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Recent progress, challenges and trends in trace determination of drug analysis using molecularly imprinted solid-phase microextraction technology

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ABSTRACT

The quantification of drugs in biological samples is a significant task for determination of the physiological efficiency in evaluated drugs in the drug discovery. To analysis of the chemical compounds at the trace and ultratrace levels, adequate analytical procedures should be applied. Therefore, sample preparation method undoubtedly is the most important stage in the trace determination process. In spite of the great growth of analytical instrumentation during the recent years, sample preparation is still nowadays considered the impasse of the all analytical procedure, especially in drugs analysis. Because of the low concentration level of drugs in blood, plasma, and the diversity of the metabolites, the chosen extraction technique should be almost perfect. Solid-phase microextraction (SPME) is a powerful, simple, fast and an equilibrium-based sample preparation method that permits integration of sampling, sample clean-up, and pre-concentration in a single solvent-free step for chemical analysis. Molecularly imprinted polymers (MIPs) that provided by the presence of a template during their synthesis are the stable polymers with molecular recognition abilities and excellent materials which provide selectivity to sample preparation. Because of its characteristics such as easy preparation, high selectivity, and chemical stability, MIP is widely utilized in many analytical fields. Accordingly, the molecular imprinting and SPME methods combination would prepare a strong analytical instrumentation which comprises simplicity, flexibility, and the selectivity characteristics of both methods. This review focuses on the application of solid-phase microextraction method coupled with molecularly imprinted polymers, namely molecularly imprinted solid-phase microextraction (MISPME), for trace determination in drug analysis.

1. Introduction

Nowadays, a high-resolution separation and low detection limits, in the picograms or below levels, can be accomplished by the analytical instrumentations. However, if an inappropriate sample preparation method has been used before the injection, the all of the advanced

Abbreviations: **AA**, Ascorbic Acid; **AAS**, Anabolic steroids; **ABA**, Abacavir; **BPA**, Bisphenol A; **CCD**, Central composite design; **CE**, Capillary electrophoresis; **CGA**, Chlorogenic acid; **CGC**, Capillary gas chromatography; **CMIP**, Conducting molecularly-imprinted polymer; **CNT**, Carbon nanotube; **CW-DVB**, Carbowax and polydivinylbenzene; **DA**, Dopamine; **DFC**, Diclofenac; **DMF**, Dimethylformamide; **DMSO**, Dimethyl sulfoxide; **DPASV**, Differential pulse anodic stripping voltammetry; **DPCSV**, Differential pulse cathodic stripping voltammetry; **DVB**, Divinylbenzene; **EE-SPME**, Electrochemical solid-phase micro extraction; **EGDMA**, Ethylene glycol dimethacrylate; **FA**, Folic acid; **FID**, Flame ionization detector; **FQ**, Fluoroquinolone antibiotic; **GC**, Gas chromatography; **GC-MS**, Gas chromatography-mass spectrometry; **HF-LPME**, Hollow fibers liquid phase microextraction; **HPLC**, High-performance liquid chromatography; **HPLC/FD**, High-performance liquid chromatography analysis with fluorescence detection; **HPLC/PAD**, High-performance liquid chromatography with photodiode-array detector; **HPLC/UV**, High performance liquid chromatography analysis with UV detection; **HPTLC**, High performance thin layer chromatography; **In-tube SPME**, In-tube solid-phase microextraction; **LC-MS**, Liquid chromatography-mass spectrometry; **LLE**, Liquid–liquid extraction; **LOD**, Limit of detection; **LOQ**, Limit of quantification; **LPME**, Liquid phase microextraction; **MAA**, Methacrylic acid; **MAMP**, Methamphetamine; **MEPS**, microextraction packed sorbent; **MIMSPE**, Molecularly-imprinted micro-solid-phase extraction; **MIP**, Molecularly-imprinted polymer; **MIPMME**, Molecularly imprinted polymer monolith microextraction; **MISPME**, Molecularly Imprinted Solid-Phase Microextraction; **MTMOS**, Methyltrime-thoxysilane; **MWCNTs**, Multi-walled carbon nanotubes; **OFL**, Ofloxacin; **OPPy**, Overoxidized polypyrrole; **PA**, Polyacrylate; **PAD**, Photodiode array detector; **PDMS**, Polydimethylsiloxane; **PDMS-DVB**, Polydimethylsiloxane and poly(divinylbenzene); **PEEK**, polyetheretherketone; **PMMA**, Polymethyl methacrylic acid; **ppb**, Parts per billion; **PPPY**, Poly-N-phenylpyrrole; **PPy**, Polypyrrole; **PVC**, Poly (vinylchloride); **RSM**, Response surface methodology; **SA**, Salicylate; **SBSE**, stir-bar sorptive extraction; **SEMs**, Scanning electron micrographs; **SLM**, Supported liquid membrane; **SMO**, Sulfamethoxazole; **SMT**, Sulfamethazine; **SPE**, Solid-phase extraction; **SPME**, Solid-phase microextraction; **SSF**, Stainless steel fiber; **TAOS**, Tetraalkoxysilane; **TAP**, Thiamphenicol; **TBZ**, Thiabendazole; **TCs**, Tetracyclines; **TRIM**, Trimethacrylate; **UV**, Ultraviolet-visible spectroscopy

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analytical processes can be impaired. So, sample preparation acts a crucially important role in the analytical procedures especially in drugs analysis which is the theme of our discussion. The sample preparation has many different roles such as the elimination of interferences and preconcentration of the analyte, converting the analytes to appropriate form for separation and detection. Because of the low concentration levels of drugs in plasma and the variety of the metabolites, the selected extraction technique should be virtually exhaustive [1].

Till now, several methods for the quantification of drugs in pharmaceutical preparations [2,3] and in biological samples [4,5] have been described utilizing HPLC with UV detection [6,7], fluorescence detection [8], liquid chromatography-mass spectrometry [9,10], HPTLC [11], spectrofluorometric [8] and densitometric methods [11]. In the complex matrices, a sample pretreatment process requires for determination of organic pollutants that presenting at trace levels. Solid-phase extraction (SPE) [12] and liquid-liquid extraction (LLE) [13] were often applied historically for the separation of analytes from aqueous matrices. However, some defects are coupled with LLE such as generally labor-intensive, time-consuming, and needs large quantities of expensive, toxic and environmentally unfriendly organic solvents which often combined with environmental and health risks. Also, SPE requires less solvent but still needs multiple steps and additionally, the enrichment performance of SPE is comparatively low. Accordingly, these methods cannot be used in low concentration levels of analytes and complex matrices [14,15]. Nowadays, novel sample-preparation procedures are likely to play a significant role in sample pretreatment of analytical chemistry which has many advantages compare to conventional methods such as removing of additional sample clean-up and concentration stages before chromatographic analysis, reduction in organic-solvent consumption and in sample degradation, and enhancement in extraction performance and selectivity. Usually, a favored sample pretreatment process includes three main purposes:

1. Sample matrix simplification;
2. Analyte enhancement or concentration; and,
3. Sample clean-up [16].

Therefore, because of using either no or very little amounts of toxic organic solvents, the simplification and miniaturization of sample preparation methods are recommended. In recent years, the solid phase microextraction (SPME) technique is one of the most favorite and applicable techniques for sample preparation in the green analytical chemistry. Since its introduction by Arthur and Pawliszyn in 1990 [17], many researchers worldwide has been utilized and performed this technique regarding its rapid development, basic understanding, development of instruments and novel applications. Hence SPME becomes widely used in many various fields such as environmental analysis [18,19], food analysis [20–22], bioanalysis [23–25], drug monitoring [26], pharmaceutical samples [27,28] and toxicology [29]. Also, SPME has been used in coupled with various instrumental analytical procedures, especially high-performance liquid chromatography (HPLC) and gas chromatography (GC) to determine trace levels of analytes from samples. This popularity of SPME can be due to its enormous advantages such as solvent-free nature, possibility of full automation, operation simplicity, relatively short extraction time, and easy coupling with chromatography (such as GC), all of which reduce contamination of the original sample and loss of analytes [16].

The SPME procedure is based on the partitioning of the analytes among the sample and the coating. The coating that uses in the SPME is fixed on the surface of a metal wire or a fused silica fiber. So, to obtain high extraction performance, an excellent material for coating acts a very important role. Until now, several SPME coating materials have been commercially used, including polydimethylsiloxane (PDMS), carboxen/PDMS, PDMS/divinylbenzene (DVB), polyacrylate (PA), carbowax/DVB and carbowax/templated resin [30]. In addition, several new laboratory techniques such as physical and vapor deposition technology, sol-gel technology, and electrochemical procedure, have been investigated to made applicable SPME fibers. In some applications of real sample analysis, these laboratory-made coated fibers have been successfully exerted which is because of their high extraction capacity and good analytical precision. However, with all of these mentioned advantages, the lack of selectivity of these laboratory-made coated fibers is the initial drawback associated during the extraction of target analytes. Due to their unsatisfactory selectivity, these traditional coatings usually cannot efficiently extract analytes in complex biological or environmental samples [15].

Based on recent studies, molecularly imprinted polymers (MIPs) have many prominent advantages such as stability, recognition ability, simplicity and low cost of preparation and also potential application to a wide range of target molecules. Due to their practical features, MIPs have possessed much consideration in the separation and extraction field of analytical chemistry. The selectivity of MIPs has been used in several applications, such as sensors [31,32], capillary electrochromatography [33,34], enantiomeric separations [35], SPE [36–38] and catalysis [39,40]. One of the most promising technical applications which is a very advanced methodology that solves the drawback of selectivity of the coatings [41,42] and is used many recently, has been molecularly imprinted solid-phase microextraction (MISPME). Thus far to our knowledge, the MISPME technology with all of these mentioned advantages has not been reviewed especially in the drugs analysis.

In this article, we review several configurations of MISPME techniques that were applied in drugs and pharmaceutical sample analysis, which can be improved the analysis process more sensitive, more selective, and more environment-friendly. These techniques include MIPs as SPME-fiber coatings (MIP-coated SPME fiber), MIPs and in-tube SPME (MIP in-tube SPME), monolithic MIP fiber for SPME (monolithic MIP-SPME fiber), sol-gel MIP and SPME (sol-gel MIP-SPME fiber), membrane MIPs and SPME and Other MIP-SPME techniques that used for drug analysis. These methods were accountable for extracting the most of the analytes from the sample matrix before the analysis based on the partition or adsorption of analytes. We are discussed on brief descriptions of advantages and capabilities of each modern extraction technique, and how these techniques could improve the absorption and extraction for a variety of analytes.

2. Molecularly-imprinted polymers

MIPs are the newly synthesized polymers that can be used for the selective extraction of selected molecules. These new synthetic polymeric materials, display high selectivity and binding capacity toward a target molecule that purposely participates in the synthesis process. They have high chemical, mechanical, and thermal stabilities. Because of these applicable advantages, MIPs are used for the separation or detection of many compounds in different applications in the analytical chemistry. They are also applied in catalysis and organic synthesis. However, MIPs have a great potential in the drug delivery, where they could be used as new and selective drug dosage forms [43]. Applications of the MIPs in sample preparation techniques are illustrated in Fig. 1.

2.1. Synthesis of MIPs

The primary polymerized materials in the production of a MIP included the functional monomer, the cross-linking agent, and the template molecule. Because of its task in the pendent of the functional groups to the functional monomers, the template molecule acts an important role in all molecular imprinting processes. So, the subsequent properties of the binding sites are dependent on the structure and functionalities of this molecule. The ability criteria of the template molecule to interact strongly with monomers was defined when candidate molecule features comprises its cost, availability, and the