Analytical and Bioanalytical Chemistry

Electronic Supplementary Material

Combination of magnetic dispersive micro solid-phase extraction and supramolecular solvent-based microextraction followed by high-performance liquid chromatography for determination of trace amounts of cholesterol-lowering drugs in complicated matrices

Somayeh Arghavani-Beydokhti, Maryam Rajabi, Alireza Asghari
**Effect of salt addition**

The presence of salts in aqueous media may have different effects on the extraction efficiency. In general, the addition of a salt to an aqueous sample solution causes a decrease in the solubility of the analytes present in the solution, thereby, the extraction efficiency can improve significantly (a phenomenon referred to as the salting-out effect). However, at a high salt concentration, the thickness of the Nernst diffusion film is larger, leading to a considerable reduction in the rate of diffusion of the solutes from the sample solution to the sorbent surface, and ultimately, a decrease in the efficiency of drug extraction (the salting-in effect). Therefore, the effect of salt (NaCl) concentration was studied in the range of 0-20% (w/v). As it can be seen in Fig. S1, salt addition causes a noticeable reduction in the drug microextraction, which can be due to the significant increase in the thickness of the Nernst film and the subsequent reduction in the drug diffusion rate.

![Fig. S1](image.png)

**Fig. S1** Effect of salt addition on Mdμ-SPE-SSME efficiency. Extraction conditions: volume of aqueous solution, 10 mL (containing 100 µg L⁻¹ of each cholesterol-lowering drug); pH value, 7.0; amount of magnetic LDHs, 5 mg; number of air agitation cycles, 20 cycles; elution volume, 100 µL
**Effect of number of extraction cycle**

The extraction time is defined as the repeated suction/injection cycles of the extraction solvent and sample solution mixture into a sample glass tube using a 10-mL glass syringe. Obviously, the extraction time plays an important role in obtaining the highest extraction efficiency within a least period of time. To achieve the best performance, the number of air-agitation cycles was investigated in the range of 1-20 cycles. By increasing the number of air-agitation cycles, the analytical signal improved up to 15 cycles of air agitation, and then remained constant (Fig. S2). Hence, 15 air agitation cycles were selected as the optimum extraction cycles for the further studies.

**Fig. S2** Effect of number of air agitation cycles on Mdμ-SPE-SSME efficiency. Extraction conditions: volume of aqueous solution, 10 mL (containing 100 µg L\(^{-1}\) of each cholesterol-lowering drug); pH value, 7.0; amount of magnetic LDH, 5 mg; no salt addition; elution volume, 100 µL
**Effect of eluent volume**

The dissolution of LDHs immediately after extraction, with pH adjustment, as well as releasing the adsorbed analytes into the sample solution is a superior advantage, leading to a great improvement in the extraction efficiency and a decrease in the analysis time. In this work, trifluoroacetic acid (TFA) solution (8%, v/v) was also selected as an eluent for the dissolution of the LDH sorbent. To obtain an optimized volume of the elution solvent, various experiments were performed using different volumes of the TFA solution (50-125 µL). As it could be seen in Fig. S3, with the increment of the eluent volume up to 100 µL, the extraction efficiency promoted but then it was not effective. In other words, for a complete elution of the LDH sorbent, 100 µL of the TFA solution was sufficient, and no specific improvement was observed in the analytical signal with a higher eluent volume.

![Graph](image)

**Fig. S3** Effect of elution volume on Mdµ-SPE-SSME efficiency. Extraction conditions: volume of aqueous solution, 10 mL (containing 100 µg L\(^{-1}\) of each cholesterol-lowering drug); pH value, 7.0; amount of magnetic LDHs, 5 mg; no salt addition; number of air agitation cycles, 15 cycles
Effect of type of extraction phase

The type of supramolecular solvent (SUPRAS) is a key factor that greatly influences the extracting capability of the target compounds. In other words, the length of the hydrocarbon chain of alkylcarboxylic acids, the extracting component of SUPRAS, is extremely effective on the uptake of target analytes. It must be noted that the dissolution increases by increment of the alkyl chain length. Thus shorter alkylcarboxylic acids are preferred for analytical applications. For this purpose, three alkylcarboxylic acids, namely octanoic, decanoic and oleic acids, were tested. The results obtained (Fig. S4) showed that quantitative extraction efficiencies were obtained using a SUPRAS made up of decanoic acid, a medium-length hydrocarbon chain alkylcarboxylic acid. Therefore, it was selected for further experiments. On the other hand, coacervation was only obtained in solvents possessing a high ability to dissolve alkylcarboxylic acids, allowing the self-assembly of these amphiphiles, and being water-miscible. According to the above-mentioned statements, THF was the best choice for analytical purposes due to the higher dissolution of alkylcarboxylic acids.

![Graph showing effect of type of alkylcarboxylic acid on Mdµ-SPE-SSME efficiency under optimum condition for SPE method. Extraction conditions: pH, 2.5; no salt addition; amount of DeA, 40 mg; THF volume, 0.5 mL](image)

**Fig. S4** Effect of type of alkylcarboxylic acid on Mdµ-SPE-SSME efficiency under optimum condition for SPE method. Extraction conditions: pH, 2.5; no salt addition; amount of DeA, 40 mg; THF volume, 0.5 mL
**Effect of salt addition**

The effect of an added salt on the extraction efficiency was investigated in the concentration range of 0-20%. As it can be seen in Fig. S5, an added salt has a negative effect on a drug microextraction. This phenomenon can be related to the increment of electrostatic interactions between polar compounds and salt ions, ultimately reducing the microextraction of target compounds. Therefore, the experiments were carried out in the absence of a salt.

![Graph](image)

**Fig. S5** Effect of salt addition on Mdµ-SPE-SSME efficiency under optimum condition for SPE method. Extraction conditions: pH, 3.0; amount of DeA, 40 mg; THF volume, 0.5 mL