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Molecularly imprinted sol-gel nanofibers based solid phase microextraction coupled on-line with high performance liquid chromatography for selective determination of acesulfame

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ABSTRACT

Sol-gel based molecularly imprinted polymer (MIP) nanofiber was successfully fabricated by electrospinning technique on the surface of a stainless steel bar. The manufactured tool was applied for on-line selective solid phase microextraction (SPME) and determination of acesulfame (ACF) as an artificial sweetener with high performance liquid chromatography (HPLC). The selective ability of method for the extraction of ACF was investigated in the presence of some selected sweeteners such as saccharine (SCH), aspartame (ASP) and caffeine (CAF). Electrospinning of MIP sol-gel solution on the stainless steel bar provided an unbreakable sorbent with high thermal, mechanical, and chemical stability. Moreover, application of the MIP-SPME tool revealed a unique approach for the selective microextraction of the analyte in beverage samples. In this work, 3-(triethoxysilyl)-propylamine (TMSPA) was chosen as a precursor due to its ability to imprint the analyte by hydrogen bonding, Van der Walls, and dipole-dipole interactions. Nylon 6 was also added as a backbone and support for the precursor in which sol could greatly growth during the sol-gel process and makes the solution electrospinable. Various effective parameters in the extraction efficiency of the MIP-SPME tool such as loading time, flow rate, desorption time, selectivity, and the sample volume were evaluated. The linearity for the ACF in beverage sample was in the range of 0.78–100.5 ng mL^{-1}. Limit of detection (LOD) and quantification (LOQ) were 0.23 and 0.78 ng mL^{-1} respectively. The RSD values ($n=5$) were all below 3.5% at the 20 ng mL^{-1} level.

1. Introduction

Solid phase microextraction (SPME) has been the center of focus by many researchers ever since it emerged in early of 1990 s [1]. SPME is a green, fast, simple, adsorbtion-desorbtion based, and single step sample preparation process. It has been well accepted as a powerful sample preparation technique and widely used in different area of analytical, bioanalytical, and environmental chemistry [2–5]. Although, there have been many improvements in this regard such as preparation of biocompatible sorbent for in-vivo extraction, unbreakable fibers, and nano composite sorbent [6–10], it is still needed to be improved in some aspects. Preparations of selective sorbents, unbreakable substrates, and sol-gel based fibers have been challenging issues in recent years and they have been studied with some research groups [8,11]. In addition, common conventional SPME fibers are breakable and sensitive when exposed to organic solvents. Some studies have been developed for the preparation of unbreakable sorbents with molecularly imprinted polymers and sol-gel [12–17]. Demand for the preparation of the sorbents with high chemical and thermal stability, long lifetime, and good repeatability has directed research groups toward sol-gel technology. Sol-gel technology has been successfully applied for the preparation of sorbents, but it still has a few problems. Lack of selectivity is the main problem of sol-gel technology. Recently molecularly imprinted sol-gel sorbents have been prepared [12,18], but it still needed more attentions and investigations. A further issue of sol-gel technology for preparation of sorbents, particularly molecularly imprinted sol-gel, could be attributed to inappropriate homogeneity and aggregation during gelation.

New methodology named electrospinning was recently developed for preparation of nanofibers while the acceptable homogeneity could be obtained. It has been used for preparation of fibers and mats for SPME [19–22]. Electrospinning of polymeric

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fibers provides the capability to create micro/nanofibers through an inexpensive and simple method. Electrospun micro/nanofibers have been applied to many different applications ranging from tissue scaffolds, and electronics [23–27]. The electrospinning process is based on similar phenomena in electrospray ionization mass spectrometry (ESI/MS) [28]. Unlike the ESI, here, producing the fiber jet is preferred over the formation of the charged droplets in ESI/MS. Therefore, in the electrospinning process, a solution of high molecular weight polymer with high viscosity is used. This method consists of placing a high electric field between a polymer solution and a conductive collector. When the electric field is strong enough to overcome the surface tension of the droplet, a Taylor cone is formed. Following the creation of the Taylor cone, polymeric nanofibers are ejected toward the conductive collector [29,30].

This method can be used to fabricate SPME fibers with various polymers. This technique should provide an approach to generate high surface area fibers and the versatility to alter the SPME nanofiber composition by changing the polymer solution for electrospinning.

Molecularly imprinted polymers (MIPs) have been largely applied to the extraction of target analytes from a variety of complex matrices. Most of these applications were based on off-line procedures. Until now, a very few applications were carried out in on-line mode [31–33] while trends in analytical chemistry are for high throughput approaches that involve to minimize the time spent performing analysis. Therefore, MIP coupled on-line with HPLC can create a straightforward and fast pretreatment due to their specific recognition properties. We applied MIPs as artificial receptors for off-line solid-phase extraction of bromhexine [34], metoclopramide [35], verapamil [36], and tramadol [37] in biological fluids. Recently, in our research group the applicability of on-line solid phase extraction method using molecularly imprinted polymers in monolithic column [38] or cartridges [33,39] for the extraction and determination of tramadol, dextromethorphan, and insulin in biological fluids and pharmaceutical samples were studied.

In this work, a simple and novel route for the preparation of unbreakable molecularly imprinted sol-gel nanofibers with electrospinning technique was developed. Nylon 6 as a backbone and support of the precursor in the MIP sol-gel process was used to facilitate the electrospinning procedure. The developed method was used for on-line SPME and determination of acesulfame coupled with HPLC. The selectivity of method for the extraction of acesulfame was evaluated in the presence of some sweets (saccharine, caffeine, and aspartame) in the beverage sample. This robust tool can be used for fifty extractions without special obstacle.

2. Experimental

2.1. Reagents

Acesulfame (ACF), saccharine (SCH), aspartame (ASP), and caffeine (CAF) were obtained from Merck (Darmstadt, Germany). 3-(triethoxysilyl)-propylamine (TMSPA) with purity higher than 98% and nylon 6 were purchased from Aldrich (Darmstadt, Germany). Methanol (MeOH), acetonitrile (ACN), trifluoroacetic acid (TFA), and formic acid (FA) were supplied from Merck (Darmstadt, Germany). The stock solution was prepared in distillated water at concentration of 1000 μg L^{-1} and stored at 4 °C. Working standard solutions of different concentrations were prepared daily by diluting the intermediate standard solution with mobile phase solution and spiked in beverage samples for all sections. Also, beverage sample was purchased from local market.

2.2. Apparatus

A DIONEX HPLC instrument was used for chromatographic analysis of ACF. This chromatographic system was composed of a multi solvent gradient pump, a UVD170U detector and an on-line degasser. A Rheodyne model 7725i injector with a 20 μL loop was used to inject the samples. Chromatographic separation was achieved on an ACE C18, 5 μm, 4.6 mm × 250 mm column. For the mobile phase, a degassed mixture of ACN: Phosphate buffer (0.02 M) (85:15) was prepared and delivered in isocratic mode at flow rate of 0.8 mL min^{-1}. All of the analyses were carried out at 220 nm and HPLC data were acquired and processed using a PC and Chromeleon Ver. 6.60 chromatography manager software.

The electrospinning setup also contains a high voltage power supply (Gamma High Voltage ES 50 P-10 W) and a syringe pump (JZB 1800D Double Channel Syringe pump from China). The SPME tool for this study was a stainless steel bar which electrospuned by MIP sol-gel. For on-line connecting SPME stainless steel bar to HPLC a homemade cupper tube (3 cm length × 0.3 cm i. d.) tool which has input and output streams for solutions utilized. SPME nanofiber bar was fixed in this cupper tube and ends of the tube sealed carefully with plastic screw to prevent from any leakage. Then, input and output streams were connected to HPLC by peristaltic pump for on-line extraction. The prepared nanofibers were used for on-line SPME and determination of acesulfame coupled with HPLC. SPME process was performed by passing the spiked aqueous samples through SPME nanofiber tool.

2.3. Preparation of MIP- and NIP-SPME nanofiber

For preparation of sol solution with electrospun capability in optimized concentration and ratio (MIP1, Table 1), 0.15 mL of standard of ACF solution (0.8 mmol L^{-1}, as the template molecule), 0.3 mL of TMSPA as the precursor was mixed and sonicated for 10 min. Then, 0.3 mL ACN as solvent, 0.2 mL of TFA (100%) as catalyst was slowly added in four steps (each time 0.05 mL). Then, 0.05 mL distillate water was added to start the hydrolysis process and solution was kept in this state for 30 min.

In addition, Nylon 6 solution (12% w/w) in 4 mL FA as backbone solution was prepared and was added to the above solution and sonicated for 20 min. This solution was used for electrospinning process to prepare MIP sol-gel nanofiber.

Electrospinning of MIP sol-gel solution without backbone compounds is a complicated process, to overcome this problem, nylon 6 as a backbone for precursor was used. This backbone is needed to have some functional group to produce hydrogen bonding with silane groups. The schematic process of this binding is shown in Fig. 1.

Electrospinning of imprinted polymer nanofibers were carried out at room temperature at a high voltage of 15 kV (Fig. 2A). The syringe used in the experiments had a capillary tip with a diameter

Table 1
Optimization of compounds ratio of sol solution with electrospun capability.

MIP/ NIP	ACF (mL)	TMSPA (mL)	TFA (mL)	Distillated water (mL)	Extraction (%) (mean ± RSD)[a]
MIP1	0.15	0.2	0.2	0.05	69 (± 1.3)
MIP2	0.15	0.3	0.2	0.05	91 (± 2.3)
MIP3	0.15	0.4	0.2	0.05	77 (± 1.1)
MIP4	0.15	0.5	0.2	0.05	60 (± 3.3)
NIP1	—	0.2	0.2	0.05	29 (± 1.1)
NIP2	—	0.3	0.2	0.05	30 (± 3.1)
NIP3	—	0.4	0.2	0.05	38 (± 4.1)
NIP4	—	0.5	0.2	0.05	40 (± 2.2)

[a] Average of five determinations

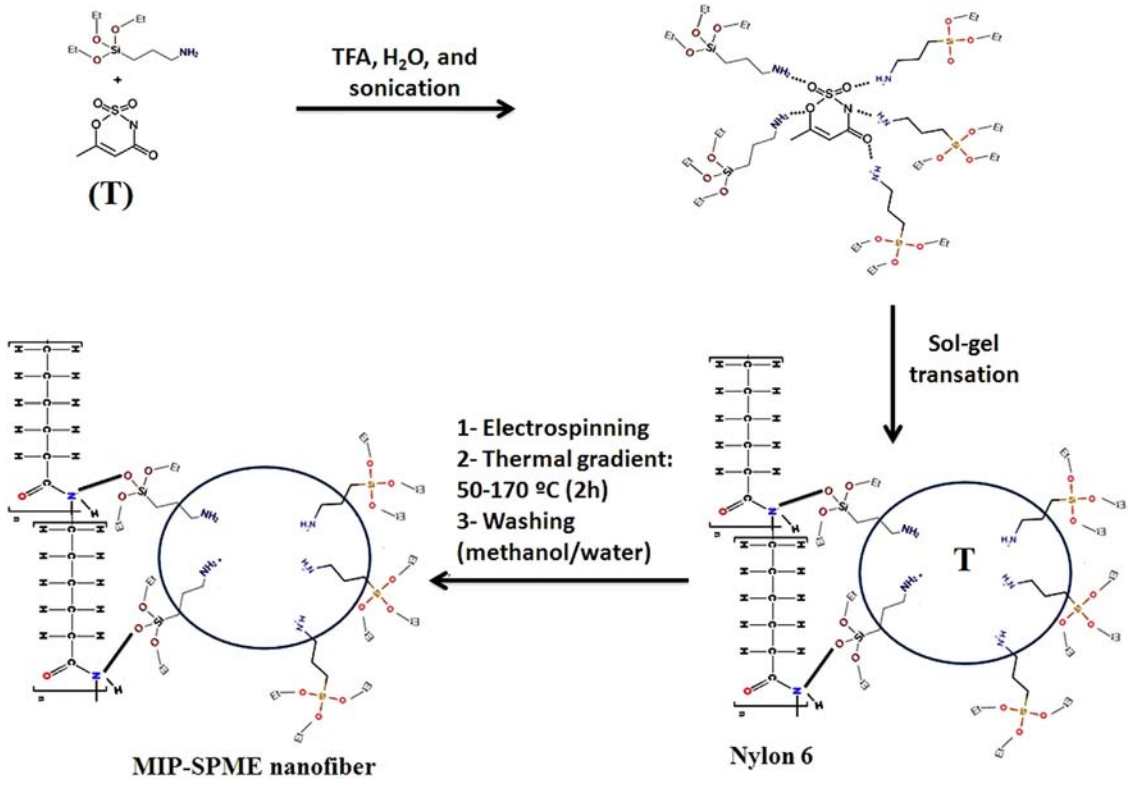

Fig. 1. Schematic MIP sol-gel and binding with Nylon 6 process.

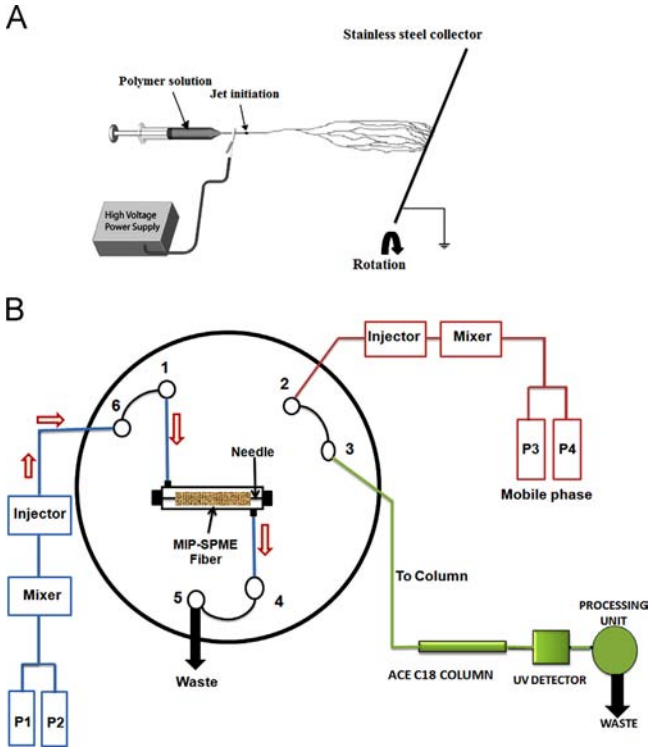

Fig. 2. Schematic diagram for electrospinning (a) and on-line MIP-SPME tool coupled with HPLC (b).

of 0.9 mm. A grounded stainless steel was used as the counter electrode and mounted at a distance of 15 cm from the capillary tip. Continuous SPME fibers were collected on the stainless steel bar. The prepared MIP-SPME was placed into a desiccator for 12 h for further aging and growing the number of bonds between the colloids. To complete the polycondensation step, prepared MIP-SPME nanofibers were placed in vacuum oven for 3 h (gradient range between 50–170 °C). Finally, MIP-SPME nanofibers were washed with methanol and distillated water to remove template and other unreacted materials. In order to verify that retention of template on nanofibers was due to molecular recognition and not to non-specific binding, a control non-molecularly imprinted polymer nanofiber (NIP-SPME) were also prepared according to the above procedures just without ACF.

2.4. On-line MIP-SPME combination with HPLC for determination of acesulfame

The prepared electrospun MIP-SPME nanofibers bar was used for on-line SPME and determination of acesulfame coupled with HPLC relatively similar setup to our previous work (Fig.2B) [38]. SPME process was performed peristaltic pumps (P1 and P2) by passing 0.5 mL ultra pure water (P1) and then 4 mL the spiked aqueous samples (flow rate= 0.8 mL min^{-1} and NaCl 50 mM) at the load position through MIP-SPME tool by P2. After extraction, by changing to elution mode the HPLC mobile phase was used for on-line desorption and elution of the extracted analytes from the MIP-SPME tool to the HPLC column. To this aim, extracted analyte was passed through the analytical HPLC column by an isocratic elution of mobile phases of ACN: Phosphate buffer (0.02 M) (85:15) through P43 and P4 peristaltic pumps. This easy, robust, and efficient setup can easily apply for on-line extraction of ACF from beverage samples and after at least 50 runs nanofiber bar needs to change. Typical chromatograms for the extraction of ACF (20 ng mL^{-1}) in an optimized situation in beverage sample with MIP- and NIP-SPME are shown in Fig. 3A. The results were shown the ability, selectivity, and efficiency of MIP-SPME compare with NIP-SPME for the extraction of ACF. Also, study of MIP-SPME nanofiber selectivity for ACF was evaluated in the presence of some selected sweets SCH, ASP, and CAF that spiked in beverage sample (concentration of all

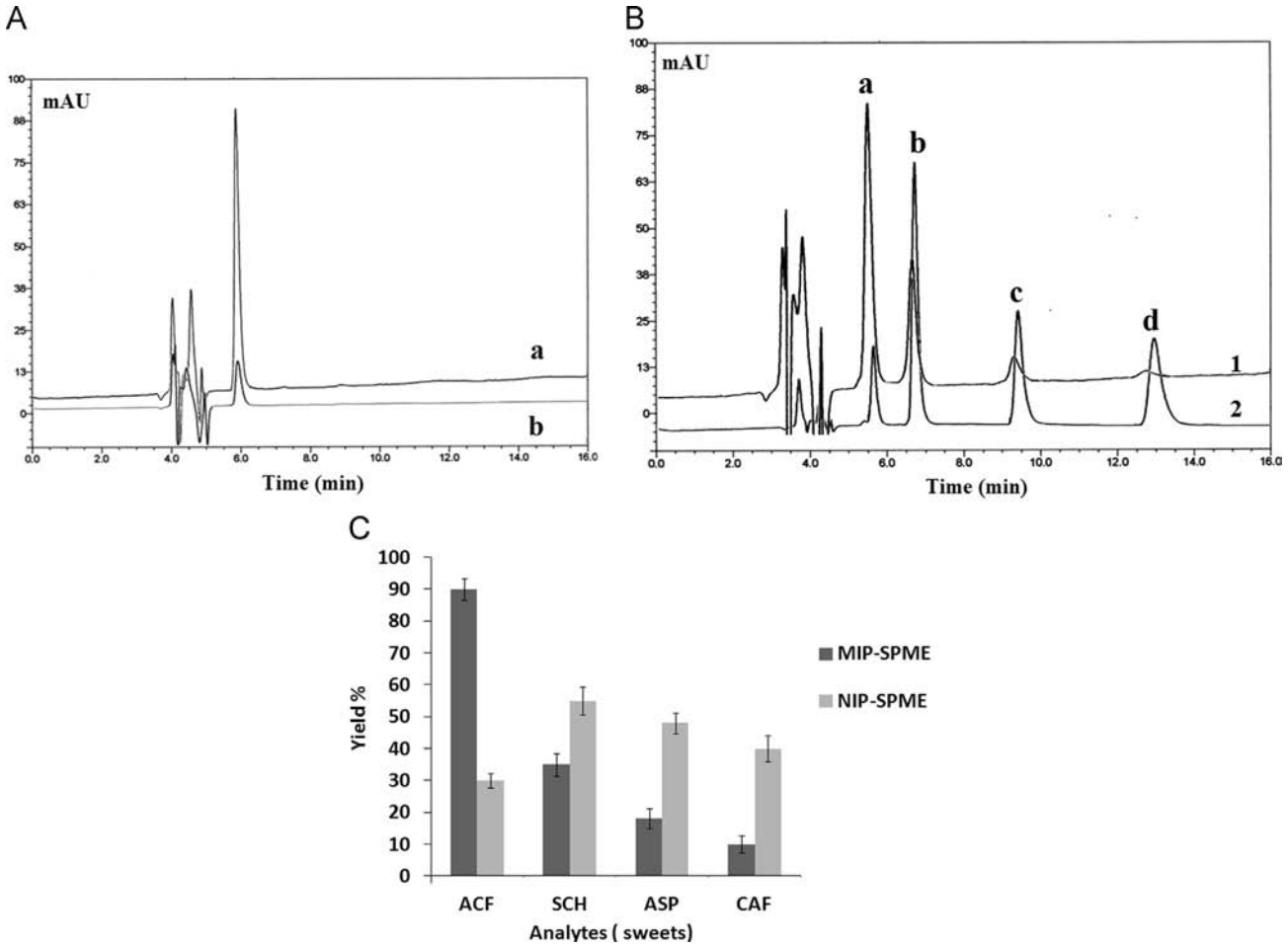

Fig. 3. HPLC chromatograms obtained on-line after clean-up acesulfame in beverage sample (A) and after percolation of beverage sample (B) spiked of acesulfame (a), saccharine (b), aspartame (c), and caffeine (d), with a clean-up step comprising MIP-SPME (1) and NIP-SPME (2). Recovery percent in beverage sample for study of MIP- and NIP-SPME selectivity (C) (monitored at 220 nm; conditions: column ACE C18, 5 μm, 4.6 mm × 250 mm, mobile phase: ACN: Phosphate buffer (0.02 M) (85:15); Flow rate: 0.8 mL min^{-1}; Desorption time: 1.0 min, Loading time: 5 min, sample volume: 4 mL; analytes concentration: 20 ng mL^{-1}).

analytes were 20 ng mL^{-1}). Typical chromatogram of extraction process in optimized situation is shown in Fig. 3B which shows the ability and selectivity of this method for extraction of ACF in the presence of some selected sweets.

3. Results and discussion

3.1. Characterization and optimization of preparation process of MIP-SPME nanofiber

The surface characteristics of the SPME nanofibers were investigated by SEM. Fig. 4 shows the micrographs of the MIP- and NIP-SPME surface. Obviously, both MIP- and NIP-SPME fibers show porous structures, which are due to the inherent properties of sol-gel process but porosity of the MIP is significantly higher than the non-imprinted one in the same surface area. Moreover, thicker diameter was obtained for MIP-SPME toward NIP-SPME which can create more surface area for the better extraction of ACF. The MIP-SPME surface possesses high porous matrices, which could significantly increase the surface area availability and better mass transfer during extraction as well as analyte desorption process. In addition, the MIP-SPME nanofibers are smooth morphology and without bead.

Electrospinning of MIP sol-gel solution without backbone compounds is a complicated process, to overcome this problem, nylon 6 as a backbone for precursor was used. This backbone is needed to have some functional group to produce hydrogen bonding with silane groups. The amount of Nylon 6 as a backbone and support of the precursor in which sol could greatly growth during sol-gel process and give electrospinable property to sol-gel solution is a critical issue. In addition, Nylon 6 has great ability for hydrogen binding and creates strong, dense membrane polymer structure. The range of 5–20% of Nylon 6 in formic acid was studied and results showed better repeatability, stability, and recovery for extraction of ACF was observed when 12% of Nylon 6 was used. In this ratio the nanofibers structures were homogenise and bead-free. Therefore, this ratio was selected for further studies.

It should be also mentioned that prepared MIP-SPME nanofibers have a rather high stability in organic solvents. The MIP-SPME stability in various solvents was tested and it was found that the nanofiber was stable in most solvents including methanol, ethanol, acetonitrile, chloroform, acetone, dichloromethane, tetrachloromethane, diethyl ether, ethyl acetate, cyclohexane, hexane, and toluene. The MIP-SPME could be dissolved in formic acid and N,N-dimethylformamide since both of them simply dissolve Nylon 6. The MIP-SPME nanofiber was quite stable and reusable for more than 50 times of usage without a significant change in recovery percentage.

3.2. Evaluation of extraction process

To achieve the best performance for this method some critical factors including the sample flow rate through the MIP-SPME tool,

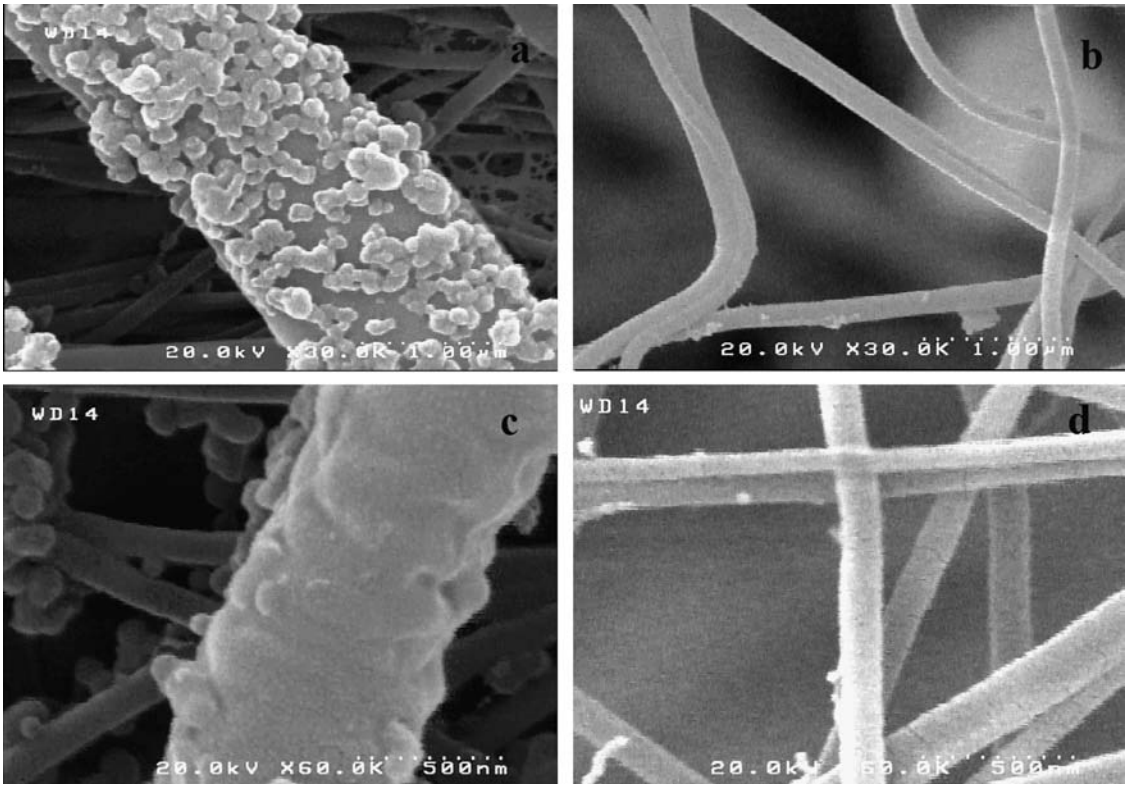

Fig. 4. Scanning electron microscopy (SEM) of MIP-SPME (a, c) and NIP-SPME (b, d).

the loading time, desorption time, the loading sample volume, elution solution volume, and adsorption capacity are urgent to be evaluated.

3.2.1. Optimization of the sample flow rate, loading time, desorption time, and sample volume through the MIP-SPME tool

It has been demonstrated that the required time to achieve extraction equilibrium is relative to the length of the SPME bar, the analyte distribution constant, and the volume of the coating, while it is inversely relative to the extraction flow rate [40,41]. According to these works, the flow rate should optimize by maintaining total sample solution volume and concentration constant. Therefore, the MIP-SPME tool used to obtain a suitable flow rate for the extraction. To this aim, a range of flow rates from 0.1 to 2 mL min^{-1} were investigated. According to the results the best and maximum of extraction efficiencies was obtained at flow rates 0.8 mL min^{-1} (Fig. 5A). Finally, flow rate of 0.8 mL min^{-1} was elected as the optimized amount for further studies.

Also, SPME is an equilibrium sample preparation technique which finding optimum time for loading the sample on sorbent is a critical issue and it is depended to some factors such as the distribution constant between sorbent and solution, thickness of sorbent and diffusion coefficient of analytes [42]. To achieve the best performance, the analyte sample was crossed through the MIP-SMPE tool in different ranges of time. According to precise investigation 5 min is a sufficient time for absorption of analyte on surface of the MIP-SPME (Fig. 5B).

In addition, when SPME method combined with HPLC, quick desorption of analyte from sorbent by efficient mobile phase elution is a serious issue. Moreover, it is very important for on-line systems desorption of analyte from sorbent could be easily happen by switching the sampling valve position from the load to the inject mode. Based on studied results (Fig. 5C) by utilizing ACN: phosphate buffer (0.02 M) (85:15) as a mobile phase desorption of analyte from SPME bed was completed after 1 min but for prevent of any carry-over 5 min time out was chosen between each sample running.

Moreover, amount absorbed analyte at equilibrium time between loading sample and SPME sorbent is calculated by following equation [42,43].

$$n = \frac{(K_{fs} V_f V_s C_0)}{(K_{fs} V_f + V_s)}$$

where n is the mass of analyte extracted by the coating, K_{fs} is a fiber coating–sample matrix distribution constant, V_f is the fiber coating volume, V_s is the sample volume and C_0 is the initial concentration of a given analyte in the sample. According to this equation the mass absorbed by the SPME nanofiber after equilibrium is calculable. Also it can be inferred that n is increased as long as sample volume (V_s) increased, until $K_{fs}V_f \leq V_s$; At this point amount of analyte extracted is independent of sample volume:

$$n = K_{fs} V_f C_0$$

The effect of sample volume was considered in range between 1 to 10 mL. As Fig. 5D shows, the extraction efficiency was increased up to 4 mL of the sample, and then it was independent of sample volume. Obviously, in this sample volume the equilibrium is easily obtainable and the rise of sample volume has no effect on the extraction efficiency.

3.2.2. Study of MIP selectivity

For surveying selectivity of ACF MIP-SPME nanofiber, some sweets such saccharine, caffeine, and aspartame with relatively similar properties were evaluated. Solutions of all sweets were prepared individually with the concentration of 20 ng mL^{-1} and spiked in the beverage sample. Elution solvent for tool was ACN: Phosphate buffer (0.02 M) (85:15). The extraction yields of the selected sweets with the MIP-SPME and NIP-SPME are shown in Fig. 3C.

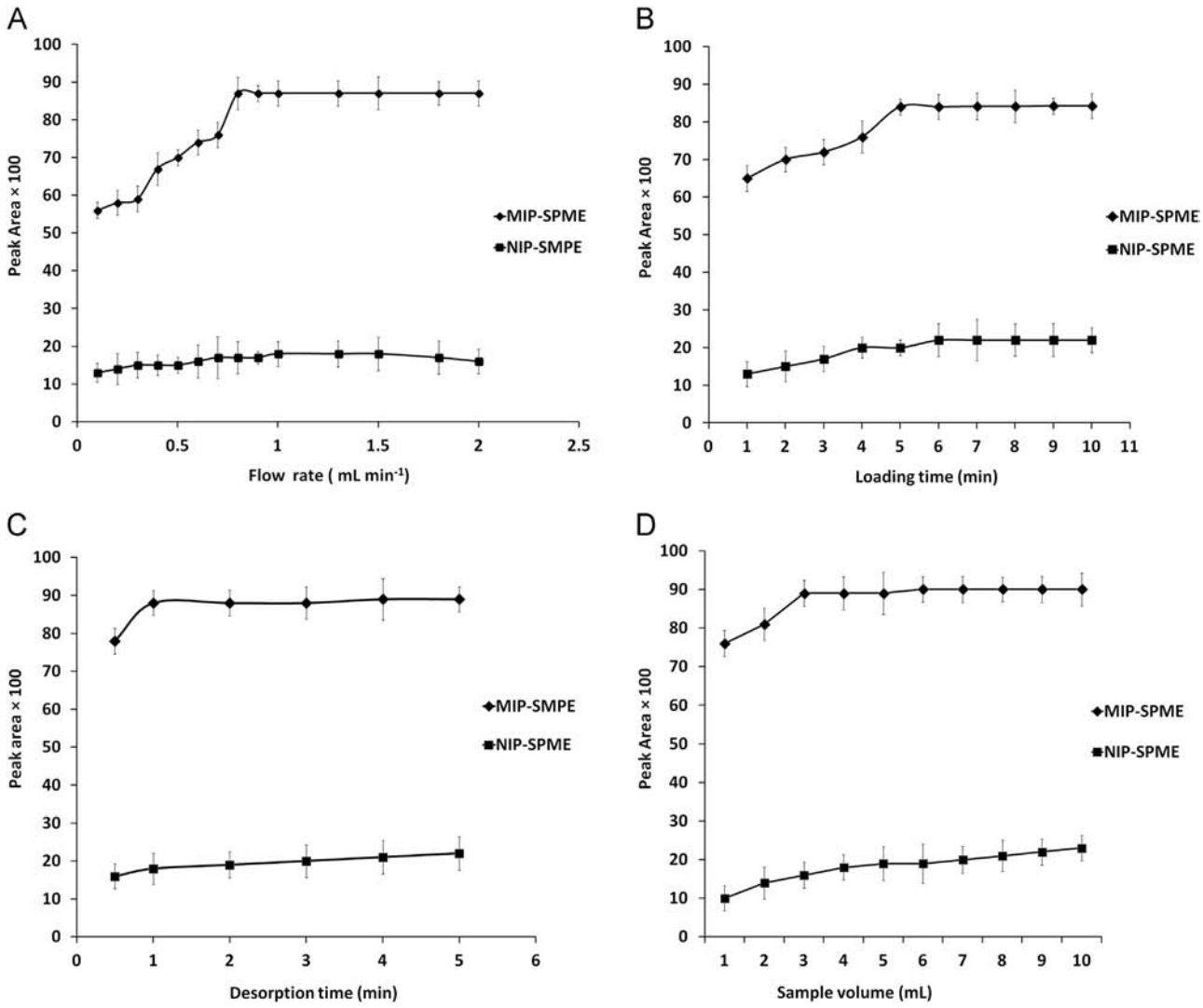

Fig. 5. Effect of sample flow rate (A), loading time (B), desorption time (C), and **s**ample volume (D) through the MIP- and MIP-SPME tool. Loading time: 5 min, Sample volume: 4 mL; analyte concentration: 20 ng mL^{-1}.

Table 2
Results of MIP- and NIP-SPME selectivity for different analytes.

Analyte[a,b]	K(MIP-SPME) (cm^2 mol^{-1})	K(NIP-SPME) (cm^2 mol^{-1})
ACF	0.428	0.021
SCH	0.025	0.067
ASP	0.0125	0.05
CAF	0.005	0.033

[a] Analyte concentration: 20 ng mL^{-1}
[b] Average of five determinations.

Also, Langmuir model well describes the process of adsorption and desorption with a solid porous coating SPME fiber. It is assumed that a monolayer of the adsorbate can be formed at the surface. The amount of analyte adsorbed by the nanofiber is given by [43,44]

$$n = \frac{n_{fA}^{\infty}}{K(n_{fmax} - n_{fA}^{\infty})}$$

That, C_0 is the initial concentration of analyte, $n_{fA}^{\infty}$is the amount of analyte adsorbed on the nanofiber at equilibrium, $n_{fmax}$is the maximum amount of the analyte that can be adsorbed on the active sites on the fiber, which corresponds to the maximum amount of active sites, assuming a 1:1 ratio of active sties to adsorbed analyte and K is adsorption equilibrium constant (in cm^2 mol^{-1}). The results of this part are shown in Table 2.

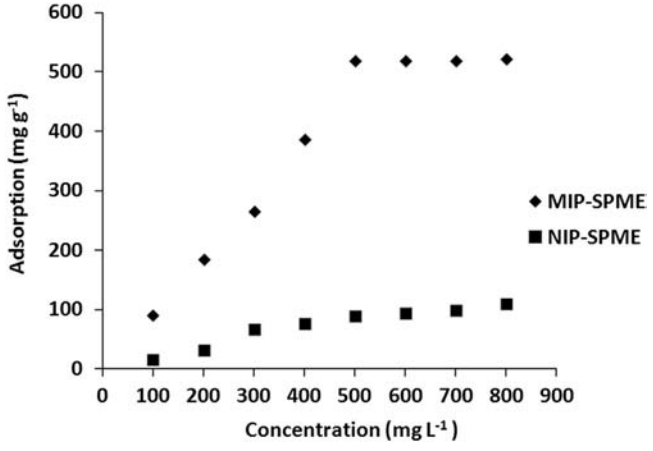

Fig. 6. Effect of ACF concentrations on the retention capacities of MIP- and NIP-SPME.

3.2.3. Adsorption capacity

The capacity of sorbent is an important factor determining how much of the analyte can absorb by sorbent from the solution quantitatively. In considering the measurement of the adsorption capacity MIP-and NIP-SPME, 4 mL ACF solutions at concentrations of 100–800 mg L^{-1} were crossed through the fibers (weight of MIP- and NIP-SPME sorbent 10 mg) at room temperature. The absorbed ACF was measured by HPLC. The isothermal adsorptions are plotted in Fig. 6. According to these results, the maximum amount of ACF absorbed by MIP-SPME was found to be 450 mg g^{-1}. Regarding higher ACF amounts, a slight increase of retained ACF was observed on MIP-SPME capacity curve. Since all the accessible specific cavities of the MIP-SPME are saturated, the retention of the analyte is only due to non-specific interactions which can be approximately identical for MIP- and NIP-SPME.

3.2.4. IF and effect of salt study

In order to evaluate the extraction efficiency of MIP-SPME and obtain the optimized extraction conditions, enrichment factor (EF) and extraction recovery (ER) were used [45]. According to this study, the enrichment factor was defined as the ratio between the analyte concentration in eluent (C_{elu}) and the initial concentration of analyte (C_0) within the sample.

$$EF = \frac{C_{elu}}{C_0}$$

Moreover, the imprinting factor (IF) was used to evaluate the recognition abilities of the MIP-SPME.

$$IF = \frac{EF_{MIP-SPME}}{EF_{NIP-SPME}}$$

Where the $EF_{MIP\text{-}SPME}$ is the enrichment factor of ACF extracted in MIP-SPME and $EF_{NIP\text{-}SPME}$ is the enrichment factor of ACF extracted in NIP-SPME under the same conditions.

In order to considering IF of MIP- and NIP-SPME for separation of ACF in solvent media and beverage sample were considered at the same process and the results are shown in Table 3 According to the results MIP-SPME is shown good selectivity in separation of ACF compare to NIP-SPME.

Moreover, the effect of salt on recovery of extraction ACF by MIP-SPME was considered. For this aim, different range of NaCl (1–100 mM) was added to solution and at the same extraction process by MIP-SPME. The results shown in special point (50 mM) this can help for increasing recovery percent of ACF in beverage sample. The results of this work are shown in Fig. 7.

Table 3
The selectivity of MIP-SPME for separation of ACF compare to NIP-SPME.

ACF media [a,b]	EF		IF
	MIP-SPME	NIP-SPME	
Solvent	0.96	0.33	2.9
Beverage	0.90	0.30	3.0

[a] Analyte concentration: 20 ng mL^{-1}
[b] Average of five determinations

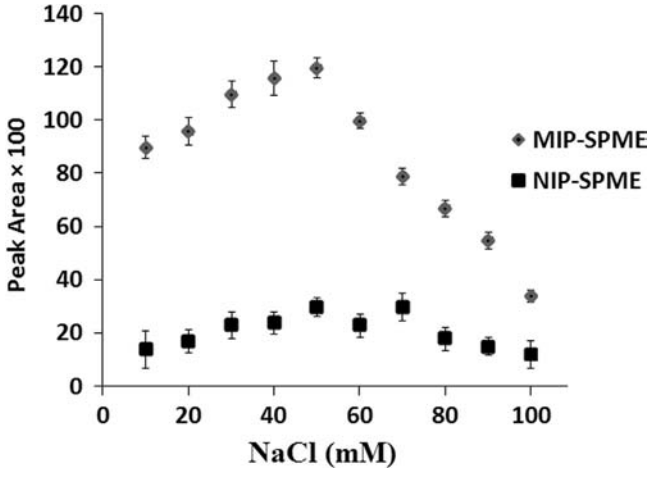

Fig. 7. Salt effect on ACF extraction recovery in beverage sample.

4. Method validation

Based on the developed method, a sampling flow rate of 0.8 mL min^{-1}, loading time of 5 min, desorption time of 5 min and sample volume of 4 mL were chosen as the optimum set of conditions. Beverage sample was spiked with the analyte to evaluate the precision of the measurements, LOD, and the dynamic range of method. The linearity of the method was tested by preparing the calibration curve for analyte with 8–10 points. The linearity for the ACF was in the range of 0.78–100.55 ng mL^{-1}. The regression coefficient obtained for ACF was (R^2=0.997).The values of LOD (S/N=3) was 0.23 ng mL^{-1} and LOQ (S/N=10) was 0.78 ng mL^{-1}.The precision of the method was determined by performing five consecutive extractions from the aqueous solutions. To evaluate the applicability of the proposed method, extraction analysis was performed on beverage sample. The beverage sample was spiked at a concentration level between 1–50 ng mL^{-1} and the analyses were carried out under the optimized conditions. As Table 4 shows good relative recoveries were achieved for the ACF more than 89% in the presence of other sweets. The intra- and inter-day precision and accuracy of method were assessed by analyzing in beverage sample spiked with ACF at three different concentration levels over the calibration range tested, (in replicates five) of 1, 20 and 80 ng mL^{-1}, respectively. All samples were prepared either at the same day or at five consecutive days. The inter-day precision was less than 3.1% and the intra-day precision was lower than 4.9% in beverage sample, respectively.

Table 4
Assay of ACF in beverage sample by means of the described on-line MIP- and NIP-SPME-HPLC procedure.

Sample	Spiked Value (ng mL^{-1})	Found [a](ng mL^{-1})	Proposed on-line SPME-HPLC procedure (Found ± RSD)[a] (ng mL^{-1})	
			MIP-SPME	NIP-SPME
Beverage	1	0.89	89.4 ± 2.5	29.3 ± 1.4
	20	18.2	90.2 ± 3.2	30.4 ± 3.5
	30	27.33	91.1 ± 1.2	31.3 ± 2.1
	50	45.2	90.4 ± 3.5	32.3 ± 3.2

[a] Average of five determinations.

Table 5
Determination of ACF with different methods.

Method	Linear range	LOQ	Recovery (%)	RSD (%)	Reference
RP-HPLC	125–5000 ng mL^{-1}	250 ng mL^{-1}	94 ≤	0.72 ≤	[46]
LC/MS/MS	0.25–2000 ng g^{-1}	0.3 ng g^{-1}	95	16.0	[47]
SPME-HPLC	0.78–100.5 ng mL^{-1}	0.78 ng mL^{-1}	89 ≤	3.5	Present work

4.1. Comparing between developed method for ACF separation

In this section, results of some works for detection of ACF RP-HPLC [46] and LC/MS/MS [47] with our study were compared. The results are listed in Table 5.

5. Conclusion

An unbreakable MIP sol-gel nanofiber tool, fabricated by the electrospinning technique, has been shown to be a selective sorbent for extracting ACF, as a sweetener, from beverage samples in the presence of some selected sweets. This unbreakable tool was connected on-line to HPLC system to facilitate the extraction speed and solvent consume. This nanofiber tool can be used for fifty runs without special problem. Influential parameters in on-line MIP-SMPE process were investigated and optimized. The proposed method presents a rather straightforward, easy, rapid, and inexpensive microextraction method for the determination of various kinds of analytes and metabolites with good selectivity, sensitivity and reproducibility from complex matrices.

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