, since it reduces the use of additional steps, such as precipitation, centrifugation, and filtration, what decreases at the same time sample manipulation. One of the most common magnetic sorbents developed and applied in MSPE, consists on Fe_3O_4 nanoparticles encapsulated in a silica shell by sol-gel polymerization, and sometimes subsequently modified with some organic ligands. The advantages of these potential sorbents in sample preparation have promoted the interest of their combination with MIT, so not only materials with specific selective binding capacity could be achieved, but also with outstanding magnetism (Ansari, 2017). This type of sorbents are known as magnetic MIPs (MMIPS), and

compared to conventional MIPs, they show superior characteristics involving fast and effective binding to target analytes, magnetically susceptible characteristics and shorter pre-treatment time.

For instance, Ma and Shi (2015) prepared a MMIP for quercetagetin, a flavonol, by SMIP method using Fe_3O_4 particles as support coated with a silica layer ($Fe_3O_4@SiO_2$), acrylamide as functional monomer, EGDMA as crosslinker and ACN as porogen. The resultant MMIP was characterized and its selectivity towards quercetagetin was evaluated according to its recognition to the template and its analogues. Results revealed excellent adsorption capacity for the target analyte, and the adsorption isotherms models analysis showed that the binding sites were homogenously distributed on the surface of the MMIP, therefore the material presented a great potential in the recognition, extraction and separation of quercetagetin, and it was applied for its determination in *Calendula officinalis* extracts, with recovery values ranging from 83 to 95% and RSD values between 3.90 and 7.08%. Also, a MMIP for selective extraction of vanillin was prepared by coating a layer of silica and MIPs on the surface of the Fe_3O_4 nanoparticles (Ning et al., 2014). The resultant MMIP showed some attractive characteristics, such as high binding capacity, fast binding kinetics, and quick separation. Adsorption equilibrium was reached within 100 min, and the apparent maximum adsorption quantity and dissociation constant were 64.12 µmol g-1 and 58.82 µmol L-1, respectively. The MMIP was applied as sorbent for the pre-concentration and selective separation of vanillin from spiked food samples (bread, milk powder, biscuits and chocolate), achieving recoveries values between 84 – 96%.

Xie et al. (2014) also prepared a MMIP by SMIP using $Fe_3O_4@SiO_2$ as supporter to selectively extract protocatechuic acid from fruit juices. Results suggested that the prepared MMIP possessed high binding capacity, fast binding kinetics, excellent selectivity, quick separation ability, and good reusability as a result of the combination of the benefits of SMIP technology and the magnetic core. In this sense, the MMIP showed maximum adsorption capacity at 7.5 mg g^{-1}, pseudo-second-order reaction kinetics with fast binding kinetics with equilibrium time at 40 min, rapid magnetic separation (10 s) and reusability (95% retention after six cycles). Additionally, it was applied for selective enrichment and determination of protocatechuic acid from different fruit juices with satisfactory recoveries (92 – 107%).

On the other hand, Fan et al. (2016) proposed the synthesis of a novel type of MMIP sorbents known as hollow molecular imprinted polymers (HMIPs), using caffeic acid as template, 4-VP as functional monomer and $Fe_3O_4@SiO_2$ as sacrificial support. For this purpose, once MMIPs were prepared, HMIPs were achieved by removing $Fe_3O_4@SiO_2$ from MMIPs in 10% hydrogen fluoride water solution for 12 h. The obtained HMIP presented a

hollow structure with large surface area (325.8 m^2 g^{-1}) that provided most recognition sites located on the surface of the material, resulting in high binding capacity (21.10 mg g^{-1}) and fast kinetic binding (35 min) in comparison with the synthesized MMIPs. The HMIP was successfully applied as dSPE sorbent to selectively extract and enrich caffeic acid from fruits with recovery values ranging between 86 - 103%.

Sometimes, to avoid interferences due to the leaching of the residual template molecules during the extraction procedure, the dummy molecularly imprinting process can be used as an alternative strategy to prepare this type of materials. In this context, Chen et al. (2013) prepared a dummy MMIP (DMMIP) for resveratrol by SMIP technique using Fe$_3$O$_4$@SiO$_2$ as supporter and rhapontigenin (an analogue compound of resveratrol) as dummy template in order to avoid the leakage of trace amounts of resveratrol. Acrylamide and EGDMA were used as functional monomer and cross-linker, respectively. The resultant MMIP was characterized and its selectivity recognition properties were evaluated showing high adsorption capacity and selectivity for resveratrol. The DMMIP was applied for the determination of resveratrol in wine samples, with recoveries between 79 - 91%.

MMPIs using Fe$_3$O$_4$ particles coated with mesostructured silica layers (Fe$_3$O$_4$@mSiO$_2$) as sacrificial support have also been developed in order to promote mass transfer and achieved higher binding kinetics, since it has been proved that this kind of materials greatly decrease mass-transport resistance and increase binding capacity. Therefore, the combination of the advantageous concepts of magnetic materials, mesostructured silicas and SMIP technology in one system, results in the development of novel advanced magnetic porous MIPs (MPMIPs). In this sense, Shi et al. (2017) prepared a novel MPMIP for highly selective extraction of cinnamic acid, using cinnamic acid as template, 4-VP as functional monomer, and magnetic Fe$_3$O$_4$ particles coated with mesostructured silica layer as sacrificial support. The material showed towards cinnamic acid a maximum adsorption capacity at 4.35 mg g^{-1} and pseudo-second-order reaction kinetics with equilibrium time at 60 min. The application of MPMIPs in the selective extraction of cinnamic acid from apple juices was successfully performed with high recovery (93 –101%) and reproducibility (RSD from 3.0 to 7.0%) values. Also, a hydrophilic MPMIP for gallic acid (Fe$_3$O$_4$@SiO$_2$@mSiO$_2$@MIPs) was prepared by self-polymerization of dopamine on magnetic mesostructured silica (Hu et al., 2015). For this purpose, Fe$_3$O$_4$@SiO$_2$ microspheres were first synthesized according to previous reports (Zhang et al., 2014) and then were coated with a mesostructured silica layer through a surfactant based sol–gel approach. Finally, the magnetic particles were polymerized using dopamine as functional monomer and gallic acid as template. The resultant material showed a maximum adsorption capacity of 88.7 mg g^{-1} and pseudo-second-order reaction kinetics

reaching equilibrium at 100 min. The synthesized MPMIP showed rapid magnetic separation (10 s) and stability (95% retention after six cycles). Lastly, the proposed MPMIP was successfully applied for the selective extraction of gallic acid from grape, apple peach and orange juices, with good recovery values (92 – 102%).

A MPMIP was also synthesized for the selective recognition of protocatechuic acid and was applied for selective and efficient extraction of protocatechuic acid from *Syzygium aromaticum* (Xie et al., 2015). The adsorption properties of the prepared MPMIP were further compared under same conditions with MIPs imprinted on magnetic non-mesostructured silica nanoparticles (MMIPs). The maximum adsorption capacity of protocatechuic acid on MPMIP was 17.2 mg g^{-1} (2.3 times higher than on MMIPs). This material showed an equilibrium time of 140 min and high stability (94.4% of retention after six cycles). Another MPMIP for the selective extraction of protocatechuic acid from *Syzygium aromaticum* was developed by the same research group (Li et al., 2015). A novel and alternative synthetic approach using MCM-48 mesostructured silica as sacrificial support was proposed to obtain a magnetic hollow porous molecularly imprinted polymer (MHPMIP). In first place, the HPMIP was synthesized by using protocatechuic acid as template, MCM-48 as sacrificial support, 4-VP as functional monomer and glycidilmethacrylate (GMA) as co-monomer. Subsequently, for magnetic properties, the epoxide ring of GMA was opened with perchloric acid for chemisorbing Fe$_3$O$_4$ nanoparticles *via* a simple co-precipitation process. The resultant material presented high adsorption capacity (38 mg g^{-1}) and fast binding kinetic (25 min), being highly superior to other reported protocatechuic acid MIPs prepared by traditional or SMIP technology. The selective recognition experiments also demonstrated the high selectivity of the developed MHPMIP towards protocatechuic acid over other compounds with an analogue structure, such as 4-hydroxybenzoic acid, salicylic acid, caffeic acid and gallic acid.

4. Integration of new silica-based sorbent materials in micro-extraction techniques for isolation of dietary polyphenols

The performance of sorbent-based micro-extraction techniques using new advanced silica-based sorbent materials allows combining and integrating the advantages of both concepts into one, what may lead to development of high-throughput sample preparation methods which can meet the requirements of the GAC approach and solve the intrinsic problems associated with the complexity of food matrices. In this sense, the miniaturization of sample preparation techniques and their combination with the development of more selective, robust, affordable and easily-prepared sorbents is a new research area that will

become an important trend in analytical chemistry in the coming years (Table 3), since the development of these new materials and their application as sorbents in micro-extraction techniques can result in more environmentally friendly methods, by reducing consumption of solvents, samples and time and saving money, while improving results without losing sensitivity or reproducibility.

Table 3. Application of silica-based sorbent materials in micro-extraction techniques for isolation of dietary polyphenols from food samples.

Micro-extraction technique	Sorbent (amount)	Food matrix	Analytes	Determination	Recoveries (%)	LOQ	Additional information*	Ref.
μ-SPE	SBA-15 (25 mg)	Citrus fruits	Narirutin, naringin, hesperidin, neohesperidin, naringenin, hesperetin	UHPLC-Q-TOF-MS/MS	89 - 103	$1.57 - 4.26$ ng mL^{-1}	Extraction time: 5 min Analysis time: 6 min	Cao et al. (2015)
μ-MSPD	SBA-15 (25 mg)	Orange fruit peels	Hesperidin, nobiletin, tangeretin	UHPLC-UV	89 - 105	$0.02 - 0.03$ μg mL^{-1}	Extraction time: 2.5 min Analysis time: 11 min	Cao et al. (2016)
MEPS	HPTES-SBA-15 (2 mg)	Pomegranate and grape juices	Ellagic acid	HPLC-UV	94 - 100	0.8 mg L^{-1}	Extraction time: 4.2 min 10 extraction cycles. Analysis time: 15 min	Rahimi et al. (2016)
PT-SPE	MISM (90 μL)	Orange juice	Gallic acid	HPLC–UV	92 -100	7 μg L^{-1}	Extraction time: 40 min Analysis time: 12 min	Arabi et al. (2017)

* Extraction time: refers to interaction time between sorbent and sample; Analysis time: refers to chromatographic separation time

In this context, the mesostructured silica SBA-15, which presents hexagonal ordered pore arrangement, has been successfully evaluated as sorbent for the extraction of 6 flavanones by miniaturized SPE (μ-SPE) and 3 flavonoids by μ-MSPD from citrus fruits and fruit peels, respectively (Cao et al., 2016 and 2015). Both works proved the excellent advantages of the mesostructured silica on the extraction of the target analytes thanks to its specific textural characteristics, providing rapid, simple and sensitive methods with very low LODs which meet the GAC requirements (low sample and sorbent amount and low elution volume consumption). However, although both methods used the same sorbent amount (25 mg) and recovery values were very similar among them, it was observed that LODs were lower when using UHPLC-Q-TOF than UHPLC-UV, due to the advantages of the accurate mass measurement and the abundant ion information provided by mass spectrometry detectors. Moreover, in the case of the μ-SPE method, the extraction performance of SBA-15 towards the 6 target flavanones was compared with the ones obtained using as well other mesostructured silicas (PCMA-60 and KIT-6) and mesoporous carbon (CMK-3) as sorbents. According to the authors, SBA-15 possessed better adsorption capability than the other tested sorbents due to the strong polarity and Coulomb field inside the cavities of the material and its unique rod-like shape (Fig. 4).

Rahimi and co-workers (2016) also used SBA-15 as sorbent for the micro-extraction of ellagic acid from pomegranate and grape juices using a semi-automated MEPS method. In this case, the silica was functionalized with three different ligands: 3-[*bis*(2-hydroxyethyl)amino]propyl-triethoxysilane (HPTES-SBA-15), dendrimer-like groups (G1-SBA-15) and propylthiols (YCSS-SBA-15), and the resulting materials were evaluated as sorbents. HPTES-SBA-15 showed the best extraction efficiency and the highest selectivity for ellagic acid, therefore, it was chosen as sorbent for the MEPS procedure, and only 2 mg of the material packed in the syringe's hub were enough for a quantitative recovery of ellagic acid from the analyzed samples, achieving recovery values between 94 and 100% with an average RSD value of 4.4% for six replicates.
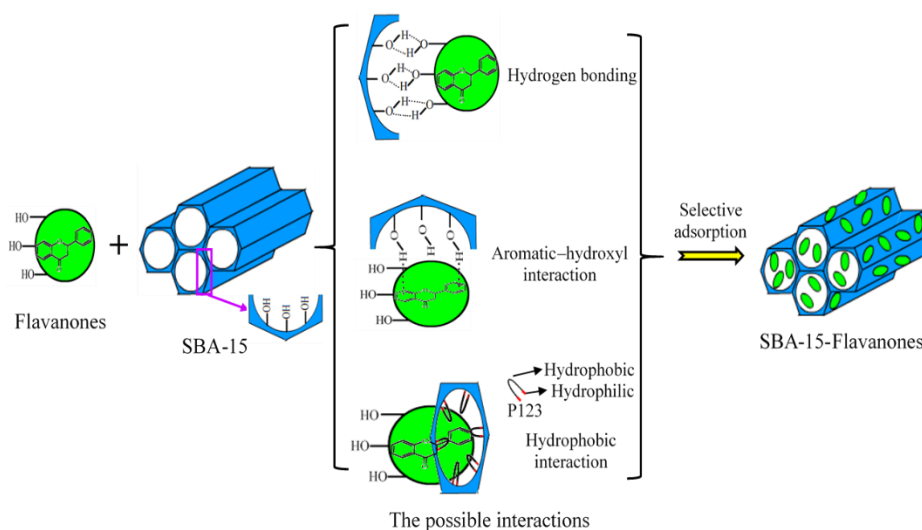
Figure 4. Mechanism of adsorption process by SBA-15 (Cao et al., 2015).

More recently, a new strategy combining the development of an advanced sorbent material with a novel micro-extraction technique, known as PT-SPE, was proposed by Arabi et al. (2017) for the selective extraction of gallic acid from orange juice samples. PT-SPE was developed as a miniaturized version of conventional SPE, where the sorbent material is packed inside plastic micropipette tips and extraction is performed by repeated aspiration and desorption of the sample solution using single channel and multichannel pipettors. The material exhibited high extraction efficiency, specific recognition capability and high extraction recovery (92 – 100%) with RSD values between 1.0 – 3.8%. Additionally gallic acid was efficiently extracted without significant matrix interferences, but it was not quantified in the sample analysed.

5. Conclusions and future perspectives

Most of the literature reported for polyphenols determination in food samples deals with the use of conventional extraction techniques, such as LLE and SPE, which require large amounts of sample, solvents and time. However, as it has been described in this review, these traditional sample preparation techniques are evolving into more sophisticated and environmentally friendly modes, according to the demands of the GAC, by scaling down the processes, what involves minimal requirements of sample, solvents and sorbents, so consequently they are less time-consuming and more cost-effective methods.. Thus, SPE has been replaced by novel and more efficient micro-extraction techniques, such as d-MSPE, μ-MSPD, MEPS, μSPEed®, SPME, PT-SPE, etc. As it has been reviewed, these techniques present multiple advantages, therefore, miniaturization, micro-extraction, and, in the near future, nano-extraction, are techniques with

promising perspectives aimed at solving problems related to the determination of compounds in food samples, in an environmentally friendly way and approaching to the standards of the GAC.

On the other hand, recent advances in the development of new sorbent materials have offered new opportunities for improving analytical performance of the developed methods. In this sense, mesostructured silicas have successfully been applied as sorbents for the extraction of polyphenols from different food samples due to their unique and advantageous properties. Magnetic materials have also proved their great potential as sorbents, providing simple, effective and quick extraction methods for isolation of polyphenols from foodstuffs. In the same way, the combination of MIT with silica-base materials is highly recommended in those processes where high extraction selectivity is required. In this context, new trends will be directed towards research and development of new materials and their application as sorbents in green micro-extraction techniques, expanding their integration to other kind of matrices and more types of analytes. As it has been reported, some works have already successfully combined these two issues. However, new perspectives should be focused on improving some characteristics of the materials, by coupling different types of materials, performing multi-functionalization and carefully considering issues related to their structural characteristics, such as mesoporous structure, wall composition, functionalization degree, pore size, particle size and morphology, etc., which are crucial to enhance efficiency of sample preparation.

Acknowledgments

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