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Automated Dispersive Solid-Phase Extraction Using Dissolvable Fe_3O_4-Layered Double Hydroxide Core–Shell Microspheres as Sorbent

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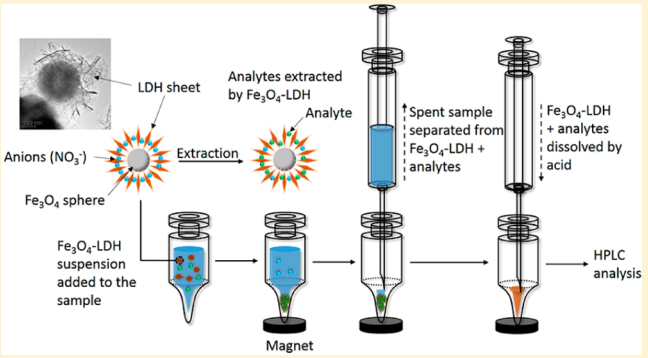
Supporting Information

ABSTRACT: Automation of dispersive solid-phase extraction (d-SPE) presents significant challenges. Separation of the sorbent from the spent sample cannot be conducted without manual operations, including centrifugation, a widely used means of isolating a solid material from solution. In this work, we report an approach to d-SPE using dissolvable magnetic Fe_3O_4-layered double hydroxide core–shell microspheres as sorbent to enable automation of the integrative extraction and analytical processes. Through magnetic force, the sorbent, after extraction, was isolated from the sample and then dissolved by acid to release the analytes. Thus the customary analyte elution step in conventional SPE was unnecessary. The automated d-SPE step was coupled to high-performance liquid chromatography (HPLC) with photodiode array detection for determination of several pharmaceuticals and personal care products (PPCPs) [acetylsalicylic acid (ASA), 2,5-dihydroxybenzoic acid (DBA), 2-phenylphenol (PP), and fenoprofen (FP)] in aqueous samples. For the automated d-SPE process, experimental parameters such as agitation speed, temperature, time, and pH were optimized. The results showed that this method provided low limits of detection (between 0.021 and 0.042 μg/L), good linearity ($r^2 \geq 0.9956$), and good repeatability of extractions (relative standard deviations ≤4.1%, $n = 6$). The optimized procedure was then applied to determination of PPCPs in a sewage sample and ASA and FP in drug preparations. This fully automated extraction–HPLC approach was demonstrated to be an efficient procedure for extraction and analysis of ASA, DBA, PP, and FP in these samples.



In the past few years, various solid-phase extraction (SPE) methods have been widely applied as sample preparation technology in water analysis, such as cartridge-, column-, and membrane disk-based SPE,[1−3] headspace or direct immersion solid-phase microextraction (SPME),[4,5] microextraction by packed sorbent (MEPS),[6] and stir-bar sorptive extraction (SBSE).[7] These procedures represent the trend toward miniaturization and/or possible automation or semiautomation, affording environmental friendliness and higher extraction efficiency.[1,2,4−9] For instance, some of the above-mentioned methods can be fully automated (e.g., cartridge-based SPE and SPME). However, for these methods, specialized devices to hold or immobilize the sorbents are needed.[1−10] This can have some disadvantages. Taking SPE as an example, immobilization of the sorbent with a cartridge limits the contact between sorbents and analytes. In addition, in this procedure, relatively large sorbent amounts (typically hundreds of milligrams) and sample volumes are required.

Dispersive solid-phase extraction (d-SPE), which was advanced by Anastassiades et al. in 2003,[11] has been developed as a valuable alternative SPE technology.[12−24] It forms part of the QuEChERS (quick, easy, cheap, effective, rugged, safe) procedure that usually includes salt-out extraction as the first step and d-SPE as the second. QuEChERS has been mainly applied to analysis of pesticides in fruits and vegetables.[25,26] However, d-SPE, by itself as an independent sample preparation method, has been used in analysis of a wider range of analytes (pharmaceuticals,[21] UV filters,[16] food additives,[27] etc.) in various aqueous samples (water,[14,22] urine,[27] or blood[21]). In d-SPE, the sorbent is dispersed in a sample solution and separated from the latter after extraction. Compared to other sorbent-based procedures (e.g., cartridge-based SPE), the extraction efficiency of d-SPE is high since there is increased active contact area between the analytes and the dispersed sorbent. Thus, extraction time is generally reduced and some disadvantages such as channeling or blockage, that occur frequently in conventional SPE, can be

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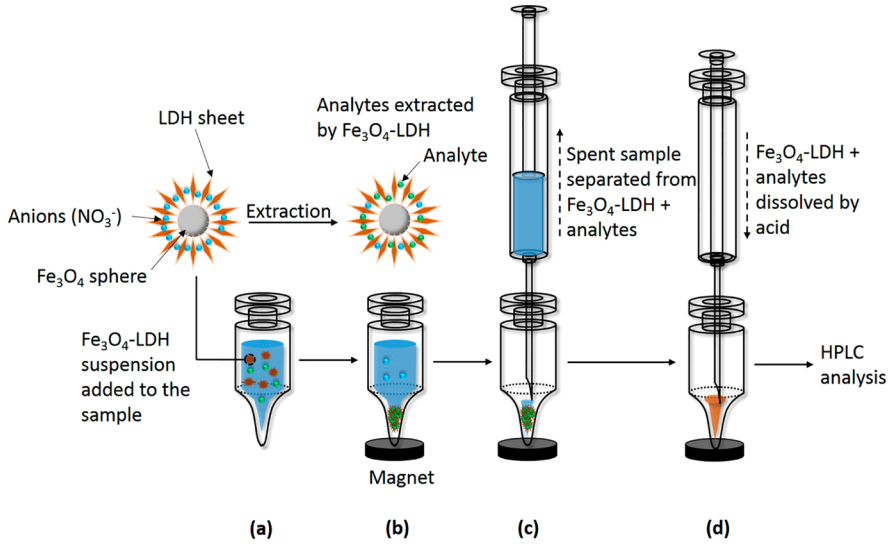

Figure 1. Schematic of automated d-SPE. Collection of the final extract and injection into the HPLC system are also automated.

avoided.[16] Unlike cartridge-based SPE, an additional benefit of d-SPE is that in-house-prepared sorbents may be used conveniently without requiring them to be immobilized in a cartridge. On the other hand, there are difficulties in automating d-SPE since the two separation steps (isolation of sorbent from sample solution after extraction, and separation of eluent and analyte-enriched sorbent after elution) usually require centrifugation. Filtering may be used as in a new filter-vial d-SPE concept, but it is not uncommon for some analytes to be retained by the filter material.[28] These steps are also difficult to couple with others (e.g., analysis) automatically and seamlessly. This disadvantage limits the applicability of d-SPE when a large number of samples are considered, since in such a situation, automation would be desirable.

Notwithstanding the above, a commercial automated d-SPE approach, called disposable pipet extraction (DPX), is available.[29,30] Here, loose sorbent is encased in a proprietary closed pipet device. The method is limited, however, by the types of sorbents available that are supplied only in the pipet format, by a small number of vendors. It is generally troublesome to attempt to use one's own sorbent for DPX, since the pipet device is a specialized item. So far DPX is generally limited to analysis of pesticides in fruits and vegetables.[29−31] To conduct DPX, the sample (fruits and vegetables) needs to be pretreated (homogenized), and the analytes are taken into a relatively cleaner liquid sample. DPX is then conducted on the latter. For DPX, the amount of sorbents used is >100 mg,[29,30,32] making it less than environmentally friendly (i.e., wasteful). Thus, an automated d-SPE approach that allows wider accessibility to those who wish to apply their own specially tailored sorbents is desirable.

Layered double hydroxides (LDHs) are a class of two-dimensional layered materials that have the general formula $[M^{2+}_{1-x}M^{3+}_{x}\ (OH)_2]^{q+}(X^{n-})_{q/n}{\cdot}yH_2O$, where M^{2+} is a divalent cation, M^{3+} is a trivalent cation, and X is an interlayer anion.[33] LDHs have high anion-exchange capacities, with large surface area, and the interlayers have variable sizes. They have good thermal stabilities and are water resistant.[34] Due to these advantageous properties, the application of LDHs as sorbents has been actively investigated.[35] An interesting feature of these sorbents is that they dissolve when the pH of the solution is lower than 4. Thus the analyte elution step, as needed in conventional SPE, can be obviated by dissolving the sorbent in acid after extraction and separation from the sample solution, as reported previously.[27] Earlier, Duan and co-workers[36] reported the use of LDHs coated on the surface of Fe_3O_4 microspheres for removal of proteins from biosamples. Magnetism was utilized for phase separation of the sorbent from the sample solution. In this manner, the centrifugation step was rendered unnecessary, although all the other usual SPE operations were conducted manually.

Pharmaceuticals and personal care products (PPCPs) include thousands of chemicals that are found in medicinal drugs and active ingredients of personal care products, as well as those chemicals used in the agricultural and animal husbandry industries.[37] They have been detected in water supplies and sewage effluents from all over the world.[38−41] They are considered as harmful contaminants affecting wildlife and humans[37] and have thus been attracting attention from environmental scientists.

The aim of this work is to synthesize Fe_3O_4-layered double hydroxide (Fe_3O_4-LDH) core−shell microspheres and utilize them as a dissolvable sorbent in a new, fully automated d-SPE approach for determination of four types of PPCPs [Table S1 in Supporting Information: acetylsalicylic acid (ASA), 2,5-dihydroxybenzoic acid (DBA), 2-phenylphenol (PP), and fenoprofen (FP)] in aqueous samples. The main parameters influencing extraction efficiency were investigated and optimized. The procedure was applied to high-performance liquid chromatographic (HPLC) determination of PPCPs in a sewage sample and ASA and FP in drug preparations in capsule form to demonstrate the feasibility of the automated approach.

EXPERIMENTAL SECTION

Apparatus and Reagents. ASA (99%), DBA (99%), PP (99%), FP (99%), and sodium acetate (99%) were purchased from Sigma−Aldrich (St. Louis, MO). Magnesium nitrate hexahydrate (98%) and aluminum nitrate nonahydrate (98%) were purchased from Alfa Aesar (Heysham, England). Sodium hydroxide (99%) was obtained from Dickson (Singapore). Iron(III) chloride (98%) was bought from Acros Organics (Geel, Belgium). HPLC-grade acetonitrile was procured from Tedia (Fairfield, IA). Trifluoroacetic acid (TFA, 98%) was obtained from Fluka (St. Louis, MO). A sewage sample was

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collected from a wastewater treatment plant. Aspirin and fenoprofen calcium capsules were bought from a local drugstore.

X-ray diffraction (XRD) measurements were made on a Siemens (Karlsruhe, Germany) D5005 X-ray diffractometer (Cu Kα = 1.5418 Å). Magnetic hysteresis data were obtained on a Lakeshore 7404 vibrating sample magnetometer (Westerville, OH). Transmission electron micrographs (TEM) were taken on a JEOL JEM-3010 instrument (Tokyo, Japan) at 300 kV.

Synthesis of Fe_3O_4-LDH Core–Shell Microspheres. Fe_3O_4-LDH core–shell microspheres were synthesized according to a previous report.[36] (Complete details are given in Supporting Information.)

Automated d-SPE Procedure. d-SPE was performed automatically by a CTC Analytics CombiPAL autosampler with a built-in agitator (Zwingen, Switzerland) and with the aid of Cycle Composer software (CTC Analytics). A 100 μL Hamilton G100-22S-3 syringe (Reno, NV) controlled by the autosampler was used for both extraction and injection of the extracts into the HPLC system. All the following steps were performed automatically: First, a vial (1.5 mL) containing the sorbent suspension (5 mg of Fe_3O_4-LDH in 1 mL of pure water) was transferred by the autosampler to the agitator and agitated at 600 rpm for 15 s to maintain its homogeneity. After agitation, 20 μL of the suspension was withdrawn into the syringe and then injected into the aqueous sample (1 mL) (Figure 1a). The sample vial was transferred to the agitator and agitated during d-SPE. After extraction, the sample vial was transferred to an autosampler tray position in which a magnet was prepositioned. The vial was seated in this position for 1 min in order for the magnet to attract, immobilize, and isolate the sorbent (Figure 1b). With the vial maintained as such, the syringe was programmed to remove and discard 1010 μL of supernatant [(100 μL × 10 times) + (10 μL × 1 time)]. (Since the autosampler is a one-syringe system, all operations were conducted with this single syringe.) Ten microliters of supernatant and sorbent was left in the vial (Figure 1c). The syringe, after rinsing, was then controlled to withdraw 10 μL of 50% TFA from a reagent vial to add to the sample vial, which was then transferred to the agitator for agitation at 600 rpm at 50 °C for 5 min to dissolve the sorbent. After this, the vial was transferred out of the agitator. Finally, 10 μL of the extract was collected and injected into the HPLC system (Figure 1d). The syringe was rinsed, and the d-SPE and HPLC analysis cycle was then repeated for each subsequent sample. In this work, we demonstrated the conduct of six automated d-SPE–HPLC analysis experiments (i.e., involving six extract injections) consecutively and uninterruptedly. (Sample pretreatment of drug preparations prior to d-SPE was conducted automatically as well; details are provided in Supporting Information.)

HPLC Analysis. Chromatographic analysis was carried out on a Shimadzu 8080 LC system (Kyoto, Japan) consisting of two pumps, a column oven, and a photodiode array detector. The CTC Analytics CombiPAL autosampler was directly coupled to the HPLC system. Data acquisition and processing were accomplished by use of LC-Solution (Shimadzu) data analysis software. A Phenomenex Kinetex-C18 (Torrance, CA) column (100 mm × 4.60 mm internal diameter, 2.6 μm particle size) was used for separation. The column temperature was held at 40 °C. The mobile phase consisted of water (0.1% TFA) and acetonitrile (0.1% TFA) and was applied in a gradient mode. The gradient was started with 20% acetonitrile (0.1% TFA) and linearly increased to 80% over 20 min at a flow rate of 0.4 mL/min. The detection wavelength was set at 226 nm.

RESULTS AND DISCUSSION

Characterization of Fe_3O_4-LDH Core–Shell Microspheres. TEM images of pristine Fe_3O_4 and Fe_3O_4-LDH core–shell microspheres are shown in Figure 2. It can be observed that the spherical pristine Fe_3O_4 particles (Figure 2a) are approximately 300 nm in diameter. In Fe_3O_4-LDH (Figure 2b,c), the LDH sheets are coated in a flowerlike morphology. With the added layer of LDH on the surface, the Fe_3O_4-LDH core–shell microspheres have a diameter of ca. 500–600 nm. [More detailed descriptions (XRD patterns and magnetic properties) of the sorbent are given in Supporting Information.]

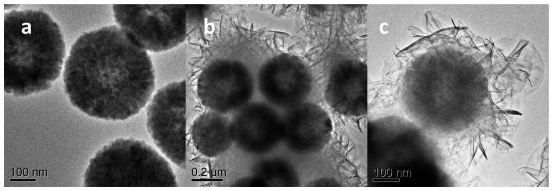

Figure 2. TEM images of (a) Fe_3O_4 and (b, c) Fe_3O_4-LDH.

Extraction Optimization. In d-SPE, extraction efficiency depends on the contact probability between analytes and sorbent. Without stirring, the sorbent could precipitate. Thus agitation is needed to maintain the dispersion of the sorbent. Agitation speeds from 200 to 700 rpm were investigated. It can be seen from Figure 3a that enrichment factors (EFs, where EF is defined as the ratio of analyte concentration in extraction solvent after extraction to initial analyte concentration in aqueous sample solution) increased with increasing agitation speed and reached a maximum at 600 rpm. In general, high agitation speed leads to high dispersity of the sorbent that enhances extraction, via provision of the maximum contact area. Thus, 600 rpm was chosen as the most favorable agitation speed.

The Fe_3O_4-LDH extracted analytes through a direct anion-exchange process. The extraction temperature can affect the orientation of analytes in the interlayers of LDHs, and proper orientation is conductive to the formation of interlayered LDHs.[42] The effect of temperature on extraction was thus evaluated by considering a range between 30 and 70 °C. Figure 3b shows that the EFs (except for ASA and PP) increased significantly with increasing temperature. From the plots shown, we can conclude that the proper arrangement can be achieved for most analytes at above 60 °C. To achieve the best extraction efficiency with minimal energy consumption, 60 °C was considered as the most favorable extraction temperature.

A series of extraction times ranging from 10 to 60 min was studied to evaluate the effect of this parameter. The results are shown in Figure 3c. When extraction time was increased from 10 to 20 min, the EFs of all the analytes increased quickly and then remained constant beyond 20 min. Thus, 20 min was adopted as the extraction time.

The influence of pH on extraction based on LDH was investigated. The pH values of the sample solution were adjusted in a range of between 5 and 11 to investigate the effect. As can be seen in Figure 3d, initially the EFs increased when pH was raised, since the ionization of analytes was enhanced at

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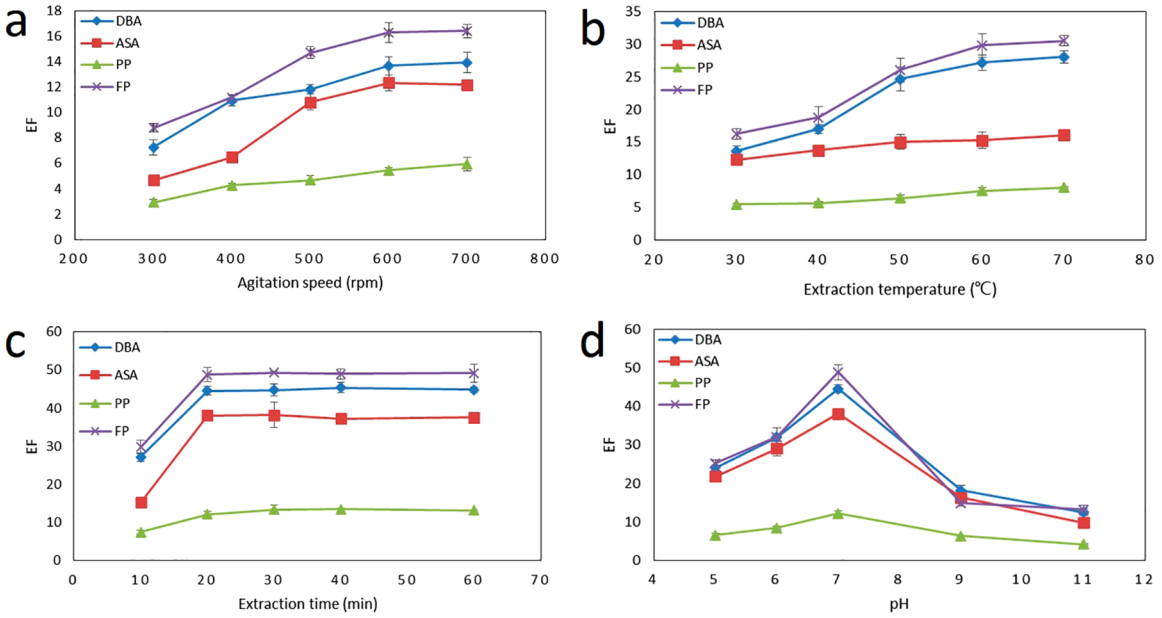

Figure 3. Effect of various parameters on extraction. Conditions: 50 μg/L analytes in spiked sample solution; sample volume, 1 mL. (a) Effect of agitation speed: extraction time 10 min, temperature 30 °C, pH 7. (b) Effect of extraction temperature: agitation speed 600 rpm, extraction time 10 min; pH 7. (c) Effect of extraction time: agitation speed 600 rpm, extraction temperature 60 °C, pH 7. (d) Effect of pH: agitation speed 600 rpm,; extraction temperature 60 °C, extraction time 20 min. Error bars show the standard deviation (n = 3).

a higher pH. However, at a pH value >7, since the concentration of competing OH^- ions increased,[43] all the analytes showed a drop in EFs. In consideration of these observations, a pH of 7 was considered optimal in d-SPE. The difference in EF values among the four analytes is mainly due to their negatively charged molecular structures. Since PP only has one phenolic hydroxyl group, its anion-exchange ability is weakest compared to the other three analytes. The influence of ionic strength on extraction was also investigated. No effect on extraction efficiency was observed. Full details are provided in Supporting Information.

Method Evaluation. Linearity, precision, repeatability, limits of detection (LOD), and limits of quantitation (LOQ) were measured to assess the performance of the present method by using pure water spiked with the analytes as sample. From the results in Table 1, it can be seen that good linearity of

Table 1. Quantitative Results of Automated d-SPE–HPLC

analyte	linearity (μg/L)	r^{2a}	RSD,[b] % (n = 6)	LOD (μg/L)	LOQ (μg/L)	EF[c]
ASA	0.1–100	0.9956	3.0	0.021	0.071	46
DBA	0.1–100	0.9981	4.1	0.022	0.074	38
PP	0.5–100	0.9990	2.9	0.042	0.139	14
FP	0.5–100	0.9975	2.5	0.037	0.122	49

[a]Coefficient of determination. [b]Calculated from samples spiked at LOQ levels. [c]Calculated from samples spiked at a concentration of 50 μg/L.

the calibration plots, with coefficients of determination (r^2) ≥ 0.9956, were obtained. To evaluate the precision of the method, the relative standard deviations (RSD, %, n = 6) were calculated for the extraction and analysis of spiked water samples at LOQ levels of the analytes. Based on a signal-to-noise (S/N) ratio of 3, the LODs ranged from 0.021 to 0.042 μg/L. The LOQ, based on S/N = 10, ranged from 0.071 to 0.139 μg/L. As can be seen in Table 2, for ASA and DBA, the LODs obtained were lower than those achieved by other types of SPE.[44−47] The LODs for FP and PP were slightly higher than those reported in other cartridge-based SPE methods but still within the same order of magnitude.[48−50]

A comparison of our results with those of other fully automated SPE procedures is shown in Table 3. It can be seen that dedicated, and mainly commercial, devices are required in all the latter methods.[1,2,4−10,15,29,30,51] Therefore, in these cases, if researchers wished to use their own specially prepared, customized sorbents, these must be fixed in the devices (cartridges, membranes, fibers, capillaries, stir bars, syringe insets, pipets etc.) before use. On the other hand, our work provides an approach that allows in-house-synthesized sorbent to be applied to automated SPE without any specialized devices required. Compared to most fully automated methods (cartridge or membrane disk-based online SPE, headspace SPME, direct immersion SPME, in-tube SPME, MEPS, DPX), in the present work only 1 mL of sample and 0.01 mL of acid (as solvent) were needed. Although SBSE is solventless, a cold trap (−5 °C) and thermal desorption processes (290 °C) make this technology hard to implement without additional accessories and therefore expense. Moreover, the extraction time is considerable (250 min) due to the low extraction efficiency. For DPX, due to the small ratio of sample volume to elution solvent volume,[29,30] the EF value is low (2–5-fold) and possibly cannot provide satisfactory LODs for low concentration analytes. In contrast, the present procedure consumed only 0.1 mg of sorbent and much higher EFs (14–49-fold) could be obtained. Moreover, it did not require any specialized device to hold the sorbent.

Real Sample Analysis. A sewage sample was subjected to automated d-SPE–HPLC to evaluate the real-world applicability of the method. In the sample, ASA was detected at a concentration of 2.39 μg/L. The existence of this compound in sewage and river has been reported previously.[52] In one study, the average concentration of ASA was determined to be ca. 1 μg/L in the effluents of municipal sewage treatment plants in

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Table 2. Comparison of Limits of Detection of Different Methods

method[a]	sorbent or cartridge	sample	LOD (μg/L)	ref
		ASA		
SPE−LC/MS	Fe_3O_4−SiO_2 nanoparticles	wastewater	0.05	44
SBSE−HPLC-DAD	polyurethane	river water	0.8	45
		DBA		
MEPS−UHPLC-PDA	C8	wine	0.085	46
SPE−LC/MS^2	Oasis HLB	human plasma	5.05	47
		PP		
SPE−GC/MS	C18	wastewater	0.25	48
SPE−GC/MS	Oasis MAX	sewage	0.01	49
		FP		
online SPE−LC-DAD/MS	LiChrosphere RP-18	tap water	0.03	50
SPE−GC/MS	Oasis MAX	sewage	0.01	49

[a]MS, mass spectrometry; SBSE, stir-bar sorptive extraction; DAD, diode array detection; MEPS, microextraction by packed sorbent; UHPLC-PDA, ultra-high-pressure liquid chromatography with photodiode array detection.

Table 3. Comparison with Other Fully Automated SPE Methods

method[a]	device/sorbent[b]	sorbent mass (mg)	sample volume (mL)	solvent volume (mL)	extraction elution time (min)	ref
online SPE (cartridge-based)	PLRP-S cartridge /cross-linked styrene−divinylbenzene		5−250	0.5−1	60	1,8
online SPE (membrane disk-based)	XAD-2 membrane extraction disks		10.5	2.5	55	2
headspace SPME	fiber/polyacrylate; derivatization with PFBAY		10	0.2 (PFBAY)	25	4
direct immersion SPME	fiber/polyacrylate; derivatization with BSTFA		100	0.05 (BSTFA)	>60	5
in-tube SPME	capillary GC column with coating/Omegawax 250; styrene−divinylbenzene polymer		1−1.4	0.038−0.04		10,51
MEPS	MEPS syringe with barrel insert and needle/C18	1−4	2−4	0.025−0.05	ca. 10	6,9
SBSE	fiber/poly(dimethylsiloxane)		20−40		250	7
DPX	DPX tip/anhydr $MgSO_4$, 1° and 2° amine, graphitized carbon black, and C18	112.5−250	0.5−1	0.25−0.5		29,30
d-SPE	Fe_3O_4-LDH (prepared in house)	0.1	1	0.01	30	this work

[a]DPX methods were conducted on juice from fruits and vegetables; all other references reported methods that were conducted on water samples. MEPS, microextraction by packed sorbent; SBSE, stir-bar sorptive extraction; DPX, disposable pipet extraction; [b]PLRP, polymeric reversed phase; PFBAY, pentafluorobenzaldehyde; BSTFA, *N*,*O*-bis(trimethylsilyl)trifluoroacetamide.

Table 4. Summary of Results from Analysis of PPCPs in Sewage by Fully Automated d-SPE−HPLC

	nonspiked		spiked at 0.5 μg/L		spiked at 10 μg/L		spiked at 100 μg/L	
analyte	concn (μg/L)	RSD, % (n = 6)	RR[a] (%)	RSD, % (n = 6)	RR[a] (%)	RSD, % (n = 6)	RR[a] (%)	RSD, % (n = 6)
ASA	2.40	2.6	99.7	3.3	97.9	1.3	98.3	2.2
DBA	nd		97.2	2.4	96.3	2.4	97.4	3.0
PP	<LOQ		100.5	1.7	97.5	4.1	96.8	1.5
FP	<LOQ		102.3	3.9	100.2	1.9	99.1	3.4

[a]Relative recovery (RR) = ($concn_{total}$ − $concn_{nonspiked}$)/$concn_{spiked}$.

Germany.[53] The levels of PP and FP were found to be below their LOQs. DBA was not detected, indicating its absence or that its concentration was below the LOD of the method. To assess matrix effects, the sewage sample was also spiked at 0.5, 10, and 100 μg/L concentration levels of each compounds, respectively, and subjected to the procedure. The results are shown in Table 4. The relative recoveries (RRs) of four analytes were ≥96.3%. The RSDs were ≤4.1%, n = 6. Figure 4 shows the chromatogram of the unspiked and spiked sewage sample extracts.

To further demonstrate the applicability of the present procedure, aspirin and fenoprofen calcium capsules (containing ASA and FP, respectively) were considered. The powder (1 mg) from each capsule was placed separately in 20 mL of 0.2% HCl solution (complete extraction and analytical processes were conducted automatically, as described in Supporting Information). From the results shown in Table 5, it can be seen that the determined amounts of active ingredients were 101% ASA (in aspirin, labeled amount 90−110%) and 98.4% FP (in fenoprofen calcium, labeled amount 95−105%), respectively. These values agree very well with the information given on the labels of the drugs. The above results indicate the applicability of automated d-SPE to real sample analysis.

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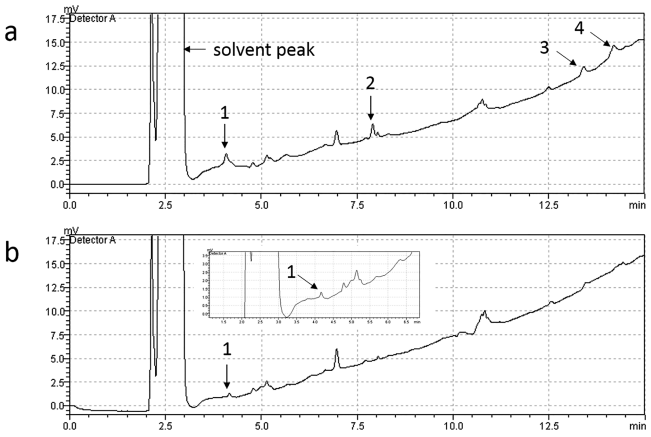

Figure 4. Liquid chromatogram of extract after automated d-SPE of (a) sewage sample spiked with analytes at concentration levels of 10 μg/L of each compound and (b) unspiked sewage sample. Conditions: agitation speed 600 rpm, extraction temperature 60 °C, extraction time 20 min, pH 7. Peak identities: (1) ASA, (2) DBA, (3) PP, and (4) FP.

Table 5. Results of Analysis of Aspirin and Fenoprofen Calcium Capsules by Fully Automated d-SPE–HPLC

drug	active ingred (g/g)	expected value (g/g)	determined amount (%)	RSD, % (n = 3)	labeled amount (%)
aspirin	ASA, 0.873	0.864	101	2.5	90–110
fenoprofen calcium	FP, 0.984	1	98.4	3.7	95–105

CONCLUSION

In the present work, we propose a fully automated procedure integrating dispersive solid-phase extraction (d-SPE), with magnetic dissolvable Fe_3O_4-LDH core–shell microspheres as sorbent, and HPLC to determine PPCPs in aqueous samples and pharmaceuticals in drug preparations. Due to the properties of the microspheres (magnetic and dissolvable), the phase separation steps in d-SPE could be completely automated, the first time this has been done for dissolvable LDH. Thus, the advantages of d-SPE (simplicity and effectiveness) and automation (speed and precision) were retained. The present procedure also afforded manual labor-free convenience after extraction and in the seamless integration with HPLC analysis. Additionally, in the developed method, only small volumes of both sample (1 mL) and solvent (10 μL) were required. Moreover, even though the sorbent could not be recycled (since it was dissolved before analysis), only a small amount (ca. 0.1 mg) was needed each time. The entire process was thus efficient and economical. This fully automated method was demonstrated successfully for its practicality and applicability to the analysis of PPCPs in water samples and pharmaceuticals in drug preparations and can be considered for other compounds in similar matrices. With new and tailor-made dissolvable LDHs, it should be possible to extract contaminants in water by this sample preparation approach. For example, LDH intercalated chelating agents (e.g., ethylenediamintetraacetic acid) can be applied to extract cations (e.g., Cu^{2+}). There is, therefore, great potential to further expand the applicability of the developed procedure.

ASSOCIATED CONTENT

Supporting Information

Additional text describing synthesis and characterization of Fe_3O_4-LDH core–shell microspheres, sample pretreatment, and effect of ionic strength on extraction; three figures showing XRD patterns and magnetic hysteresis loops for LDH, Fe_3O_4, and Fe_3O_4-LDH and effect of ionic strength on extraction; and two tables listing structures of analytes and binding capacities. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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