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# Understanding Solid-Phase Microextraction: Key Factors Influencing the Extraction Process and Trends in Improving the Technique

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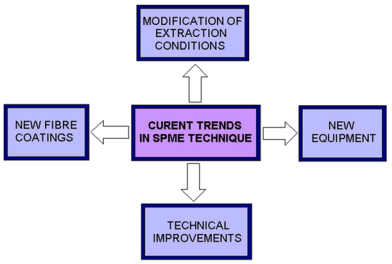


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## 1. INTRODUCTION

Analytical chemists are faced with the daunting challenges of accurately monitoring the state of the environment and the processes taking place in it and of determining an enormous range of analytes often present in trace and ultratrace amounts in sample matrixes with complex or variable compositions. Further challenges are presented by the need to introduce new methodologies into current analytical practice and equipment to comply with the principles of sustainable development and green chemistry. Highest among these principles is the elimination or at least the substantial reduction of the quantities of reagents consumed (especially organic solvents and toxic compounds), solid and liquid wastes produced, and vapors and gases emitted. In analytical chemistry these principles are implemented above all by the utilization of ever more sensitive and automated instruments and of monitoring equipment which allows many analytes to be determined in a single analytical run, by the wide application of direct analytical techniques, operating in situ, and by the introduction of additional isolation and/or preconcentration steps prior to the final determination.

*Solventless* or *solvent-free techniques* are new approaches to sample preparation, and if these approaches are extended to the entire analytical procedure, they come under the heading of *green analytical chemistry*.[1,2] Solventless sample preparation chiefly involves the preconcentration of an analyte to a level above the limit of detection of the measuring instrument; solvent-free techniques are also used for extract cleanup, interferent removal, and matrix simplification to eliminate sample constituents strongly adsorbed in chromatographic columns and thus accelerate their consumption. Therefore, sample preparation is one of the first steps in determining the quality and reliability of the final results of the analyses.

One of the most popular techniques for preparing samples for analysis which satisfies the requirements of green analytical chemistry is solid-phase microextraction (SPME), developed in the 1990s by Pawliszyn and implemented in analytical practice by his team.[3] SPME is the subject of numerous review papers and books and is very widely applied for sampling a broad spectrum of analytes from gaseous, liquid, and solid media with diverse matrix compositions.[4−7] The enormous popularity of

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SPME is due to its undoubted merits: simplicity of operation, short extraction time, solvent-free nature of the process, possibility of full automation, and easy coupling with GC, which reduces contamination of the original sample and partial loss of analytes. In addition, using SPME, samples can be collected in situ, and reliable results can be obtained for analytes present in trace quantities.[8] However, in its basic form, SPME is not without its drawbacks: poor selectivity, low mechanical resistance of the fiber, and limited choice of commercially available fiber coatings. In addition, the technique's efficiency is relatively low, particularly in the case of polar analytes in media containing mainly polar matrix components and when analytes are extracted from contaminated or complex matrix samples.

It is worth observing that besides SPME there are other techniques belonging to the group which one can generally describe as microextractive ones. This group embraces, for example, hanging drop techniques,[9−11] stir bar sorptive extraction,[12,13] dispersive liquid−liquid extraction,[14,15] etc. Despite the fundamental similarity—reduced amount of the sorptive medium—these techniques differ significantly in many details of the employed instrumentation. These differences make a generalized theoretical analysis of this group as a whole almost impossible. Therefore, this work is concentrated on the most widespread of the microextraction techniques, aiming at a thorough and detailed analysis of its most important aspects, at the same time stressing that SPME is one of the many available microextraction techniques.

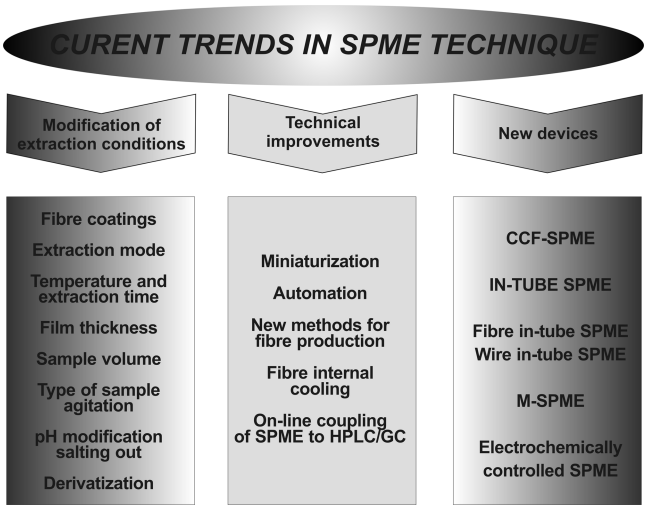


**Figure 1.** Current trends in solid-phase microextraction.

Because of the advantages of SPME and the enormous potential it has in analytical practice, a series of studies have been undertaken to develop new methodologies and interface SPME with measuring instruments, leading to improvements in the efficiency/sensitivity of the technique (Figure 1). These studies have been aimed not only at completely new designs but also at the possibility of modifying existing solutions, which includes their miniaturization and automation as a result of simplified coupling with existing final measurement instruments. Work is also in progress on the design of instruments using mechanically and more thermally resistant extraction fibers. Separately from this, efforts are being undertaken to improve the efficiency of extraction through the proper selection of sample preparation conditions, where the most important parameters are the type of extraction coating, sorbent film thickness, effect of the matrix pH, presence of other compounds, temperature and duration of extraction, and stirring technique.

## 2. THEORETICAL PRINCIPLES OF SPME

SPME is mainly based on a partition mechanism and on achieving a state of equilibrium of an analyte between the extractant and the other constituents of the system, i.e., the sample matrix or corresponding headspace. The SPME device consists of a fused silica fiber coated with a thin film of a suitable polymeric sorbent or an immobilized liquid. The fiber itself is placed inside the needle of a syringelike arrangement. In most cases, extraction is performed by immersing the fiber directly into the sample. Extraction from the headspace is a possible alternative (HS-SPME), a useful approach for analyzing samples that are solid or contain matrix components capable of contaminating the fiber, such as biological and petrochemical samples.[16] Following extraction, the fiber is inserted into the injector of the measuring device (GC, HPLC, or capillary electrophoresis (CE)), where the analytes are desorbed.[17]

The quantity of analyte in the system is constant and equal to the amount of analyte introduced to the system from the original sample (os), so that, at equilibrium (eq), the distribution of the analyte between the sample (s) and the extractant (e) can be described by the material balance:

$$C_{os}V_s = C_{s,eq}V_s + C_{e,eq}V_e \tag{1}$$

Moreover, two-phase extraction at equilibrium is described by two quantities—the ratio of the extractant volume to sample volume, $\beta_{e/s}$, and the partition coefficient of the analyte between the two phases, $K_{e/s}$—described by eqs 2 and 3, respectively.

$$\beta_{e/s} = \frac{V_e}{V_s} \tag{2}$$

$$K_{e/s} = \frac{C_{e,eq}}{C_{s,eq}} \tag{3}$$

Transformation of eqs 1 and 3 yields the following equation, describing the quantity (number of moles) of extracted analyte by the coating at equilibrium:

$$n_{e,eq} = \frac{K_{e/s}V_eC_{os}V_s}{K_{e/s}V_e + V_s} \tag{4}$$

Furthermore, the sample−analyte−extractant system and the preconcentration process can be described by two parameters: the fraction extracted, $R$

$$R = \frac{n_{e,eq}}{n_{os}} = \frac{K_{e/s}\beta_{e/s}}{1 + K_{e/s}\beta_{e/s}} = \frac{K_{e/s}}{K_{e/s} + \beta_{e/s}^{-1}} \tag{5}$$

and the preconcentration coefficient, $E$

$$E = \frac{C_{e,eq}}{C_{os}} = R\frac{V_s}{V_e} = \frac{K_{e/s}}{1 + K_{e/s}\beta_{e/s}} \tag{6}$$

From eq 4 one can draw an important conclusion that, at equilibrium conditions, knowledge of the sample volume is not needed to obtain direct proportionality between $n_{e,eq}$ and the concentration in the sample, providing that the equilibrium


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concentration in the sample is not much lower than the initial concentration of the analyte (see also sections 3.4 and 4).

The terms describing the two quantities are given here in accordance with the IUPAC Gold Book.[18] The former is also known as "recovery" (recovery factor), treated by the Gold Book as obsolete. In SPME, however, it is most frequently referred to as the "extraction efficiency".[6] The extraction efficiency is not yet defined by IUPAC, yet its meaning as the fraction (or percentage) of an analyte transferred from the original sample to the measuring device is quite clear in sample pretreatment procedures (see collection efficiency).[11] It should be remembered, however, that in the case of SPME this value alone does not define the limit of determination of the complete analytical procedure and the desorption efficiency (transfer from the fiber to the analytical instrument) must also be included. Its importance may also be seen when its values approach 100%, thus permitting simplification of the calibration procedure. Formally, if not expressed as a percentage, the same quantity may also be treated as the sensitivity (ratio of the output signal to the input signal, both in moles) of the preconcentration step. One can notice that, in the literature, both terms are frequently used interchangeably. The second quantity is also known as the "enrichment coefficient". Both quantities are measures of the overall success of the extraction. The term "extraction efficiency" is used in this paper in the meaning explained before.

Extraction from the headspace is a particular case of extraction in a triple-phase system, in which the indirect extractant (ie) is a neutral gas, the process being described by the following quantities: $\beta_{ie/s}$, the ratio of the volume of the indirect extractant (ie) to that of the original sample, $\beta_{e/ie}$, the ratio of the volume of the coating material (e) to that of the indirect extractant, and the corresponding partition coefficients $K_{ie/os}$ and $K_{e/ie}$. The analyte is divided among all the phases of the system in accordance with the following equation:

$$C_{os}V_s = C_{s,eq}V_s + C_{ie,eq}V_{ie} + C_{e,eq}V_e \quad (7)$$

In this system the deciding factor is the change in analyte concentration in the primary and coating material, so for all practical purposes, the coefficients $K_{ie/os}$ and $K_{e/ie}$ are neglected and the partition coefficient of the analyte in the primary sample/coating material system is taken into consideration. This latter coefficient is described by the following equation:

$$K_{e/s} = \frac{C_{e,eq}}{C_{os,eq}} = K_{ie/os}K_{e/ie} \quad (8)$$

Rearrangement of eqs 7 and 8 leads to a relationship from which the quantity of analyte in the extractant at equilibrium ($n_{e,eq}$) can be calculated:

$$n_{e,eq} = \frac{K_{e/os}V_eC_{os}V_s}{K_{e/os}V_e + K_{ie/os}V_{ie} + V_{os}} \quad (9)$$

## 3. PARAMETERS AFFECTING THE EFFICIENCY OF ANALYTE EXTRACTION USING SPME

### 3.1. Types of Fiber Coatings

The choice of commercially available fiber coatings is rather limited, and these do not always meet expectations, e.g., in highly specific applications.[19] Furthermore, the available extraction fibers have a number of shortcomings: they are thermally unstable and mechanically rather weak, their selectivity is low, and they do not meet expectations for high recovery of polar analytes from samples with a polar matrix composition.

In practice, the choice of SPME fiber coatings is limited to poly(dimethylsiloxane) (PDMS), divinylbenzene (DVB), polyacrylate (PA), Carboxen (CAR), and poly(ethylene glycol) (PEG; Carbowax, CW), available in various thicknesses and combinations.[20] Combinations of polar/nonpolar sorbents such as PDMS/DVB, PDMS/CAR, or CW/DVB provide extraction coatings that yield larger recoveries of polar, organic analytes from polar matrixes.[21,22] The guiding principle when selecting extractants is that polar and nonpolar sorbents reveal greater affinity for polar and nonpolar analytes, respectively. Therefore, in accordance with this principle, extraction coatings such as PA are used for sampling polar analytes, such as phenols[23,24] and some pesticides and herbicides,[25,26] while even more polar coatings, such as PDMS/DVB, PDMS/CAR, and CW/DVB, are used for extracting highly polar compounds such a alcohols, amines, and ethers.[27,28] Correspondingly, the nonpolar PDMS is used mainly for extracting nonpolar compounds such as BTEX or PAHs.[29,30] PDMS/CAR coatings, with their poly(diethylene glycol) cross-links, have a larger surface area-to-volume ratio, ensuring better extraction efficiency of BTEX analytes.[31]

The most common sorbent in SPME is PDMS, existent, within the temperature range at which extraction is performed (usually 25−60 °C), in a form of immobilized liquid. This material is routinely used as the stationary phase in GC and is readily identified in MS, since its decomposition products are known (cyclic oligomers). Moreover, this material is thermally stable up to 300 °C and is chemically neutral. Finally, desorption can be carried out at moderate temperatures, so target analytes do not decompose.[32]

Because of the restricted range of commercially available extraction fiber coatings and the limited applicability, the need arose to synthesize completely new sorption materials for SPME purposes. Synthesis of fiber coatings in the laboratory may be quite complicated and difficult to reproduce, due to the need for accurate control of many conditions. Despite this, recent years have witnessed an upsurge in the number of publications dealing with innovative methods for preparing new types of extraction fiber coatings, the conditions of their synthesis, and their applicability.

One possible way of enhancing the efficiency of extracting polar analytes from a medium using SPME could be to increase the polarity of the sorbent, the effect of which would be to increase its affinity for polar analytes. Unfortunately, however, raising the sorbent polarity does not solve the problem, because at the same time it increases the affinity for the matrix, which could lead to competing sorption processes and eventually to the leaching of the analyte. To achieve a better extraction efficiency with SPME, one uses highly specific sorbents with a high affinity for the target analytes, providing sufficient overall sensitivity, despite the small volume of sorbent used.

With these new technologies, SPME fiber coatings can be produced from fairly cheap polymers; these coatings are stable right across the pH range, and at high temperatures, they are mechanically strong and are reusable with good reproducibility of results. The sorbents synthesized for the needs of SPME most often mentioned in the literature include conducting polymers, molecularly imprinted polymers,[33] sol−gel coatings,[34] and immunosorbents.[35] With these new coatings, SPME


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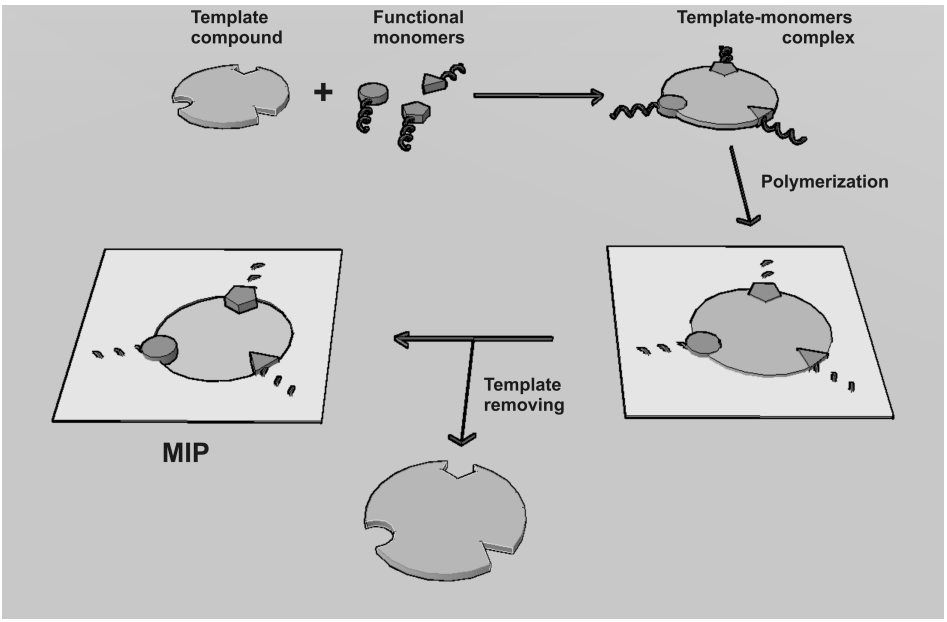


**Figure 2.** Synthesis of molecularly imprinted polymers.

can be used to sample a wide range of analytes from biological media, often with a complex matrix composition.

An important problem involving perhaps all types of fiber coatings is conditioning of the new SPME fibers.[36] Typical conditioning times vary from 30 min to 4 h and temperatures from 210 to 320 °C, depending on the manufacturers' recommendations (sometimes even higher values are needed for ultraclean conditions). The goal of this procedure is to remove any residual monomers or other chemicals remaining in the fiber coating since its manufacturing or sorbed during storage. A similar procedure is sometimes recommended for cleaning the fibers after a series of analyses to prevent carryover or cross-contamination.

**3.1.1. Conducting Polymers.** Conducting polymers were introduced as SPME fiber coatings to overcome the problems in sampling polar analytes from a medium of mainly polar matrix components. The conducting polymer usually used for this purpose is polypyrrole (PPy) and its derivatives (PPPy, PPy-DS).[37] The polymers from this group can be synthesized chemically or electrochemically[38] from commercially available monomers.[39] Polypyrrole fiber coatings adhere very well to the fiber core, which is usually a metal wire made from platinum, gold, or stainless steel. With a metal core, the extraction fiber is mechanically very strong.[40] These coatings give excellent recoveries of polar and aromatic compounds such as PAHs,[31] phenols,[32] and VOCs,[29] as well as metamphetamine and its derivatives.[41] Even ionic analytes may be extracted with these coatings.[42]

Utilization of conducting polymers may lead to quite new methods of extraction (sorption)/desorption control, i.e., utilizing electric potential of the fiber, treated as an electrode. The coating can change its chemical properties drastically when reduced or oxidized. Attempts have been made employing P3DDT on platinum for successful extraction of arsenate ions and organometallic arsenobetaine.[43,44]

**3.1.2. Molecularly Imprinted Polymers.** Molecularly imprinted polymers (MIPs) are used as SPME extraction fiber coatings because their properties are governed by the method used to produce them. MIPs are obtained by the copolymerization of functional monomers with a template molecule, which are covalently or noncovalently bonded, after which the template monomers are cross-linked. Following polymerization, the template is leached with a suitable solvent, leaving an imprint of a given shape and size in the polymer structure (Figure 2). The molecular imprint and the presence of characteristic groups that transport analytes are responsible for the sorption properties of these materials. MIPs very selectively recognize compounds, the structure of which is the same as or similar to that of the template molecule.[45,46]

By altering the composition of the reaction mixture and the conditions of polymerization, the shape and selectivity of the MIP can be customized. MIPs are inexpensive, are thermally and chemically stable, and are easily synthesized.[47,48] A drawback of these materials, however, is that, even though they work efficiently in aqueous media, in some organic media regrouping of the polymer chains deforms the polymer's internal structure; moreover, during thermal desorption the polymer is frequently decomposed to the monomers. MIPs are synthesized mainly for analytical purposes; they are used in SPME as highly selective fiber coatings for sorbing a wide range of analytes from a variety of media,[28] for example, to extract herbicides,[49] triazines,[50] phenols, heavy metals, and antibiotics,[51] other pharmaceuticals (diacetylmorphine and analogues),[52] and many other compounds from samples with complex matrix compositions, such as blood,[53] urine,[54,55] food,[56] environmental samples,[57,58] and other complex samples.[47,59,60] It is interesting that sometimes MIPs may be employed for both the sample pretreatment and the final determination.[52] A brief review on applications of MIPs in solid-phase extraction (SPE) and SPME was published elsewhere.[61]

**3.1.3. Sol−Gel Sorbents.** The problems with commercially available extraction fibers arise from their low working temperatures, swelling in organic solvents, poor mechanical strength and thermal stability, possible leaching of the extraction layer, and difficulties in obtaining homogeneous coatings. Some of these difficulties have been overcome by applying the sol−gel technique to bind the polymeric extraction


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layers to the fiber surface.[62] This process is based on the hydrolysis of an organic precursor (a metal alkoxide—usually a

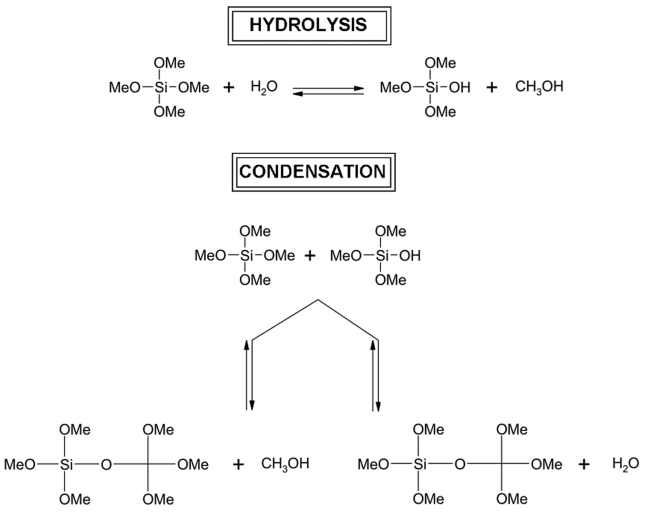


**Figure 3.** Diagram illustrating the sol–gel process.

tetraalkoxysilane) followed by the alcoholic or aqueous condensation of that precursor. The product is then hydrolyzed and condensed; its viscosity increases because the sol molecules aggregate as a result of bonds being formed between the chains (Figure 3). Finally, the physical structure of the sol changes to that of a three-dimensional lattice, a rigid gel.

The sol–gel technique is a universal, inexpensive method for conveniently obtaining, under mild conditions, both inorganic and hybrid organic–inorganic polymers with the desired molecular shape and unique properties: resistance against chemical and photochemical agents,[63,64] enhanced thermal stability,[56] stability in a wide pH range,[65] and high purity and homogeneity. From a suitable reaction mixture, a polymeric stationary phase with the desired surface properties and structure can be obtained.[27,56] Such coatings are chemically and mechanically stable and can be used over a wider range of working conditions and to determine compounds with high boiling points.[56] In addition, their porosity, resulting in a high specific surface area, ensures usage of thin films, while maintaining high extraction recoveries.[56] Obviously, this technique also reveals defects and limitations: the most important of them include the complexity of the method, the need to optimize many parameters, and the difficulties in reproducing procedures described in the literature.

The sol–gel technique enables a diversity of compounds to be included in the polymer gel; as a result extraction coatings with specific properties are produced[66] and used in SPME to sorb a broad spectrum of polar and nonpolar analytes from samples of water, air, food, biological fluids, and other media with a complex matrix composition.[27,56] For the purposes of SPME, fiber coatings have been prepared containing poly(vinyl alcohol) (PVA),[67,68] phenyltrimethoxysilane,[69] anilinemethyltriethoxysilane,[70] hydroxyfullerene compounds,[71] and octyltriethoxysilane compounds ($C_8$-TEOS),[72] the latter used for sampling mercury and tin compounds. The sol–gel coatings most commonly synthesized are polymers containing calix[4]arenes in their structures. These materials can be used to sample phenols,[73−75] aromatic amines,[76−78] BTEX and PAHs,[69] pesticides,[79] etc. Another very common sol–gel coating for SPME contains crown ethers and is also used to sample phenols,[80,81] aromatic amines,[73,82] BTEX and chlorobenzenes,[73,83] and pesticides.[84,85]

**3.1.4. Ionic Liquids.** Application of ionic liquids in separation techniques has recently become a hot topic in analytical chemistry.[86] This special interest is due to the unique properties of the ionic liquids (very low vapor pressure, high thermal stability, inflammability, ability to dissolve a wide range of both inorganic and organic substances, high viscosity),[87,88] which make possible their usage as universal "green" solvents in chromatography, electrochemistry, and extraction techniques of sample preparation.[89,90] There have also been attempts to apply ionic liquids as coatings in SPME.[91] The first papers on the subject were published in 2005.[92] Consecutive studies of the preparation of such fiber coatings examined the possibility of deposition of ionic liquids on a fiber precoated with a Nafion membrane.[93] This approach, however, did not permit a permanent deposition, and after each extraction the procedure had to be repeated. A breakthrough was achieved by introduction of polymeric ionic liquids as the extraction medium[94,95] and either polymerization of ionic liquids on the silica molecules[96] or cross-linking of a silicone prepolymer saturated with an ionic liquid.[97] Quite recently the sol–gel technique has been employed for these purposes.[98,99] Mixtures of polymeric ionic liquids have also been tested.[100] In practice, however, these procedures of extraction coating syntheses are too complicated and poorly reproducible. The SPME technique with an ionic liquid extraction agent is used for isolation of analytes from groups such as BTEX,[81] PAHs,[85,87,101] phenols,[87] alcohols,[91] aromatic amines,[88,90] and fatty acid esters,[86,102] as well as in analyses of biological fluids.[89,103] ILs can also be employed as desorption solvents for SPME[104] or mediators for in-tube SPME.[105]

**3.1.5. Nanotubes.** Carbon nanotubes have also been used to form a sorption layer on SPME fibers. Their affinity for relatively strong sorption of hydrophobic organic pollutants, combined with other properties (very large specific surface, durability, and chemical stability), makes them a promising option. To date, though, they remain at the testing stage. The first paper on this subject was published in 2006.[106] Fibers coated with multiwalled carbon nanotubes (MWCNTs) have been employed in sampling of polybrominated diphenyl ethers from real samples, including river water, wastewater, and milk, while fibers coated with single-walled carbon nanotubes (SWCNTs) have been used in sampling chlororganic pesticides from lake water and wastes,[107] as well as phenols from aqueous media.[108] Phenols were also determined with an extraction layer made of carbon nanotubes modified by introducing carboxyl groups on their surface, thus increasing the polarity of the coating.[109] Usage of nanotubes was also described in determination of organophosphorous pesticides.[110] In 2011, a new technique of using the sol–gel technique for deposition of carbon nanotubes on the SPME fibers was developed. The solution of the sol was introduced into a polypropylene tube, and a gel was formed directly on the fiber. Such fibers were subsequently utilized for sampling of phenobarbital in wastewater.[111] Due to flexibility of the sol–gel technique, combined with the unique features of the carbon nanotubes, this method of fiber preparation may lend itself to wide applications in SPME to determine different analytes. These fibers were much cheaper, as compared with commercial SPME fibers, were more chemically and thermally stable, and could be reused for a longer period of time with comparable or better extraction efficiency.[101]


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**3.1.6. Other Types of Fiber Coatings.** There are also literature references to other materials used as fiber coatings in SPME: the cheap and chemically resistant polycrystalline graphites,[112,113] the thermally and mechanically very stable polysilicone fullerenes (PFs) with enhanced selectivity in regard to the extraction of aromatic compounds,[106] and perfluorinated resins (Nafion).[114] Mesoporous silicates (silica gels modified with octadecyl ($C_{18}$), octyl ($C_8$), or phenol groups), which are extremely strong mechanically, have been used for sampling aromatic hydrocarbons.[115−118] One can find literature mentioning usage of the phenyl-$C_{18}$- and $C_8$-bonded silica particles as the porous layer coating a stainless steel or nickel−titanium wire in SPME.[119] Particles are immobilized using a high-temperature epoxy glue; these fibers have been used to extract polychlorinated biphenyls and BTEX from water.[109,120] In a similar way cyclodextrin-bonded silica particles attached to a stainless steel or fused silica fiber could be used for determination of phenols.[121] Porous silica particles provide a large specific surface area, and the diffusion process is very fast. The separation efficiency is thus improved and its time reduced. Another interesting, though not very popular, new solution in SPME is employment of coatings with properties resembling those of immunosorbents (ImS's), which are more frequently used in the SPE technique.[122] This type of coating has been developed to increase the selectivity of extraction, a feature important in determination of analytes in complex samples.[28] ImS's are produced by binding natural antibodies to a solid substrate, and the resulting material exhibits immunological affinity. The first step in this process is to react the substrate (usually a silica, agarose, or cellulose polymer) with (3-aminopropyl)triethoxysilane (APTES); this is followed by activation with glutaraldehyde, after which the antibodies are immobilized on it.[123] So far, ImS-type coatings have been used in SPME for extraction of theophylline from serum samples,[114] as well as for determination of 7-amnoflunitrazepam and other benzodiazepines from urine and water samples.[124,125]

### 3.2. Structure of the Fiber Core and Methods of Depositing the Extraction Coating

One of the shortcomings of SPME is the low mechanical strength and thermal stability of the extraction fibers. The problem can be solved by making the fibers from materials stronger than glass fiber. For this purpose the extraction layer can be coated onto a core of silver, which is stable up to 300 °C,[126] or stainless steel cores are coated with a porous siliceous material.[106,107,109] Some thermally stable materials with an affinity for target analytes can be used directly in SPME without having to be coated with a sorbent film: for example, zinc fiber cores have been used for extracting thiols from gaseous and aqueous samples,[127] and aluminum fibers have been used for sampling aliphatic alcohols and BTEX from gases.[128]

Also available as extraction fiber cores are thin wires made from nitinol, an alloy containing 49% nickel and 51% titanium. Nitinol is a material with shape memory; that is, upon being deformed, it regains its original shape. This alloy is also highly elastic, biocompatible, and resistant to corrosion.[129,130] Not only the fiber but also the needle and plunger are made from this material. SPME equipment manufactured from this inert alloy is very strong and resistant to mechanical damage and high temperatures (melting point >1300 °C); it can deal with large numbers of analyses without compromising efficiency and/or reproducibility.[131]

The method of depositing the extraction layer on the SPME fiber may differ, depending on the type of sorbent. The simplest way is to immerse the core in a solution of molten polymer, after which the fiber may be conditioned or heated to stabilize it. This method is quick and very convenient, but the coatings have an irregular structure, and the sorbent film is not of uniform thickness. Electrochemical techniques provide an alternative: cyclic voltammetry (CV) or potentiometric methods. These methods rapidly coat any fiber, including those with an irregular or porous surface. The sorbents in these methods are conducting polymers such as polythiophenes (P3DDT)[35,36] or polypyrrole and its derivatives,[30,32,33] which are used to coat a metal core, usually made from platinum.[132,133] The extraction coatings formed in this way are extremely homogeneous and pure. Using electrochemical techniques to apply extraction layers, coatings can be obtained in the oxidized or reduced form of the polymer, for example, an SPME coating made from overoxidized sulfonated polypyrrole (OSPPy).[124] With electrodeposited extraction layers, SPME can be used for sampling analytes that are inactive in electrochemical reactions,[36] cationic, anionic, and neutral analytes,[124] for example, trace amounts of nickel(II) and cadmium(II) ions.[123,124] Electrodeposition can also be used to produce metal coatings, for example, thin layers of gold deposited on a carbon steel core for determining mercury,[134] coatings of copper chloride deposited on a copper core,[135] or coatings made from polyaniline (PANI) deposited on a platinum core for sampling polar and nonpolar aromatic compounds and alcohols.[136,137]

### 3.3. Mode of Extraction

SPME can be used for the direct sampling of analytes from gases and fairly pure liquids by exposing the fiber coating to the sample. Analytes are moved directly from the sample matrix to the extraction fiber. SPME can also be used in an indirect manner to analyze the composition of liquid and solid samples: the target analytes are sampled from the gaseous headspace above the medium (HS-SPME).

The mode of extraction is selected on the basis of the volatility of the target analytes and their affinity for the sample matrix and the state of matter and composition of the matrix. Headspace sampling is usually favored for the extraction of volatile analytes (PAHs, BTEX, VOCs) and for sampling analytes from solid matrixes and water contaminated with suspended particulate matter or oils. In headspace sampling, the sample is placed in a hermetically sealed container and the remaining free space is filled with a neutral gas. The SPME fiber is then inserted into the container, where extraction is allowed to continue usually until the system reaches equilibrium; thereafter, the fiber is placed in the GC injector port where the retained analytes are thermally desorbed. If a hydrophobic material is used for the SPME fiber coating, the problems of the influence of water on the process of an analyte sorption, e.g., blocking the active centers by water molecules, are eliminated.

The direct insertion of the extraction fiber into the measuring instrument's injector greatly limits analyte losses and means that the analytical process can be automated. Headspace sampling reduces the risk of contamination of and damage to the extraction fiber, which could occur if the fiber comes into direct contact with a sample of the investigated medium containing nonvolatile compounds, high-molecular-weight compounds, proteins, or humus compounds as interferents.[5] Moreover, as there is no contact between the fiber and the


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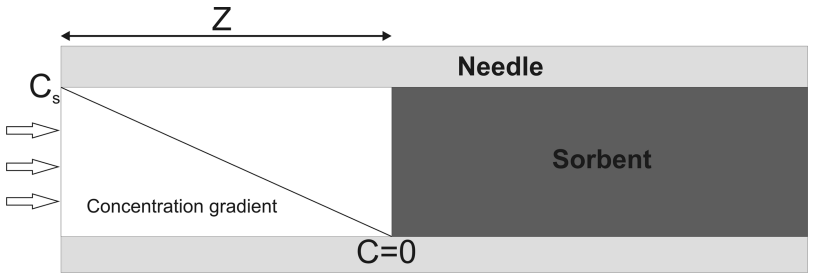


**Figure 4.** Application of an SPME device for the determination of time-weighted averages.

sample medium in headspace sampling, further manipulations can be performed on a liquid matrix, for example, changing the pH without running the risk of damaging the extraction layer or performing extractions from samples with a complex matrix composition. Finally, the selectivity of headspace sampling is superior to that achievable with direct sampling.[138] Nonetheless, HS-SPME does have its limitations: the most important ones are associated with calibration and the necessity of keeping constant the parameters affecting the state of equilibrium, such as the extraction time, phase volume of the system, temperature, or stirring speed.

HS-SPME is usually used to sample highly volatile analytes regardless of their polarity. Since the most suitable extractant can be selected in this technique, this technique can also be used to determine analytes from samples with a complex matrix composition as well as from aqueous, environmental, and biological[139] and food[129,140−143] samples. The SPME fiber can also be used as a passive sampler for collection of some indoor air pollutants (such as biogenic VOCs).[144] It is worth noting that SPME may serve in transfer of some very volatile compounds (components of the wine aroma) also to such instruments as the artificial nose which also require a certain degree of both enrichment and matrix simplification.[132,134]

**3.3.1. Passive Mode of Extraction: Determination of the Time-Weighted Average Concentration.** Besides the aforementioned modes of SPME extraction by exposure of the fiber to the analyzed sample, it is possible to employ the SPME device as a passive sampler for the determination of time-weighted averages (TWAs).[145,146] While in the former applications the fiber coated with a sorbent layer is pushed off the device needle, in the passive sampler case, the fiber is retracted back to the needle by known distance $Z$ (Figure 4).

In this configuration, when there is no mixing of the medium within the needle, separating the sorbent from the bulk sample beyond the needle tip, transport of analytes in the needle is diffusion controlled and may be described by the first Fick law, which finally leads to the following equation:[147]

$$m = D\frac{A}{Z}\int_0^t C_s \, dt \tag{10}$$

where $m$ denotes the mass of the analyte retained (extracted) in the sorbent, $D$ the diffusion coefficient of the analyte in the phase filling the needle between its tip and the sorbent, $C_s$ the concentration of the analyte in the bulk of the sample (or just outside the needle tip), $A$ the area of the needle cross-section, and $t$ the time of the sampling procedure.

Applicability of this equation depends on three factors. First, the sorbent layer must behave toward the analytes as a "zero sink" ($C = 0$). This means that a molecule of analyte arriving at the interface undergoes immediate sorption, finally leading to the dependence of transport of the analytes exclusively on their concentration at the needle tip (with all other conditions constant) and its independence of the concentration (or amount) of the analyte already extracted. Second, the analyte concentration at the needle tip ($Z = 0$) should be equal to its concentration in the bulk sample. Third, the amount of the extracted (sorbed) analyte must be proportional to its concentration at the needle tip. The results of studies on isolation of alkanes from air samples demonstrate that the first condition is fulfilled when sorbents demonstrating strong interactions with analyte molecules and high sorption capacity are used (e.g., Carboxen/PDMS or PDMS/DVB[143]). The same study also revealed another advantage of the SPME device, resulting from its small size, permitting continuous sample "renewal" at the needle tip, even at low flow rates across its section. This results in diffusion through the immobile medium layer in the needle being the sole limiting factor of the transport of analytes toward the sorbent surface. A short distance of diffusion ($Z$) ensures a rapid response of the system toward varying concentration of analytes in the sample. Moreover, this distance may be adjusted within a certain range, depending on the predicted sampling time, the concentration of analytes in the sample, and their diffusion coefficients to ensure the zero sink condition is fulfilled. SPME devices have been successfully employed for determination of TWA of VOCs in air and PAHs in water. In the latter case fiber-in-needle SPME was used.[148]

### 3.4. Extraction Time and Temperature

The temperature and extraction time are fundamental parameters governing the efficiency of the process. Utilizing the temperature influence is rather restricted, as its increase leads to improvement of the rates of mass transport between the phases, at the same time worsening the partition coefficient(s).[149] For this reason, manipulating the temperature applies chiefly to the headspace extraction mode, as an increase in temperature accelerates analyte transport from the solution or solid to the headspace.[150] In this mode, increasing temperature influences two partition coefficients, i.e., $K_{ie/os}$ and $K_{e/ie}$, usually improving the former and worsening the latter. Hence, one can select an optimum extraction temperature, allowing for the matrix composition of the medium under investigation, the volatility of the target analytes (increasing temperature increases the vapor pressure, thus permitting extraction of medium- and low-volatility compounds), and the type of sorbent in the SPME fiber coating.

The extraction time is affected by a number of factors: sample temperature, partition coefficient of the analyte, and means of stirring. Achieving maximum sorption of analyte means reaching equilibrium. Times required to reach equilibrium are usually long and may be shortened by intensive stirring, which is the main factor in the direct extraction mode, when increasing the temperature is not practical due to the


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aforementioned factors. These times can be shortened in the headspace mode, as the samples may be preheated to achieve os/ie equilibrium, when the interface surface area is larger; subsequently—after the fiber is placed in the headspace—the time needed to achieve ie/e equilibrium is shorter due to more rapid diffusion of analytes in a gaseous medium. An important advantage of the equilibrium approach is that calibration procedures are simplified due to the applicability of eqs 4 and/or 9.

Nevertheless, in practice, reaching equilibrium is rarely utilized because the equilibration times are still too long. Therefore, extraction is often carried out in nonequilibrium mode, and the optimum extraction time is defined on the basis of sorption diagrams—plots of the amounts of extracted analytes vs their adsorption time. In this approach, however, stirring must be kept under very strict control and calibration usually requires utilization of internal standards.

### 3.5. Thickness of the Fiber Coating

The extraction efficiency also depends on the volume of sorbent, which in the case of SPME is equivalent to the thickness of the fiber coating. The quantity of analyte adsorbed on the extraction fiber is proportional to the thickness of the sorbent coating. A thicker coating will retain larger amounts of analyte than a thin one, but the time to reach equilibrium in the former case is correspondingly longer. Thick coatings are usually used for sampling volatile analytes since they can be transferred to the injector of the measuring instrument without loss, whereas thin SPME fiber coatings ensure good recoveries of high-molecular-weight molecules and nonpolar compounds.[10]

### 3.6. Sample Volume

The sample volume is also an important parameter affecting the efficiency of SPME (eqs 4 and 9). Assuming that the composition of the primary sample is unchanged by the extraction, i.e., the quantity of analyte in the sample does not change by more than 1%, the quantity of analyte extracted on the SPME extraction fiber is proportional only to the partition coefficient and the volume of the sorbent. Ensuring the invariability of the composition of the original sample by an appropriate choice of sample volume simplifies the calibration procedure and the performance of quantitative determinations, which in this case are based solely on knowledge of the relevant partition coefficients.

In headspace extraction, the analyte is partitioned among three phases: the original sample, the headspace, and the SPME sorbent. In this case, the efficiency of extraction depends also on the volume of the indirect phase (neutral gas used).[151,152] The volume of the indirect phase should be as small as possible to prevent the excessive dilution of analytes in this phase, because this substantially influences the method's detection limit.

### 3.7. Stirring

As discussed before, stirring increases mass transfer in the system, thus shortening the extraction time, sometimes also improving reproducibility. Classic stirring with a Teflon-coated magnetic stir bar may be employed, the flask containing the sample can be vortex-vibrated, or ultrasounds can be used to agitate the sample.[153] The last way seems to be most effective, because it ensures very short extraction times (<30 s), yet the ultrasounds heat the sample; thus, the method cannot be employed with thermally unstable analytes.[4,140] One should also remember that the magnetic stirrer may itself become a source of contamination.[154,155] In some studies rotation of the fiber was also applied.[156] Detailed discussion of the sorption kinetics can be found elsewhere.[157]

### 3.8. Other Factors Influencing Extraction Efficiency

**3.8.1. Salting Out.** The addition of small amounts of salts affects the efficiency of extraction, as it raises the ionic strength of the solution. Organic constituents become less soluble, and their partition coefficients increase. The overall effect of salting out on the extraction efficiency, however, depends on the concentrations of analyte and salts in the sample. Sodium chloride and sodium sulfate are the compounds usually used for these purposes.[158] It should be remembered that the addition of a salt may substantially increase the risk of contamination of the sample. Moreover, when direct immersion of the fiber in the sample solution is applied (not in the HS-SPME mode), the fiber should be thoroughly rinsed as under these conditions it becomes much more prone to mechanical damage.

**3.8.2. Change of pH and the Matrix Effect.** The pH of a sample can also affect the amount of an analyte retained on an SPME extraction fiber.[159] The sample pH is particularly important in the case of weakly acidic or basic compounds such as amines and phenols, which should be maintained in undissociated form.[160] Moreover, the pH of the sample is a significant parameter in the context of the mechanical strength of the sorbent coating, as some of these materials are poorly resistant to strongly alkaline or strongly acidic environments.

According to the available literature, addition of a hydrophobic, organic solvent can affect the efficiency of analyte extraction, but this effect is not well understood. The addition of organic solvents to aqueous samples usually lowers the analyte extraction efficiency. Likewise, the addition of water to organic samples also reduces the extraction efficiency. In this context, even the moisture contained in the air can impair headspace extraction from organic samples, thus reducing the amounts of analytes extracted on the extraction fiber coating.[161] The presence of other hydrophobic compounds with good sorption properties, such as dissolved organic carbon, can have the same effect.[49,162] On the other hand, the addition of a hydrophobic solvent improves analyte diffusion from the sample to the sorbent, but this effect has been observed only in the case of solid samples such as sediments and mud.[163] Apart from the above-mentioned salts and solvents, other components present in the sample matrix can influence extraction; for example, humic and fulvic acids, originating from biodegradation of dead organic matter and present in water and soil samples in dissolved form (dissolved organic matter), can reduce the amounts of analytes retained by the sorbent layer.[164,165] One can also say that SPME may be used as a tool for studying the effects discussed here.

**3.8.3. Derivatization of Analytes.** The cases when the analytes demonstrate poor affinity to the extraction phase, and no better phase may be found for a given problem, become very troublesome in the sampling of analytes present in trace quantities and in the extraction of analytes from media with complex matrixes. A good way of improving the efficiency of SPME in such situations is to convert the target analytes into their derivatives, which have a different chemical structure and properties, thus revealing better affinity toward the extraction phase, i.e., more favorable partition coefficients. The same is true in th eHS-SPME mode, when one can produce more volatile derivatives. Derivatization can be carried out at various

stages of the extraction: prior to sampling (when analyte conversion is carried out in the original sample), after the analyte has been adsorbed on the SPME fiber, or during analyte desorption onto the chromatographic column.[166,167] Derivatization also enhances applicability of SPME to a wider range of analytes.

The type of derivatization best suited to SPME is the conversion of analytes on the fiber coating itself, since this avoids the side reactions that are almost inevitable if the process is carried out in the original sample. The derivatizing agent is brought to the SPME fiber coating by placing the fiber in the vapors of the agent or immersing it in a solution of the agent. Derivatization is carried out after the extraction proper, when the target analytes have already been adsorbed on the fiber (thus influencing the desorption and final determination only), or the derivatizing agent is brought to the fiber before extraction, in which case the analytes are converted at the same time as they are extracted. The simultaneous sampling of analytes from the medium and their on-fiber derivatization have been used in the analysis of environmental samples,[168,169] food samples,[170] and biological samples,[171,172] whereas analyte conversion on the fiber after the actual extraction has been used for the analysis of biphenyls from urine samples,[173] narcotics and steroids from samples of water and biological fluids,[174,175] and herbicides from water samples.[176]

Usually, polar and/or thermally unstable analytes are derivatized to improve their properties under the conditions of chromatographic separation. Derivatization usually involves the esterification of strongly acidic compounds such as acetic acid[177,178] and the conversion of amines and amphetamines to less polar and more volatile derivatives,[179,180] aldehydes and ketones to more stable oximes,[145,181] and phenols to acetates;[182] organometallic compounds are converted to more volatile or more thermally stable derivatives.[183,184] The applications of chemically modified extraction fiber coatings are described in numerous review papers; they usually refer to the analysis of water, food, blood, and urine samples.[185−187]

## 4. CALIBRATION PROCEDURES

Comparison of calibration methods used in SPME with those used in conventional extraction techniques (such as liquid−liquid extraction (LLE), SPE, or Soxhlet extraction) demonstrates high flexibility of the SPME technique toward varying conditions of extraction. Aforementioned conventional extraction techniques usually permit quantitative extraction, which leads to a very simple calibration procedure (one can determine the analyte concentration in the sample knowing only its volume). On the contrary, the SPME technique rarely permits complete isolation of analytes from the sample to be achieved (fraction extracted $R > 0.95$). This results from the small volume of the sorbent layer on the SPME fiber (ca. 0.5 $\mu$L). Equation 5 demonstrates that $R$ is defined by two parameters, $K$ and $\beta$. These parameters are so related that quantitative extraction requires $1/\beta \ll K$, which leads to the denominator in eq 5 converging to $K$ and $R$ to unity. Consequently, in some cases it is possible to choose a suitable, permitting quantitative extraction, sample volume. For example, for PAHs, whose PDMS/water partition coefficients are on the order of $10^5$ or more, the sample volume should not be larger than 2.5 mL. One can observe that the question exists of whether the chosen final determination technique is capable of measuring the amount of analyte contained in such a small sample volume. Favorable partition coefficients may be achieved by adequate selection of the sorbent phase, an approach widely discussed in the next paragraphs. One can also utilize the dependence of the partition coefficients on the temperature (see also section 5.1). Another method of quantitative isolation of analytes from the sample is multiple extraction of the same sample. This approach has been successfully employed for determination of VOCs in solid samples (solid multiple HS-SPME).[188] Generally, however, one must remember that quantitative extraction is rather slow, due to the still decreasing concentration of analytes with the equilibration time, which is long as compared with that in cases when this concentration is kept at a relatively constant level.

In most cases, when SPME is utilized, traditional quantitation/calibration techniques, such as external standard, internal standard, and standard addition, are employed.

External standard means finding the dependence of the signal (e.g., peak area) on the amount/concentration of a given analyte in a series of standard solutions or extracted from such solutions, maintaining constant conditions influencing the extraction kinetics. This approach, due to the necessary reproducibility of these conditions, is primarily used in laboratories. Nevertheless, if extraction is carried out in equilibrium mode and the matrix influence on the equilibrium is negligible, external standard based SPME may also be used in on-site analyses.[189]

The standard addition procedure means adding known amounts of analyte/analytes to the samples and preparation of the dependence of the detector response on the amount added. The intercept of such a plot reveals the concentration of analyte in the sample. The principal advantage of this procedure is avoidance of problems of any matrix influence, which is fully compensated here. In the case of SPME, this method is recommended for solid and complex matrix samples.[190]

The internal standard method means adding to the sample not the analyte (target compound) but another compound, usually revealing similar properties, yet allowing its independent identification. The latter usually results from the separation technique employed or from using isotope-labeled internal standards. In this case, quantitation is achieved by determining the ratio of detector responses toward the standard to that toward the analyte. Also in this procedure, the influence of the sample matrix has been eliminated. The internal standard procedure permits determinations even in cases when reproducibility of the sample preparation or final determination steps is not quite ensured.[191]

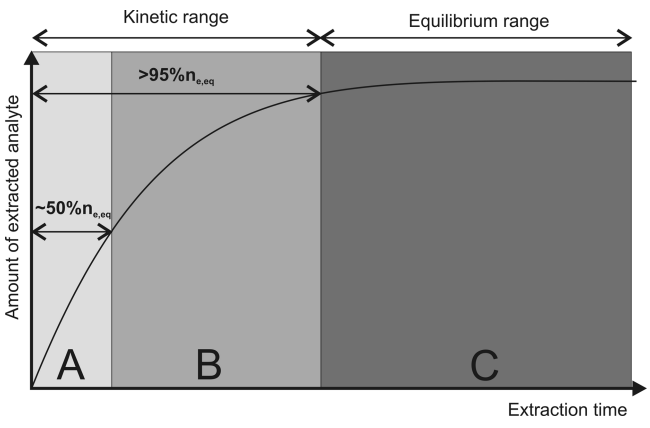


**Figure 5.** Sorption profile in an SPME device.


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Calibration methods typical for SPME may be characterized by analysis of the sorption profile shown in Figure 5. Generally, one can distinguish two ranges of the sorption profile: the kinetic one (with subranges A and B) and the equilibrium one (C). The latter range is relatively simple in regard to calibration procedures. Two extreme cases are possible here: aforementioned quantitative extraction and extraction from such a volume of the sample which ensures its relatively constant composition. In the latter case, for determination of the amount of analyte in the sample, one must know the partition coefficient at the extraction conditions and volume of the sample, while controlling parameters influencing the extraction kinetics is not necessary. The former case (kinetic region of the sorption profile) consists of two subranges. In the first one (A), the amount of analyte extracted increases linearly with time, and in the second one (B), the dependence is not linear. Even in subrange A, the assumption of linearity is rather a simplification. A 50% saturation of the sorbent with analyte is conventionally treated as an A−B threshold value, yet in many cases this value may be significantly lower. Within this subrange, it is possible to adopt calibration methods based on the transport rate of analytes to the fiber surface, as this is the rate-determining step of the whole extraction procedure. Depending on the details of the exposition of the SPME fiber extraction layer to the sample, different theoretical models have been developed. In the case when the fiber is retracted back to the needle, knowledge of the diffusion coefficient of an analyte and the geometric parameters of a given SPME device permits determination of TWA of this analyte in a given sample (see section 3.3.1). In this case, when the fiber protrudes from the needle and is exposed to the sample, two models have been developed to describe the analyte transport kinetics:

(a) Assuming linear flow of the sample in the direction normal to the fiber main axis, known as the cross-flow model and described by the equation[192]

$$C_s = \frac{n_e \ln((b + \delta)/b)}{2\pi DLt} \quad (11)$$

where $L$ is the length of the exposed sorbent layer, $b$ the radius of the sorbent layer, $\delta$ the thickness of the boundary layer, a parameter which is a function of the Reynolds and Schmidt numbers, and $t$ the fiber exposition time.

(b) Assuming the existence of a diffusion layer characterized by parameters invariable along the whole fiber (the sample medium rotates around the cylindrical fiber and its sorbent coating), known as the interface model and described by the equation[193]

$$C_s = \frac{n_e d}{E(Re)^m (Sc)^{1/3} ADt} \quad (12)$$

where $E$ and $m$ are constants depending on the Reynolds number, $Re$ is the Reynolds number, $Sc$ is the Schmidt number, $A$ is the fiber surface area, and $d$ is the external diameter of the fiber.

Both cases may be simplified to the following form:

$$C_s = \Delta \frac{n_e}{D} t \quad (13)$$

where $\Delta$ is a constant including characteristic parameters of the extraction system, resulting from its geometry and the sample flow dynamics.

Even this simple model reveals proportionality of the amount of an analyte extracted with time, while the proportionality constant depends upon the geometric and flow parameters of the system. Therefore, determination of these parameters, as well as maintaining their constancy during the extraction procedure, permits a relation to be found between the amount of the analyte extracted and its concentration in the sample without employing either the external or internal standard method.

## 5. NEW APPROACHES TO SPME EQUIPMENT

### 5.1. Cooled Coated Fiber SPME

The best way to achieve maximum extraction efficiency is to reach equilibrium between the sorbent and the sample matrix as quickly as possible, but the time to reach this equilibrium may vary from a few seconds to a few hours, depending on the thickness of the SPME fiber coating, the type of sorbent, the concentration and volatility of the analyte, the state of matter and characteristics of the sample matrix, and the conditions of the extraction. As mentioned earlier, raising the temperature accelerates the diffusion of analytes to the headspace and the extraction process in general, but on the other hand, this lowers the partition coefficients of the analytes between the extraction phase and the sample matrix. A new approach to improving extraction efficiency in this way is to heat the sample and simultaneously cool the SPME fiber and/or the headspace; this intensifies the mass transfer and increases the partition coefficients. The temperature is easily controlled by cooling the fiber coating from the inside with a coolant and by altering the core diameter of the arrangement.[194] In the first report describing the internal cooling of the SPME extraction coating (cooled coated fiber SPME, CCF-SPME), the coolant was liquid $CO_2$,[195] while in later reports the coolant was alcohol precooled in a cryostat.[196] This technique is used especially in the case of analytes with low partition coefficients and to collect analytes from highly viscous samples, such as glues, where stirring could be problematic.

The first internally cooled fibers were used to extract VOCs and BTEX from air,[176] and the equipment used for this purpose was miniaturized and automated in 2006.[175] Subsequent reports describe the application of CCF-SPME for sampling volatile compounds in tropical fruits,[197] flavors and fragrances in water and shampoos,[198] PAHs in sediments,[199] and chloroanisoles in the corks used to seal wine bottles.[200] In the latest studies, CCF-SPME equipment was used for sampling nanoparticles from aerosols.[201] CCF-SPME extraction fibers can be placed directly in the injector of the chromatographic column, which ensures the long lifetime of such equipment. The fibers in this apparatus have also turned out to be relatively strong mechanically and have been used up to 100 times before having to be replaced. CCF-SPME extracts analytes from the headspace and from highly contaminated liquid samples with a complex matrix composition with excellent efficiency.[176,178,180]

### 5.2. In-Tube SPME

To overcome the problems caused by the mechanical weakness of the extraction fiber, its poor efficiency, and the leaching of the coating, and also the difficulties of combining this technique with HPLC and the poor selectivity of this method, a novel piece of apparatus has been designed for solid-phase microextraction. Other factors have also fueled the search for new solutions in SPME technology—the small number of


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commercially available fiber coatings and the problems involved with the automation of the process—which would improve reproducibility and minimize technical defects.

One such fresh approach is to combine SPME with in-tube/in-needle extraction (ITE). In-tube SPME was introduced in

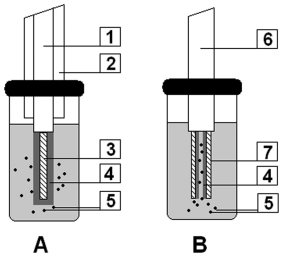


**Figure 6.** Diagram of devices for fiber SPME (A) and in-tube SPME (B): 1, inner needle; 2, outer needle; 3, fused silica fiber; 4, stationary phase; 5, analyte; 6, injection needle; 7, fused silica capillary column.

1997;[202] since then it has been widely applied to collect analytes from environmental samples, biological samples and foods, and especially polar and thermally sensitive analytes.[203]

The extraction phase in in-tube SPME is immobilized as the inner coating of the needle or part of the chromatographic column (Figure 6). In the latter case a further advantage is that commercial columns are chemically and thermally very resistant and are available in a wide range of polarities. Analytes are retained in the extraction medium during a few draw/eject cycles of the sample. Analytes are then desorbed directly in the injector of the measuring instrument: the needle is flushed with a mobile phase which is then transferred to the HPLC column.[204] Analytes can also be desorbed off-line if the in-tube SPME equipment is rinsed with a small amount of solvent. This method of desorption prevents peak broadening, which sometimes happens when desorption takes place directly in the desorption chamber; at the same time it improves limits of detection of the whole analytical procedure. If the sample contains nonvolatile, high-molecular-weight compounds, such as proteins or humus compounds, analysis with in-tube SPME may be troublesome; in this case, porous cellulose filters protecting the sensitive fiber are preferable.[205]

Apart from the materials used as internal wall coatings in capillary chromatographic columns, the internal needle coatings for in-tube SPME equipment are also made from molecularly imprinted polymers,[206] conducting polymers,[207−209] and immunosorbents.[210] Because of the means by which analytes are released, in-tube SPME is used mainly to sample polar and thermally labile analytes from food[211] and medical[212] samples. The standard types of SPME fiber coatings, such as PDMS, CW, or PEG (e.g., Omegawax 250), are used, for example, to sample pesticides from aqueous solutions[183] and narcotics and $\beta$-blockers from biological media and body fluids[213,214] and to extract BTEX and phenols from aqueous samples.[215]

The in-tube SPME technology also uses monolithic capillary columns, especially those made from fused silica, the stationary phase of which has been additionally modified with $C_{18}$ groups to achieve a better porosity and a minimal pressure drop at high flow rates.[216] This type of coating has been used, for example, for sampling polycyclic aromatic hydrocarbons[197,217] and estrogens as well as narcotics and medicines.[218,219] The inner walls of the in-tube SPME apparatus can also be coated using the sol−gel technique;[54,57,220] as a result, both inorganic and hybrid organic−inorganic polymers of the desired shape can be obtained. These materials are characterized by a high degree of purity, homogeneity, and enhanced thermal stability at all pH values, as well as excellent analyte recovery rates. The better porosity of the extraction coating, and hence the greater specific surface area, means that even a thin layer ensures a very good extraction efficiency. Such coatings are used in in-tube SPME to sample phenols, alcohols, and amines from aqueous media.[221] Table 1 lists basic information on the possible uses of different sorbents in in-tube SPME.

In-tube SPME equipment is easily coupled to final determination systems such as HPLC, LC−MS, ion chromatography (IC), and CE;[184] it can also be connected directly to most GC arrangements, although in this case the needle has to be dried before thermal desorption in the GC injector.[222] The in-tube SPME apparatus is readily automated by connecting it to a commercially available HPLC automatic sampling device. With such an automated system, analyses can be completed in less time, and with better precision and reproducibility of results.[183,223] This technique has its limitations, however: it can

**Table 1. Applications of Different Sorbents for In-Tube SPME**

| stationary phase | final determination technique | analyte | matrix | ref |
|---|---|---|---|---|
| MIPs | HPLC | propranolol | biological fluids | 206 |
| conducting polymers (PPy) | LC−ESI-MS | $\beta$-blockers | urine and serum | 207 |
| | HLPC | aromatic compounds | tap and lake water | 208 |
| | LC−ESI-MS | organoarsenic compounds | tap water, seafood | 209 |
| immunosorbents | HPLC | drugs | biological material | 210 |
| Omegawax 250 | HPLC | phenylurea pesticides | distilled water | 202 |
| | LC−ESI-MS | $\beta$-blockers | urine and serum | 213, 214 |
| | GC | volatile compounds, BTEX | deionized water | 176 |
| monolithic capillary columns | HLPC | alkylphenols; pesticides; | distilled water | 216 |
| | HLPC | PAHs | distilled water | 217 |
| | HPLC | ketoprofen, fenbufen, ibuprofen | urine samples | 220 |
| | HLPC | acidic drugs, phenols, endocrine-disrupting chemicals | lake water | 218 |
| sol−gel sorbents | GC | PAHs, aldehydes, ketones, phenols, amines | deionized water | 221 |
| | HPLC | ketamine | urine samples | 219 |
| | HLPC | PAHs, ketones, alkylbenzenes | deionized water | 62 |
| | CME−GC | PAHs, aldehydes, ketones | deionized water | 65 |


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only be used with very pure samples, not containing large solid particles that could block the capillary tube or needle.

**5.2.1. Fiber-in-Tube/Wire-in-Tube SPME.** A new approach to the in-tube SPME technique is based on improving the on-line LC connection. To this end, two interesting devices have been developed: a stainless steel core (wire-in-tube SPME)[224] or a polymer core (fiber-in-tube SPME)[225−227] is inserted into the capillary of the in-tube SPME arrangement. In the wire-in-tube system, the core reduces the capillary volume, but the surface area of the sorbent is not reduced, as would be the case if the capillary diameter were made smaller. The combination of this system with LC is extremely efficient and has been used to extract analytes from biological samples.[205] Moreover, the on-line combination of in-tube SPME arrangements with LC makes it possible to perform quick and reliable analyses of samples with a complex matrix composition such as biological material (blood or urine) for the presence of narcotics or medicines. It can also be combined with CE or capillary electrochromatography (CEC).

### 5.3. Membrane SPME (M-SPME)

The concept of using a membrane in SPME appeared in the mid-1990s with the membrane playing different roles (e.g., a protective sheath) by Pawliszyn et al. One example where the membrane (hollow cellulose) was a more active element of the system, i.e., cutting out some high-molecular-weight interfering compounds, was published in 1996.[205] Since then, several papers have been published where the membrane played chiefly a protective role. In 2004, a system including a hollow fiber (polypropylene) membrane-protected solid-phase microextraction system (commercial solid phases) was used for determination of triazine herbicides in bovine milk and sewage sludge samples.[228] The same group suggested using a similar membrane to protect a multiwalled carbon nanotube microextraction system for determination of organophsophorous pesticides in sewage sludge[109] and extraction of acidic drugs from wastewater samples, this time a porous membrane protecting a $C_{18}$ sorbent.[229]

As described above, the extraction of polar analytes from samples containing polar constituents using SPME still requires improvements in a number of areas and the elimination of problems reducing recoveries and reproducibility of results. The difficulties with sampling polar analytes are due, among other things, to the low affinity of extraction coatings for polar compounds, but if the polarity of the sorbent is increased, its affinity for the matrix, especially water, also increases, and the coating partially dissolves in the matrix. Introducing a membrane separating the polar retention medium from the sample was one of the concepts for overcoming the problems with isolating polar analytes from samples with a polar matrix composition.[230] In such a system, polar analytes migrate from the sample matrix across a hydrophobic, mechanically strong, and thermally stable membrane and are retained in a suitable SPME fiber coating underneath. The glass SPME fiber is coated with two layers of sorbent: an inner layer of highly polar PEG, which is the extraction medium proper, and an outer, hydrophobic, nonpolar layer of PDMS, which acts as the membrane separating the extraction medium from the sample (Figure 7).

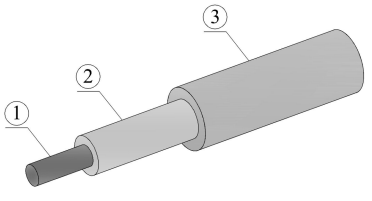


**Figure 7.** Fiber structure in an M-SPME device: 1, glass fiber; 2, extraction medium (PEG); 3, polymeric membrane (PDMS).

Both layers are produced using the procedure described in section 3.2: the fiber is immersed in molten polymer, and the membrane is applied using the sol−gel technique. In this simple way, highly selective, thermally and mechanically very resistant membranes with customized properties can be obtained from polymeric materials. The membrane can also be made from a pseudoliquid, but the choice of these materials is limited to the two most commonly used ones available on the market, i.e., PDMS and PA.[231]

These double-layered fibers are strong and thermally resistant, so thermal desorption of adsorbed analytes is feasible. In addition, the fiber fits entirely within the GC injector, so analytes are not lost from the nonpolar phase. Experiments using the PEG/PDMS system on a standard mixture of phenols have given a 10-fold better extraction efficiency than commercially available polyacrylic coatings. The method of preparing fibers enables usage of highly polar sorbents without the risk of their dissolving in the sample matrix.[214] Quite recently, another example of covering a commercial SPME fiber with an extra layer of PDMS, increasing its robustness in direct extraction from food samples, was also published.[232]

## 6. AUTOMATION OF SPME

An important practical aspect of implementation of the SPME technique in analytical laboratories is its automation-oriented nature. A typical SPME device is just an appropriately modified syringe; therefore, quite naturally, its automation started with suitable modifications of existing autosamplers used for injection of liquid samples in chromatography and related techniques. Nonetheless, such modifications had to account for some specific requirements of the technique. For example, due to high throughput of samples, special septa were employed, more robust, especially resistant against coring (e.g., predrilled). Another option is to use septumless systems, manufactured, for example, by Merlin Microseal, which, according to the manuals, permit at least 1000 faultless insertions. The same reasons led to modifications of the needles, the tips of which are now shaped in a special manner.

The necessity of quite frequently stirring the sample led to implementation of different stirring techniques in automated SPME devices. However, fiber vibration or sample tray rotation may result in significant mechanical strain, leading to damage of the fiber. To increase the fiber lifetime, Supelco introduced a new type of elastic steel with which all the basic elements of a system, such as needles, plungers, and fiber cores, are made. Miniature magnetic stirring bars are also employed in most of the available commercial systems.[233] Several manufacturers make systems, such as the MultiPurpose sampler (Gerstel GmbH), Combi PAL (CTC Analytics), and TriPlus RSH (Thermo Scientific), offering automation of the whole procedure of sample preparation. The following stages of such a procedure are included: extraction of analytes from liquid samples and from the headspace (samples are thermostated and agitated), fiber conditioning (thermally and by pure solvent), derivatization of the analytes (in the sample phase or on-fiber), and preparation of the secondary sample (liquid desorption of the analytes from the fiber).


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**Table 2. Summary of the Problems Raised/Discussed in This Paper: Quick Reference Table**

| params affecting extraction of analytes | analytical procedure | analytes | LOD | | ref |
|---|---|---|---|---|---|
| Coatings | | | | | |
| Conducting polymers | determination of PAHs by HS-SPME-GC using 16 $\mu$m PPy-DS and 100 $\mu$m PDMS fibers | analytes | (PPy-DS) (pg/mL) | (PDMS) (pg/mL) | 39 |
| | | Naphthalene Acenaphthylene Acenaphthene | 160 | 180 | |
| | | | 90 | 270 | |
| | | | 55 | 100 | |
| Molecularly imprinted polymers | determination of triazines by MIP-coated SPME-HPLC | The extraction yields of six triazine analogues with the MIP-coated fibers were much higher than that of the nonimprinted polymer (NIP) coated fibers (for prometryn it was 10 times as much as that with the NIP-fibers) | | | 50 |
| Immunosorbents | Determination of theophylline by immobilized antitheophylline-coated fiber SPME-HPLC | Theophylline | antitheophylline-coated SPME fiber | CW/DVB fiber and capillary GC/NPD | 123 |
| | | | 0.0001 $\mu$g/mL | 0.6 $\mu$g/mL | |
| Sol−gel sorbents | determination of BTEX and PAHs, HS and direct SPME with GC-FID | | C[4]−OH-TSO coating | PDMS coating | 77 |
| | | Benzene | 35.2 ng/l | 2.2 times more than for C [4] | |
| | | Ethylbenzene | 17.7 | 2.1 | |
| | | Naphthalene | 2.5 | 5.0 | |
| | | Biphenyl | 1.2 | 5.8 | |
| | | Acenaphthylene | 5.6 | 6.1 | |
| Ionic liquids | determination of fatty acid methyl esters by polymeric ionic liquids-coated SPME-GC-FID | | (Poly(ViHDIm$^+$ NTf$_{2-}$) PIL | (7 $\mu$mPDMS) ($\mu$g/l) | 94 |
| | | Isopropyl butyrate | 50 | 100 | |
| | | Methyl enanthate | 25 | 50 | |
| | | Methyl caprylate | 5 | 50 | |
| | | Methyl decanoate | 2.5 | 5 | |
| | | Furfuryl octanoate | 2.5 | 10 | |
| Other types of fiber coatings | determination of nonionic surfactants by polycrystalline graphite-coated fiber SPME reversed-phase HPLC-fluorescence | Triton-X | (Polycrystalline graphites-coated SPME fiber) 0.50 mg/L | (Carbowax/TPR) 1.57 mg/L | 113 |
| Other modifications/ improvements | | | | | |
| Metal core | high mechanical strength and thermal stability: silver core,[117] stainless steel core,[106] platinum,[127] highly elastic, biocompatible and resistant to corrosion core made from Nitino.[102] | | | | |
| Methods of depositing the extraction coating | rapid deposition of many coating, even on irregular or porous surfaces, using cyclic voltammetry (CV).[35,36,123] Coatings formed in this way are extremely homogeneous and pure; coatings can be obtained in the oxidized or reduced form of the polymer. | | | | |
| Mode of extraction | Headspace sampling: reduced risk of contamination of and/or damage to the fiber, for example, changing pH of the sample is possible; selectivity is superior to direct sampling. Limitations: more demanding calibration (necessity of maintaining constant the parameters affecting the state of equilibrium).[129,131] | | | | |
| Extraction time vs temperature and stirring | Temperature increase leads to improvement of the rates of mass transport between the phases, at the same time worsening the partition coefficients, therefore, manipulating temperature applies chiefly to HS extraction mode. Times required to reach equilibrium are usually long and may be shortened by intensive stirring, which is the main factor in direct extraction mode, when temperature manipulations are limited. Stirring increases mass transfer, shortening the extraction time, and sometimes also improves reproducibility. Vortex-vibrators or ultrasounds can be used to agitate the sample, ensuring very short extraction times.[140] | | | | |
| Thickness of the fiber coating | Thicker coatings retain larger amounts of analytes, but the equilibration times are longer. | | | | |
| Sample volume | When extraction does not reduce the amount of analyte in the sample by more than 1%, the quantity of an analyte adsorbed is proportional only to the partition coefficient and the volume of the sorbent. In such cases, calibration procedure may be simplified. Generally, increasing sample volume is favorable for analytes of high partition coefficients. | | | | |
| | In HS mode, the efficiency of extraction depends also on the volume of the intermediate phase (neutral gas used), which should be as small as possible to prevent the excessive dilution of analytes in this phase, because this substantially influences the overall detection limit.[138,139] | | | | |
| Salting out | Adding salt to a liquid sample improves extraction via increased ionic strength of the solution, leading to lower solubility and larger partition coefficients of organic components.[145] | | | | |



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**Table 2. continued**

| params affecting extraction of analytes | analytical procedure | analytes | LOD | | ref |
|---|---|---|---|---|---|
| Change of pH | pH of samples can affect the amount of an analyte retained,[146] particularly in cases of weakly acidic or basic compounds like amines and phenols, which should be maintained in undissociated form. Extreme pH values can, however, influence the mechanical strength of the sorbent coating. | | | | |
| Matrix effect | Effects of influencing the extraction by addition of a hydrophobic organic solvent to aqueous samples is not well understood (usually extraction is worse; likewise, adding water to organic samples also reduces extraction). It improves, however, diffusion of analytes from the sample to the sorbent in the case of solid samples, like sediments and muds. Also, some components of the sample matrix can influence extraction; for example, humic and fulvic acids, present in water and soil samples as dissolved organic matter, can reduce amounts of analytes retained by the sorbent layer.[149,150] | | | | |
| Derivatization of analytes | This approach may be recommended in the cases when analytes are present in trace quantities and in the extraction from complex matrices (derivatives may reveal more favorable partition coefficients). Derivatization also enhances applicability of SPME to a wider range of analytes.[172] | | | | |
| Internally cooled SPME | Determination of chloroanisoles in cork by PDMS-coated HS-SPME-GC-TOF-MS | | (PDMS) ICC-HS-SPME (ng/g) | (PDMS/DVB) HS-SPME (ng/g) | 181 |
| | | | 0.28 | 1.8 | |
| | | 2,4-dichloroanisole | 0.25 | 1.6 | |
| | | 2,6-dichloroanisole | 0.25 | 1.2 | |
| | | 2,4,6-trichloroanisole pentachloroanisole | 0.49 | 1.6 | |
| In-tube SPME | Determination of carbamates in-tube SPME−HPLC−UV | | In-tube-SPME ($\mu$g/l) | EPA/NPS Method ($\mu$g/l) | 204 |
| | | Carbaryl | 1 | 2 | |
| | | Propham | 5.1 | 11 | |
| | | Methiocarb | 4 | 4 | |
| | | Chlorpropham | 8.5 | 0.5 | |
| | | Barban | 7.5 | 3.8 | |
| M-SPME | determination of phenols by PDMS-coated SPME-GC and M-SPME-GC | | (PEG/PDMS) M-SPME ($\mu$g/l) | (PA) SPME ($\mu$g/l) | 210 |
| | | 2-chlorophenol | 43 | 530 | |
| | | 2,4-dichlorophenol | 15 | 120 | |
| | | 2,4-dimethylphenol | 9 | 110 | |
| | | 2,4-dinitrophenol | 110 | 950 | |
| | | 2-nitrophenol | 9 | 60 | |



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An important step in full automation of SPME-based analytical procedures was introduction of the module permitting automatic change of fibers (e.g., of different polarities), which made possible automated analyses of different classes of analytes from the same sample. Currently available instrumentation performs not only the traditional version of SPME but also internally cooled SPME and in-tube SPME. A somewhat different approach is represented by the multifiber/thin film SPME system (Professional Analytical Systems Technology) in the format of a 96-well plate permitting screening analyses to be carried out.[234] One should stress that currently available systems permit linking the extraction/sample preparation step with GC and LC.[235,236]

## 7. SUMMARY

In view of the demands made of contemporary analytical techniques and the need to implement green technologies in analytical practice, solvent-free techniques of preparing samples for analysis, such as SPME, are taking on a greater significance. With this technique, analytes can be sampled from media with a complex composition, from contaminated media, and from media with polar matrix constituents. The cited literature presents information on modifications of existing approaches in regard to the SPME apparatus (miniaturization, automation, combination with monitoring and measurement instrumentation) and on completely new devices such as CCF-SPME, in-tube SPME, and M-SPME, which guarantee high recoveries of a broad spectrum of analytes. Studies of the effects on the extraction process of parameters such as the extraction time and temperature, the type of extraction coating and its thickness, and fiber derivatization have provided the opportunity to control both its efficiency and, to some extent, its selectivity. SPME has achieved enormous significance in analytical practice as far as the preparation of samples for analysis is concerned. Thanks to the merits of this technique and the possibilities of improving it through novel design approaches and the implementation of new, highly selective extraction fiber coatings, one can expect further developments in this field. For the readers' benefit, Table 2 was prepared as a kind of quick reference tool to the problems raised in this paper.

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### Notes

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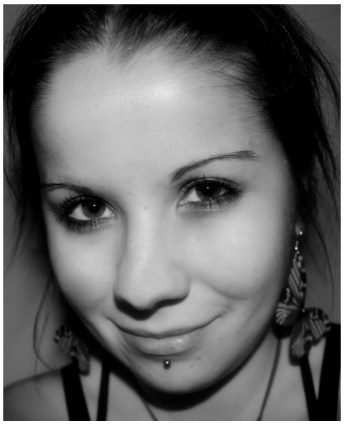

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## ACRONYMS

| | |
|---|---|
| BTEX | benzene, toluene, ethylbenzene, xylenes |
| CAR | Carboxen |
| CE | capillary electrophoresis |
| CV | cyclic voltammetry |
| CW | Carbowax |
| DVB | divinylbenzene |
| GC | gas chromatography |
| GPE | gum-phase extraction |
| HPLC | high-performance liquid chromatography |
| HS-SPME | headspace solid-phase microextraction |
| ICP | inductively coupled plasma |
| IL | ionic liquid |
| MAH | monocyclic aromatic hydrocarbon |
| MESI | membrane extraction with a sorbent interface |
| M-SPME | membrane solid-phase microextraction |
| OTT | open-tubular trapping |
| P3DDT | poly(3-dodecylthiophene) |
| PA | polyacrylate |
| PAH | polycyclic aromatic hydrocarbon |
| PANI | polyaniline |
| PIL | polymeric ionic liquid |
| PCB | polychlorinated biphenyl |
| PDMS | poly(dimethylsilane) |
| PEG | poly(ethylene glycol) |
| PEO | poly(ethylene oxide) |
| PPy | polypyrrole |
| PT | purge and trap |
| S-HS | static headspace |
| SBSE | stir bar sorptive extraction |
| SFC | supercritical fluid chromatography |
| SPE-DT | solid-phase extraction thermal desorption |
| SPME | solid-phase microextraction |
| VOC | volatile organic carbon |

## Variables

| | |
|---|---|
| $\beta_{e/ie}$ | volume ratio of extractant (coating material) to indirect extractant |
| $\beta_{e/s}$ | volume ratio of extractant to sample |
| $\beta_{ie/s}$ | volume ratio of indirect extractant to sample |
| $C_{e,eq}$ | analyte concentration in extractant phase at equilibrium after extraction |
| $C_{os}$ | analyte concentration in original sample |
| $C_{s,eq}$ | analyte concentration in sample at equilibrium after extraction |
| $E$ | coefficient of enrichment |
| $K_{e/ie}$ | partition coefficient of analyte between extractant and indirect extractant phases |
| $K_{e/s}$ | partition coefficient of analyte between extractant and sample phases |
| $K_{ie/os}$ | partition coefficient of analyte between indirect extractant and sample phases |
| $n_{e/eq}$ | amount of analyte in extractant phase after extraction at equilibrium |
| $R$ | extraction recovery |
| $V_e$ | extractant volume |
| $V_s$ | sample volume |

## REFERENCES


(1) Tobiszewski, M.; Mechlińska, A.; Zygmunt, B.; Namieśnik, J. *Trends Anal. Chem.* **2009**, *28*, 943.
(2) Tobiszewski, M.; Mechlińska, A.; Namieśnik, J. *Chem. Soc. Rev.* **2010**, *39*, 2869.
(3) Arthur, C. L.; Pawliszyn, J. *Anal. Chem.* **1990**, *62*, 2145.
(4) Pawliszyn, J. *Solid Phase Microextraction: Theory And Practice*; Wiley-VCH Inc.: New York, 1997.
(5) Theodoridisa, G.; Kosterb, E. H. M.; de Jong, G. J. *J. Chromatogr., B* **2000**, *745*, 49.
(6) Pawliszyn, J. *Application of Solid-Phase Microextraction*; Royal Society of Chemistry: Cambridge, U.K., 1999.
(7) Lord, H.; Pawliszyn, J. *J. Chromatogr., A* **2000**, *885*, 153.
(8) Zhang, Z. Y.; Yang, M. J.; Pawliszyn, J. *Anal. Chem.* **1994**, *66*, 844A.
(9) Lopez-Jimenez, F. J.; Rubio, S.; Perez-Bendito, D. *J. Chromatogr., A* **2008**, *1195*, 25.
(10) He, Y.; Vargas, A.; Kang, Y.-J. *Anal. Chim. Acta* **2007**, *589*, 225.
(11) Wang, Q.; Qiu, H.; Li, J.; Liu, X.; Jiang, S. *J. Chromatogr., A* **2010**, *1217*, 5434.
(12) Prieto, A.; Basauri, O.; Rodil, R.; Usobiaga, A.; Fernández, L. A.; Etxebarria, N.; Zuloaga, O. *J. Chromatogr., A* **2010**, *1217*, 2642.
(13) Krüger, O.; Christoph, G.; Kalbe, U.; Berger, W. *Talanta* **2011**, *85*, 1428.
(14) Shi, Z.-G.; Lee, H. K. *Anal. Chem.* **2010**, *82*, 1540.
(15) Zhou, S.; Chen, H.; Wu, B.; Ma, C.; Ye, Y. *Microchim. Acta* **2012**, *176*, 419.
(16) Mills, G. A.; Walker, V. *J. Chromatogr., A* **2000**, *902*, 267.
(17) Wardencki, W.; Curyło, J.; Namieśnik, J. *J. Biochem. Biophys. Methods* **2007**, *70*, 275.
(18) IUPAC. *Compendium of Chemical Terminology*, 2nd ed. (the "Gold Book"); compiled by A. D. McNaught and A. Wilkinson; Blackwell Scientific Publications: Oxford, U.K., 1997.
(19) Dietz, C.; Sanz, J.; Cámara, C. *J. Chromatogr., A* **2006**, *1103*, 183.
(20) Sigma-Aldrich. Solid Phase Microextaction. http://www.sigmaaldrich.com/analytical-chromatography/sample-preparation/spme/literature.html.

(21) Huang, C.-T.; Su, Y.-Y.; Hsieh, Y.-Z. *J. Chromatogr., A* **2002**, *977*, 9.
(22) Barro, R.; Ares, S.; Garcia-Jares, C.; Llompart, M.; Cela, R. *J. Chromatogr., A* **2004**, *1045*, 189.
(23) Endo, S.; Droge, S. T. J.; Goss, K.-U. *Anal. Chem.* **2011**, *83*, 1394.
(24) Barták, P.; Čáp, L. *J. Chromatogr., A* **1997**, *767*, 171.
(25) Sampedro, M. C.; Martin, O.; Lopez de Armentia, C.; Goicolea, M. A.; Rodriguez, E.; Gomez de Balugera, Z.; Costa-Moreira, J.; Barrio, R. J. *J. Chromatogr., A* **2000**, *893*, 347.
(26) Berrada, H.; Font, G.; Molto, J. C. *J. Chromatogr., A* **2004**, *1042*, 9.
(27) Llorente, D. D.; Abrodo, P. A.; de la Fuente, E. D.; Gonzalez Alvarez, J.; Gutierrez Alvarez, M. D.; Gomis, D. B. *J. Sep. Sci.* **2011**, *34*, 1293.
(28) Krüger, R. L.; Dallago, R. M.; Nascimento Filho, I.; Di Luccio, M. *Environ. Monit. Assess.* **2009**, *158*, 355.
(29) Xiong, G.; Koziel, J. A.; Pawliszyn, J. *J. Chromatogr., A* **2004**, *1025*, 57.
(30) Tang, B.; Isacsson, U. *Energy Fuels* **2008**, *22*, 1425.
(31) Tumbiolo, S.; Gal, J.-F.; Maria, P.-Ch; Zerbinati, O. *Anal. Bioanal. Chem.* **2004**, *380*, 824.
(32) Baltussen, E.; Cramers, C. A.; Sandra, P. J. F. *Anal. Bioanal. Chem.* **2002**, *373*, 3.
(33) Augusto, F.; Carasek, E.; Silva, R. G. C.; Rivellino, S. R.; Batista, A. D.; Martendal, E. *J. Chromatogr., A* **2010**, *1217*, 2533.
(34) Kumar, A.; Gaurav; Malik, A. K.; Tewary, D. K.; Singh, B. *Anal. Chim. Acta* **2008**, *610*, 1.
(35) Mullett, W. M.; Pawliszyn, J. *J. Sep. Sci.* **2003**, *26*, 251.
(36) Koziel, J. A.; Shurmer, B.; Pawliszyn, J. *J. High Resolut. Chromatogr.* **2000**, *23*, 343.
(37) Wu, J.; Pawliszyn, J. *J. Chromatogr., A* **2001**, *909*, 37.
(38) Sadki, S.; Schottland, P.; Brodie, N.; Sabouraud, G. *Chem. Soc. Rev.* **2000**, *29*, 283.
(39) Mohammadi, A.; Yamini, Y.; Alizadeh, N. *J. Chromatogr., A* **2005**, *1063*, 1.
(40) Alizadeh, N.; Zarabadipour, H.; Mohammadi, A. *Anal. Chim. Acta* **2007**, *605*, 159.
(41) Alizadeh, N.; Mohammadi, A.; Tabrizchi, M. *J. Chromatogr., A* **2008**, *1183*, 21.
(42) Wu, J.; Mullett, W. M.; Pawliszyn, J. *Anal. Chem.* **2002**, *74*, 4855.
(43) Gbatu, T. P.; Ceylan, O.; Sutton, K. L.; Rubinson, J. F.; Caruso, J. A.; Mark, H. B., Jr. *Anal. Commun.* **1999**, *36*, 203.
(44) Yates, B. J.; Temsamani, K. R.; Ceylan, O.; Oztemiz, S.; Gbatu, T. P.; Larue, R. A.; Tamer, U.; Mark, H. B. *Talanta* **2002**, *58*, 739.
(45) Martín-Esteban, A. *Fresenius' J. Anal. Chem.* **2001**, *370*, 795.
(46) Pichon, V. *J. Chromatogr., A* **2007**, *1152*, 41.
(47) Kloskowski, A.; Pilarczyk, M.; Przyjazny, A.; Namieśnik, J. *Crit. Rev. Anal. Chem.* **2009**, *39*, 43.
(48) Cormack, P. A. G.; Elorza, A. Z. *J. Chromatogr., B* **2004**, *804*, 173.
(49) Hua, X.; Daia, G.; Huanga, J.; Yea, T.; Fanb, H.; Youwena, T.; Yua, Y.; Lianga, Y. *J. Chromatogr., A* **2010**, *1217*, 5875.
(50) Hu, X.; Hu, Y.; Li, G. *J. Chromatogr., A* **2007**, *1147*, 1.
(51) Hua, X.; Pan, J.; Hua, Y.; Huoa, Y.; Li, G. *J. Chromatogr., A* **2008**, *1188*, 97.
(52) Djozan, D.; Baheri, T. *J. Chromatogr., A* **2007**, *1166*, 16.
(53) Hu, X.; Pan, J.; Hu, Y.; Li, G. *J. Chromatogr., A* **2009**, *1216*, 190.
(54) Koster, E. H. M.; Crescenzi, C.; den-Hoedt, W.; Ensing, K.; de-Jong, G. J. *Anal. Chem.* **2001**, *73*, 3140.
(55) Qiu, L.; Liu, W.; Huang, M.; Zhang, L. *J. Chromatogr., A* **2010**, *1217*, 7461.
(56) Jing, T.; Wang, Y.; Dai, Q.; Xia, H.; Niu, J.; Hao, Q.; Mei, S.; Zhou, Y. *Biosens. Bioelectron.* **2010**, *25*, 2218.
(57) Zeng, J.; Chen, J.; Chen, L.; Wang, Y.; Chen, W.; Huang, X.; Chen, X. *Anal. Chim. Acta* **2009**, *648*, 194.
(58) Li, M. K.-Y.; Lei, N.-Y.; Gong, C.; Yu, Y.; Lam, K.-H.; Lam, M. H.-W.; Yu, H.; Lam, P. K. *Anal. Chim. Acta* **2009**, *633*, 197.
(59) He, J.; Lv, R.; Zhan, H.; Wang, H.; Cheng, J.; Lu, K.; Wang, F. *Anal. Chim. Acta* **2010**, *674*, 53.
(60) Prasad, B. B.; Tiwari, K.; Singh, M.; Sharma, P. S.; Patel, A. K.; Srivastava, S. *J. Chromatogr., A* **2008**, *1198*, 59.
(61) Tamayo, F. G.; Turiel, E.; Martín-Esteban, A. *J. Chromatogr., A* **2007**, *1152*, 32.
(62) Kim, T.-Y.; Alhooshani, K.; Kabir, A.; Fries, D. P.; Malik, A. *J. Chromatogr., A* **2004**, *1047*, 165.
(63) Hofacker, S.; Mechtel, M.; Mager, M.; Kraus, H. *Prog. Org. Coat.* **2002**, *45*, 159.
(64) Chong, S. L.; Wang, D.; Hayes, J. D.; Wilhite, B. W.; Malik, A. *Anal. Chem.* **1997**, *69*, 3889.
(65) Alhooshani, K.; Kim, T.-Y.; Kabir, A.; Malik, A. *J. Chromatogr., A* **2005**, *1062*, 1.
(66) Basheer, C.; Jegadesan, S.; Valiyaveettil, S.; Lee, H. K. *J. Chromatogr., A* **2005**, *1087*, 252.
(67) Lopes, A. L.; Augusto, F. *J. Chromatogr., A* **2004**, *1056*, 13.
(68) Zuin, V. G.; Lopes, A. L.; Yariwake, J. H.; Augusto, F. *J. Chromatogr., A* **2004**, *1056*, 21.
(69) Azenha, M.; Malheiro, C.; Silva, A. F. *J. Chromatogr., A* **2005**, *1069*, 163.
(70) Hu, Y.-l.; Fu, Y.-l.; Li, G.-K. *Anal. Chim. Acta* **2006**, *567*, 211.
(71) Yu, J.; Dong, L.; Wu, C.; Wu, L.; Xing, J. *J. Chromatogr., A* **2002**, *978*, 37.
(72) Gbatu, T. P.; Sutton, K. L.; Caruso, J. A. *Anal. Chim. Acta* **1999**, *402*, 67.
(73) Li, X.; Zeng, Z.; Zhou, J. *Anal. Chim. Acta* **2004**, *509*, 27.
(74) Zhou, F.; Li, X.; Zeng, Z. *Anal. Chim. Acta* **2005**, *538*, 63.
(75) Liu, M.; Zeng, Z.; Lei, Y.; Li, H. *J. Sep. Sci.* **2005**, *28*, 2306.
(76) Xiu-juan, L.; Rui-min, X.; Hai-bing, L.; Zeng Zhao-rui, J. *Wuhan Univ. J. Nat. Sci.* **2003**, *8*, 1153.
(77) Li, X.; Zeng, Z.; Gao, S.; Li, H. *J. Chromatogr., A* **2004**, *1023*, 15.
(78) Wang, W.; Gong, S.; Cao, Q.; Chen, Y.; Li, X.; Zeng, Z. *Chromatographia* **2005**, *61*, 75.
(79) Dong, C.; Zeng, Z.; Li, X. *Talanta* **2005**, *66*, 721.
(80) Zeng, Z.; Qiu, W.; Huang, Z. *Anal. Chem.* **2001**, *73*, 2429.
(81) Wang, D.; Xing, J.; Peng, J.; Wu, C. *J. Chromatogr., A* **2003**, *1005*, 1.
(82) Zeng, Z.; Qiu, W.; Yang, M.; Wei, X.; Huang, Z.; Li, F. *J. Chromatogr., A* **2001**, *934*, 51.
(83) Yun, L. *Anal. Chim. Acta* **2003**, *486*, 63.
(84) Cai, L.; Gong, S.; Chen, M.; Wu, C. *Anal. Chim. Acta* **2006**, *559*, 89.
(85) Yu, J.; Wu, C.; Xing, J. *J. Chromatogr., A* **2004**, *1036*, 101.
(86) Soukup-Hein, R. J.; Warnke, M. M.; Armstrong., D. W. *Annu. Rev. Anal. Chem.* **2009**, *2*, 145.
(87) Weingärtner, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 654.
(88) Roth, M. *J. Chromatogr., A* **2009**, *1216*, 1861.
(89) Liu, R.; Liu, J.; Yin, Y.; Hu, X.; Jiang, G. *Anal. Bioanal. Chem.* **2009**, *393*, 871.
(90) Aguilera-Herrador, E.; Lucena, R.; Cardenas, S.; Valcarcel, M. *Trends Anal. Chem* **2010**, *29*, 602.
(91) Ho, T. D.; Canestraro, A. J.; Anderson, J. L. *Anal. Chim. Acta* **2011**, *695*, 18.
(92) Liu, J. F.; Li, N.; Jiang, G. B.; Liu, J. M.; Jonsson, J. A.; Wen, M. J. *J. Chromatogr., A* **2005**, *1066*, 27.
(93) Hsieh, Y. N.; Huang, P. C.; Sun, I. W.; Whang, T. J.; Hsu, C. Y.; Huang, H. H.; Kuei, C. H. *Anal. Chim. Acta* **2006**, *557*, 321.
(94) Zhao, F.; Meng, Y. J.; Anderson, J. L. *J. Chromatogr., A* **2008**, *1208*, 1.
(95) López-Darias, J.; Pino, V.; Anderson, J. L.; Graham, C. M.; Afonso, A. M. *J. Chromatogr., A* **2010**, *1217*, 1236.
(96) Wanigasekara, E.; Perera, S.; Crank, J. A.; Sidisky, L.; Shirey, R.; Berthod, A.; Armstrong, D. W. *Anal. Bioanal. Chem.* **2010**, *396*, 511.
(97) He, Y.; Pohl, J.; Engel, R.; Rothman, L.; Thomas, M. *J. Chromatogr., A* **2009**, *1216*, 4824.
(98) Liu, M.; Zhou, X.; Chen, Y.; Liu, H.; Feng, X.; Qiu, G.; Liu, F.; Zeng, Z. *Anal. Chim. Acta* **2010**, *683*, 96.

(99) Amini, R.; Rouhollahi, A.; Adibi, M.; Mehdinia, A. *J. Chromatogr., A* **2011**, *1218*, 130.
(100) Graham, C. M.; Meng, Y.; Ho, T.; Anderson, J. *J. Sep. Sci.* **2011**, *34*, 340.
(101) López-Darias, J.; Pino, V.; Meng, Y.; Anderson, J. L.; Afonso, A. M. *J. Chromatogr., A* **2010**, *1217*, 7189.
(102) Meng, Y.; Pino, V.; Anderson, J. L. *Anal. Chem.* **2009**, *81*, 7107.
(103) Yang, P.; Lau, C. W.; Liu, X.; Lu, J. Z. *Anal. Chem.* **2007**, *79*, 8476.
(104) Martin-Calero, A.; Ayala, J. H.; González, V.; Afonso, A. M. *Anal. Bioanal. Chem.* **2009**, *394*, 937.
(105) Shearrow, A. M.; Harris, G. A.; Fang, L.; Sekhar, P. K.; Nguyen, L. T.; Turner, E. B.; Bhansali, S.; Malik, A. *J. Chromatogr., A* **2009**, *1216*, 5449.
(106) Wang, J. X.; Jiang, D. Q.; Gu, Z. Y.; Yan, X. P. *J. Chromatogr., A* **2006**, *1137*, 8.
(107) Lu, J.; Liu, J.; Wei, Y.; Jiang, K.; Fan, S.; Liu, J.; Jiang, G. *J. Sep. Sci.* **2007**, *30*, 2138.
(108) Li, Q.; Wang, X.; Yuan, D. *J. Chromatogr., A* **2009**, *1216*, 1305.
(109) Liu, X.; Ji, Y.; Zhang, Y.; Zhang, H.; Liu, M. *J. Chromatogr., A* **2007**, *1165*, 10.
(110) Basheer, Ch.; Alnedhary, A. A.; Madhava Rao, B. S.; Valliyaveettil, S.; Lee, H. K. *Anal. Chem.* **2006**, *78*, 2853.
(111) Eshaghi, Z.; Rezaeifar, Z.; Rounaghi, G.-H.; Nezhadi, Z. A.; Golsefidi, M. A. *Anal. Chim. Acta* **2011**, *689*, 122.
(112) Wan, H. B.; Chi, H.; Wong, M. K.; Mok, C. Y. *Anal. Chim. Acta* **1994**, *298*, 219.
(113) Aranda, R.; Kruus, P.; Burk, R. C. *J. Chromatogr., A* **2000**, *888*, 35.
(114) Górecki, T.; Martos, P.; Pawliszyn, J. *Anal. Chem.* **1998**, *70*, 19.
(115) Hou, J.; Ma, Q.; Du, X.; Deng, H.; Gao, J. *Talanta* **2004**, *62*, 241.
(116) Du, X.-Z.; Wang, Y.-R.; Tao, X.-J.; Deng, H.-L. *Anal. Chim. Acta* **2005**, *543*, 9.
(117) Hashemi, P.; Shamizadeh, M.; Badiei, A.; Poor, P. Z.; Ghiasvand, A. R.; Yarahmadi, A. *Anal. Chim. Acta* **2009**, *646*, 1.
(118) Liu, Y.; Lee, M. L.; Hageman, K. J.; Yang, Y.; Hawthorne, S. B. *Anal. Chem.* **1997**, *69*, 5001.
(119) Azenha, M.; Ornelas, M.; Silva, A. F *J. Chromatogr., A* **2009**, *1216*, 2302.
(120) Liu, Y.; Shen, Y.; Lee, M. L. *Anal. Chem.* **1997**, *69*, 190.
(121) Hu, Y.; Zheng, Y.; Li, G. *Anal. Sci.* **2004**, *20*, 667.
(122) Pichon, V.; Bouzige, M.; Miége, C.; Hennion, M.-C. *Trends Anal. Chem.* **1999**, *18*, 219.
(123) Yuan, H.; Mullett, W. M.; Pawliszyn, J. *Analyst* **2001**, *126*, 1456.
(124) Lord, H. L.; Rajabi, M.; Safari, S.; Pawliszyn, J. *J. Pharm. Biomed. Anal.* **2006**, *40*, 769.
(125) Lord, H. L.; Rajabi, M.; Safari, S.; Pawliszyn, J. *J. Pharm. Biomed. Anal.* **2007**, *44*, 506.
(126) Farajzadeh, M.; Rahmani., N. A. *Anal. Sci.* **2004**, *20*, 1359.
(127) Djozan, D.; Abdollahi, L. *Chromatographia* **2003**, *57*, 799.
(128) Djozan, D.; Assadi, Y.; Haddadi, S. H. *Anal. Chem.* **2001**, *73*, 4054.
(129) Nitinol Home Page. http://www.nitinol.com/.
(130) Kujala, S.; Pajala, A.; Kallioinen, M.; Pramila, A.; Tuukkanen, J.; Ryhänen, J. *Biomaterials* **2004**, *25*, 353.
(131) Setkova, L.; Risticevic, S.; Linton, C. M.; Ouyanga, G.; Bragg, L. M.; Pawliszyn, J. *Anal. Chim. Acta* **2007**, *581*, 221.
(132) Uğur, T.; Yücel, Ş.; Nusret, E.; Yasemin, U.; Kadir, P.; Attila, Y. *J. Electroanal. Chem.* **2004**, *570*, 6.
(133) Tamer, U.; Ertaş, N.; Udum, Y. A.; Şahin, Y.; Pekmez, K.; Yıldız, A. *Talanta* **2005**, *67*, 245.
(134) Guo, F.; Górecki, T.; Irish, D.; Pawliszyn, J. *Anal. Commun.* **1996**, *33*, 361.
(135) Farajzadeh, M. A.; Rahmani, N. A. *Talanta* **2005**, *65*, 700.
(136) Bagheri, H.; Mir, A.; Babanezhad, E. *Anal. Chim. Acta* **2005**, *532*, 89.
(137) Bagheri, H.; Babanezhad, E.; Es-haghi, A. *J. Chromatogr., A* **2007**, *1152*, 168.
(138) Stashenko, E. E.; Martínez, J. R. *J. Biochem. Biophys. Methods* **2007**, *70*, 235.
(139) Kasiotis, K. M.; Souki, H.; Tsakirakis, A. N.; Carageorgiou, H.; Theotokatos, S. A.; Haroutounian, S. A.; Machera, K. *Int. J. Mol. Sci.* **2008**, *9*, 906.
(140) Lambropoulou, D. A.; Konstantinou, I. K.; Albanis, T. A. *J. Chromatogr., A* **2007**, *1152*, 70.
(141) Guadarrama, A.; Fernández, J. A.; Íñiguez, M.; Souto, J.; de Saja, J. A. *Sens. Actuators, B* **2001**, *77*, 401.
(142) Lozano, J.; Santos, J. P.; Gutíerrez, J.; Horrillo, M. C. *Sens. Actuators, B* **2007**, *126*, 616.
(143) Lozano, J.; Santos, J. P.; M. C. Horrillo, M. C. *J. Food Compos. Anal.* **2008**, *21*, 716.
(144) Huang, Y.; Ho, S. S. H.; Ho, K. F.; Lee, S. C.; Gao, Y.; Feng, N. S. Y. *Anal. Methods* **2012**, *4*, 277.
(145) Chen, Y.; Pawliszyn, J. *Anal. Chem.* **2003**, *75*, 2004.
(146) Sheehan, E. M; Limmer, M. A.; Mayer, Ph.; Karlson, U. G.; Burken, J. G. *Environ. Sci. Technol.* **2012**, *46*, 3319.
(147) Martos, P. A.; Pawliszyn, J. *Anal. Chem.* **1999**, *71*, 1513.
(148) Ouyang, G.; Chen, Y.; Pawliszyn, J. *Anal. Chem.* **2005**, *77*, 7319.
(149) Haddadi, S. H.; Pawliszyn, J. *J. Chromatogr., A* **2009**, *1216*, 2783.
(150) Panavaite, D.; Padarauskas, A.; Vičkačkaite, V. *Anal. Chim. Acta* **2006**, *571*, 45.
(151) Kalua, C. M.; Boss, P. K. *J. Chromatogr., A* **2008**, *1192*, 25.
(152) Page, B. D.; Lacroix, G. *J. Chromatogr., A* **1997**, *757*, 173.
(153) Motlagh, S.; Pawliszyn, J. *Anal. Chim. Acta* **1993**, *284*, 265.
(154) Pedersen-Bjergaard, S.; Rasmussen, K. E. *Anal. Chem.* **1999**, *71*, 2650.
(155) Baltussen, E.; Sandra, P.; David, F.; Janssen, H.-G.; Cramers, C. *Anal. Chem.* **1999**, *71*, 5213.
(156) Geppert, H. *Anal. Chem.* **1998**, *70*, 3981.
(157) Louch, D.; Motlagh, S.; Pawliszyn, J. *Anal. Chem.* **1992**, *64*, 1187.
(158) Bao, M. L.; Pantani, F.; Griffini, O.; Burrini, D.; Santianni, D.; Barbieri, K. *J. Chromatogr., A* **1998**, *809*, 75.
(159) Doorn, H.; Grabanski, C. B.; Miller, D. J.; Hathorne, S. B. *J. Chromatogr., A* **1998**, *829*, 223.
(160) Yang, S. S.; Huang, C. B.; Smetena, I. *J. Chromatogr., A* **2002**, *942*, 33.
(161) Martos, P. A.; Pawliszyn, J. *Anal. Chem.* **1997**, *69*, 206.
(162) Valor, I.; Molto, J. C.; Apraiz, D.; Font, G. *J. Chromatogr., A* **1997**, *767*, 195.
(163) Sarrion, M. N.; Santos, F. J.; Galceran, M. T. *J. Chromatogr., A* **1998**, *819*, 197.
(164) Rogers, H. R.; Comber, S. D. W. *Chemosphere* **1998**, *37*, 1413.
(165) Ohlenbusch, G.; Kumke, M. U.; Frimmel, F. H. *Sci. Total Environ.* **2000**, *253*, 63.
(166) Alzaga, R.; Bayona, J. M. *J. Chromatogr., A* **2004**, *1042*, 155.
(167) Alzaga, R.; Peña, A.; Ortiz, L.; Bayona, J. M. *J. Chromatogr., A* **2003**, *999*, 51.
(168) Lee, I. S.; Tsai, S. W. *Anal. Chim. Acta* **2008**, *610*, 149.
(169) Tsai, S. W.; Chang, C. M. *J. Chromatogr., A* **2003**, *1015*, 143.
(170) Pizarro, C.; Perez-del-Notario, N.; Gonzalez-Saiz, J. M. *J. Chromatogr., A* **2007**, *1143*, 26.
(171) Chafer-Pericas, C.; Campins-Falco, P.; Herraez-Hernandez, R. *J. Pharm. Biomed. Anal.* **2006**, *40*, 1209.
(172) Domeno, C.; Ruiz, B.; Nerin, C. *Anal. Bioanal. Chem.* **2005**, *381*, 1576.
(173) Hong, J. E.; Pyo, H.; Park, S. J.; Lee, W. *Anal. Chim. Acta* **2005**, *539*, 55.
(174) Rodríguez, I.; Carpinteiro, J.; Quintana, J. B.; Carro, A. M.; Lorenzo, R. A.; Cela, R. *J. Chromatogr., A* **2004**, *1024*, 1.
(175) Okeyo, P. D.; Snow, N. H. *J. Microcolumn Sep.* **1998**, *10*, 551.
(176) Rodríguez, I.; Rubí, E.; González, R.; Quintana, J. B.; Cela, R. *Anal. Chim. Acta* **2005**, *537*, 259.

(177) Wittmann, G.; Van Langenhove, H.; Dewulf, J. *J. Chromatogr., A* **2000**, *874*, 225.
(178) Sarrión, M. N.; Santos, F. J.; Galceran, M. T. *J. Chromatogr., A* **1999**, *859*, 159.
(179) Zimmermann, T.; Ensinger, W. J.; Schmidt, T. C. *Anal. Chem.* **2004**, *76*, 1028.
(180) Pan, L.; Chong, J. M.; Pawliszyn, J. *J. Chromatogr., A* **1997**, *773*, 249.
(181) Cancho, B.; Ventura, F.; Galceran, M. T. *J. Chromatogr., A* **2002**, *943*, 1.
(182) Llompart, M.; Lourido, M.; Landín, P.; García-Jares, C.; Cela, R. *J. Chromatogr., A* **2002**, *963*, 137.
(183) Davis, W. C.; Vander, P. S. S.; Schantz, M. M.; Long, S. E.; Day, R. D.; Christopher, S. J. *J. Anal. At. Spectrom.* **2004**, *19*, 1546.
(184) Centineo, G.; González, E. B.; Sanz-Medel, A. *J. Chromatogr., A* **2004**, *1034*, 191.
(185) Stashenko, E. E.; Martinez, J. R. *Trends Anal. Chem.* **2004**, *23*, 553.
(186) Stalikas, C. D.; Fiamegos, Y. C. *Trends Anal. Chem.* **2008**, *27*, 533.
(187) Kumar, A.; Gaurav,; Malik, A. K.; Matysik, F.-M. *Bioanal. Rev.* **2009**, *1*, 35.
(188) Carrillo, J. D.; Tena, M. T. *Flavour Fragrance J.* **2006**, *21*, 626.
(189) Ventanas, S.; Ruiz, J. *Talanta* **2006**, *70*, 1017.
(190) De Jager, L. S.; Perfetti, G. A.; Diachenko, G. W. *J. Chromatogr., A* **2008**, *1192*, 36.
(191) Melo, L. P.; Queiroz, R. H. C.; Queiroz, M. E. C. *J. Chromatogr., B* **2011**, *879*, 2454.
(192) Koziel, J.; Jia, M.; Pawliszyn, J. *Anal. Chem.* **2000**, *72*, 5178.
(193) Chen, Y.; Koziel, J. A.; Pawliszyn, J. *Anal. Chem.* **2003**, *75*, 6485.
(194) Chen, Y.; Pawliszyn, J. *Anal. Chem.* **2006**, *78*, 5222.
(195) Zhang, Z.; Pawliszyn, J. *Anal. Chem.* **1995**, *67*, 34.
(196) Chia, K.-J.; Lee, T.-Y.; Huang, S.-D. *Anal. Chim. Acta* **2004**, *527*, 157.
(197) Carasek, E.; Pawliszyn, J. *J. Agric. Food Chem.* **2006**, *54*, 8688.
(198) Chen, Y.; Begnaud, F.; Chaintreau, A.; Pawliszyn, J. *J. Sep. Sci.* **2007**, *30*, 1037.
(199) Ghiasvand, A. R.; Hosseinzadeh, S.; Pawliszyn, J. *J. Chromatogr., A* **2006**, *1124*, 35.
(200) Carasek, E.; Cudjoe, E.; Pawliszyn, J. *J. Chromatogr., A* **2007**, *1138*, 10.
(201) Koziel, J. A.; Haddadi, S. H.; Koch, W.; Pawliszyn, J. *J. Sep. Sci.* **2009**, *32*, 1975.
(202) Eisert, R.; Pawliszyn, J. *Anal. Chem.* **1997**, *69*, 3140.
(203) Kataoka, H. *Anal. Bioanal. Chem.* **2002**, *373*, 31.
(204) Lord, H. L. *J. Chromatogr., A* **2007**, *1152*, 2.
(205) Zhang, Z.; Poerschmann, J.; Pawliszyn, J. *Anal. Commun.* **1996**, *33*, 219.
(206) Mullett, W. M.; Martin, P.; Pawliszyn, J. *Anal. Chem.* **2001**, *73*, 2383.
(207) Wu, J. C.; Lord, H. L.; Pawliszyn, J.; Kataoka, H. *J. Microcolumn Sep.* **2000**, *12*, 255.
(208) Wu, J.; Pawliszyn, J. *Anal. Chem.* **2001**, *73*, 55.
(209) Wu, J.; Mester, Z.; Pawliszyn, J. *Anal. Chim. Acta* **2000**, *424*, 211.
(210) Queiroz, M. E. C.; Oliveira, E. B.; Breton, F.; Pawliszyn, J. *J. Chromatogr., A* **2007**, *1174*, 72.
(211) Kataoka, H.; Pawliszyn, J. *Chromatographia* **1999**, *50*, 532.
(212) Saito, K.; Yagi, K.; Ishizaki, A.; Kataoka, H. *J. Pharm. Biomed. Anal.* **2010**, *52*, 727.
(213) Kataoka, H.; Narimatsu, S.; Lord, H. L.; Pawliszyn, J. *Anal. Chem.* **1999**, *71*, 4237.
(214) Kataoka, H.; Lord, H. L.; Yamamoto, S.; Narimatsu, S.; Pawliszyn, J. *J. Microcolumn Sep.* **2000**, *12*, 493.
(215) Tan, B. C. D.; Marriott, P. J.; Lee, H. K.; Morrison, P. D. *Analyst* **1999**, *124*, 651.
(216) Shintani, Y.; Zhou, X.; Furuno, M.; Minakuchi, H.; Nakanishi, K. *J. Chromatogr., A* **2003**, *985*, 351.
(217) Zheng, M. M.; Lin, B.; Feng, Y. Q. *J. Chromatogr., A* **2007**, *1164*, 48.
(218) Fan, Y.; Zhang, M.; Feng, Y.-Q. *J. Chromatogr., A* **2005**, *1099*, 84.
(219) Fan, Y.; Feng, Y.-Q.; Da, S.-L.; Gao, X.-P. *Analyst* **2004**, *129*, 1065.
(220) Fan, Y.; Feng, Y.-Q.; Da, S.-L.; Wang, Z. H. *Talanta* **2005**, *65*, 111.
(221) Bigham, S.; Medlar, J.; Kabir, A.; Shende, C.; Alli, A.; Malik, A. *Anal. Chem.* **2002**, *74*, 752.
(222) Gupta, M.; Pillai, A. K. K. V.; Jain, A.; Verma, K. K. *Anal. Chim. Acta* **2008**, *618*, 61.
(223) Gou, Y.; Eisert, R.; Pawliszyn, J. *J. Chromatogr., A* **2000**, *873*, 137.
(224) Saito, Y.; Kawazoe, M.; Hayashida, M.; Jinno, K. *Analyst* **2000**, *125*, 807.
(225) Saito, Y.; Nakao, Y.; Imaizumi, M.; Takeichi, T.; Kiso, Y.; Jinno, K. *Fresenius' J. Anal. Chem.* **2000**, *368*, 641.
(226) Zheng, F.; Hu, B. *Talanta* **2011**, *85*, 1166.
(227) Saito, Y.; Ueta, I.; Ogawa, M.; Abe, A.; Yogo, K.; Shirai, S.; Jinno, K. *Anal. Bioanal. Chem.* **2009**, *393*, 861.
(228) Basheer, Ch.; Lee, H. K. *J. Chromatogr., A* **2004**, *1047*, 189.
(229) Basheer, Ch.; Chong, H. G.; Hii, T. M.; Lee, H. K. *Anal. Chem.* **2007**, *79*, 6845.
(230) Jönsson, J. Å. *Chromatographia* **2003**, *57*, 317.
(231) Kloskowski, A.; Pilarczyk, M.; Namieśnik, J. *Anal. Chem.* **2009**, *81*, 7363.
(232) Souza Silva, É. A.; Pawliszyn, J. *Anal. Chem.* **2012**, *84*, 6933.
(233) Kohlert, C.; Abel, G.; Schmid, E.; Veit, M. *J. Chromatogr., B* **2002**, *767*, 11.
(234) Xie, W.; Mullett, W. M.; Miller-Stein, C. M.; Pawliszyn, J. *J. Chromatogr., B* **2009**, *877*, 415.
(235) Bianchi, F.; Dugheri, S.; Musci, M.; Bonacchi, A.; Salvadori, E.; Arcangeli, G.; Cupelli, V.; Lanciotti, M.; Masieri, L.; Serni, S.; Carini, M.; Careri, M.; Mangia, A. *Anal. Chim. Acta* **2011**, *707*, 197.
(236) Chen, Y.; Sidisky, L. M. *Anal. Chim. Acta* **2012**, *743*, 61.