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Liquid chromatographic determination of certain isoquinoline alkaloid by a cloud-point extraction method with diatomite bonding magnetite

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ABSTRACT

A synthesis of magnetic Fe_3O_4-doped diatomite nanoparticles (MNPS) to capture an anionic surfactant (SDBS) was described this paper, Using the above surfactant as an extractant to concentrate three kinds of isoquinoline alkaloids in which measured human urine by HPLC. The method affords significant simplification of the conventional CPE procedures without requiring specialized apparatus, thereby alleviating the need for specific sample handling treatment such as centrifugation. Furthermore, compared with conventional sorbents, analytes can be extracted from larger sample volumes at lower extraction times without any filtration step. The lower limits of quantification were 0.3 ng/mL for all analytes. The extraction recoveries were 87.5% for coptisine, 92.1% for palmatine, and 95.2% for berberine on average. The validated method was used to study the pharmacokinetic profile of the three isoquinoline alkaloid in urine after oral administration of the tablets.

KEYWORDS

Berberine;
Palmatine;
Coptisine;
Magnetic microsphere;
HPLC-UV.

INTRODUCTION

Sample preparation is considered as the most critical step in overall analytical process since it has a multifarious role related to analyte extraction, preconcentration and clean-up from co-existing species. Cloud point extraction (CPE) with dispersive micro solid phase extraction (D-μ-SPE)[1] (C–Fe_3O_4/CMNP)[2] solid-phase extraction and preconcentration of trace amounts Hg(II) from environmental samples was developed by using sodium dodecyle sulphate-coated magnetite nanoparticles (SDS-coated Fe_3O_4 NPs)[3] Simple cloud-point extraction (CPE) for SDBS extraction in herbal medicine does not lead to phase separation, and as a result, CPE process can only be carried out by centrifugation (C-CPE). Centrifugal operation, however, has limited processing capacity owing it to the small operation volume of the centrifuge tube. In view of the above discussion, a modification to CPE is described by resorting to the benefits of hydrophobic magnetic nanoparticles as a collection medium of the extraction phase. If CPE must be enlarged for drug measure analysis for continuous operation, the MNPS-CPE has to be adopted. Using anionic surfactant (SDBS) in CPE under the conditions of phase separation results to a high cloud point. The high temperature required to make the insulation and the strong thermal motion makes phase separation hard to accomplish, thus rendering it unsuitable for the separation of heat-labile substances. If surfactant (SDBS) synthesized MNPS were to be combined with an easily extractable enrichment structure, the MNPS-CPE-based systems

are likely to have a low cloud point, a characteristic that is suitable for the enrichment of alkaloids.

In recent years, due to their large surface area, high number of surface active sites, and relatively rapid and easy magnetic separation via magnetic field, magnetic polymeric particles have been used in biomedical and bioengineering[4-6]. Moreover, because of their unique characteristic and strong adsorption ability, they also offer great potential in several areas of application, such as being an adsorbent for removal and/or preconcentration of many kinds of inorganic and organic pollutants including pesticides and metal ions[7-9].

Coptidis Rhizoma (Huanglian), a widely used traditional Chinese medicine (TCM), has been used for centuries for treating dysentery, hypertension, inflammation, and liver diseases[10,11]. This TCM is derived from the dried rhizome of ranunculaceous plant such as *Coptis chinensis* Franch, *Coptis deltoidea* C.Y. Cheng et Hsiao., or *Coptis* teeta Wall. and is known to contain berberine, palmatine, and coptisine (structures shown in Figure 1). These protoberberine alkaloids are the major bioactive components.

In previous pharmacokinetics studies, berberine has been reported in humans using non-specific methods such as UV spectrophotometry, fluorometry, tritium-labeling, gas chromatography-chemical ionization mass spectrometry, and HPLC[12,13]. The quaternary protoberberine-type alkaloids berberine and palmatine are the main active components of C. rhizome, and P. cortex. Despite the extensive literature on the pharmacology of berberine and palmatine, little information is available relating to their pharmacokinetics.

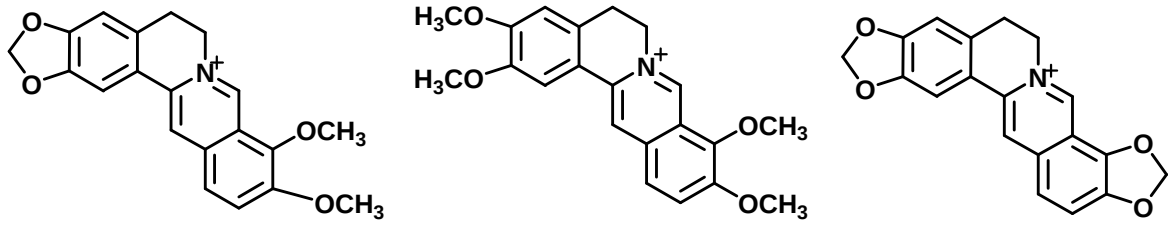

Figure 1 : The structures of berberine, palmatine, and coptisine

The present study introduces a new type of magnetic microsphere, the CPE method supplemented with high-performance liquid chromatography (HPLC) and UV-visible detection, for the determination of berberine, almatine, and coptisine in Traditional Chinese Medicine. Experimental parameters of the method were optimized, and the reliability of the actual drugs were evaluated. The method can accurately measure and determine the presence of the three alkaloids in different Chinese herbal medicine and biological fluids, thus demonstrating the feasibility of MNPS-CPE.

EXPERMENTAL DETAILS

Materials

Berberine, palmatine, and coptisine (purchased from Chengdu Must Bio-Technology Co., Ltd.) were used as reagents without further purification. The stock solution (1.0 mg mL^{-1}) was prepared by dissolving 100 mg of the drug in 100 mL of methanol. Working standard solution was obtained through the appropriate dilution of the stock solution. HPLC-grade acetonitrile was purchased from Tianjin Guangfu Fine Chemical Research Institute (Tianjin, China). Sodium dodecyl benzene sulfonate (SDBS) was obtained from Acros Organics (Geel, Belgium). Water extracted with the Milli-Q Purification System (Millipore, Bedford, MA, USA) was used throughout the study. All reagents used are of analytical grade, and all the solutions used for HPLC were filtered through 0.45 μm membranes prior to the experiment.

The Shuang huang lian and Yi qing ke li medicines were purchased from Hebei province in China. Chromatographic analysis was performed on an Agilent1200 HPLC system (California, USA) equipped with a variable wavelength detector, and an automatic sample injector. The analytes were separated on a Spursil C_{18} column (5 μm, 4.6 mm × 250 mm, Dikma Limited) with Spursil C_{18} Guard Cartridges (5 μm, 2.1 mm × 10 mm, Dikma Limited). The mobile phase was a combi-

nation of 0.1% phosphoric acid and 0.02% SDS, which was delivered at a flow rate of 1 mL/min. The column temperature was 30 °C, whereas the wavelength used was 345 nm. A vortex shaker (QL-861, Haimen,China) and an ultrasonic cleaner (KQ3200DE, Kunshan, China) were used for the treatment of the samples. All glassware used in the experiments were washed with deionized water and acetone and then dried at room temperature prior to use.

Methods

(a) Synthesis of pure maghemite nanoparticles

Pure maghemite nanoparticles were prepared according to existing literature[14,15]. In the typical synthesis of monodisperse Fe_3O_4 NPS with mesoporous structure, $FeCl_3 \cdot 6H_2O$ (0.8 g) was dissolved in EG (16 mL) to form a thick yellow liquid, to which NaAc (2.4 g) and ETH (8 mL) were added. The mixture was vigorously stirred for half an hour, and then sealed in a teflon-lined stainless-steel autoclave (50 mL capacity). The autoclave was heated to and maintained at 200 °C for 8 h before it was allowed to cool to room temperature. The resulting black products were washed several times with distilled water and ethanol, and dried at 60 °C in vacuum for 8 h.

(b) Fabrication of Fe_3O_4-doped diatomite nanoparticles (MDDNPS)

The above process can be extended to the synthesis of Fe_3O_4-doped diatomite nanoparticle through hydrothermal synthesis. The 0.3 g of diatomite in 24 mL of EG was subjected to ultrasound dissolution to form a viscous yellow liquid. This was followed by the addition of 0.6 g of $FeCl_3 \cdot 6H_2O$ and 1.2 g of NaAc. The mixture was vigorously stirred for half an hour, and sealed in a teflon-lined stainless-steel autoclave in the same manner the maghemite nanoparticles were stored. Prior to drying at 60 °C in vacuum for 8 h, the products were washed several times with distilled water and ethanol[16,17].

Extraction procedure

(a) SUF-DLLME step

Aliquots of standard drug solution were mixed with 1 mL of Britton–Robinson buffer solution (pH 4.0) and 0.4 mL of SDBS extracting solution before the volume of the whole mixtures were increased to 10 mL with double distilled water, and 1.2 g of $MgCl_2$ was added. All experiment process were performed in an ice bath. After the manual concussion, the mixture was dispersed throughout the comparison tube.

(b) MR- SUF step

A magnet was held at the bottom of the graduated centrifuge tube containing 0.035 NPs, while another one was gently swept around the outer wall of the centrifuge tube to concentrate the nanoparticles. After the sedimentation of Fe_3O_4 MNPS, the sample solution was carefully removed using a drip tube and a microsyringe. Subsequently, 0.2 mL of organic solvents, including methanol and acetonitrile, was injected into the centrifuge tube to desorb the surfactant (SDBS). Sonication for 60 s was performed, before the nanoparticles were isolated from the solution using a magnet. On the other hand, 10 µL of the collected organic solvent was injected into the HPLC system for analysis. All experiments were conducted in triplicates.

Chromatographic conditions

The flow rate was set to 1 mL/min. The mobile phase and the sample solution were filtered through a 0.45µm membrane before they were injected into the HPLC system. The detection wavelength was set at 345 nm, and the column temperature was maintained at 30 °C. Mobile phase A was composed of 0.1% phosphoric acid and 0.02% SDS, whose pH value was adjusted to 3.0 with triethylamine, whereas mobile phase B contained acetonitrile. Gradient elution conditions were set at 0–15 min for 30%–40% B, and at 15–25 min for 40%–50% B. UV absorbances at 345 nm were monitored by using a UV detector, and the resulting peak area was used for quantification.

RESULT AND DISCUSSION

Characterization of magnetic particles

The morphologies of the Fe_3O_4 and the Fe_3O_4@diatomite samples were examined by SEM and XRD, as shown in Figure 2. Figure 2a shows the SEM image of the Fe_3O_4 sample, and it can be clearly seen that the sample is composed of many spherical particles with diameter measurements of about 90 nm. This

image exhibits that the surfaces of prepared Fe_3O_4 magnetic nanospheres are not smooth. SEM image of the Fe_3O_4@diatomite sample is shown in Figure 2b, and it could be observed that Fe_3O_4@ diatomite nanocomposite has a smooth silica shell with a diameter of about 5–10 nm.

XRD was used to characterize the chemical structure of the samples obtained. Figure 3 shows the XRD patterns of the Fe_3O_4, the diatomite and the Fe_3O_4@diatomite nanocomposites. All the expected diffraction peaks at $2\theta = 30.26°, 35.69°, 37.2°, 43.1°, 53.55°, 57.38°$, and $63.02°$ for Fe_3O_4@ diatomite (curves a) nanocomposites were observed, a result which is in agreement with the XRD peaks of pure Fe_3O_4 nanospheres (curve C). These peaks correspond to the (2 2 0), (3 3 1), (2 2 2), (4 4 0), (4 2 2), (5 1 1), and (4 4 0) Bragg reflections of Fe_3O_4, respectively, indicating that the Fe_3O_4@diatomite nanocomposites did not result to any change in the crystal structures of the Fe_3O_4 nanospheres. The absence of the diatomite peak in the XRD pattern of the Fe_3O_4@ diatomite sample is due to its amorphous structure coated on the Fe_3O_4 nanospheres. In addition to the diffraction peaks that correspond to Fe_3O_4, there also exists three other dif-

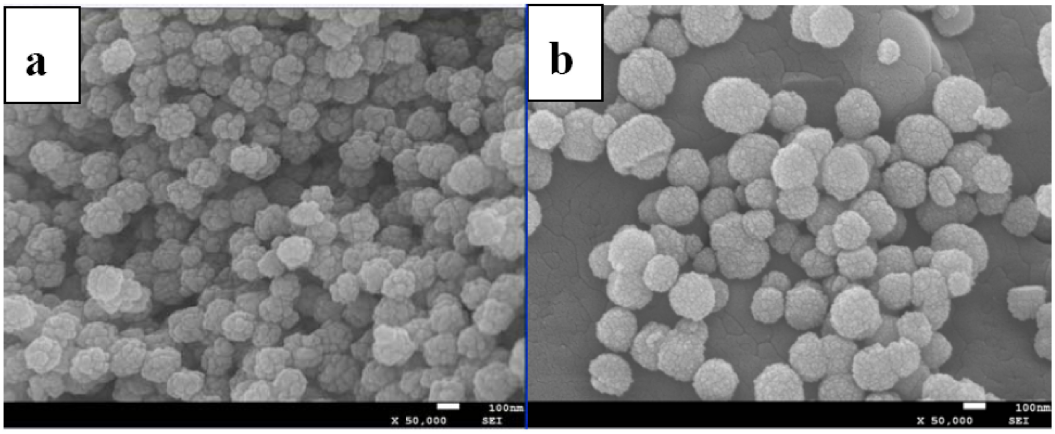

Figure 2 : (a,b) SEM images of Fe_3O_4, Fe_3O_4@ diatomite samples

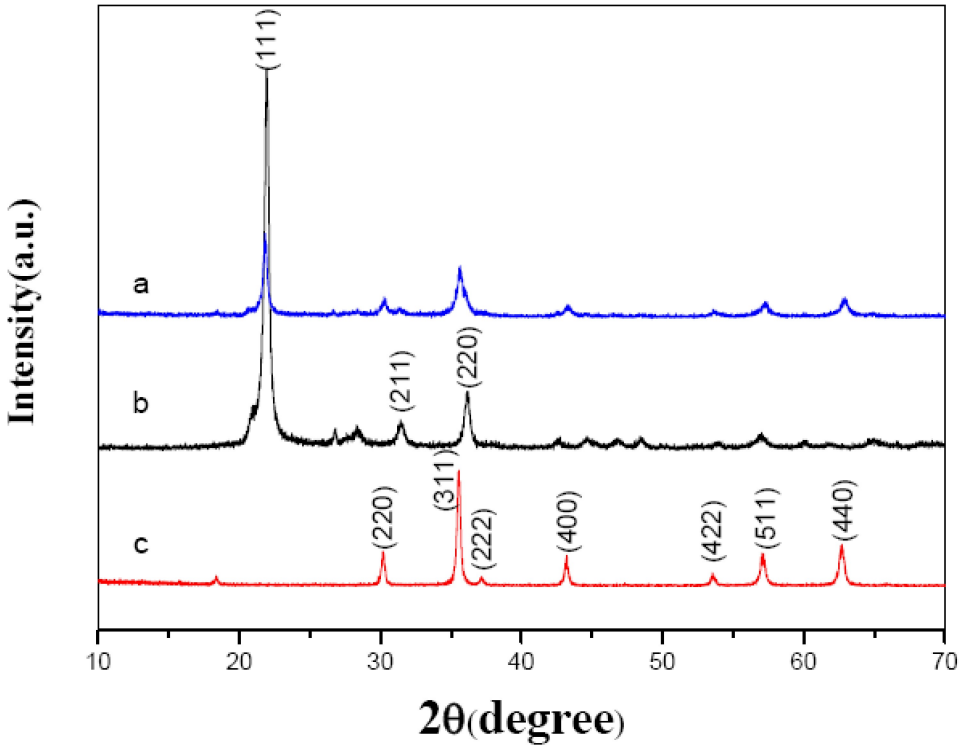

Figure 3 : Typical XRD patterns (a) Fe_3O_4@ diatomite (b) diatomite (c) Fe_3O_4.

fraction peaks (labeled with the symbol #). The position and intensity of the diffraction peaks match well with (1 0 1), the crystal faces of cubic phase diatomite.

Calibration of enrichment factor and extraction recovery

To evaluate the performance of the proposed method, the values for extraction recovery and enrichment factor were calculated. Eqs. (1) and (2) were applied for calculating enrichment factor (EF) and recovery (R), respectively:

$$\mathrm{EF} = \frac{C_{\mathrm{sed}}}{C_0} \quad (1)$$

where C_{sed} is the concentration of the analyte in enriched phase; and C_0 is the initial concentration of analyte in the sample solution.

$$R = \frac{C_{\mathrm{sed}} \times V_{\mathrm{sed}}}{C_0 \times V_{\mathrm{aq}}} \times 100\% = EF \times \frac{V_{\mathrm{sed}}}{V_{\mathrm{aq}}} \times 100\% \quad (2)$$

where Vsed is the volume of the enriched phase; and Vaq is the volume of the sample solution.

Optimization of the parameters affecting MNPS-CPE

To optimize the described method for the separation and preconcentration of the alkaloids in Traditional Chinese Medicine, various analytical parameters were optimized including the pH of the sample solution, type and concentration of the surfactant, quality of the MNPS, and the effect of salt usage in the aqueous sample and desorption condition. All the experiments were conducted using a standard mixture containing 10 μg/mL berberine, 10 μg/mL palmatine, and 10 μg/mL coptisine. All the optimization experiments were conducted three times.

(a) Type and quantity of the surfactant

There are various kinds of surface-active agents that may be employed in classical CPE[18], and the most often being used are of the anionic, double ionic (zwitterionic), and non-ionic types. The outer surface of hemimicelles is hydrophobic whereas that of admicelles is ionic, two characteristics which provide different mechanisms for the retention of organic compounds, but are both suitable for the SPE method. In the mixed hemimicelle phase, both hemimicelles and admicelles are formed in the surface of mineral oxides, and the adsorption is driven by both hydrophobic and electrostatic interactions. Between the two surfactants used, SDBS was better at the separation and preconcentration of the alkaloids. Moreover, the concentration of surfactant is also an important parameter to consider, because the concentration should be sufficient for the quantitative extraction of the target analyte. As shown in Figure 4, the recovery of three alkaloids initially increased when volume of the surfactants rose up to 0.4 mL, and from that point onwards, it remained constant. According to these results, 0.4 mL of SDBS is ideal for the method being developed.

(b) Ionic strength

Ionic strength is also one of the factors to consider in optimizing the performance of CPE[19,20]. The addition of salt can cause anionic or cationic surfactant solutions to separate into immiscible surfactant-rich and surfactant-poor phases. Several inorganic salts, including $MgCl_2$, NaCl, and $GaCl_2$. were tested. $MgCl_2$ emerged to be the best, because of the high recovery efficiency value obtained for it. Results show that the addition of $MgCl_2$ facilitates the separation between the surfactant-rich phase and the aqueous phase. To study the influence of the ionic strength on the extraction recovery, the quantity of $MgCl_2$ was varied from 0.6 g to 1.4 g. A rise in the quantity of salt causes the increase in the micelle size and the aggregation number, while the critical micellar concentration remains constant. In addition, analytes possibly become less soluble in the solution at higher salt concentrations, and thus this contributes to higher extraction recoveries. The result obtained from Figure 5 indicates that the CPE at salt quantity of 1.2 g gives the optimum extraction recovery.

(c) Amount of MNPS

The selection of desired functional MNPS is extremely important to the method because it significantly influences the extraction efficiency. MNPS, such as Fe_3O_4 nanoparticles, have found wide acceptance in many chemical analyses because of the advantages they boast, which include their simple, inexpensive and high-yielding preparation method, their good adsorption capacity, their superparamagnetism, and their low toxicity[21,22]. Substantial effort has been expended toward

modifying the nanoparticles before utilizing them in various separation procedures[23,24]. The amount of the MNPS was varied from 10 mg to 40 mg. As shown in Figure 6, the highest recoveries (87.5–92.1%) for three target analytes were obtained at 35 mg of MNPS. Masses greater than 35 mg led to a decrease in recovery, which indicates that target analytes could not be completely eluted with methanol.

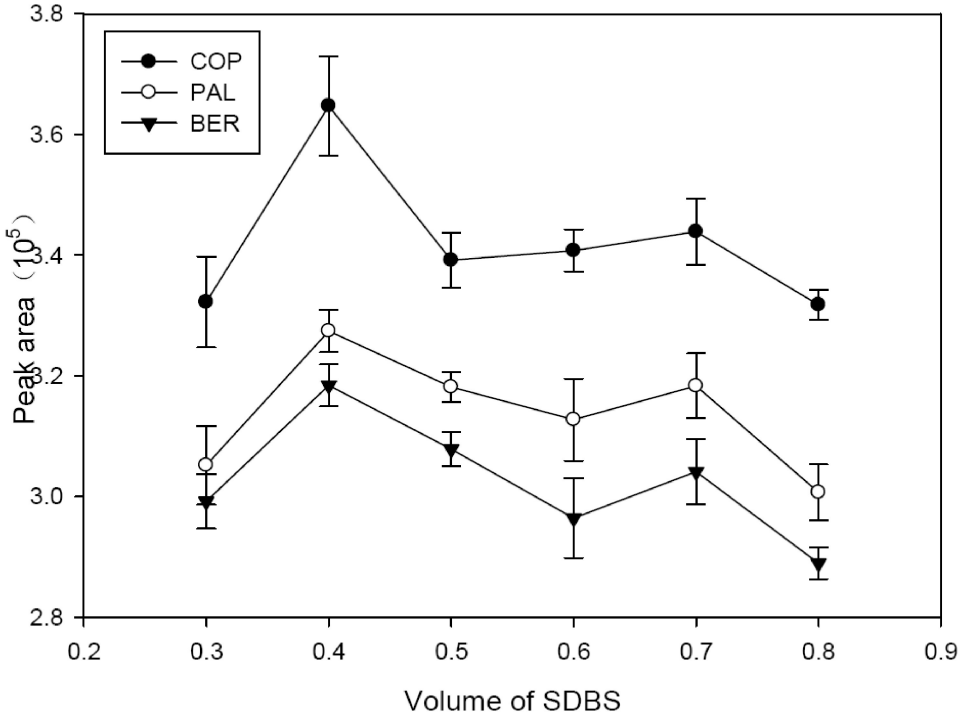

Figure 4 : Effect of the volume of SDBS experiment conditions: concentration of drugs, 200 ng/mL; amount of $MgCl_2$, 1.2g; pH, 4.0; amount of MNPS, 35mg.

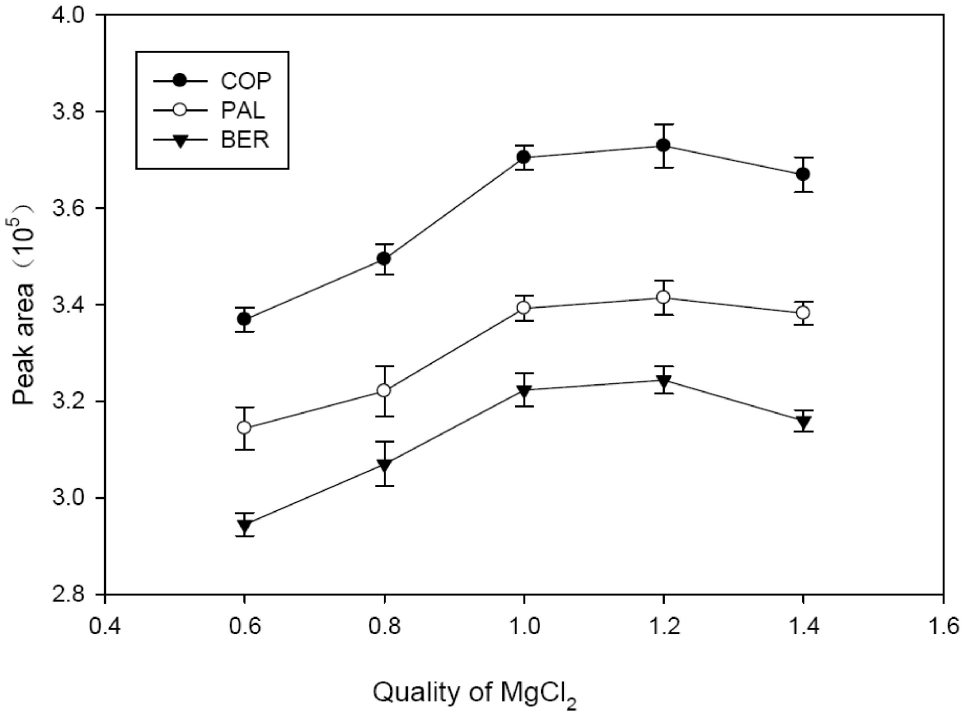

Figure 5 : Effect of the amount of $MgCl_2$ experiment conditions: concentration of drugs, 200 ng/mL; volume of SDBS, 0.4mL; pH, 4.0; amount of MNPS, 35mg.

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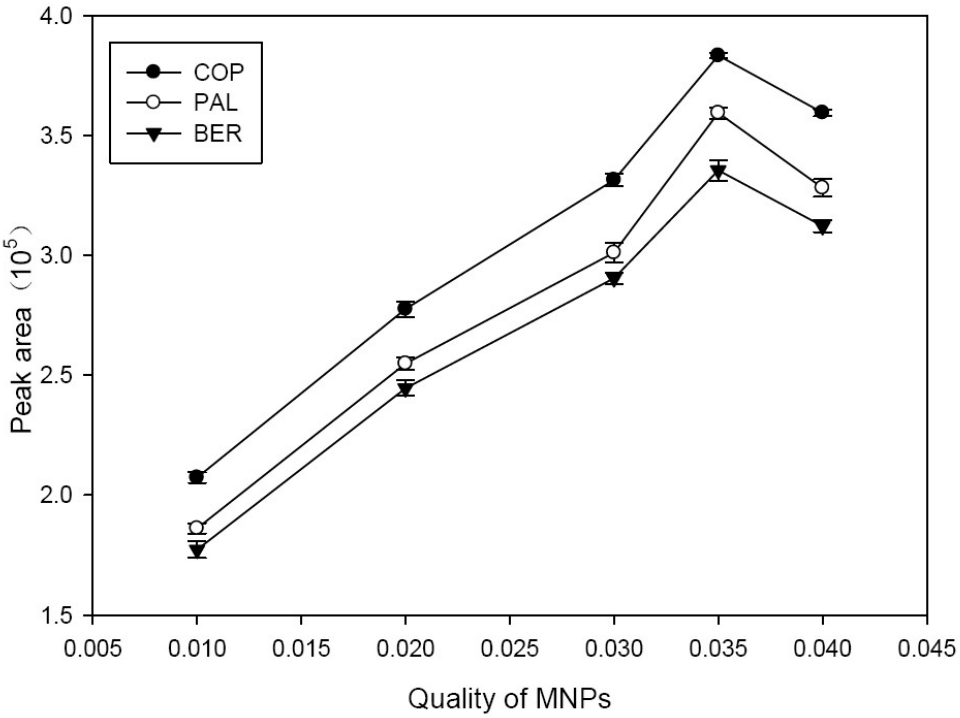

Figure 6 : Effect of the amount of MNPS experiment conditions: concentration of drugs, 200 ng/mL; volume of SDBS, 0.4mL; amount of $MgCl_2$, 1.2g; pH, 4.0.

(d) pH

In recently developed CPEs, schemes based on ionic surfactants were used to effectively extract charged analytes[25]. The charge density of the minera oxide surface is a main factor affecting the adsolubilization of analytes, and it varies strongly with pH. In effect, pH is a very important parameter for the adsorption of target compounds. The pH of the standard solution was adjusted with the addition of 10 mL of buffer solution, and its value was varied from 2.0 to 7.0. The results for the optimization of the pH value are shown in Figure 7. The analytical signal for the extraction recovery reached its maximum at pH 4.0.

(e) Desorption condition

Organic solvents can easily disrupt the mixed hemimicelle structures, and the attachment of the analyte to the surface of the MNPS. The desorption of the analyte from the diatomite-coated Fe_3O_4 NPS was studied using different organic solvents, including acetonitrile, methanol, acetone, and the mixture of methanol/acetonitrile (1:1). The maximum extraction rate was observed when 0.2 mL of both methanol and acetonitrile (1:1 methanol/acetonitrile) was used. To improve the recoveries, diatomite-coated Fe_3O_4 NPS were sonicated for 20 s during each desorption process.

Method validation

To evaluate the proposed MNPS-CPE method, some parameters such as linearity, reproducibility, and EFs were determined under the described extraction conditions. The results are listed in TABLE 1. The calibration graph for each analyte was constructed by performing extraction from three standard solutions containing all the analytes at concentrations ranging from 1 ng/mL to 1000 ng/mL in triplicates. The calibration curve was linear in the range of 0.1–1000 ng/mL for the three target analytes. The calibration curves gave a high level of linearity, yielding coefficients of estimation (R^2) of 0.9998, 0.9999, and 0.9999 for berberine, palmatine, and coptisine respectively. The limit of detection (LOD) for the analytes, calculated at a signal-to-noise (S/N) ratio of 3, ranged around 0.3 ng/mL. The repeatability of the method, expressed as percentage relative standard deviations (%RSDs), was evaluated for five replicate experiments of aqueous standard solutions with concentrations of 10 μg/mL each alkaloid. The %RSDs were illustrating satisfactory repeatability. The EFs of the three alkaloid, which were derived from the chromatographic peak areas of a standard solution before and after extraction, were in the range of 40–50[26].

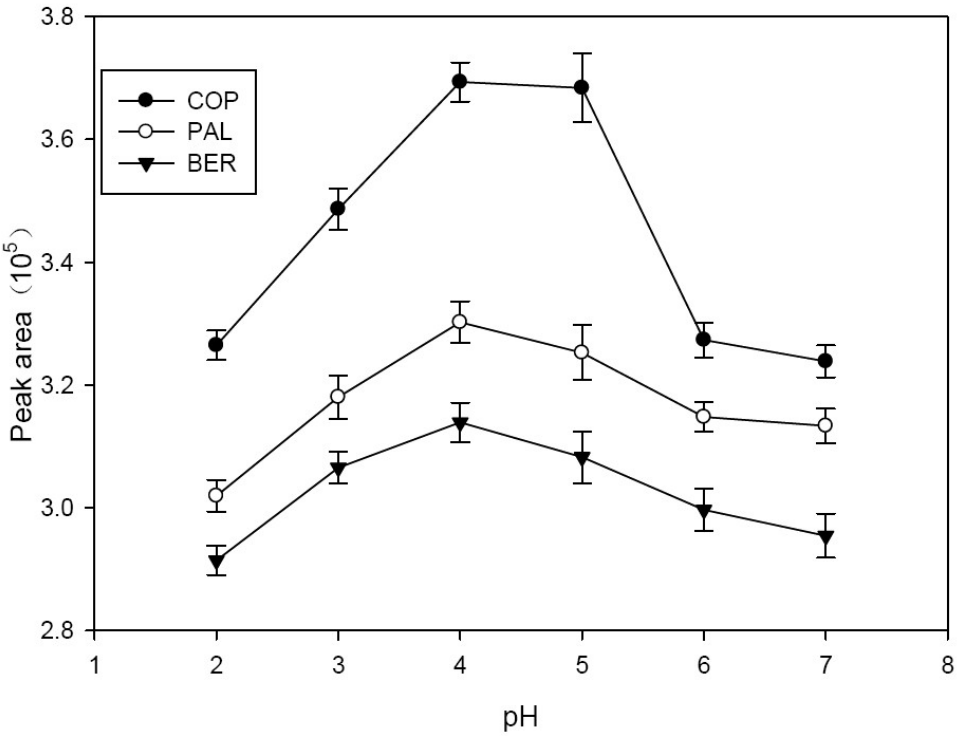

Figure 7 : Effect of the pH experiment conditions: concentration of drugs, 200 ng/mL; volume of SDBS, 0.4mL; amount of $MgCl_2$, 1.2g; amount of MNPS, 35mg.

TABLE 1 : Analytical parameter for the three isoquinoline alkaloid (n = 8)

Analyte	Linearity range (ng mL^{-1})	R^2	Precision (RSD, %), n = 8	Enrichment factor	LOD (ng mL^{-1})	LOQ (ng mL^{-1})
Berberine	5-2000	0.9998	1.28	43.7	0.03	0.05
Palmatine	5-2000	0.9999	1.32	46.1	0.03	0.05
Coptisine	5-2000	0.9999	1.14	47.6	0.03	0.05

Application of the method to actual samples

(a) Analysis of tablets

To validate the accuracy and precision of the proposed method under the selected conditions, Shuang huang lian and a clear particle pills were obtained, and milled through a 100 mesh sieve. Ten mg of the samples were taken, and boiled for half an hour. Afterwards, 0.1 mol hydrochloric acid was added. The sample was filtered with a 0.45μm film, and its pH value was adjusted to 4. accurate shift 2 mL of the above mentioned solution of Memberto colorimeter tube and then by the above extraction step enrichment and separation analysis liquid. Results of the analysis of the liquid sample and the spiked samples with HPLC-UV are shown in TABLE 2.

(b) Pharmacokinetic analysis

After oral administration of three 0.1 g berberine hydrochloride tablets by five healthy volunteers, the concentrations of berberine in their urine were determined by the MNPS-CPE method being described in the present study. The measured mean urine concentration–time profiles (n = 5) are represented in Figure 8.

Comparison of MR-SUF-DLLME method with other sample preparation techniques

Comparisons between the present MNPS-CPE method and other sample preparation techniques such as[27-35] in the aspects of linearity, LODs, %RSDs, and EFs are shown in TABLE 3. The analytical performance of the present MR-SUF-DLLME-HPLC method is comparable to that of other reported microextraction methods coupled with HPLC for the determination of the Chinese herbal medicine. Moreover, no centrifugation step is needed in MNPS-CPE, thus resulting in

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TABLE 2 : Determination of the recovery for this method (n = 5)

Sample	Base value (ng mL^{-1})			Quantity added (ng mL^{-1})			Mean recovery (%)		
	Berberine	Palmatine	Coptisine	Berberine	Palmatine	Coptisine	Berberine	Palmatine	Coptisine
Yiqingkeli	79.4	23.9	17.2	50	10	10	95.95 ± 1.25	97.56 ± 1.53	100.44 ± 2.01
				100	20	20			
Huanglian shuang qingwan	83.8	22.4	16.2	50	10	10	102.21 ± 1.70	98.65 ± 1.82	95.06 ± 1.54
				100	20	20			

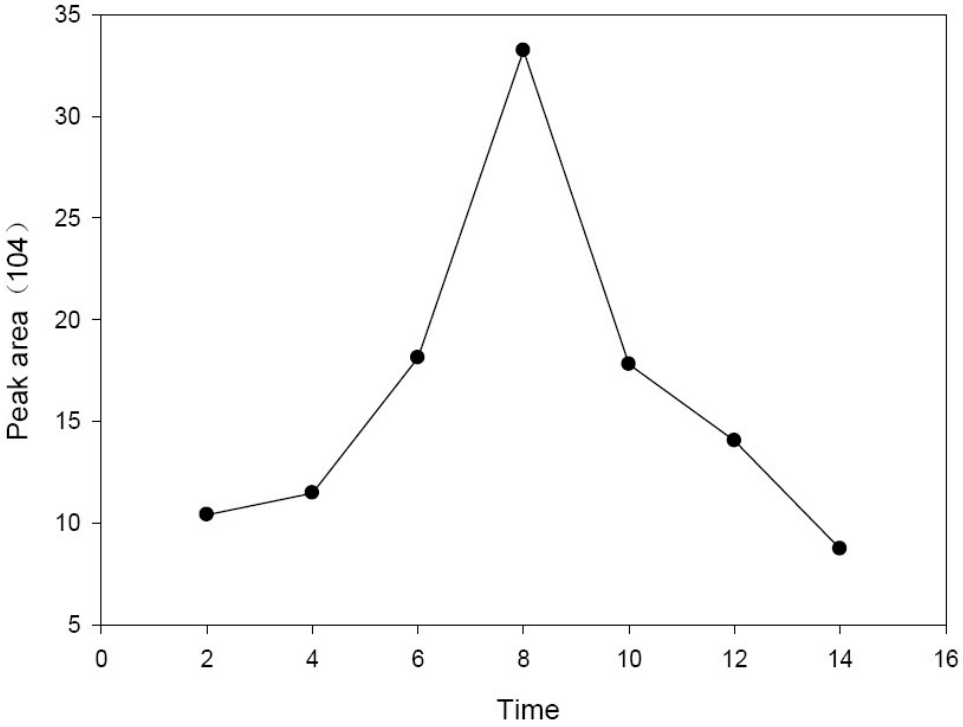

Figure 8 : The mean urine concentration–time profiles (n = 5)

TABLE 3 : Comparison linearity and LOD with other methods

Technique	Linear range (ng mL^{-1})			LOD (ng mL^{-1})			Reference
	BER	PAL	COP	BER	PAL	COP	
HPLC-UV	50-50000	–	–	10.0	–	–	[27]
HPLC-DAD	100000-880000	12500-300000	13500-270000	104	113	143	[28]
HPLC-MS-MS	1.0-250	1.0-250	–	1.0	1.0	–	[29]
HPLC-MS-MS	–	0.1-500	–	–	0.1	–	[30]
LC-ESI-MS	0.31-20	0.31-20	0.31-20	0.31	0.31	0.31	[31]
UPLC–PDA	322-96600	375-12500	–	60	75	–	[32]
UPLC-MS	6.45-645	4.5-450	–	1.2	1.5	–	[33]
Sweeping-CE	10-50	10-50	10-50	2.5	2.5	2.5	[34]
MEKC	103000-620000	20000-241000	31000-187000	34300	6700	13300	[35]
MNPS-CPE-HPLC-DAD	0.1-1000	0.1-1000	0.1 -1000	0.03	0.025	0.025	This work

EFs that are higher than most of the other reported extraction methods. Furthermore, the extraction process was modified into a single step, making it simpler than other DLPME-based methods[26].

CONCLUSIONS

A new magnetic adsorbent was prepared based on

modified Fe_3O_4 nanoparticles and incorporated into a diatomite. The developed MNPS-CPE method was successfully applied to the efficient enrichment of some Chinese herbal medicine samples. Based on the results obtained, the method simplified conventional CPE procedures without requiring any specialized apparatus, thereby eliminating specific sample handling treatments such as centrifugation. Furthermore, MNPS is stable, which means it could be used for many cycles with minimal loss on its recovery. To the best of our knowledge, this is the first report on the use of MNPS-CPE extract for the three alkaloids, namely berberine, palmatine, and coptisine. The MNPS-CPE has a great potential in exploring ways to improve other CPE methods.

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REFERENCES

[1] D.L.Giokas, Q.Zhu, Q.Pan; Journal of Chromatography A, **1251**, 33-39 **(2012)**.
[2] H.Heidari, H.Razmi, A.Jouyban; Journal of Chromatography A, **1245**, 1-7 **(2012)**.
[3] M.Faraji, Y.Yamini, M.Rezaee; Talanta., **81**, 831-836 **(2010)**.
[4] J.Chen, F.Wang, J.Liu, F.S.C.Lee, X.Wang, H.Yang; Anal.Chim.Acta, **613**, 184-195 **(2008)**.
[5] S.W.Sun, H.M.Tseng; J.Pharm.Biomed.Anal., **37**, 39-45 **(2005)**.
[6] L.Liu, X.Chen, Z.Hu; Microchim.Acta, **159**, 125-13 **(2007)**.
[7] C.G.Pinto, J.L.P.Pavon, B.M.Cordero, E.R.Beato, S.G.Sánchez; Journal of Analytical Atomic Spectrometry, **11**, 37-41 **(1996)**.
[8] J.L.Manzoori, G.Karim-Nezhad; Analytical Sciences, **19**, 579-583 **(2003)**.
[9] C.C.Nascentes, M.A.Z.Arruda; Talanta[J], **61**, 759-768 **(2003)**.
[10] S.Bova, R.Padrini, W.F.Goldman, D.M.Berman, G.Cargnelli; Exp.Therap., **261**, 318 **(1992)**.
[11] W.F.Chiou, M.H.Yen, C.F.Chen; Eur.J.Pharmacol., **204**, 35 **(1991)**.
[12] M.B.Bhide, S.R.Chavan, N.K.Dutta; Indian J.Med.Res., **57**, 2128 **(1969)**.
[13] H.Miyazaki, E.Shirai, M.Ishibashi, K.Niizima; J.Chromatogr., **152**, 79 **(1978)**.
[14] S.Guo, D.Li, L.Zhang, et al.; Biomaterials, **30**, 1881-1889 **(2009)**.
[15] H.Deng, X.Li, Q.Peng, et al.; Angewandte Chemie, **117**, 2842-2845 **(2005)**.
[16] A.Z.M.Badruddoza, K.Hidajat, M.S.Uddin; J.Colloid Interface Sci., **346**, 337-346 **(2010)**.
[17] A.Badruddoza, G.S.S.Hazel, K.Hidajat, M.Uddin; Colloids Surf.A: Physicochem.Eng.Aspects, **367**, 85-95 **(2010)**.
[18] K.Madej; TrAC Trends in Analytical Chemistry, **28**, 436-446 **(2009)**.
[19] Z.S.Ferrera, C.P.Sanz, C.M.Santana, J.J.S.Rodriguez; Trends Anal.Chem., **23**, 469-479 **(2004)**.
[20] T.Madrakian, F.Ghazizadeh; Journal of Hazardous Materials, **153**, **(2008)**.
[21] Yan Liu, Hai Fang Li, Jin-Ming Lin; Talanta., **77**, 1037-1042 **(2009)**.
[22] J.Ding, Q.Gao, D.Luo, Z.G.Shi, Y.Q.Feng; J.Chromatogr.A, **1217**, 7351 **(2010)**.
[23] H.F.Zhang, Y.P.Shi; Analyst., **137**, 910 **(2012)**.
[24] H.Xu, N.Tong, L.Cui, et al; Journal of Magnetism and Magnetic Materials, **311**, 125-130 **(2007)**.
[25] E.K.Paleologos, D.L.Giokas, M.I.Karayannis; TrAC Trends in Analytical Chemistry, **24**, 426-436 **(2005)**.
[26] Y.Zhang, H.K.Lee; Journal of Chromatography A, **1249**, 25-31 **(2012)**.
[27] P.L.Tsai, T.H.Tsai; J.Chromatogr.A, **961**, 125-130 **(2002)**.
[28] L.H.Yin, B.N.Lu, Y.Qi, L.N.Xu, X.Han, Y.W.Xu, J.Y.Peng, C.K.Sun; J.Pharm.Biomed.Anal., **49**, 1101-1108 **(2009)**.
[29] Y.Deng, Q.Liao, S.Li, K.Bi, B.Pan, Z.Xie; J.Comatogr.B, **863**, 195-205 **(2008)**.
[30] J.Huang, G.Wang, Y.Jin, T.Shen, W.Weng; J.Chromatogr.B, **854**, 279-285 **(2007)**.
[31] S.Yu, X.Pang, Y.Deng, L.Liu, Y.Liang, X.Liu, L.Xie, G.Wang, X.Wang; Int.J.Mass Spectrom., **268**, 30-37 **(2007)**.
[32] J.Chen, F.Wang, J.Liu, F.S.C.Lee, X.Wang, H.Yang; Anal.Chim.Acta, **613**, 184-195 **(2008)**.
[33] S.W.Sun, H.M.Tseng; J.Pharm.Biomed.Anal., **37**, 39-45 **(2005)**.
[34] L.Liu, X.Chen, Z.Hu; Microchim.Acta, **159**, 125-131 **(2007)**.
[35] K.L.Li, S.J.Sheu; Anal.Chim.Acta, **313**, 113-120 **(1995)**.