Current development and applications of ordered mesoporous silicas and other sol-gel silica-based materials in food sample preparation for xenobiotics analysis

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In the last years, sample preparation has been playing an important role in the analysis of xenobiotics in complex matrices, such as food samples. Recent advances in the development of new materials, such as ordered mesoporous silicas (OMSs) and other sol-gel silica-based materials, have gained increasing research interest in sample preparation and analytical chemistry due to their desirable characteristics and advantages versus traditional and commercial sorbents, since they enhance the analytical performance of many existing techniques or allow new ones to be developed. The aim of this review is to provide an overview with the most relevant achievements in the preparation and functionalization of OMSs and other sol-gel organic-inorganic hybrid silicas, and to give some recent examples from the last six years (from 2010 to 2016) regarding the analytical applications of these materials in sample preparation and extraction of xenobiotics from food products, including beverages and drinking water samples.

Keywords: Ordered mesoporous silicas, Silica-based materials, Sample preparation, Molecularly imprinted silica, Organic-inorganic hybrid silicas, Food, Xenobiotics, Water, Solid-phase extraction.
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1. Introduction

The presence of potentially harmful contaminants and their organic residues in food is one of the main concerns in food safety. Contaminants might be present in food as a result of its production, treatment, packaging, transport or storage. Moreover, new toxic residues in food, the so-called emerging contaminants (e.g. pharmaceuticals, steroids, surfactants, pesticides, etc.), are increasing as a result of new industrial processes, agricultural practices, environmental pollution and climate change. The occurrence of these compounds can cause potential risk for human health [1]. Therefore, monitoring of these residues in food products has become nowadays the main demand in the food field, in order to ensure food safety, what has led to the need to develop quick, sensitive and selective analytical methodologies for determination of trace residues and contaminants in food samples.

Food samples are highly complex matrices, since they often contain proteins, fat, salts, acids, bases, and food additives with different chemical properties. In this sense, the determination of contaminants in food samples constitutes a difficult task, since normally they occur at very low concentrations and are subjected to interferences caused by the matrices. Matrix effects may produce a detrimental impact on important method parameters, such as limit of detection (LOD), limit of quantification (LOQ), linearity, accuracy, and precision. Therefore, an appropriate sample pretreatment method is indispensable in the analytical process [2]. The main purposes of sample preparation are to isolate and concentrate target compounds from the matrices and make the analytes more suitable for separation or detection. The typical steps within sample preparation include sampling/homogenization, filtration, extraction, clean-up and evaporation followed by the final analysis [3]. The final analysis is usually performed
using powerful separation techniques, typically chromatographic, combined with mass spectrometry or other appropriate detectors.

Sample preparation steps are often the most time and labor consuming parts of the analytical process. For this reason, there has been a tendency in the last years to develop new extraction and clean-up approaches, by minimizing the number of steps to reduce both time and sources of error, moving towards more environmentally friendly techniques, such as reduction in organic-solvent consumption and in sample degradation, and improving the extraction efficiency and selectivity with the application of new advanced sorbents [4-6]. Up to date, many sample preparation techniques have been applied in the food field to extract and to enrich trace-level analytes from complex matrices. These techniques include liquid-liquid extraction (LLE), liquid-solid extraction (LSE), microwave-assisted extraction (MAE), ultrasound assisted extraction (UAE), solid-phase extraction (SPE), micro-solid-phase extraction (μ-SPE), dispersive solid-phase extraction (d-SPE), molecularly imprinted solid-phase extraction (MISPE), solid-phase micro extraction (SPME), matrix solid-phase dispersion (MSPD), magnetic solid-phase extraction (MSPE), stir-bar sorptive extraction (SBSE), liquid-phase micro extraction (LPME), supercritical fluid extraction (SFE), super-heated water extraction (SHWE) and pressurized liquid extraction (PLE), among others, which have been previously reviewed by other authors [2-4, 7]. Each technique has its advantages and drawbacks, and the method selection depends on the properties of the target analytes and matrices.

However, considering the complexity of food products, attention should be focused on those extraction techniques with enhanced efficiency and sensitivity and on the highly selective sorbents that have been recently applied in food sample preparation. In recent years, new sorbent materials have promoted the development on extraction
and clean-up technologies, especially, SPE. Great efforts have been made on the improvement and investigation of these new advanced materials [2, 5-10]. Among them, ordered mesoporous silicas (OMSs) are gaining increasing research interest in sample preparation, since they present a number of desirable characteristics, such as high surface area, large pore volume, well defined pore-size distribution, controllable wall composition and modifiable surface properties [6]. For all these reasons, these materials may be a good alternative to classical sorbents, such as amorphous silica and polymeric materials, and they can allow an efficient extraction of the target compounds. Besides OMSs, other sol-gel silica-based materials have been developed in the last years and interesting advantages versus traditional sorbents have also been found for sample preparation.

This review aims to provide an overview of the most relevant achievements in the preparation of OMSs and other sol-gel organic-inorganic hybrids silicas, and give some recent examples, from the last six years (from 2010 to 2016), regarding the application of these materials in sample preparation and extraction of xenobiotics from food products, including beverages and drinking water.
2. Ordered mesoporous silicas (OMSs) for food sample preparation

OMSs where prepared for the first time in 1992 by the Mobil Oil Company [11, 12], known as the M41S phase (Mobil Composition of Mater No. 41) (Fig. 1). OMSs show very high specific surface areas (typically between 500 and 1000 m$^2$ g$^{-1}$), regularly ordered pore arrangement, well-defined pore size distribution, and pore diameters from approximately 20 to 100 Å. These materials are synthesized from molecular precursors using the hydrolytic sol-gel process which requires the participation of a templating or structure-directing agent, often a neutral or charged surfactant in aqueous solution or a water-soluble polymer. This templating effect directs the polymerization and condensation of silica precursors under mild chemical conditions. Once the synthesis process has concluded, the surfactant template is removed by calcination or solvent extraction.

The characteristics of the OMSs, such as particle size and morphology, surface area, pore diameter, etc., highly depend on the experimental synthesis conditions [13 - 15]. Thus, through innovative combinations of templates or texturing agents, starting from different mineral precursors and using a range of sol-gel reaction conditions, a wide number of OMSs have emerged (e.g. Santa Barbara amorphous (SBA) [16], Hexagonal mesoporous silica (HMS) [17], Fudan University (FDU) [18], etc.) with different structures (cubic, 3D hexagonal, 2D hexagonal, 2D rectangular, etc.). On the other hand, the functionalization of these materials with organic groups offers a further possibility of tailoring their physical and chemical properties, and therefore these materials can potentially be used for different applications such as adsorption of contaminants [19, 20], substance-delivery [21, 22], sensor-development [23, 24], chromatographic and electrophoretic separations [25, 26], etc.
The post-synthetic (PS) grafting procedure for modifying the surface of mesoporous silicas involves grafting a ligand (chloroorganosilane, alkoxyorganosilane or silazane), usually made in an organic solvent under reflux conditions, onto the surface of a previously prepared silica. The silanol groups (\(-\text{Si-OH}\)) of the silica surface are replaced by the desired organic ligands via single-step or multi-step attachment (Fig. 2a). The PS procedure allows the introduction of a wide variety of functional groups thanks to the reactive surface of silanols and has the advantage that, under the synthesis conditions used the mesostructure of the starting silica is usually maintained. However, there is no guarantee of a uniform distribution of the grafted functional groups. Other disadvantage of this method is the reduction in the porosity (surface area, pore volume and size) of the functionalized material, which depends on the size of the organic ligand and the degree of functionalization [27, 28]. An alternative method to directly obtained hybrid mesoporous silicas in one-step procedure is the co-condensation (CO) or direct synthesis (Fig. 2b). This method consists in the hydrolysis and co-condensation of tetraalkoxysilanes with one (or more) organoalkoxysilanes in the presence of a structure-directing agent leading to materials with organic residues anchored covalently to the pore walls. The CO procedure overcomes the main drawbacks of the PS method since the functional groups are direct components of the silica matrix and generally they are more homogeneously distributed inside the pore channels, so pore blocking is not a problem. However, there are also some disadvantages in this method. The appropriate selection of the organosilane and its compatibility with the reaction conditions are of vital importance, in order to avoid the perturbation of the micelles. Consequently the degree of functionalization that can be achieved with this method is limited, since increasing too much the amount of organosilane in the reaction mixture may ultimately lead to obtain totally disordered materials. Furthermore, considerable care must be taken
to retain the organic ligand during surfactant removal; therefore only extractive methods
can be used for this purpose and calcination is not suitable [27, 28].

In 1999 the preparation of the so-called periodic mesoporous organosilicas
(PMOs) represented a landmark in the field of mesoporous silicas [29 - 31]. PMOs with
organic groups integrated in the framework have offered a new family of materials with
very interesting surface and mechanical properties and improved hydrothermal stability.

PMOs are obtained by hydrolytic polycondensation of bridged organosilane precursors
of the type \([ (R’O)_3Si ]_n \) \( R \) (\( n \geq 2 \)) in the presence of a structure directing agent. The
organic units are incorporated in the 3D network structure of the silica matrix through
covalent bonds and thus distributed totally homogenously in the pore walls. Therefore,
the organic bridges are integral components of the silica network (Fig. 3). These
materials are characterized by periodically organized pore system and a very narrow
pore radius distribution. Changing the nature of the organic bridges includes specific
optical, electrical and surface properties in the material. The main advantage of
introducing any functional group within the pore walls of the mesoporous materials is
that the non-siliceous group will not partially block the mesopores, so a better diffusion
of the ion or molecules of interest through the pores can be achieved. Nevertheless, the
groups introduced generally affect the hydrophilic-lipophilic balance of the system what
makes difficult to determine the synthetic conditions required to simultaneously obtain
well-ordered pores and a specific particle size and morphology. One way to locate
functional groups in the framework is to modified the channel pores by employing
mixtures of bridged silsesquioxanes and terminal trialkoxysilyorganosilanes
\([ (R’O)_3SiR” ] \). This results in bi-functional PMOs with distinct locations of the organic
groups, a combination of bridging organic units inside the framework and terminal
organic groups whose ends point into the channels [32].
Once these OMSs had been synthesized and modified, different techniques can be used to characterize them in order to obtain information about their structural, morphological and textural properties, and regarding the functional groups attached to the silica. Low-angle powder X-ray diffraction (XRD) and transmission electron microscopy (TEM) are usually used to measure the pore structure (Fig. 4a and 4b). Pore volume, pore size distribution and specific surface area are typically measured by N₂ adsorption-desorption, what reveals type IV isotherms according to IUPAC classification which are characteristic of mesoporous materials with a high surface area and a narrow pore-size distribution (Fig. 4c and 4d). The combination of the XRD data with the average pore diameter obtained from N₂ adsorption-desorption analysis is often used to determine the wall thickness of the material. Scanning electron microscopy (SEM) is used to determine the particle morphology and size. The incorporation of functional groups can be verified by powerful techniques like NMR spectroscopy (especially ¹³C and ²⁹Si MAS-NMR) and FTIR spectroscopy which enable the simultaneous identification of multiple functionalities as well as the different types of silanol groups and the effectiveness of the covalent bonding of the ligand to the silica framework. Other techniques that provide information on chemical composition of the material include ultraviolet/visible, Raman, infrared, fluorescence and electron paramagnetic resonance spectrosopies. Elemental chemical analysis and thermogravimetric analysis (TGA) are also used to quantify the incorporation of organic groups and to estimate the thermal stability of the hybrid material [33].

To assess the potential of OMSs as sorbents in food sample preparation, different studies have been carried out in the last years for SPE [34-41], µ-SPE [41] and MSPD [42, 43] applications (Table 1). In most of these works, results have been compared with those obtained with commercial products, in terms of sensitivity and
selectivity, demonstrating their promising application for this purpose. Scheme 1 depicts the principles and the main differences of these three sample preparation techniques.

2.1 Applications for SPE

SPE is the most widely used procedure for extraction and pre-concentration of organic compounds from food and beverages samples, mainly due to its simplicity and limited usage of organic solvents. This technique involves a liquid-solid partition, where the extracting phase is a solid sorbent extensively used to remove and concentrate organic compounds from liquid samples or solutions. In comparison with liquid-liquid extraction, SPE is easy to use, and reduces solvent consumption and the time for sample preparation (Scheme 1). The procedure consists of a first conditioning step by passing organic solvents or water through the SPE cartridge (column filled with the sorbent) to increase the effective surface area and to reduce interferences. Then, the sample solution is loaded onto the cartridge and the target analytes are retained by the sorbent. Once the sample has been loaded, a washing step is performed in order to wash away undesired components which may interfere. After drying the sorbent, the interactions between the desired analytes and the sorbent are disrupted by passing small volumes of organic solvents, this leads to desorption of the analytes from the solid phase which are collected for its subsequent analysis.

One drawback of SPE is that the packing of the cartridge must be uniform to avoid poor efficiency, and although pre-packed commercial cartridges are considered reliable, automated systems can have difficulties with reproducibility for some sample types. On the other hand, it is very important to consider the particle size effect on the SPE
procedure, since the overall particle size for the different sorbents can be very different, what imposes many influences, such as, mass diffusion and a drop in pressure of the extraction device. Moreover, the sample matrix can also affect the ability of the sorbent to extract the analytes due to competition for retention. Thus, it is important to select a suitable sorbent, in order to control parameters such as selectivity, affinity and capacity. This choice highly depends on the target analytes and the interactions between the chosen sorbent and the functional groups of the analytes. It also depends on the kind of sample matrix involved and its interactions with both the sorbent and the analytes. In this sense, a wide range of materials have been used as sorbents in SPE (e.g. activated carbon, modified amorphous silica, clays, zeolites, organic chelating resins, carbon nanotubes, polyurethane foam, polymers, etc.). However, many of these materials present inherent problems such as low capacity, low selectivity, long equilibrium times, and mechanical/or thermal instability [5, 44 - 49]. Therefore, the aim of some research groups in this field has been to develop new materials with enhanced selectivity, better adsorptive capacity, enhanced thermal, chemical or mechanical stability and improved lifetime.

Various promising sorbents prepared by functionalization of new OMSs have been studied for the SPE of organic compounds from food, beverages and drinking water samples due to their remarkable characteristics, especially their large surface area, ease of functionalization, high adsorption capacity, excellent mechanical resistance, non-swelling behavior, and excellent stability. Over the past few years, different hybrids OMSs have been evaluated in our research group for analytical applications, including sample preparation. For example, Gañán et al. [34] prepared two OMSs with different morphology and structure, SBA-15 with cylindrical shape and well ordered 2D hexagonally structured pores (1.7 µm average particle length) and SM with spherical
shape and 3D wormhole framework structure (diameters ranging from 3 to 5.5 µm). Both silicas were modified with octadecyl (C18) groups by CO or PS procedure to achieve SBA-15-C18 and SM-C18, respectively. Functionalized and non-functionalized silicas were examined as sorbents for the extraction and preconcentration of 17β-estradiol from drinking water. Among the prepared materials, SBA-15-C18 had the highest adsorption capacity towards the extremely hydrophobic target analyte, what was mainly attributed to its very high functionalization degree (1.17 mmol/g). Under optimized conditions (200 mg of sorbent) the mean recovery obtained in spiked water samples was of 82% (RSD ≤ 3%) with a preconcentration factor of 150 (Fig. 5). Since SBA-15 proved to give better results than SM, this material was also tested as SPE sorbent for the extraction of twelve endocrine disrupting compounds in drinking waters. In this later study, the functionalization of the material by CO procedure was modified in order to obtain a carbon loading similar to the commercial amorphous silica ExtraBond C18 (17% C). Results obtained indicated that the prepared mesoporous sorbent enabled the extraction of the twelve estrogenic hormones in tap and mineral waters with recoveries between 70 and 111% (RSD ≤ 10%) for the lowest concentration level tested. A preconcentration factor of 1000 was achieved under optimized conditions, and three loading and elution cycles could be applied without a significant decrease in the adsorption capacity [35].

In milk samples, Pérez-Fernández et al. [36] examined SBA-15 and SM silicas both functionalized by the PS procedure with C18 groups as sorbents for the extraction and preconcentration of seven steroids. SBA-15-C18 showed a better behaviour for the SPE of these steroids in milk than SM-C18, which was mainly attributed to the different pore distribution and particle size of both sorbents since the functionalization degree was similar in both cases (0.26-0.28 mmol/g). Moreover, this SBA-15-C18 material showed
great extraction potential in comparison with other commercial sorbents, such as Oasis HLB cartridges and amorphous silica functionalized with C18 and NH2 groups (MFE-Pack C18 and DSC-NH2 cartridges, respectively). Thus under optimized conditions, 100 mg of sorbent allowed achieving recoveries between 62 and 108%. More recently, one-pot synthesized functionalized SBA-15 with C18 groups (0.69 mmol/g) was also successfully evaluated as reversed-phase SPE sorbent for the extraction of twelve endocrine disrupting compounds in milk, commonly used as growth promoters in cattle. Compared with other methods, the sample treatment procedure optimized in this work was simpler and/or faster, with satisfactory recoveries (between 72 and 105%, except for diethylstilbestrol, with RSD ≤ 10%) in whole and skimmed milks spiked at two concentration levels [37].

The application of this type of materials as SPE sorbents has also been recently demonstrated in our research group in bovine meat, which is a more complex food sample due to its high content of proteins and fats. For this purpose, Casado et al. [38] prepared SBA-15 functionalized with C18 groups by the PS procedure (0.23 mmol/g), and after the optimization of the solvent extraction protocol for meat samples, 100 mg of this material were successfully applied as SPE sorbent in the multi-residue extraction of 23 veterinary drugs (β-blockers, β-agonists and non-steroidal anti-inflammatory drugs) from the resulting extracts prior to their analysis by UHPLC-IT-MS/MS. The advantages of this material towards commercial C18 amorphous silica (0.23 mmol/g) were demonstrated under the same conditions, since recoveries obtained were higher for all compounds (Fig. 6). These results were attributed to the fact that hybrid SBA-15 contained more accessible functional groups than the commercial sorbent. In addition, in the mesoporous material the target analytes experienced a reversed-phase sorption with the C18 groups (by hydrophobic interactions) and polar secondary interactions (by
hydrogen bonding) as a result of the high number of residual non-modified silanol groups in the mesoporous silica. This fact was evidenced since more pronounced effect on the retention was observed for the most polar drugs. Additionally, bi-functionalized SBA-15, with C18 or C8 and SO$_3^-$ groups, have recently been prepared by Casado et al. [39] in order to obtain materials with reversed-phase/strong cation-exchange mixed-mode retention mechanism. The bi-functionalized materials were evaluated as SPE sorbents for the multi-residue extraction of 26 veterinary drug residues in meats. The mixed-mode retention mechanism of the prepared silicas was confirmed by comparing them with mono-functionalized SBA-15 with C18 or C8 groups. Best results were achieved with 200 mg of SBA-15-C18-SO$_3^-$ obtaining recoveries higher than 70% for the majority of analytes. However, besides the interactions of the analytes with the functionalites present on the material, it is also essential to consider the importance of some other parameters. In that respect, six different mesoporous silicas were functionalized with C18 groups (Casado et al. unpublished results) in order to evaluate the influence of the pore structure (hexagonal parallel channels versus wormhole-like pore arrangement), pore diameter (from 23 to 64 Å), particle morphology (spherical versus rod-like) and particle size (from 1 to 2.5 µm) on the extraction efficiency of 7 β-blockers, 9 β-agonists, 9 non-steroidal anti-inflammatory drugs and 1 mycotoxin in bovine meat extracts. On the basis of the results obtained, it was demonstrated the importance of the structural properties of the OMSs in their effectiveness as SPE sorbents. Thus, in comparison with SBA-15-C18, MCM-41-C18 and MSU-2-C18, HMS-C18 mesoporous silica showed to have a big potential as sorbent. This fact was attributed to its medium particle (1.7 µm) size and spherical morphology that provided better access to the wormlike-framework-confined mesopores of this material in the adsorption process. In addition, the mean diameter of this material and morphology was
favourable to pack homogeneously the cartridges and to reduce the drop in the pressure of the device (in comparison with smaller particles), achieving a higher reproducibility in the SPE procedure.

Unlike mesoporous silicas, PMOs are highly hydrophobic due to the uniform distribution of organic moieties throughout their pore wall, so they can be excellent adsorbents for organic molecules. In this regard, Carpio et al. [40] evaluated for the first time a PMO (phenylene-bridged material) as SPE sorbent for the extraction of five pesticides in grape must prior to their determination by CE-UV (Fig. 7). Results demonstrated that the prepared PMO (smooth, unevenly shaped particles with sizes 3 and 12 µm) was similar in terms of selectivity and sensitivity, and sometimes even better than commercial C18 and HLB sorbents in extracting the target analytes (recoveries between 86 – 105%). In the opinion of the authors, these results highlighted the outstanding properties of this type of material and stated that is the starting point to develop a new family of PMOs which can be apply as potential SPE sorbents in the determination of organic pollutants in food products.

2.2 Applications for µ-SPE

Micro-extraction techniques (such as SPME, SBSE, µ-SPE, d-SPE, etc.) have several advantages over traditional approaches such as LLE and conventional SPE. µ-SPE is a miniaturized mode of sorption-based extraction. Like SPE, this extraction procedure involves analyte adsorption followed by solvent desorption but on a much smaller scale. It was developed to reduce solvent consumption, sorbent usage and sample handling, without the need of special auxiliary device for extraction [49]. It is an interesting alternative to the multi-step SPE method for the extraction of analytes in
complex matrices, such as food samples, since sample clean-up and extraction step are carried out simultaneously (Scheme 1). The µ-SPE procedure involves the use of a sorbent material enclosed in a porous membrane sheet, which ends are sealed with heat. For extraction, this µ-SPE device which contains the sorbent is directly placed into the sample solution. Due to the porosity of the membrane, analytes are able to diffuse freely and are extracted by the sorbent. While the extraction is performed, the sample is stirred and the movement of the µ-SPE device enables mass transfer. In that respect, the use of nanoparticles (particle sizes between 1 and 100 nm) as sorbent enhances the interactions with the analytes in the extraction process, due to their surface properties (area, roughness, surface potential and electron distributions) [50]. After the extraction, the µ-SPE device is removed from the solution using a pair of tweezers, and immersed into a suitable organic solvent to carry out the analyte desorption by ultrasonification.

Lashgari and Lee [41] determined ten perfluorinated carboxylic acids (PFCAs) in fish fillet samples by HPLC-MS/MS using uncalcined MCM-41 mesoporous silica (denoted as CTAB-MCM-41) as µ-SPE sorbent for the extraction and pre-concentration of the target analytes. Results obtained indicated that the hydrophobic and positively charged surface of CTAB on the CTAB-MCM-41 could trap PFCAs with high extraction efficiency due to its anionic properties (recoveries between 77 – 120%, RSD ≤ 5 – 14%). Moreover, the protective role of the polypropylene membrane used in µ-SPE for the elimination of matrix effects was evaluated by parallel trials using classical d-SPE. Results showed that the polypropylene membrane was significantly effective in reducing matrix effects, and the recoveries obtained proved the feasibility and reliability of the proposed method for the determination of PFCAs in fish samples at the ng/g concentration range.
2.3 Applications for MSPD

MSPD procedure combines aspects of several analytical techniques, performing sample disruption while dispersing the components of the sample on a solid support (Scheme 1). First, the sample is placed in a glass mortar and mixed with a solid support using a glass pestle to obtain complete disruption and dispersion of the sample on the solid support. Once blending is complete, the mixture can be packed into an empty column. Elution is performed with a small volume of solvent and it can be achieved in two different ways. One possibility is to carry out a first washing step where interfering compounds are eluted while, next, analytes are eluted by a different solvent. On the other hand, analytes can be directly eluted if interfering matrix compounds are selectively retained on the column. Finally, the sample extract can be directly analyzed or, in some cases, additional clean-up is performed by SPE to remove interfering matrix components, particularly with fatty samples, prior to the analysis.

Some OMSs had been used as MSPD sorbents in food sample preparation. For example, Barreto et al. [42] successfully tested non-functionalized MCM-41 as MSPD sorbent for the extraction of six pesticides from mango fruit prior to their analysis by GC-MS. Recoveries ranged between 73-103% (RSD ≤ 9 %). Comparison of MCM-41 with commercially available silica gel provided significant cost advantage over the conventional sorbent since a smaller amount of sorbent was needed for the extraction and because MCM-41 is cheaper than other commercial sorbents. However, an aspect to optimize in this study, in order to reduce solvent consumption, would be the amount of sample and sorbent employed, since 2 g of each one were used for the MSPD procedure.
More recently, our research group has also demonstrated the application of OMSs as sorbents for MSPD. In this regard, Gañán et al. [43] developed a MSPD method using SBA-15 functionalized with C18 groups as sorbent for the simultaneous determination of five steroids in milk. For this purpose, 200 µl of goat milk sample and 100 mg of material were used and, after washing the cartridge with hexane, the target analytes were eluted with methanol. The mesoporous material proved high affinity towards the target analytes, therefore the resulting sample extract was sufficiently clean to be directly analysed by micellar electrokinetic chromatography (MECK) with UV-VIS detection. Good average recoveries (between 70 – 100%, RSD ≤ 13%) were obtained for the target analytes in the spiked goat milk samples.

3. Molecularly imprinted OMSs for food sample preparation

Traditional molecularly imprinted polymers (MIPs) are prepared by bulk polymerization or precipitation polymerization processes which use a template molecule and a functional monomer for co-polymerization in the presence of a cross linking agent and an initiator in a porogenic solvent. After polymerization, the template is removed, resulting in a polymer network with strategically positioned functional groups in binding sites that are complementary in size and shape to the template molecule. Therefore, the MIP can potentially recognize and bind with high selectivity to the template molecule or to other molecules with similar molecular structure. However, although MIPs exhibit high selectivity and have extensively been used as sorbents for SPE (the so called MISPE), the kinetics of the sorption/desorption process are unfavorable and mass transfer is slow in the bulky MIP [51]. In addition, leaching of template molecules can be produced, because the imprinted polymer matrices are
usually thick and the template molecules are too deeply embedded to be fully eluted before their use. Therefore, to overcome these drawbacks different molecular imprinting methods have been developed, such as surface molecular imprinting (SMIP). SMIP consist of localizing the recognition sites on the surface of a supporter, this strategy greatly increases the efficiency of adsorption and desorption, reducing the leakage of the residual template by reducing the diffusion length.

For SMIP process, OMS can be used as support materials because of their good stability in acidic or alkaline solutions and because the channels, instead of closed pores, of this kind of materials facilitate the diffusion of solvent and template, what makes the removal of template easier. In addition, these molecularly imprinted OMSs have an extremely high surface-to-volume ratio; therefore most of the template molecules are situated at the surface or in the vicinity of the material surface. This fact is expected to improve the binding capacity, binding kinetics and accessibility of the recognition sites. For these reasons, some authors have prepared composite materials (OMSs@MIPS) by post-modification of OMSs, and have demonstrated important advantages of these sorbents for MISPE in food sample preparation, by combining the selectivity of MIPs and the binding capacity of OMSs [52-54]. On the other hand, other alternative strategies to achieve imprinted mesoporous silicas have been developed, for example using a complex of template-monomer with covalent bonding in the OMSs synthesis. This strategy also allows improving the site accessibility of MIP and increases the efficiency of MISPE, since the high pore volume and nano-sized wall thickness of the material allows high accessibility for the target molecule [55, 56]. However, a limitation of this approach is that the monomer has to be able to form a reversible covalent bond with the template molecule. Table 2 shows applications of OMSs in food and drinking sample preparation.
3.1 Applications for MISPE

Mehdinia et al. [52] used non-functionalized SBA-15 as support for the synthesis of an imprinted polyaniline-based MIP. Polymerization occurred inside the channels of the SBA-15 thanks to the negatively charged internal surface of the material that allowed the attachment of positively charged anilinium ions and 2,4-dinitrophenol as template (Fig. 8). The prepared SBA-15@MIP nanocomposite was characterized and results revealed that it possessed a highly ordered mesoporous structure. The material was used as a selective sorbent for MISPE of 2,4-dinitrophenol in the presence of phenolic compounds in tap water samples, analysed by HPLC-UV, showing a high adsorption capacity, selectivity and good site accessibility for the target analyte (recoveries higher that 96%, RSD ≤ 3.2%).

To avoid interferences due to the leaching of the template molecules during the extraction procedure, an alternative strategy to prepare this type of materials consist in the replacement of the template by other molecule with analogue structure (dummy molecularly imprinting process, DMIP). Therefore, Li et al. [53] prepared a MCM-48@DMIP composite using tetrabromobisphenol A as dummy template, 4-vinylpyridine as functional monomer and MCM-48 nanospheres (525 nm average diameter) as support. The material was evaluated for the isolation and determination of bisphenol A in drinking waters, and it exhibited satisfactory results with good recoveries (between 95 – 105%, RSD ≤ 6%), high selectivity and repeatability. In addition, the developed extraction protocol eliminated the effect of template leakage on quantitative analysis.

More recently, Yang et al. [54] developed a new strategy to prepare SBA-15@MIP composites using the atom transfer radical polymerization (ATRP) in the
imprinting process in order to create more homogeneous polymer layer on the silica surface. The results demonstrated that the material (spherical particles with diameters between 3-5µm and 45 Å of pore size) had both advantages of MIP and OMSs, as it proved to have good selectivity, high binding capacity and fast binding kinetics for the target analyte (bisphenol A). On-line MISPE experiments were carried out to demonstrate the application of the material as sorbent for the efficient determination of bisphenol A in tap water by HPLC. Moreover, bisphenol A and its analogues showed less peak tailings, what was attributed to the thin MIP film and less mass transfer resistance of the material.

With the aim to improve the site accessibility of this type of materials and increase the extraction efficiency of bisphenol A in waters by MISPE, Cheng et al. [55] prepared new imprinted OMSs, based on MCM-41 and SBA-15, by incorporation of a semicovalently bond molecule into the skeletons of the mesoporous materials for imprinting (Fig. 9a). Results revealed that the MIP-SBA-15 not only showed high selectivity to the target molecule because of the existence of molecularly imprinted sites, but also its recognition capability was four fold of MIP-MCM-41, suggesting that the structure of the mesoporous material greatly influence the recognition efficiency (Fig 9b). Therefore, the molecularly imprinted SBA-15 resulted to be an efficient SPE sorbent for bisphenol A in waters with mean recoveries higher than 87%.

In order to avoid the interference of the residual template molecules and reduce the number of non-specific binding sites Yu et al. [56] combined for the first time a DMIP with a new synthesis strategy to prepare mesoporous silicas (irregular shape particles with size of 10-20µm). A new covalent template-monomer complex (BPAF-Si) was first synthesized with 2,2-bis(4-hydroxyphenyl)hexafluoropropane (BPAF) as the dummy template. Then, the imprinted silica was obtained via sol-gel process of
BPFA-Si with tetraethoxysilane, and the subsequent removal of template by thermal cleavage of the urethane bonds. When used as MISPE sorbent for bisphenol A, the new imprinted silica presented high extraction efficiency, high enrichment factor (up to 200) and acceptable reusability (20 cycles). Therefore, owing to these benefits the material was successfully used as SPE sorbent for detecting trace amount of bisphenol A in tap waters (recovery 99-105%, RSD 3-5%).

4. Other sol-gel organic-inorganic hybrid silicas in food sample preparation

4.1 Applications of ORMOSILs and molecularly imprinted ORMOSILs

Some new sol-gel organic–inorganic hybrid silica-based materials, the so-called ORMOSILs (organically modified silicas), had been prepared and employed in the last years as SPE sorbents in food and beverage analysis (sample preparation) (Table 3). For example, Ibrahim et al. [57] synthesized a novel organic-inorganic silica based on methyltrimethoxysilane-tetraethoxysilane (MTMOS-TEOS) and used it as SPE sorbent for the determination of five organophosphorus pesticides by GC-MS. The sorbent (with 50 Å of pore size and around 1 µm of particle size) showed superior extraction performance in comparison to other sol-gel hybrid materials, probably due to the porous nature and large surface area of the sol-gel material. The introduction of the MTMOS to TEOS helped to increase the hydrophobicity of the material and promote the interaction between the hydrophobic pesticides and the sorbent. The high surface area and the mesoporous nature of the material also facilitated the adsorption process and increased the sensitivity. Excellent recoveries of the pesticides in water and fruit samples were
obtained (97-11%, RSD between 0.4 – 4%), so the material resulted as an inexpensive alternative to commercially available C18 sorbents.

A novel ampholine-functionalized hybrid organic-inorganic silica material was prepared by Wang et al. [58] via glutaraldehyde crosslinking reaction and applied as SPE sorbent for the extraction of acidic and basic compounds in beverage Coca-Cola®. Ampholine was chemically bonded on the surface of the hybrid organic-inorganic silica, and it was observed that this material showed three types of interactions: electrostatic interaction, hydrophobic interaction, and hydrogen bonding, exhibiting high extraction efficiency and good reproducibility towards the tested compounds, which were comparable to those obtained with commercial Oasis WAX and Oasis WCX sorbents. Two years later, the same research group applied this material as sorbent for the extraction and purification of melamine from milk samples by SPE [59]. The adsorption capacity towards melamine of the developed ampholine-functionalized hybrid organic-inorganic silica, based on hydrophilic interactions, was 30 μg of melamine per gram of sorbent, and it showed excellent extraction efficiency and repeatability. Under optimized conditions high recoveries were achieved (between 86 and 102%, RSD ≤ 8%), so the developed SPE method was proposed as a promising tool for daily monitoring of milk infant formulas.

Molecularly imprinted ORMOSILS are prepared by a conventional sol-gel process with incorporation of the template molecules into the synthesis reaction mixture. After removal of the template, molecular cavities with distinct pore size, functionality and shape remain in the host. These molecularly imprinted cavities show high affinity for the target compound over other structurally related compounds. In this sense, Silva et al. [60] prepared a novel molecularly imprinted ORMOSIL. The material was synthesized by a sol-gel route through hydrolysis and condensation reactions using
3-aminopropyltrimethoxysilane as functional monomer, tetraethylorthosilicate as reticulating agent and atrazine as template. The material was then evaluated as a specific sorbent for the extraction of triazine herbicides from sugar cane juice. Results showed that the material was highly selective for the template molecule as well as for other structurally related compounds. The results were also comparable with those obtained using commercial SupelMIP SPE cartridges (recoveries between 79–116%, RSD ≤ 9%), with the advantage of being reusable.

4.2 Applications of other hybrid silica-based composite materials

Different hybrid silica-based composite materials have been prepared in the last years using different synthetic routes. Hybrid composite materials usually possess the advantages of both materials (e.g. SiO₂, MIP, Fe₃O₄, graphene, etc), and for this reason they have been studied as promising sorbents for food sample preparation (Table 3). For example, Lv et al. [61] developed a novel molecularly imprinted organic-inorganic hybrid composite material based on molecular imprinting technique in combination with hybrid composite synthesis and sol-gel technology. Methacrylic acid was used as organic functional monomer, tetraethoxysilane as inorganic precursor, oxytetracycline as template and methacryloxypropyltrimethoxysilane as the coupling agent, which was used to form the covalent bonding between the organic and inorganic phases. This synthetic method provided flexible reaction conditions which improved adsorption capacity, selectivity, hardness and toughness by changing factors such as the molar ratio of inorganic precursor and organic functional monomer. The composite material was then successfully applied for the selective extraction of tetracycline antibiotics residues.
from milk samples by MISPE. Very good recoveries in the range of 81 – 104% with RSD between 5 – 13% were found under optimized conditions.

Recently graphene has intrigued increasing interest in the separation and preconcentration field due to its excellent mechanical strength and large surface area. For these reasons, great efforts have been done to develop graphene-based composites. In this regard, Liu et al. [62] presented for the first time an easy and simple synthetic route to coat C8-modified mesoporous silica onto hydrophilic graphene nanosheets through a surfactant-mediated cocondensation sol-gel process (Fig. 10a). The material with a three-layer structure (graphene@mSiO$_2$-C8) was successfully applied for efficient extraction of glucocorticoid residues in milk by d-SPE prior to their analysis by HPLC-MS/MS (Fig. 10b). The obtained materials possessed high surface area, extended plate-like morphology in the exterior surface, highly open pore structure with uniform pore size, numerous C8-modified interior pore-walls, as well as good water dispersibility. In addition, satisfactory reusability and stability were also obtained during the extraction of glucocorticoids. In this procedure, the sorbent material was directly added into the sample, what improved the interaction area between the sorbent and the target analytes. Then, the sorbent was separated from the supernatant by centrifugation to remove interferences and, finally, analytes were eluted with different solvents. The methodology developed provided low LOD and good linearity, with recoveries between 85 – 95%. Moreover, since d-SPE avoids passing the extract through a SPE cartridge, fewer amounts of sorbent and solvent were used, reducing time and labor, therefore the method was proposed as an attractive choice for convenient, efficient and rapid extraction of glucocorticoids and other small molecules in biological samples.
The synthesis of new magnetic adsorbents has received considerable attention in the last years [2, 7, 9]. This magnetic sorbents are usually synthesized using generally magnetite, Fe₃O₄, followed by coating of the magnetic phase with diverse organic compounds or with other materials. One of the most applied magnetics sorbents consists in Fe₃O₄ nanoparticles (usually between 50-100 nm) encapsulated in a silica shell by sol-gel polymerization and subsequently modified with some organic ligands. The resultant solids are applied as sorbents during isolation, separation, and preconcentration of analytes by MSPE. Compared to classical SPE, this methodology is faster and has several benefits, since it provides simplicity, efficiency, high selectivity, minimum sample manipulation, lower solvent consumption, and consequently lower cost. Additionally, the procedure does not need additional steps that could cause loss of analytes, such as centrifugation, precipitation, or filtration of the sample. The advantages of the MSPE have promoted in recent years its application in the food field, during control and analysis of residues of organic compounds in food samples. The selection of the sorbent is a critical parameter in order to achieve the best results in the preconcentration process, and some factors must be taken into account, like for example the polarity of analytes, the nature, and the complexity of the matrix. Therefore, the preparation and application of new magnetic sorbents for MSPE has received considerable attention. For instance, Ibarra et al. synthesized different silica-based magnetic mixed-polarity sorbents functionalized with phenyl chains (Fe₃O₄@SiO₂-Phenyl-C8) for the extraction of tetracyclines [63], quinolones [64] and sulphonamides [65] in milks. These sorbents were synthesized by varying the molar ratio of phenyltrimethylsilane and tetramethyloorthosilicate, and were evaluated in terms of their pH and degree of hydrophobicity for the target analytes retention. The optimal conditions were a pH of 6 and a magnetic:sorbent ratio of 2:1 in the case of
sulphonamides, while for tetracyclines the optimal conditions were a pH of 10 and a magnetic:sorbent ratio of 4:1. The proposed methodologies demonstrated in all cases to be efficient strategies for the rapid preconcentration by MSPE of the target analytes in complex matrices samples such as milk. In other works, triphenylamine [66] and C18 [67, 68] have been used for silica modification, and the resulting materials have been successfully applied as MSPE sorbents for determination of PAHs in waters by HPLC-FLD [66], pyrethroids in vegetables by UHPLC-UV [67] and endocrine disruptors in milks by GC-MS [68]. The incorporation of surfactants, such as dioctadecyl dimethyl ammonium chloride (DODMAC), into the silica matrix of silica magnetic particles has been evaluated by He et al. [69]. The resulting material, \( \text{Fe}_3\text{O}_4@\text{DODMAC}@\text{silica} \) (with an average particle diameter ~ 3 \( \mu \text{m} \)), demonstrated to be a good candidate as MSPE sorbent for the extraction of five sulfonylurea herbicides in waters. This strategy favoured the extraction of the organic analytes when performing MSPE, and provided surfactant free extracts during the eluting step to avoid chromatographic interferences. Good recoveries (80 – 107\%, RSD ≤ 6\%) were achieved under optimized method conditions.

Alternatively, Sun et al. [70] modified silica-coated \( \text{Fe}_3\text{O}_4 \) nanoparticles by grafting graphene onto the surface by chemical bonding, and the novel nanocomposites (\( \text{Fe}_3\text{O}_4@\text{SiO}_2-G \), 5-30 nm) were applied as sorbents for the extraction of carbamates from cucumber and pear samples by MSPE prior to their determination by HPLC with UV detection. Wang et al. [71] also grafted graphene onto the surface of magnetic microspheres by chemical bonding, and used them as a novel sorbent for the preconcentration and determination by HPLC-UV of phthalate esters in soybean milk samples. Results of both works indicated that the graphene bonded on the surface of the magnetic microspheres endows the material with a high adsorption capacity towards the
target analytes. These same authors also evaluated the Fe$_3$O$_4$@SiO$_2$-G particles (15-40 nm) as sorbent for the extraction of five PAHs in drinking water samples [72]. Results revealed that satisfactory extraction can be achieved with only 15 mg of sorbent per 250 mL solution due to the high surface area and the excellent adsorption capacity of the material. Recoveries of the developed method were in the range of 83-108% (RSD ≤ 6%). More recently, Zhang et al. [73] prepared Fe$_3$O$_4$ magnetite particles (average diameter of ~ 500 nm) modified with graphene oxide (shell layer thickness of ~ 100 nm) via a microwave-assisted synthesis method, and used them in the MSPE of three phenolic compounds in drinking water. Owing to the high surface area and the excellent adsorption capacity of the prepared material, satisfactory recoveries were achieved. In addition the material could be used at least 15 times without significant decrease in the sorption capacity. On the other hand, Huang et al. [74] developed novel raisin-bread sandwich-structured magnetic graphene/mesoporous silica composites with C18-modified interior pore walls (Fe$_3$O$_4$-G@mSiO$_2$-C18) through a simple one-pot co-condensation approach for its application as MSPE sorbent for the selective enrichment of phthalates in drinking water samples. The novel hybrid material was synthesized by bonding acidized graphene with magnetic Fe$_3$O$_4$, and following coated with functional mesoporous silica. The obtained functionalized nanocomposites possessed regularly aligned pores, high surface area, strong magnetic responsivity, hydrophilic exterior surface, and C18-modified interior pore walls, which endowed them with powerful extraction capacity for selective enrichment of the target analytes. Results indicated that this novel approach offers an attractive alternative for rapid, convenient, efficient and selective extraction of hydrophobic compounds.

The adsorption ability of magnetic nanoparticles can also be improved by surface modification of the magnetic nanoparticles with an ionic liquid (IL). For this
reason, magnetic nanoparticles coated with ILs have been successfully evaluated as sorbents for the extraction of different target analytes in food samples. For example, Yang et al. [75] prepared magnetic microspheres (600 nm) functionalized with IL for the preconcentration of three chlorophenols in drinking water samples. A mesoporous silica shell was formed on the surface of the Fe₃O₄ nanoparticles by sol-gel polymerization method and then the IL N-methylimidazolium (MIM) was covalently bonded on the previous chloropropyl-modified magnetic silica microspheres. This approach earns many merits such as simplicity, ease of operation, satisfactory sensitivity, and less consumption of organic solvents compared to traditional SPE. In addition, by immobilizing IL on magnetic microspheres, the IL can be saved. Results indicated that this novel sorbent provides efficient separation, purification and preconcentration of organic pollutants. Under optimal conditions, good recoveries (70 – 89 %) were achieved with satisfactory RSD ≤ 6 %. A similar synthesis strategy was used by Galán-Cano et al. [76] who prepared Fe₃O₄@SiO₂ nanoparticles (average particle size of 12 nm) coated by covalent immobilization with the IL MIM. The material was successfully applied as MSPE sorbent for the extraction of PAHs from drinking water samples prior to their determination by GC-MS. Results obtained in both works indicated that the covalent immobilization of the IL coating provides high stability, avoiding its loss during the extraction and elution processes. This aspect was especially interesting since it allows the reuse of the sorbent up to ten times after a soft cleaning process with a negligible effect on its extraction capacity. More recently other ILs have also been successfully used for this purpose, and have been evaluated for the determination of Rhodamine B in chili powder and Chinese prickly ash samples [77] or for the selective extraction and separation of pyrethroids from fruits and vegetables samples in combination with supercritical fluid extraction [78].
Magnetic core-mesoporous shell microspheres functionalized with C18 have also been successfully evaluated as MSPE sorbent for the extraction of cephalosporins in milk samples prior their determination by HPLC-MS/MS [79]. C18-Fe₃O₄@mSiO₂ microspheres (250 nm of diameter with magnetic core and 50 nm thickness of porous silica shell) with both good dispersibility and extraction efficiency were synthesized through a one-pot sol-gel coating strategy (Fig. 11). The excellent magnetic responsibility of the microspheres made the sample extraction procedure simple and quick, with no need for any protein precipitation procedure. The cephalosporins were directly adsorbed onto the C18-Fe₃O₄@mSiO₂ microspheres through hydrophobic interactions with the C18 groups coated in the interior walls of the mesoporous channels while milk proteins were excluded out of the channels due to the size exclusion effect. Moreover, thanks to the easier preparation, the less solvent consumption, the sample handling procedure and the high extraction efficiency, the extraction procedure could be achieve with little amount of sorbent in a short time of 10 min. Thus, the newly proposed method was validated, and it offered good linearity, accuracy and precision.

Considering the advantages of mesoporous materials, Lu and Xu [80] prepared estrone imprinted mesoporous structured Fe₃O₄@SiO₂@mSiO₂ particles (particle diameter about 300 nm fully coated by silica shell with thickness about 50 nm) (Fig. 12) that were successfully applied as sorbent for selective pre-concentration and specific recognition of estrone, 17β-estradiol and estriol from drinking water samples by MSPE. Magnetic particles were introduced because magnetic properties enable simple, rapid and efficient separation. Moreover, they demonstrated that the new material presented higher binding capacity, faster mass transfer and higher extraction efficiency for the three analytes than non-porous structured Fe₃O₄@SiO₂ particles (Fig. 13).
5. Conclusions and future trends

The use of ordered mesoporous silicas and other sol-gel silica-based materials in food sample preparation is a topic of growing interest in analytical sciences. The particular characteristics of this type of materials have been extensively exploited in different extraction techniques, mainly SPE, MSPD and MSPE. These studies have demonstrated that these materials are promising sorbents in sample preparation and they offer new opportunities for improving the performance of analytical methods in terms of linear range, limits of detection and quantification, precision, accuracy and selectivity. OMSs have successfully been applied as SPE, μSPE and MSPD sorbents for the extraction of xenobiotics from food and drinking samples due to their unique characteristics, such as large surface area, ease of functionalization, high adsorption capacity, excellent mechanical resistance, non-swelling properties and stability. The use of OMSs results in markedly improved analytical features in comparison to those reported for conventional and commercial sorbents. PMOs have showed to be potential and promising SPE sorbents in the determination of organic pollutants; however, they remain unknown and are scarcely used with this purpose. In order to improve the selectivity of OMSs, the current trend is to achieve imprinted mesoporous silica, using OMSs as support materials. This strategy has demonstrated to improve the binding capacity and the accessibility of the recognition sites. Although SPE is the most often-used sample pretreatment method, the synthesis of new magnetic sorbents has received considerable attention in the last years in the food field, since this technique provides several benefits, such as simplicity, efficiency, selectivity, low solvent consumption and minimum sample manipulation. Moreover, the adsorption ability of the magnetic
particles can be improved in different ways by surface modification, using graphene or IL for instance.

In conclusion, the rapid and current research in the development of new materials linked with new analytical methods will provide a wide range of new sorbents that will have a great relevance in the future of food analysis. The major trends in this context would be focused on improving some of the characteristics of the materials, in order to increase their selectivity and the preconcentration factor in the extraction procedure. In this sense, the preparation of hybrid materials by coupling various types of materials (SiO$_2$, MIP, Fe$_3$O$_4$, graphene, etc.) is a very interesting strategy to improve the selectivity and/or adsorption ability of the sorbent. Also, due to the complexity of food matrices, it is still a huge challenge to extract trace amounts of a wide range of contaminants in these samples, so it is necessary to develop novel multi-functionalized sorbents for multi-residue analyses. In addition, although these materials have demonstrated advantages in sample preparation, some issues associated with their structural characteristics must be carefully considered (i.e. mesoporous structure, wall composition, functionalization degree, pore size, particle size and morphology, etc.) since they are crucial factors in the enhancement of efficiency of sample preparation. Finally, in order to satisfy the general objectives of sample preparation (smaller sample amounts, reduction of solvents and sorbents, reduction of preparation time, etc. and potential for automation), the development and application of new materials for on/in-line mode of extraction methods will be of special interest, as a key aspect for broadening their use in routine analyses for the monitoring and control of xenobiotics in food products in order to ensure food safety.
Acknowledgments

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Table 1. Applications of ordered mesoporous silicas (OMSs) in food and drinking sample preparation.

<table>
<thead>
<tr>
<th>Matrix</th>
<th>Analyte</th>
<th>Sorbent</th>
<th>Extraction</th>
<th>Determination</th>
<th>Recoveries</th>
<th>Ref.</th>
</tr>
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<td>17β-estradiol</td>
<td>SBA-15-C18, SM-C18</td>
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<td>HPLC-DAD</td>
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<td></td>
<td>Endocrine disrupting compounds</td>
<td>SBA-15-C18 (100 mg)</td>
<td>SPE</td>
<td>HPLC-DAD</td>
<td>70-111%</td>
<td>[35]</td>
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<td>Endocrine disrupting compounds</td>
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<td>[37]</td>
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<td></td>
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<td>MECK-UV/VIS</td>
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<td>Veterinary drugs</td>
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<td>UHPLC-MS/MS</td>
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<td>Grape must</td>
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<td>Fish</td>
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Table 2. Applications of molecularly imprinted ordered mesoporous silicas (OMSs) in food and drinking sample preparation.

<table>
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<th>Matrix</th>
<th>Analyte</th>
<th>Sorbent</th>
<th>Extraction</th>
<th>Determination</th>
<th>Recoveries</th>
<th>Ref.</th>
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<tbody>
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<td>2,4-dinitrophenol</td>
<td>SBA-15@MIP (100 mg)</td>
<td>SPE</td>
<td>HPLC-UV</td>
<td>98%</td>
<td>[52]</td>
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<td>Bisphenol A</td>
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<td>HPLC-UV</td>
<td>95-105%</td>
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<td>Bisphenol A</td>
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<td>97%</td>
<td>[54]</td>
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<td>HPLC-UV</td>
<td>88-94%</td>
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<td>Bisphenol A</td>
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<td>HPLC-UV</td>
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<td>Bisphenol A</td>
<td>mesoporous silica (MIMO) (300 mg)</td>
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<td>HPLC-UV</td>
<td>99-105%</td>
<td>[56]</td>
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Table 3. Applications of sol-gel organic-inorganic hybrid silicas in food and drinking sample preparation.

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<th>Determination</th>
<th>Recoveries</th>
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<td>Fe$_3$O$_4$@SiO$_2$-TPA (80 mg)</td>
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<td>HPLC-DAD</td>
<td>81-107%</td>
<td>[69]</td>
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<td>HPLC-FLD</td>
<td>83-108%</td>
<td>[72]</td>
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<td>Phenolic compounds</td>
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<td>HPLC-UV</td>
<td>89-104%</td>
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<td>HPLC-DAD</td>
<td>70-89%</td>
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<td>75-102%</td>
<td>[76]</td>
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<td>Fe$_3$O$_4$@SiO$_2$-mSiO$_2$ (800 mg)</td>
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<td>HPLC-UV</td>
<td>85-95%</td>
<td>[80]</td>
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<td>Coca-cola®</td>
<td>Acidic and basic compounds</td>
<td>Ampholine-hybrid organic-inorganic silica (50 mg)</td>
<td>SPE</td>
<td>HPLC-DAD</td>
<td>82-98%</td>
<td>[58]</td>
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<tr>
<td>Sugar cane juice</td>
<td>Herbicides</td>
<td>ORMOSIL (25 mg)</td>
<td>SPE</td>
<td>HPLC-UV</td>
<td>79-116%</td>
<td>[60]</td>
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<td>Category</td>
<td>Substance</td>
<td>Adsorbent Description</td>
<td>Extraction Method</td>
<td>Separation Method</td>
<td>Recovery (%)</td>
<td>Reference</td>
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<tr>
<td>Milk</td>
<td>Melamine</td>
<td>(15 mg) Ampholine-functionalized hybrid organic-inorganic silica (300 mg)</td>
<td>SPE</td>
<td>HPLC-UV</td>
<td>86-102%</td>
<td>[59]</td>
</tr>
<tr>
<td></td>
<td>Tetracyclines</td>
<td>MIP-HCM (50 mg)</td>
<td>SPE</td>
<td>HPLC-UV</td>
<td>81-104%</td>
<td>[61]</td>
</tr>
<tr>
<td></td>
<td>Glucocorticoids</td>
<td>graphene@mSiO$_2$-C8 (0.6 mg)</td>
<td>dSPE</td>
<td>HPLC-MS/MS</td>
<td>85-95%</td>
<td>[62]</td>
</tr>
<tr>
<td></td>
<td>Tetracyclines</td>
<td>Fe$_3$O$_4$@SiO$_2$-Phenyl-C8 (100 mg)</td>
<td>MSPE</td>
<td>CE</td>
<td>94-100%</td>
<td>[63]</td>
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<td>Quinolones</td>
<td>Fe$_3$O$_4$@SiO$_2$-Phenyl-C8 (130 mg)</td>
<td>MSPE</td>
<td>CE</td>
<td>74-98%</td>
<td>[64]</td>
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<tr>
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<td>Sulphonamides</td>
<td>Fe$_3$O$_4$@SiO$_2$-Phenyl-C8 (100 mg)</td>
<td>MSPE</td>
<td>HPLC-DAD</td>
<td>82-115%</td>
<td>[65]</td>
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<td></td>
<td>Endocrine disruptors</td>
<td>Fe$_3$O$_4$@SiO$_2$@C18 (17 mg)</td>
<td>MSPE</td>
<td>GC-MS</td>
<td>79-116%</td>
<td>[68]</td>
</tr>
<tr>
<td></td>
<td>Cephalosporins</td>
<td>C18-Fe$_3$O$_4$@mSiO$_2$ (1 mg)</td>
<td>MSPE</td>
<td>HPLC-MS/MS</td>
<td>85-115%</td>
<td>[79]</td>
</tr>
<tr>
<td></td>
<td>Pesticides</td>
<td>Organic-inorganic hybrid</td>
<td>SPE</td>
<td>GC-MS</td>
<td>97-111%</td>
<td>[57]</td>
</tr>
<tr>
<td>Fruits and Vegetables</td>
<td>Insecticides</td>
<td>Fe$_3$O$_4$@SiO$_2$-C18 (30 mg)</td>
<td>MSPE</td>
<td>UFLC-UV/VIS</td>
<td>76-99%</td>
<td>[67]</td>
</tr>
<tr>
<td></td>
<td>Pesticides</td>
<td>Fe$_3$O$_4$@SiO$_2$-G (20 mg)</td>
<td>MSPE</td>
<td>HPLC-UV</td>
<td>93-107%</td>
<td>[70]</td>
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<tr>
<td>Chili poder and</td>
<td>Insecticides</td>
<td>Fe$_3$O$_4$@SiO$_2$@ILs (40 mg)</td>
<td>MSPE</td>
<td>HPLC-UV</td>
<td>89-107%</td>
<td>[78]</td>
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<td>Chinese prickly</td>
<td>Rhodamine B</td>
<td>Fe$_3$O$_4$@SiO$_2$@ILs (100 mg)</td>
<td>MSPE</td>
<td>HPLC-UV</td>
<td>99-101%</td>
<td>[77]</td>
</tr>
</tbody>
</table>
**Scheme 1.** Schematic diagrams and comparison of a range of factors of the main extraction techniques used in food sample preparation.

<table>
<thead>
<tr>
<th></th>
<th>SPE</th>
<th>μ-SPE</th>
<th>MSPD</th>
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<tbody>
<tr>
<td><strong>Extraction and pre-concentration technique</strong></td>
<td>Miniaturized sorption-based extraction technique</td>
<td>Disruption and dispersion extraction technique</td>
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<tr>
<td>Cartridges and discs with a special manifold</td>
<td>Porous membrane sheet and tweezers</td>
<td>Glass mortar, glass pestle and column</td>
<td></td>
</tr>
<tr>
<td>Simplicity and flexibility</td>
<td>Inexpensive, without special auxiliary devices</td>
<td>Flexibility</td>
<td></td>
</tr>
<tr>
<td>Limited usage of organic solvents, a wide range of sorbents are commercially available</td>
<td>Reduces solvent consumption, sorbent usage and sample handling</td>
<td>Short extraction times, small amounts of sorbent and low solvent consumption</td>
<td></td>
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<tr>
<td>Cartridges must be packed uniformly to avoid poor efficiency</td>
<td>Clean-up and extraction carried out simultaneously</td>
<td>Possibility of extraction and clean-up in one step</td>
<td></td>
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<tr>
<td>Can be on-line and off-line. Automated systems may cause difficulties with reproducibility</td>
<td>Avoids high back-pressure or blockage of the column. Can be used off-line</td>
<td>Not easily automated and time consuming for a large number of samples. Can be used off-line</td>
<td></td>
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<tr>
<td>15-30 min extraction time</td>
<td>10-30 min extraction time</td>
<td>2-10 min extraction time</td>
<td></td>
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<tr>
<td>High concentration factors</td>
<td>Low concentration factors</td>
<td>Low concentration factors</td>
<td></td>
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</tbody>
</table>
**Fig. 1.** Liquid crystal templating mechanism of formation pathways for M41S family mesoporous silicas {Reprinted with permission from [13]}.  

1. Liquid crystal initiated pathway - operating in almost all situations  

2. Silicate initiated pathway - operating in almost all situations  

Increasing surfactant to silica ratio  

TEOS treatment, calcination  

Calcination  

MCM-50  

MCM-48  

MCM-41  

MCM-41 to silica ratio
Fig. 2. Synthesis of functionalized mesoporous silicas by (a) post-synthesis or “grafting” method, and (b) co-condensation or “one-pot” method. R = organic functional group {Reprinted with permission from [33]}. 
Fig. 3. Synthesis of periodic mesoporous silicas (PMOs) from bridged organosilane precursors (Reprinted with permission from [32]).
Fig. 4. (a) XRD pattern, (b) TEM image, (c) N2 adsorption-desorption isotherms, and (d) pore size distribution for a mesoporous silica (SBA-15) {Reprinted with permission from [32]}. 
Fig. 5. Scheme of SPE procedure for the extraction and preconcentration of 17β-estradiol from drinking water with SBA-15-C18 (Reprinted with permission from [34]).
Fig. 6. Comparison of the recovery percentages obtained from the analysis of meat samples spiked at the validation level extracted with SPE cartridges with 100 mg of SBA-15-C18 and 100 mg of commercial C18. Error bars represent the standard deviation of samples replicates (n = 6) [Reprinted with permission from [38]].
Fig. 7. Representation of the SPE process showing the chemical structures of the pesticides studied, a picture of the prepared cartridges and a scanning electron micrograph of the Ph-PMO sorbent for extraction before CE analysis {Reprinted with permission from [40]}. 
Fig. 8. Mechanism of surface imprinting of SBA-15/polyaniline nanocomposite [Reprinted with permission from [52]].
Fig. 9. (a) Scheme for synthesis of imprinted mesoporous silica polymer (b) Static adsorption curves of BPA on MIP-MCM-41, NIP-MCM-41, MCM-41, MIP-SBA-15, NIP-SBA-15 and SBA-15 materials [Reprinted with permission from [55]].
Fig. 10. (a) Synthetic protocol of graphene@mSiO2-C8 composites, (b) Extraction and enrichment of glucocorticoids from bovine milk using the graphene@mSiO2-C8 materials {Reprinted with permission from [39]}. 
Fig. 11. Synthetic procedure of C18-Fe3O4@mSiO2 microspheres and extraction and enrichment of cefalexin, cefazolin and cefoperazone from milk using C18-Fe3O4@mSiO2 microspheres (Reprinted with permission from [79]).
Fig. 12. Schematic illustrations for preparation estrone imprinted Fe3O4@SiO2@mSiO2 [Reprinted with permission from [80]].
Fig. 13. Binding isotherms of MIPs for estrogens in water (a) static absorption experiment, (b), kinetic up take experiment and (c) selective binding experiment [Reprinted with permission from [80]].