Review Article

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Solid-phase nano extraction as a green approach for the analyte isolation

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Abstract

Today rapid and reliable analytical method for determining the trace level of targeted analytes in biological analysis and different fields is an essential object in analysis. So we try to focus on novel methods suggested for improving solid-phase microextraction based on novel drug delivery systems, especially nanoparticles. Nanoparticles like (dendrimer, carbon-based nanoparticles, magnetic and mesoporous nanoparticles, …) and their application as a new sorbent combined with different methods such as solid microextraction and liquid microextraction techniques are discussed in this article. These nano sorbents induced the potentials like selectivity and sensitivity for these methods. Furthermore, this nano extraction caused the lower consumption of hazardous solvent and reduced the total time needed for the extraction procedure, especially in biological analysis. The beneficial effects of nanoparticles indicated that a meaningful future was expected for their application. These new sorbents can be evolved the analytical methods and create reliable and rapid analytical methods.

Keywords: Microextraction, Nanoparticle, Nanosorbent, Nanoextraction, Biological Analysis

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1. Introduction

Today rapid and straightforward analysis methods for drugs in biological samples and the pharmaceutical dosage form are fundamental due to the necessity of these methods to determine the toxic effects of drugs (1). These methods are desired to understand drug levels in different biological matrices like urine, serum, forensic chemistry, clinical control, doping inspection, and optimize pharmacotherapy and pharmacokinetics (2).

The first step in bioanalysis is extracting specific analytics like drugs which is a highly complex and challenging task (3). Interfering compounds like proteins, salts, acids, bases, and other compounds in biological matrices such as blood, plasma, saliva, and urine makes the analysis process more difficult (4). Among the different steps of the analytical procedure, 80% of the total analytical time is spent on sample preparation, while 30% of errors are because of mistakes in sample preparation procedures (2, 5). Therefore, one of the essential steps in the analysis is the sample preparation technique, especially in conditions with minimal therapeutic drugs in a biological sample. Ideally, sample preparation techniques should be rapid, selective, easy, solvent-free, low-price, reproducible, and high recoveries without the possibility of analyte degradation (2). Furthermore, the sample preparation should also be compatible with a wide range of separation methods, susceptible to automated and operating separation and concentration of both hydrophilic and hydrophobic compounds from aqueous media at the same time (6).

The primary goal of the sample preparation process is to concentrate the targeted analytic by eliminating the interfering substances (like

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proteins, salts, and lipids) (3). Today Different approaches are available to reduce the matrix effects, such as liquid-liquid extraction (LLE), solid-phase extraction (SPE), and protein precipitation (PPT) which are the three most commonly used sample preparation techniques (7). SPE and LLE are the most applicable sample preparation technique for LC-MS (8-10). LLE and SPE are traditionally used for non-volatile analytics. Conventional LLE and SPE methods have various limitations, including time-consuming procedures, hardly automation, the need for a large amount of solvent, and sample consumption. Therefore, a part of the low amount of samples may become wasted because of the multi-step procedures (2). Moreover, the large amount of harmful solvent increased the total cost of procedure development and waste disposal, which is considered a fundamental problem for environmental pollution and human health (11). Recently, there has been growing interest in reducing analysis time, sample volume, cost, and solvent removal. Also, increasing automation is encouraged to reduce the workload (9).

2. Microextraction

The extraction progress has been driven by developing various extraction methods using a minimal amount of samples. These miniaturized versions of extraction methods are called microextraction techniques (12). Different researchers have developed microextraction techniques by various approaches (13). Was performed in small sample volumes related to the sample volume (14). Therefore, only a small amount of the samples could be extracted. The extraction efficiency is related to the affinity of the targeted analyte to the extraction phase. When the analyte remains predominantly in the extraction phase, a more significant analyte amount has been extracted.

The partitioning of the analyte to the extraction phase can be controlled by modifying the physicochemical properties of the extraction phase, analytic, and sample matrix (14). Also, the microextraction techniques should have spent a shorter time for sample preparation and lower cost than the conventional extraction techniques, thus reducing errors (15). So, methods like solid-phase microextraction (SPME), liquid-phase microextraction (LPME), and the use of restricted access materials (RAM) are popular extraction methods for the analysis of therapeutic drugs (9).

2.1. SPME classification

SPME is an efficient and solvent-free sampling preparation technique first established by Pawliszyn (16). In this article, fused-silica fibers are externally used and coated with an appropriate extraction phase. This technique is done in two types: static in-vessel and dynamic in-flow, using capillary tubes and fibers coated with an appropriate stationary phase. This extraction procedure includes two phases-partitioning analytics between the samples and the extraction phase. Then desorbs and detection with analytical instruments. All processes in this method can be performed in the same step. Compared to other analytical techniques, SPME provides clean and low-cost procedure conditions. Concentrating the extracts is an ideal method for a trace amount of materials in the body, like doping and toxicity (6).

The analytical sample is directly extracted to the outer fiber coating by absorption or desorption in fiber. In this method, polymer coating concentrated the targeted analytics by absorption and desorption processes. The extracted analytics is introduced to the GC injection port or transferred to the chromatogram instrument like HPLC. Then the needle was inserted into the injector, and the fiber was exposed. The analytics with the mobile phase were eventually eluted with analytical methods detected (17). The fiber SPME is combined with GC or GC-MS to detect semi-volatile and volatile compounds. Polydimethylsiloxane (PDMS) is a commercially available fiber for non-polar analytics. Polydimethylsiloxane (PDMS), while polyacrylate (PA), is a polar coating ideal for phenols extraction (18).

Stir bar desorption was a static method developed by Baltussen et al. The coated stir bar can be contacted with samples by direct immersion or headspace sampling (19). The commercially available stir bar is the Twister stir bar coated with a PMDS stir bar. Compared to the other microextraction techniques, this method is widely used for polar and semi-polar analytics in liquid samples. It is suitable for extracting volatile and semi-volatile

compounds from a small volume of liquid samples and has good selectivity for volatile compounds with different polarities. The limitation of this method include manual handling, the absence of chemical binding caused bleeding, high viscosity, and coating polymers' thickness increased the equilibrium time needed. The lack of commercially available coating caused limited development compared to the fiber SPME technique. It could be optimized by controlling the parameters like the dimension of the stir bar, stirring rate, and temperature. The washing step is a critical point in this method (13, 18, 20).

One of the newest types of stir bar is based on Sol-Gel Technology developed by Liu et al. for the first time (SOL-Gel Technology in Stir-Bar Sorptive Extraction), which is used for extraction of organophosphorus materials with good selectivity and efficient stability (21).

Another type of stir bar is Molecular Imprinted Stir Bar Sorptive Extraction (MISBSE), based on the partitioning of analytes between the stationary phase and the liquid sample. However, up to now, only the stir bar, which is coated with PDMS, is commercially available and has high selectivity and rapid equilibrium time (22)

Headspace SPME (HD-SPME) exposed to the vapor phase from the headspace above the samples was suitable for extracting volatile and semi-volatile analytics. These extracted analytes are thermally desorbed by directly transferring them to GC. Non-volatile analytes in liquid samples are extracted by Direct immersion SPME (DI SPME). The DI and HS-SPME can be combined with GC, GC-MS, HPLC-MS, and HPLC (23). Each targeted compound should optimize parameters like temperature, pH, salt concentration, polarity, and stationary phase thickness. The thickness of fiber could be affected the total time needed for extraction. Thus, stirring methods like ultrasound and agitation can decrease the extraction time. The selectivity of the extraction is affected by the type of fiber, like thick fiber used for volatile but thin fiber used for semi-volatile analytes. Non-polar and polar fiber are used, for non-polar and polar compounds (6, 24). The irreversible absorption of materials in fiber SPME can be limited by HS-SPME, while in DI-SPME, direct contact with compounds causes irreversible absorption and influences the selectivity and sensitivity of the extraction. Because of this drawback, a hollow fiber membrane is used (23). Recently, the newly biocompatible fiber SPME directly coupled with mass spectrometry was designed to analyze biological fluids. The thin-film microextraction was developed with high sensitivity, and a rapid extraction rate by the higher surface-to-volume ratio can be increased the mass uptake. There is some limitation like instability and breaking of the coating polymer. The low temperature in operating conditions with the sol-gel method could overcome these limitations (25, 26).

Solid-phase dynamic extraction (SPDE) is in needle solid-phase extraction in that the extraction device is needles coated with a polymer. The extracted analytes were concentrated on the inner surface of the needle and then introduced to GC or GC-MS for analysis. All procedure can be operated in dynamic condition, and compared to fiber, SPME has a higher volume and need a shorter time for extraction. In comparison, the desorbed compound by heating might be retained in the inner surface of the needle (27).

The tube extraction was first developed for HPLC coupling, and now, a day can be used for online coupling with LC-MS and HPLC. Capillary columns are used as an extraction device (open tubular capillary is popular). Compounds in liquid matrices are extracted directly by the internal coating of the capillary or the outer coated surface of the packed fibers. Sorbents by streaming of mobile phase in the inner surface of the capillary or for highly adsorbed materials on the capillary surface with static desorption of solvent desorbed. They are then injected into the LC instrument for detection. This method generally has two types for extraction; the first is the thorough flow type, which is applied in one direction and controlled manually or automatically. With the draw/eject cycle, the second type is controlled only automatically. Compared to the draw/eject type, the first type has a better extraction efficiency in a shorter time (28). The basic concept of the in-tube and fiber method is the same. Specific differences like the extraction of analytes are performed on the inner surface of the in-tube columns. Although on the outer surface

of the fiber is performed. In the tube, the method can be plugged; therefore, filtration of the samples before the extraction is necessary. In the filter method, this is not necessary. Fiber may be fragile, and coating polymer in the extraction and agitation processes breaks beside the macromolecules like proteins could be absorbed on the surface of the fiber and changed the extraction efficiency (6). This method does not have fiber limitations, such as low absorption capacity and fragility, but has higher mechanical stability. The retaining of hydrophobic and hydrophilic materials is selectively performed, respectively, with low polarity and high polarity columns. This method was suitable for analyzing thermo-labile and polar materials and with miniaturization performed by low solvent consumption. The online coupling with HPLC or LC-MS and their automation process from extraction, desorption, and injection could be done with the same auto-sampler. The main advantage of this technique compared to the manual technique is automation. This technique could eliminate the total time of extraction and increase the accuracy and precision of the extraction processes (28). The main disadvantage of this method was a tendency of the capillary to clog, and with the samples, not interfering could be avoided (25, 29).

New capillary tubes (such as fiber-packed, sorbent packed, rod type) and sorbent monoliths (such as silica monoliths and different monoliths based on various monomers and cross liking mixture of them) have been developed to increase the extraction specificity and efficiency by increasing the surface of extraction media and decreasing the volume of the capillary (28). Restricted access material (RAM) was developed for biological fluid direct injections to the lab-made biocompatible capillary of in-tube SPME and simultaneous extraction of macromolecules and pre-concentrated drugs from biological matrices (30).

Microextraction with packed sorbent (MEPS) or packed syringe is a novel method for sample preparation and, compared to conventional solid-phase extraction, eliminates the volume of solvent consumption. The same syringe can be used many times for biological samples. Because of its easy operation, a reduced sample volume was needed, solvent consumption was very rapid and had a high recovery rate. All extraction procedures can be online automated. Furthermore, compared to the conventional methods, the cost of the procedure is limited, and the recovery rate is high (13, 31).

In tip SPME with 96 blades as a new method developed in the same type, several samples were extracted, sample preparation was automated—all plates with shaker agitated. Then with a proper solution, easily cleaned and unwanted materials are removed. Polymer and silica-based coating for their large porously structure were used as a sorbent for the extraction of both hydrophilic and hydrophobic metabolites from a biological matrix (32)

2.2. Liquid phase micro extraction classification

The necessary step in the analysis of the targeted compounds is sample preparation. Liquid-liquid chromatography (LLE) is a conventional separation method based on different solubility of targeted compounds between aqueous and organic solvents. The presence of different drawbacks in this method like large consumption of hazardous pure organic solvent and large sample volume needed, the tedious and expensive procedure caused an urgent need for new miniaturized extraction method for extraction of trace amount of analytes like liquid-liquid microextraction method (LLME) (33) . Less solvent, rapid and straightforward operation and easy handling device, automated method coupled with the different analytical instrument could be applied to extract trace material in different fields (34) . By controlling the critical parameters such as temperature, sample volume and concentration, pH, the time needed for exposure, and extraction time, the choice of appropriate solvent and volume of solvent can be optimized for this method. Generally, this method is classified into two types. The first is membrane-assisted liquid microextraction, and the second is single-drop microextraction (35). Each of them has a different subtype. The first subtype includes two-phase (include direct immersion (DI), continuous flow (CF), drop to drop (DD), and directly suspended droplet (DSD) LME) and three-phase microextraction that includes headspace and liquid-liquid LME, and two-phase. The

single-drop microextraction includes hollow fiber, membrane bag, and flat sheet membrane microextraction method. Another type is the dispersive liquid-liquid microextraction (DLLM) method (36).

2.2.1. Single drop micro-extraction (SDME)

This method is the earliest LLME method in which the extraction media is the single drop. Performed with the microsyringe and water-immiscible organic solvent. Directly suspended to the surface of the aqueous sample by the tip of the needle, known as direct immersion(DI) mode. The organic solvent should be water insoluble and cannot be used as polar solvent for extraction of polar or semi-polar analytes (37).

2.2.2. Drop to drop(DD) microextraction method

In this method, the droplet of the organic solvent was immersed in the larger stirred aqueous phase by the Teflon rode, and after a certain period, the Teflon rode was removed. Then extracted phase with a microneedle is injected into an analytical instrument (38). The organic solvent was passed through the microsyringe, and the needle was immersed in the sample solution. Subsequently, the droplet of the solvent was suspended in the tip of a needle in the stirred liquid samples. The extracted organic solvent, after the extraction, is sent back to the microsyringe and directly injected into the GC (39). In the dynamic method, repeated movement of the microsyringe plunger increased the agitation in both solvents and improved the mass transfer. The microsyringe has both the solvent holder and GC injector roles in the static and dynamic method. SDME with automation has higher validity, better control of time consumption, and increased extraction efficiency (40).

2.2.3. Headspace(HD) SDME

In this method, the microdroplet of organic solvent is suspended at the tip of the needle of a micro syringe and subsequently exposed above the aqueous sample and pre-concentrated analytes droplets. Returned to the micro-needle and directly injected into the suitable analytical instrument (38). This method is widely used for the extraction of volatile and semi-volatile analytes. Easily coupled with an analytical instrument like GC or GC-MS, the targeted analytes distributed among the three-phase include the organic solvent, aqueous sample, and head space (39). This method could have limited the interfering effect of a non-volatile matrix. Compared to the HD-SPME, the choice of solvent is widely selected, and the price of organic solvents compared to the fibers is very low (41). The dynamic mode was developed to improve the extraction efficiency and then completely automated to increase the procedure's validity. Furthermore, all steps can be operated in the same step in a shorter time and increasing the efficiency and lower solvent consumption (42).

2.2.4. Continues flow(CF) SDME

In this method, employing an HPLC pump, the aqueous samples continuously flow into the extraction chamber with a steady-state flow rate. The extraction of solvent droplets using the microsyringe was injected into the chamber and kept at the outlet of the connecting tube, then continuously immersed in the sample solution. Aqueous samples were continuously pumped around the droplet and simultaneously extracted. Microneedle was used to collect the extracted and analyze. Because of the droplets' control with HPLC valves, the droplets have good stability and continuously interact with freshly aqueous samples, which increases the extraction efficiency (43).

2.2.5. Directly suspended droplet(DSD) LME

In this method, placing the stir bar at the bottom of the aqueous sample vial employing rotating in an efficient condition caused the formation of a microdroplet of the organic solvent at the surface of a sample. These droplets are manually moved by microneedle to the analytical instrument. The difficulty of pure extraction in the manual transfer is controlled with the organic solvent at a low-temperature point. After stirring, the floating organic solvent was transferred to an ice bath. The solidified microdroplets were melted and used for analytical analysis (44, 45).

2.2.6. membrane assisted liquid phase microextraction

This method could extract analytes utilizing the membrane as a supported function. Include

the porous membrane (hollow fiber, flat sheet of porous membrane) or non-porous membrane. The organic phase is placed on the surface of the porous membrane and fills the pores with the solvent, causing the thin layer of the solvent on the membrane-like in HF, and could diffuse the targeted analytes from the donor phase (aqueous sample) to the acceptor. The HFLME includes two subtypes, two-phase and three-phase microextraction. The organic solvent must have a low volatility point, compatible with the membrane, immiscible with the aqueous sample, and easily dissolve and extract the analytes (46). Firmly placed in the membrane's pores and immobilized in the extraction procedures. Passive diffusion causes mass transfer. This method could be extracted polar and ionized analytes but is limited to the acidic and basic extraction, which could be ionized (46, 47).

2.2.7. Dispersive liquid-liquid microextraction(DLLM)

Extraction in this method is based on dispersion. At first, the extraction and disperser solvents are injected into the aqueous sample. Subsequently, after dispersion preformation, centrifugation, the sedimentary phase containing extracting solvent, and targeted analysis are collected and analyzed with a suitable analytical instrument. Because of the simplicity, lower consumption of organic solvent, and rapid operation, this method is prevalent. Controlling the critical parameters like the selection of appropriate extracting and disperser solvent and volume of them can optimize this method and increase the extraction efficiency (48).

3. Solid-phase Nano extraction (SPNE)

Nanoparticles, for their small size(1-100nm) and larger surface area compared to the volume, are interesting devices in drug delivery and other applications. These excellent tiny materials are not simple. Have three different layers, the outer one can be functionalized with different molecules, and the second one or the shell is chemically different from the core materials. Nowadays, nanomaterials, with their large surface area and significant affinity to trace levels of materials, are a good candidate as a sorbent for trace levels of materials. In addition, their small size, surface property, and high affinity to trace levels of target materials caused high extraction capacity and increased the selectivity and sensitivity of analytical methods. Nowadays, different analytical methods through diverse nanoparticles like polymeric, carbon base, and magnetic nanoparticles are applied in different fields to extract and identify trace levels of targeted materials (49).

3.1. Carbon nanotube

Carbon-based nanoparticles like graphene and carbon nanotubes include single wall CNT, composed of a single layer of graphene in a cylindrical tube with a small diameter. Multi-wall CNT is composed of a multi-sheet of graphene with a larger diameter. Due to their specific and attractive properties like good chemical and mechanical strength, thermal and electrical conductivity, and high surface area, optical properties have specific roles in different fields like drug delivery, agriculture, biosensor, and chemical analysis methods. Because of the high extraction capacity, porosity, and heterogeneity in structure, CNT is utilized in SPE and SPME and increases the extraction methods' efficiency, selectivity, and recovery. The designing of fiber coating with MWCNT and SWCNT demonstrated increased extraction efficiency, precision, and accuracy. Compared to the commercially available fiber increased the recovery efficiency (50). These days with different methods like physical agglutinating technique, electrophoretic deposition method, and sol-gel technology as a new type of SPME fiber based on SWCNT coating was designed. The electrophoretic deposition method applying the electric field induced the charged nanoparticle's deposition and caused the film's production with variable thickness. Controlling the voltage and the electrophoretic deposition time can easily control the film thickness with efficient reproducibility of the coating as well as with the unique structure of CNTs and production of wander Waals bond between the surface of the CNT has the high chemical and thermal stability. In addition to the methods for SWCNTs, methods like chemical bonding and electrochemical polymerization were developed for MWCNT-based coating fibers. However, the coating fibers with sol-gel technology do not have durable stability and re-

producibility because of these drawbacks. Chemical and electrochemical methods could overcome these limitations (51).

Nanoparticles like carbon nanotube, graphene, and nano horn can be combined with monolith compounds to produce a new type of sorbents or stationary phase to increase specific interaction with targeted analytes. Due to large porosity, the single wall carbon nano horn has a cone shape, and high specific surface area was an excellent sorbent with high extraction capacity. They were widely used in microextraction methods. Recently a hybrid monolith with the monomers of methacrylate with oxidized single wall carbon nano horns was used in the spin column by photopolymerization. This new hybrid spin column was evaluated for the pre-concentration of the NSAID drugs in the urine samples. The results indicated that excellent recovery, high extraction capacity, and wide range linearity of the extraction procedure associated with the specific properties from the nano horns like porosity and large surface area and good chemical stability in the wide range of the pH caused this new hybrid column can be widely applied in biological analysis (52). The silica monoliths and CNT combination with the sol-gel method were designed as a new hybrid sorbent for extracting and detecting the non-polar materials from the water and compared with the silica monoliths lonely.

The result indicated that the hybrid type with the outstanding properties of the mesoporous silica structure and CNT-like P interaction and large specific surface area, good stability increased the extraction efficiency and selectivity of the targeted compound (53). Comparatively, one study used MWCNT and C-18 silica as a sorbent in solid phase extraction. The results indicated that MWCNT consumed a significantly lower amount of organic solvent and, at the same time, had a higher recovery and showed a 3-fold lower limit of detection of targeted analytes. The dispersive solid-phase microextraction modified with MWCNT is effective, cheap, easy, quick operation, and safe. Recently reported that MWCNT is a suitable sorbent for DSPME. It can be utilized for the extraction of different trace levels of analytes. In the magnetic molecularly imprinted dispersive solid phase extraction utilized magnetic carbon nanotube as solid sorbents for the gatifloxacin detection in a biological matrix, and detection with HPLC indicated that this method was rapid, with high extraction efficiency. By the utilized the external magnetic fields, their separation was straightforward (54). The hybrid monolithic with the multiwall carbon nanotube and methacrylate monolith was produced with the UV grafting on the inner surface of the polypropylene pipette tips for the microextraction of the antidepressant drugs in the urine samples. The results indicated that the new hybrid stationary phase with covalent interaction improved the extraction efficiency their stability during the extraction. CNT reduced the interfering compounds in the complex samples and increased the selectivity and sensitivity of the antidepressants in the extraction procedure (55).

3.2. Silica nanoparticles

Mesoporous silica Nanoparticles are a kind of inorganic nanomaterials with specific properties like less toxic, hydrophilic surface, biocompatibility, and have a large surface area with mesoporous and chemically functionalized structure and high adsorption capacity. Widely used in drug delivery, DNA conjugation and different functionalization on the inner and outer surface can be performed as a medical probe. Because of its higher surface area and smaller size, nanofiber mesoporous silica can be applied for the encapsulation of drugs, enzymes, and other materials (56, 57). These nanoparticles have different forms like the sheet, sphere or wire, with a large specific surface area and mesoporous structure are excellent sorbent. It can be modified with different compounds like amine, saline, or coated with polymers or by magnetization can increase the extraction efficiency and specificity, and stability during the extraction. In the extraction procedure with SINPs with simple optical or electrochemical methods like enzymatic or antibody-based methods can be detected the targeted analytes (58). A silica nanoparticle that functionalized with amine groups in solid phase extraction in plasma and aqueous sample was evaluated for the extraction of 5 fluorouracil and detection with HPLC. The result indicated that silica nanoparticles that are functionalized with aminopropyl with excellent extraction recovery

for different concentrations of drug in these media could be applied as a promising sorbent for bioanalysis studies (59). In recent years the use of magnetic nanoparticles with microextraction methods as the sorbents, as well as their large surface area and large extraction capacity with the external magnetic field, increased the interaction and improved the extraction efficiency compared to conventional methods. The recent study by the use of superparamagnetic porous silica nanoparticle in the capillary column for the extraction of the triazines from the water samples and detection with liquid chromatography instrument demonstrated that the functionalization of a capillary column with the magnetic porous silica nanoparticles and applied external magnetic field increased the extraction of analytes from 3% in conventional method to 60% in this new method (60). In recent years the use of magnetic nanoparticles with m Magnetic porous silica nanoparticle with large pore size and well-defined structure was evaluated as a stationary phase for extraction of anti-diabetic drugs in plasma samples (61). In another study, coating the magnetic silica nanoparticle (Fe2O3-SNPs) with gold nanoparticles increased the extraction efficiency, which was the new effective sorbent in the magnetic solid phase extraction and coupled with the dispersive liquid-liquid microextraction increased the extraction of the targeted analytes from the water sample (62). Amine functionalized silica nanoparticle was utilized as the new stationery phase for the extraction and separation of the calcium ions from the blood and urine samples in the in vitro study. After the bath sonication and centrifugation, the Ca ions concentration with the flame ionized method was detected. The result indicated that this method could be applied for in vivo studies for decreased and control the concentration of calcium in the body of patients with hypercalcemia (63). Chemically modification of the silica nanoparticles with the octadecyl deposited in capillary as a stationary phase are used for IT-SPME. The new microextraction media's extraction performance was evaluated using the non-polar, moderately polar, and hydrophobic compounds as an analytes model and detected with HPLC. The results like LOD, reproduction ability, stability during the procedure, and repeatability indicated that this new nano-sized extraction media has the best performance for different compounds (64). Some applications of different nanoparticles in extraction procedure were inserted in Table 1.

3.3. Polymeric Nano particles as a solid sorbent

The essential part of the solid phase extraction, which has a crucial role in the extraction efficacy and the capacity of the extraction, is the sorbent phase, and materials participate in the sorbent formation. Because of the necessity of this, the growing urgent for designing new packed sorbent for increased extraction capacity, selectivity, and efficacy is developed. Different polymeric compounds are designed, developed, applied for extraction analysis, and evaluated in different analytical studies. Organic and inorganic polymers have inner and outer surface areas. A reactive repeatable end group can be a promising sorbent with high extraction capacity. Polymers can be developed as a new mode of polymers with improved performance in extraction procedures and effectively used in the extraction of trace levels of analytes in complex sample matrices (65).

Dendrimer was a high-branched macromolecule with tree shaped and homogenous structure. Nanosized with a large amount of repetitive functional end groups and high surface area increased the application of the dendrimer in different fields like drug delivery systems and diagnostic and chemical analysis (66). The high surface area, hydrogen binding, and the P and hydrophobic interaction with the targeted compounds increased the extraction capacity and selectivity. This method could overcome the limitation shown in the polymers with linear structures like fragility, low extraction capacity, and decomposition during the processes, and developed an efficient sorbent for extraction (67). Hybridization of the polythiophene with the dendrimer caused a new type of sorbent in the HS-SPME with the excellent extraction of the triazole compounds from the water. Compared to the commercial type, this new type of fiber coating has a high extraction capacity, excellent thermal stability, and an increased extraction rate with remarkable selectivity (68). Combination of magnetic nanoparticles with dendrimers developed a new type of magnetic sorbent, increasing the ex-

traction efficiency. In recent study indicated that functionalized magnetic Fe3O4 nanoparticle with PAMAM dendrimer as a magnetic solid sorbent in the MSPME increased the extraction of the trace level of NSAIDs in the water samples (69). Another new type of magnetic sorbent with PAMAM dendrimer was decorated to extract the trace level of the toxic phenolic compounds like Tetrabromobisphenol A in the water samples. PAMAM dendrimer was synthesized with Michael addition and amidation with ethylene diamine (70).

Chitosan is a biodegradable, biocompatible copolymer and linear polysaccharide with a polycationic surface charged, obtained with deacetylation of chitin, especially from crustacean shells in alkaline conditions. Its outstanding characteristics like biocompatibility, biodegradability, less toxicity, cationic surface charge, and the ability for hydrogen binding caused enormous application in drug delivery systems, tissue engineering, and analytical studies (71). The chitosan derivative is functionalized with different amine and S groups and changes the affinity and selectivity toward specific metallic ions to detect trace levels of metallic ions. Recovery of cationic metals because of the insolubility of chitosan in alkaline and neutral media was easily accrued. While because of the complete solution in acidic media, application of cross-linked type and combination with carbonic and inorganic materials for extraction of metals anions are extensively used (72). The chitosan base film with a combination of chitosan and silver nanoparticles is designed. This nanofilm is efficiently designed to extract metal compounds like CD, Fe, and Zn trace levels. The results indicated excellent recovery for different trace-level metals with favorable selectivity. Predicted that this nanofilm, with good selectivity and stability, could be developed as a noble sorbent to extract metallic-based pollutants from water (73). Chitosan was grafted with anyline, and a new sorbent in DSPME was designed to extract phetalat ester in milk and detected with HPLC. The favorable efficiency of this new sorbent was indicated with LOD and LOQ and linearity range for detected analytes (74).

Mixed types of polymeric materials with cationic, anionic, or hydrophobic interaction increased extraction efficacy and selectivity. Different molecular imprinted polymers were designed as solid sorbent in solid phase extraction. The essential step in this method was the optimization and providing the appropriate polymerization methods and conditions and purified final molecules for extraction. These molecules have properties like thermal and chemical stability and mechanical and chemical strength and can be applied in offline and online techniques and combined with different analytical methods like HPLC (75). In the pre-polymerization stage, the polar and covalent interactions with template molecules and monomers caused the semi-covalent and non-covalent imprinting molecules. In the second type, the characteristics like rebinding, fast removal, and easy release of template molecules were preferred. Molecular imprinting polymers are obtained using precipitation and bulk polymerization methods. The molecules obtained from the precipitation have a spherical shape with monodispersed size from sub-micron to nanometer (1). After removing the template molecules, the final new type of polymers with a well-defined structure with monodispersed size and different active sites on the surface are constituted. Because of the selective interaction with the analytes and the easy synthesis with low cost and high stability in different conditions, these polymers were favorable compared to other polymers and conventional sorbents (76). In one study, molecular imprinting polymers as a stationary phase in the solid phase extraction to determine the level of the fluoroquinolone drugs in the milk was used. Three types of fluoroquinolone as template molecules are used in these molecules. After removing template molecules by positioning some monomers with the specific functional group around them with a cross-linking agent, produced a new type of polymer with a specific cavity and high surface area. These molecules can be reused for the specific extraction and the purification of the specific molecules with a similar structure to the template molecules (77).

In recent years use of nanoparticles as sorbent was developed like magnetic nanoparticles. Fe2O3 with applied external magnetic field increased the extraction purity and specificity, as well as the incorporation of core magnetic materi-

als with molecularly imprinted polymers shell with stable and homogeneity structure developed as a new type of sorbents, increased the selectivity of bioanalysis with a trace level of analytes (78, 79). The framework of polymeric materials with metal as an alternative sorbent in extraction is used. Polymers increase the extraction capacity and sufficient permeability by having a porous structure to increase the extraction flow rate. Consequently, reduced the organic solvent consumption and limited the procedure times. These modifications increased the extraction capacity and selectivity in the pore size and surface. In a bioanalysis study, amino and cysteine modified polymers functional-

Table 1. Some application of different nanoparticles in different microextraction methods.

Nanoparticles type	Detection technique	Extraction method	Medium and analytes	Result	Ref.
CNT	HPLC	Peptide tip SPME	Extraction of flavonoid and alkaloid from Biologic sample	Result of recovery(90.05-99.85%), LOQ was 1.02 µg/ml and good range for linearity(3-300 µg/ml) are shown.	(82)
Functionalized mesoporous silica with the CNT	HPLC	IT-SPME	Extraction of poly cyclic aromatic hydrocarbon in water	LOQ was 0.005-0.05 µg/ml, linearity range(0.016- 20 µg/ml, and correlation coefficient form 0.9921 to 0.9999 is obtained.	(83)
Magnetic nanoparticle functionalized with coating by dendrimer containing ethylene diamine and methyl methacrylate	HPLC	Magnetic-SPME	Extraction of resuvastatine in urine and blood and tablet samples	The efficiency of extraction in plasma with 54.5%, 86.6% in drug samples and 94.3% in urine was shown.	(84)
A magnetic functionalized PAMAM dendrimer	GC-MS	HS-SPME	Extraction of chlorophenol from eques samples	Linearity range from2 to 1000ng/ml, LOD 0.6-10 ng/ml and the recovery from 80 to 97% was obtained.	(85)
Dendrimer grafted with the silica mesoporous fiber	GC	HS-SPME	Extraction of solvent include hexane, toluene and benzene residue from the edible vegetable oil	LOD for three solvents was 0.9 to 1.2 mg/kg, linearity range was 6 to 300 mg/kg for hexane and 8 to 250 mg/kg for toluene and benzene detection.	(86)
Inorganic magnetic core functionalized with PAMAM dendrimer and β cyclodextrine then coated with ion liquid	HPLC	Dispersive-magnetic-SPME	Extraction of pyrethroids residue like phenothrin, bifentrin and permethrin in the juice samples	The linearity range from 3.5 to 500 µg/ml, LOD 0.36 to 1.3 µG/L and LOQ 1.2 to 4.3 µg/ml was shown.	(87)
PAMAM dendrimer inclusioned with silica with the sol-gel	HPLC	HF-SPME	Extraction and detection of citalopram from waste water samples in the hospital	Linearity range from 0.05 to 100 µg/ml, LOD 0.0095 and LOQ 0.031 was obtained.	(88)
Chitosan and copper oxide and zinc oxide nanoparticles with sol-gel method	HPLC	SPME	Extraction and clean up pesticides from the water samples	The results indicated that these cartridges compare to the standard type have a higher extraction efficiency but chitosan combined with ZO stronger than the combination of chitosan with Cuo performed in the pesticides extraction.	(89)
Magnetic hydrophobic Nano particles	GC-MS	M-SPME	The determination of paraben like methyl, ethyl and propyl paraben in waste water from sea and swimming samples.	The results indicated the best linearity range with LOD and LOQ in the ng/l range for different paraben samples.	(90)
Fe_3O_4 coated with polyaniline as an anionic exchange solid sorbent	HPLC	M-SPME	The extraction of parabens from different samples include toothpaste, sea water and cream samples.	The linear range from 0.5 to 100 µg/l, LOD from 0.3 to 0.4 µg/l was obtained. The lower extraction and desorption time indicated the efficiency and repeatability of this method.	(91)

ized with Ag and Au nanoparticles as a new stationery phase for albumin extraction are used. The result indicated that these materials with the thiol group have high recovery and loading capacity was an excellent stationery phase in protein extraction and isolation (80).

Sometimes instead of using the template molecule, the ions are used, and the ion imprinting molecules accrued the interaction between the ions and monomers. These molecules are suited for extracting water-soluble ions and selective extraction of trace levels of metal ions. This new type of sorbent with high selectivity for the trace level of the ionic analytes are used. Because of the selectivity, reusability, stability, low-cost preparation method, and large surface area have gained the great interest for ion extraction (63, 79). Bulk polymerization is widely used for these molecules' production, but the precipitation and suspension polymerization methods were the best alternatives for size control (80). After the polymerization processes, the template molecules were removed, and the cavity with a particular active binding site and appropriate size for selective extraction of targeted analytes was designed (81).

4. Conclusion

In this review, we summarized development accrued in analytical methods from extraction methods to SPME and LPME, which used less water and time than traditional methods. This new extraction method could have detected the trace level of materials in a complex matrix. We were emerging the application of different nanoparticles in analytical methods and designed a diverse new type of sorbents. Nanoparticles with specific features like large surface area, specific functional groups, and different physical and chemical binding sites increased the extraction sensitivity and selectivity. These new sorbents reduced the total volume of samples needed and reduced the extraction time. These materials could be increased the extraction feasibility for trace level materials. This method needs further progress to synthesize nano-based sorbents with the same size, morphology, and surface property besides stability during the extraction procedure. Increased reproducibility and repeatability for production on a large scale could be coupled with different detection instruments. According to the beneficial effects of nanoparticles in extraction procedures, an unknown future was predicted for nanoparticles in the extraction methods. The different studies from different fields are designed for the application of nanoparticles as a new type of sorbents, indicating that nanoparticles have an enormous potential for application in this field.

Conflict of Interest

None declared.

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