MODESTUM
OPEN ACCESS
Eurasian Journal of Analytical Chemistry
ISSN: 1306-3057
2018 13(3):em21
DOI: 10.20933/ejac/85176

Preconcentration and Determination of Ciprofloxacin with Solid-phase Microextraction and Silica-coated Magnetic Nanoparticles Modified with Salicylic Acid by UV-Vis Spectrophotometry

Mohsen Varakneshin [1], Mahmoud Ebrahimi [1*]

[1] Department of Chemistry, Mashhad Branch, Islamic Azad University, Mashhad, IRAN

Received 17 July 2017 ▪ Revised 15 November 2017 ▪ Accepted 26 December 2017

ABSTRACT

In the present age, the pharmaceutical application continues to increase and this results in the environmental pollution. As a result, pharmaceutical control is a common technique in many labs. This project is on the improvement of the procedure to determine a small amount of ciprofloxacin (CF) in bio-environmental sample. Regarding the fact that each method requires preliminary measures to preconcentrate and prepare analyte prior to measurement and recognition. In recent study, preconcentration of samples containing CF (as antibiotic) based on solid-phase microextraction method using silica-coated magnetic nanoparticles modified with salicylic acid (SA) was proposed which acted as sorbent. In addition, UV-Vis spectrophotometry was carried out to determine the amount of CF. The wavelength of maximum absorption (λ_{max}) for this drug was 275 nm. Also, the optimum conditions of various parameters such as pH of solution, amount of magnetic nanoparticles, time, the effect of stirring speed on the extraction and desorption, the rate of centrifugation, the volume of aqueous and organic-phases, temperature and salt effect were investigated. The dynamic range was obtained between 0.05-0.15 mg L^{-1}, LOD and RSD (%) were 0.002 mg L^{-1} and 1.878 respectively. Results showed using this procedure increased the concentration factor to 68.36. Relative recovery was achieved by spike method.

Keywords: ciprofloxacin, magnetic nanoparticles, solid-phase microextraction, UV-Vis spectrophotometry

INTRODUCTION

The quinolones have emerged as one of the most important classes of antibiotics of the previous decade. CF [1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperarinyl)-3-quinolone carboxylic acid] (**Figure 1**) is a synthetic fluoroquinolone derivative which has demonstrated broad-spectrum activity against many pathogenic Gram-positive and Gram-negative bacteria. The bacterial action of CF results from interference with enzyme DNA gyrase which is needed for the synthesis of bacterial DNA [1-4]. The drug is structurally related to different quinolones including cinoxacin, lomefloxacin, enoxacin, nalidixic acid, norfloxacin, pefloxacin and ofloxacin.

There is several interest in determining fluoroquinolones for the purpose of pharmaceutical quality control. Most of the analytical methods for the determination of CF employ high-performance liquid chromatography (HPLC). In 1998, Carlucci reported a review of the published HPLC assays that used fluorescence or UV detection [5]. Then, other works have been reported employing fluorescence detection [6-11] and UV detection [12, 13]. The HPTLC method has been developed for the determination and the purity control of CF in coated tablets [14, 15]. Other different methods were reported such as spectrophotometry [16-22], fluorimetry [22-24], capillary electrophoresis [25-32] and immunoassay [33, 34]. Both spectrophotometric [35-38] and chemiluminescent [39, 40] detection were proposed as automatic spectroscopy procedures.

✉ mohsenvarakneshin@yahoo.com ✉ m.ebrahimi@mshdiau.ac.ir **(*Correspondence)**

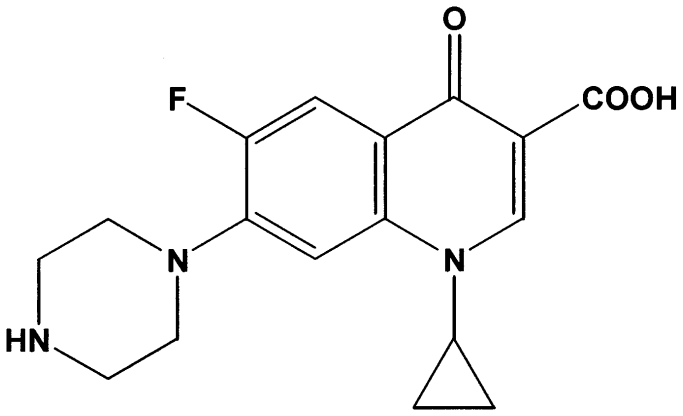


Figure 1. Structure of CF

UV-Vis spectrophotometry is considered as the most convenient analytical technique, because of its inherent simplicity and wide availability in most quality control laboratories.

Solid-phase microextraction, first introduced with Belardi and Pawaliszyn more than a decade ago [41], is a simultaneous sampling, matrix removal, preconcentration and simple technique. Solid-phase microextraction has been more and more used for sample preparations in analytical laboratories.

Magnetic nanoparticles, a new kind of nanometer-sized material, are widely used in the fields of biomedicine, biotechnology and as an efficient adsorbent with large specific surface area and small diffusion resistance [42-55].

Several methods have been reported to synthesize magnetic nanoparticles, such as hydrothermal synthesis [56], microemulsion [57], chemical co-precipitation [58], oxidation of Fe $(OH)_2$ by H_2O_2 [59], microwave irradiation [60], R-ray irradiation [61] and etc. Co-precipitation is the cheapest and simplest synthesis method.

However, it should be pointed out that pure inorganic magnetic nanoparticles (such as Fe_3O_4 and Fe_2O_3) can easily form extensive aggregates, which may alter their magnetic properties [51, 62]. Moreover, these are not target-selective and are unsuitable for several samples. A suitable coating is essential to overcome such limitations. To overcome latter problem, physical or chemical modification of the sorbent surface by some organic compounds, especially chelating ones, is usually used to load the surface with some donor atoms such as oxygen, sulfur, nitrogen and phosphorus [49, 51].

SA is a commercial ligand with a carboxylic and a phenolic functional group which can act as electron pair donors reacting with most of hard and intermediate cations. It has already been used, for example, as the modifier in chelating resins like Amberlite XAD-2-SA, Amberlite XAD-4-SA and silica gel-SA and it have shown nice sorption capacity [63-65].

The aim of this work was to develop an analytical method for the preconcentration and determination of CF with solid-phase microextraction and silica-coated magnetic nanoparticles modified with SA by UV-Vis spectrophotometry.

EXPERIMENTAL

Materials

All chemicals were of analytical-reagent grade. The following materials were used in this study:

CF from Acofarme (Spain), chloroform and methanol from BDH (England), ethanol, sodium chloride, acetic acid and borax from Merck (Germany) and $FeCl_3.6H_2O$, $FeCl_2.4H_2O$ and tetraethoxysilane (TEOS) from Sinopharm chemical Reagent Co. (China) were obtained. SA, glycerol and $NH_3.H_2O$ were analytical grade and commercially available products. Aqueous solutions of drug were prepared with distilled water. The washed magnetic nanoparticles was stored in deionized water. Buffer solutions of required pH were made from 0.1 mol L^{-1} NaOH Merck (Germany) solution and 0.1 mol L^{-1} HCl Merck (Germany) solution.

Apparatus

The following instruments were used in this study:

A single-beam model (Varian, Cary 50 Bio, Australia) UV-Vis spectrophotometer equipped with 1 mm matched quartz cells was used for absorbance measurements. A Metrohm model (780, Switzerland) pH-meter with a combined glass electrode, libra model (Sartorius, GC1603P, Germany) with an accuracy of ± 0.0001, ultrasonic

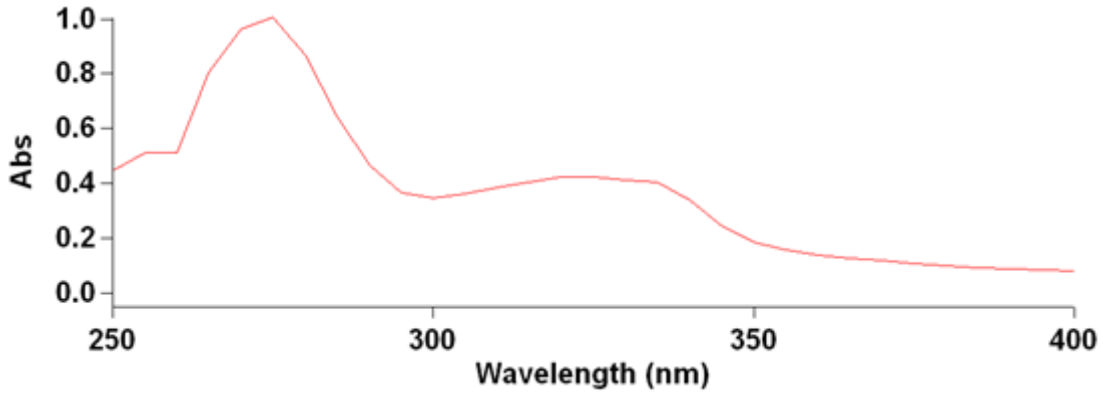


Figure 2. Absorption spectra of CF after solid-phase microextraction

processor model (Hielscher, UP100H, Germany) and centrifuge model (Dynamica Velocity, 18R, Austria) were used. Stirring of the solutions was carried out with a (Heidolph MR 3001, Schwabach, Germany) magnetic stirrer. Infrared spectra were recorded by Fourier transform infrared spectrometer (FT-IR, Perkin Elmer, spectrum 100). Scanning electron microscopy (SEM) was performed to measure the magnetic nanoparticles size and shape (SEMEDX, XL30, Philips, Netherland). X-ray diffractometer (XRD) (38066 Riva, d/G.Via M. Misone, 11/D (TN) Italy) was used.

Preparation of Silica-coated Magnetic Nanoparticles

The magnetic nanoparticles were prepared by the conventional co-precipitation method with minor modifications [44]. For this method, ultrasonic processor with an ultrasonic bath was used instead of magnetic stirring. $FeCl_3.6H_2O$ (11.68 g) and $FeCl_2.4H_2O$ (4.30 g) were dissolved in 200 mL deionized water under nitrogen gas in an ultrasonic bath at 85°C for small minutes leading to smaller and more homogenized particles. 20 mL of 30% $NH_3.H_2O$, was added to the solution. The color of bulk solution changed from orange to black fastly. The magnetic precipitates were washed twice with deionized water and once by 0.02 mol L^{-1} sodium chloride. The washed magnetic nanoparticles was stored in deionized water at a concentration of 40.0 g L^{-1}.

Then, the suspension prepared above (20 mL) was placed in a 250 mL round-bottom flask and allowed to settle. The supernatant was removed, and an aqueous solution of [TEOS, 10% (v/v), 80 mL] was added, followed by glycerol (60 mL). The pH of the suspension was adjusted to 4.5 using glacial acetic acid, and the mixture was then stirred and heated at 90°C for 2 h under a nitrogen atmosphere. After cooling to room temperature, the suspension was washed sequentially by deionized water (3 × 500 mL), methanol (3 × 500 mL) and deionized water (5 × 500 mL). The silica magnetic composite was stored in deionized water at a concentration of 40.0 g L^{-1}.

Preparation of Silica-coated Magnetic Nanoparticles Modified with SA

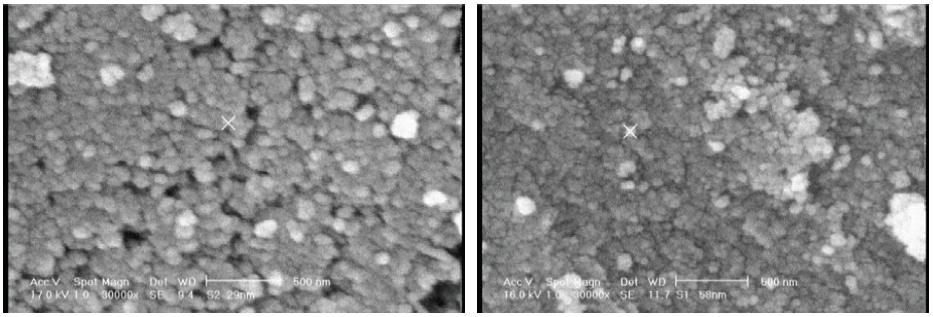
25 mL of silica-coated magnetic nanoparticles prepared as described above was washed with ethanol (2 × 100 mL) and then diluted to 150 mL with 3.3% SA solution and 16 mmol L^{-1} acetic acid solution (pH 4.5). The solution was transferred to a 500 mL 3-necked round-bottom flask and later stirred and heated at 60°C for 2 h under a nitrogen atmosphere. The resulting magnetic nanoparticles were washed with deionized water three times and twice by methanol, then dried into powders at room temperature under vacuum.

METHOD

The solution was made 0.4 mg L^{-1} of CF in chloroform. The UV-Vis spectrophotometry absorption was used and the absorbance was 0.098 at 275 nm. This value was the base of analytical comparison of CF before and after microextraction. After the microextraction with magnetic nanoparticles and at the same concentration, absorbance of CF rose to 1.005 (**Figure 2**).

To prepare a stock solution, 50 µg CF was added in to the flask 50 mL and dissolved in distilled water. The pH of the solution with 0.1 mol L^{-1} NaOH was raised to 10.5. Then the traces of borax was added and a 1 mg L^{-1} solution of CF was made.

In this method, after preparation of the solution 0.4 mg L^{-1} from CF of stock solution in pH suitable at aqueous-phase, magnetic nanoparticles was added to solution and magnetic stirring was set about 10 min. Then it centrifuged for 5 min. After this step, solution was discarded and magnetic nanoparticles with absorbed CF attached to the magnet. 3 mL of chloroform was added. Stirring for 10 min was set to be stirred by magnets and



(a) (b)

Figure 3. SEM images of synthesized magnetic nanoparticles (a) and modified magnetic nanoparticles (b) [45]

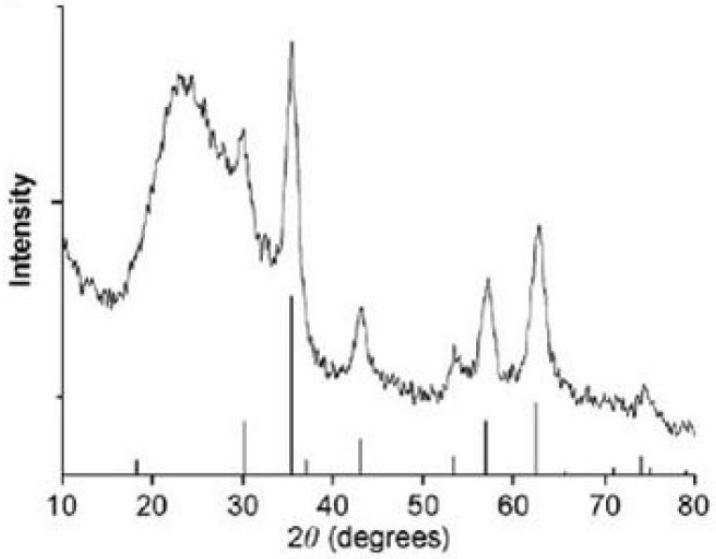


Figure 4. XRD pattern of silica-coated magnetic nanoparticles [45]

later centrifuged for 5 min. The absorption spectrum of the chloroform solution of CF after the desorption process by UV-Vis spectrophotometry was recorded. The absorbance at 275 nm was 1.005, it was reduced due to the high absorption of CF concentration. Several tests and low concentrations of CF solution, containing a concentration of 0.15 mg L^{-1} was found suitable for this solution. After solid-phase microextraction steps as above, the absorption spectra of the solution by UV-Vis spectrophotometry was 0.210.

RESULTS AND DISCUSSION

Characteristics of Modified Magnetic Nanoparticles

The surface and textural morphology of silica-coated magnetic nanoparticles with SEM image is illustrated in **Figure 3**. As shown in **Figure 3**, the pristidin magnetic nanoparticles had a mean diameter of 29 nm. Using the ultrasonic processor caused smaller and more homogenized magnetic nanoparticles prepared [66]. After modification process, the modified magnetic nanoparticles prepared are in the range of 58-73 nm in diameter. This shows that the magnetic nanoparticles have been completely coated with the silica and SA.

The typical XRD profile of silica-coated magnetic nanoparticles is shown in **Figure 4**. The broad peak at around $2\theta = 20°$ in the XRD pattern is due to the amorphous silica shell on the surface of the magnetic nanoparticles.

The FT-IR spectrum of silica-coated magnetic nanoparticles modified by SA has prominent bands at 1680 cm^{-1}, 1486 cm^{-1} and 1387 cm^{-1} due to carboxylate, OH (bending) and phenolic group vibrations, respectively (**Figure 5**).

All parts of magnetic nanoparticles production and related figures obtained from paper [67].

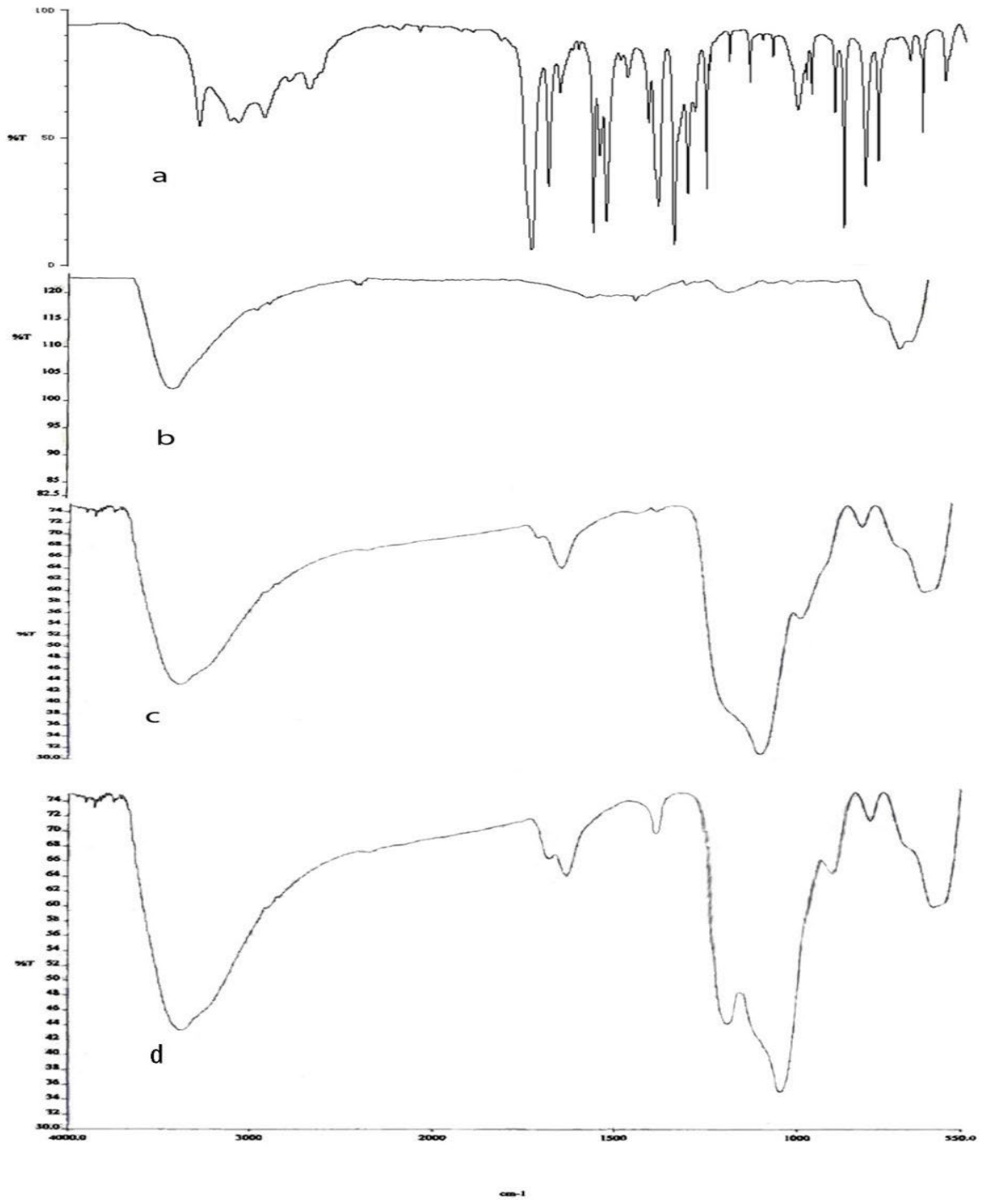


Figure 5. FT-IR spectra (a) SA (b) magnetic nanoparticles (c) SiO_2 coated magnetic nanoparticles (d) SiO_2 coated magnetic nanoparticles modified with SA [45]

Spectral Characteristic

According to the studies in the literature, absorption of CF occurs between 250 to 300 nm wavelength. The wavelength of maximum absorption (λ_{max}) of this drug is 275 nm that is found experimentally.

Effect of Experimental Variables

The optimal conditions for solid-phase microextraction, all parameters and procedures were studied and tested in this research. In the entire optimization process for the solution of CF, concentration was 0.15 mg L^{-1}. The

Table 1. The optimized parameters and maximum absorbance

Parameter	Amount	$Abs_{(max)}$
pH	11.5	0.474
Amount of magnetic nanoparticles (mg)	2	0.511
Extraction time (min)	10	0.511
Centrifuge Time (min)	20	0.516
Desorption time (min)	10	0.518
Stirring speed on the extraction process (RPM)	800	0.570
The rate of centrifugation (RPM)	5000	0.571
Stirring speed on the desorption process (RPM)	500	0.573
Volume of aqueous-phase (mL)	20	0.674
Volume of organic-phase (mL)	3	0.676
Temperature (°C)	55	0.838
Salt effect (w/v)%	1	0.887

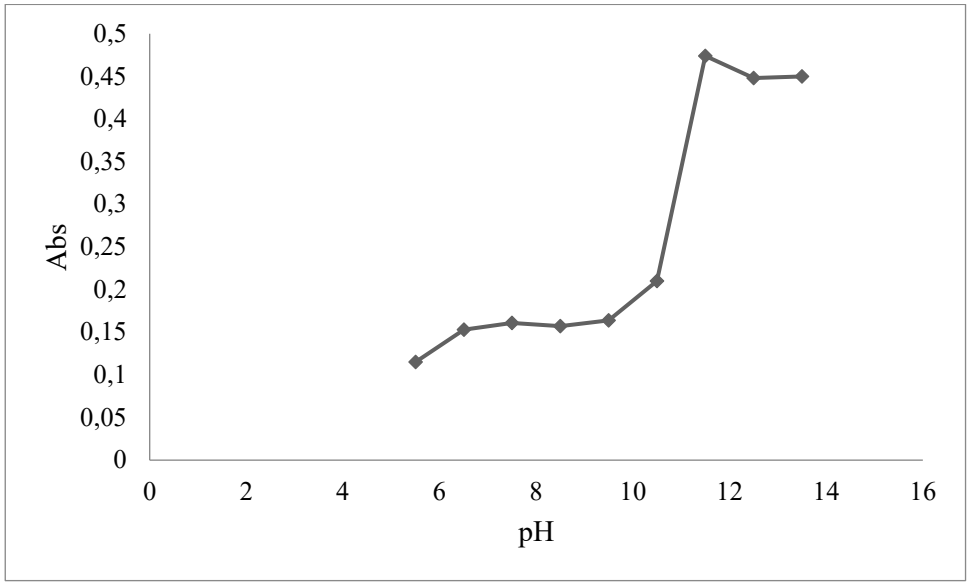


Figure 6. Effect of pH on absorption in the extraction process

optimized parameters and maximum absorbance are set in **Table 1**. In the following, the curves of some important optimized parameters are reported.

The optimum pH in the Extraction Process

pH plays an important role in the extraction. The effect of pH on extraction was studied. Therefore, pH of 5.5 to 13.5 were tested and the results obtained at pH 11.5 was the highest absorbance. This drug has a positive charge at alkaline solution and due to the fact that pH_{zpc} at pH 7 is neutral so the maximum interaction between the analyte and the magnetic nanoparticles observed at pH 11.5 (**Figure 6**).

Optimization of the Amount of Magnetic Nanoparticles

To optimize the amount of magnetic nanoparticles, different doses (1, 2, 3, 4, 5 and 6 mg) were tested and it was found that for 2 mg maximum absorption is achieved. Less than 2 mg, extraction efficiency is low because the amount of magnetic nanoparticles is not enough for extraction and cannot uptake all of the amount of analyte molecules on the magnetic nanoparticles. More than 2 mg, increasing the amount of magnetic nanoparticles does not affect the extraction efficiency (**Figure 7**).

Optimization of the Extraction Time

Extraction time affects the equilibrium conditions. In aqueous solution analyte molecules should have enough time to transfer to the magnetic nanoparticles. The optimization time of 3, 5, 10, 15, 20 and 25 min were analyzed and the conclusion was that by 10 min extraction the highest absorption is achieved. After 10 min, the extraction

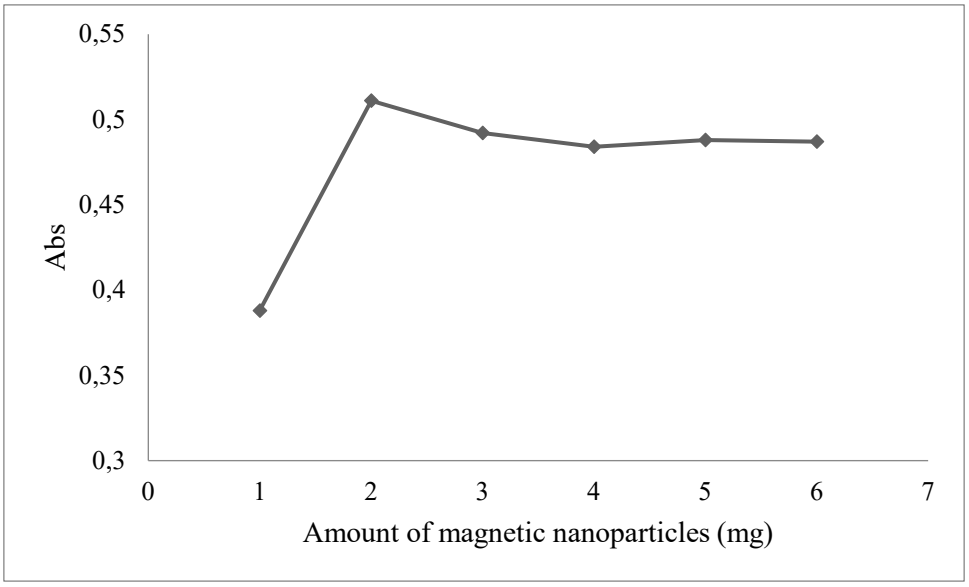


Figure 7. Effect of different amounts of magnetic nanoparticles on absorption

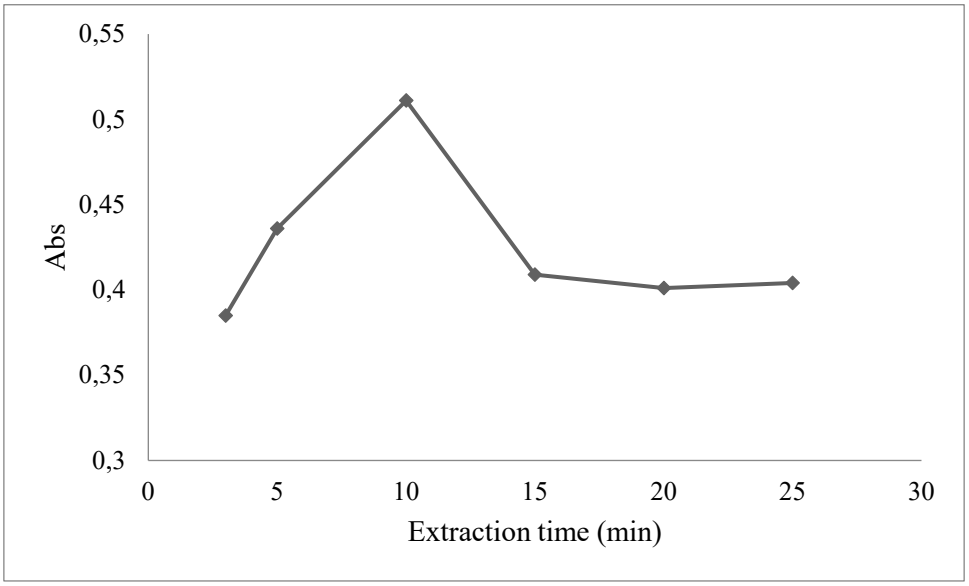


Figure 8. Influence of different extraction times on absorption

efficiency decreases which may be because all the adsorbed analyte molecules are re-entered to aqueous solution due to increasing time (**Figure 8**).

Optimization of the Volume of Organic-phase Solvent in the Desorption Process

The complete extraction of the analyte depends on the organic-phase solvent volume. Optimization was done in 5 different volumes. At higher volumes, the extraction efficiency is reduced. The main reason of reduced extraction efficiency with the increased volume of organic-phase solvent is analyte dilutions. Also, with increasing the volume of organic-phase, the analyte in the adsorbent surface decreases. The best result was obtained by 3 mL of organic-phase volume. (**Figure 9**).

The Optimum Temperature in the Extraction Process

Setting the temperature to complete the reaction is important and a suitable temperature for the reaction should be considered. To optimize the temperature, the extraction process was carried out at several temperatures. At 35°C the extraction efficiency reduced. At higher temperatures, as the temperature increases the speed of transition of

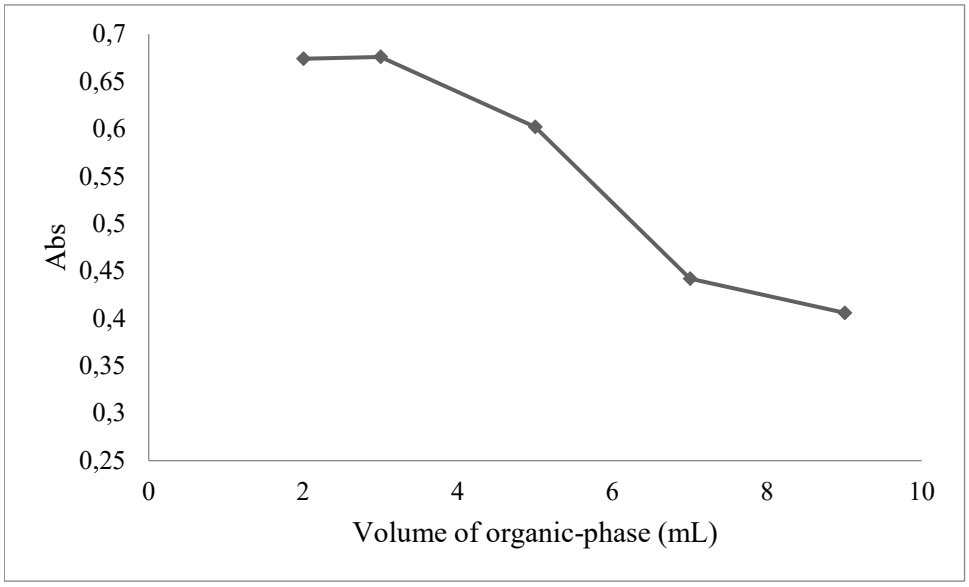


Figure 9. Effect of different volumes of organic-phase solvent on absorption

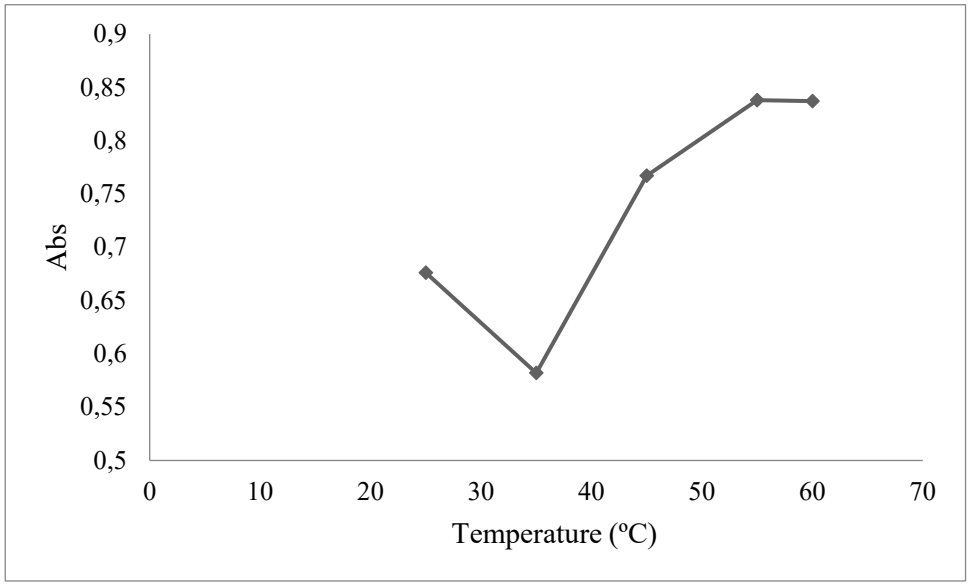


Figure 10. Effect of different temperatures on absorption in the extraction process

analyte molecules to the magnetic nanoparticles increases and the extraction efficiency rises. Then, it was concluded that the optimum temperature, is 55°C (**Figure 10**).

Analytical Parameters

The calibration curve for the sample treated according to the proposed procedure is linear for the concentration range 0.05-0.15 mg L^{-1} (**Figure 11**). The analytical parameters are summarised in **Table 2**.

Analytical Application

For real sample project, the hospital effluent was taken from Razavi hospital (Razavi Khorasan, Mashhad) and analyzed.

There was no CF in hospital effluent, so we added 0.07 mg L^{-1} drug to it and then relative recovery was done by spike method.

The relative recovery of CF was done by comparing the absorbance values obtained of the pure drug with absorbance obtained from the spiked method.

Table 2. Analytical parameters

Parameter	
Linear dynamic range (mg L^{-1})	0.05-0.15
Detection limit (mg L^{-1})	0.002
RSD (%)	1.878
Concentration Factor	68.36

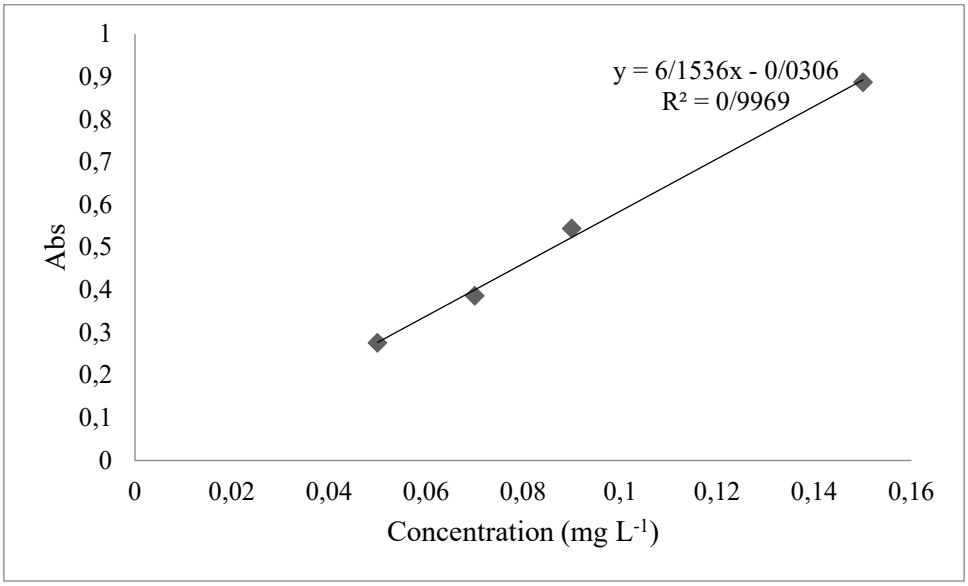


Figure 11. Calibration curve for this method

Absorbance values obtained at 0.07 mg L^{-1} for the pure drug, after solid-phase microextraction and its optimum value was 0.386. Absorbance obtained after solid-phase microextraction in optimal conditions for solution made to the spike method at the same concentration was 0.357. Relative recovery was 92.48%.

CONCLUSION

The results of the experiments show that the method of solid-phase microextraction with silica-coated magnetic nanoparticles modified with SA is a suitable extraction method for preconcentration and measurement of small quantities CF. The method of microextraction uses small amounts of magnetic nanoparticles (2 mg) that after optimization steps, is able to detect minor amounts of CF. These magnetic nanoparticles have relatively high adsorption as compared to the similar materials because of their smaller size. The size of the produced magnetic nanoparticles was determined by XRD analysis and SEM. Also, magnetic nanoparticles can be separated from the aqueous solution easily. The measurement of these drugs using UV-Vis spectrophotometry is done precisely. The benefits of this method are low detection limit, high levels of accuracy, concentration factor and relative recovery. This method is very fast, easy and efficient for a wide variety of analytes. In general, the discussed method is a reliable technique for measuring drugs in environment and other real samples.

REFERENCES

1. Directors of the American Society of Hospital Pharmacists, Drug Information 88, Bethesda, MD. 1988;415-420.
2. World Health Organization Meeting, Use of Quinolones in Food Animals and Potential Impact on Human Health, Geneva, Switzerland. 1998.
3. Sharma VK, Johnson N, Cizmas L, McDonald TJ, Kim H. A review of the influence of treatment strategies on antibiotic resistant bacteria and antibiotic resistance genes. Chemosphere. 2016;150:702-714.
4. Masadeh MM, Alzoubi KH, Khabour OF, Al-Azzam SI. Ciprofloxacin-Induced Antibacterial Activity Is Attenuated by Phosphodiesterase Inhibitors. Current Therapeutic Research. 2015;77:14-17.
5. Carlucci G. Analysis of fluoroquinolones in biological fluids by high-performance liquid chromatography. J. Chromatogr. 1998;812:343-367.

6. Wright DH, Herman VK, Konstantinides FN, Rotschafer JC. Determination of quinoline antibiotics in growth media by reversed-phase high-performance liquid chromatography. J. Chromatogr. B. 2000; 709:97-104.
7. Cohen E, Maxwell RJ, Donoghue DJ. Automated multiresidue isolation of fluoroquinolone antimicrobials from fortified and incurred chicken liver using on-line microdialysis and high-performance liquid chromatography with programmable fluorescence detection. J. Chromatogr. B Biomed. Sci. Appl. 1998;724:137-145.
8. Yorke JC, Froc P. Quantitation of nine quinolones in chicken tissues by high-performance liquid chromatography with fluorescence detection. J. Chromatogr. A. 2000;882(1-2):63-77.
9. Holtzapple CK, Buckley SA, Stanker LH. Determination of fluoroquinolones in serum using an on-line clean-up column coupled to high-performance immunoaffinity-reversed-phase liquid chromatography. J. Chromatogr. B. 2001;754:1-9.
10. Golet EM, Alder AC, Hartmann A, Ternes TA, Giger W. Trace determination of fluoroquinolone antibacterial agents in urban wastewater by solid-phase extraction and liquid chromatography with fluorescence detection. Anal. Chem. 2001;73(15) 3632-3638.
11. Zotou A., Miltiadou N. Sensitive LC determination of ciprofloxacin in pharmaceutical preparations and biological fluids with fluorescence detection. J. Pharm. Biomed. Anal. 2002;28:559-568.
12. Kamberi M, Tsutsumi K, Kotegawa T, Nakamura K, Nakano KS. Analysis of fluoroquinolones in biological fluids by high-performance liquid chromatography. Clin. Chem. 1998;44:1251-1255.
13. Maya MT, Gonc¸Alves NJ, Silva NB, Morais JA. Simple high-performance liquid chromatographic assay for the determination of ciprofloxacin in human plasma with ultraviolet detection. J. Chromatogr. B. 2001;755:305-309.
14. Novakovic J, Nesmarak K, Nova H, Filka K. An HPTLC method for the determination and the purity control of ciprofloxacin HCl in coated tablets. J. Pharm. Biomed. Anal. 2001;25(5-6):957-964.
15. Mirzajani R, Kardani F. Fabrication of ciprofloxacin molecular imprinted polymer coating on a stainless steel wire as a selective solid-phase microextraction fiber for sensitive determination of fluoroquinolones in biological fluids and tablet formulation using HPLC-UV detection. Journal of Pharmaceutical and Biomedical Analysis. 2016;122:98-109.
16. El Walily AF, Belal SF, Barry RS. Spectrophotometric and spectrofluorimetric estimation of ciprofloxacin and norfloxacin by ternary complex formation with eosin and palladium (II). J. Pharm. Biomed. Anal. 1996;14(5):561-569.
17. Nagaralli BS, Seetharamappa J, Melwanki MB. Sensitive spectrophotometric methods for the determination of amoxycillin, ciprofloxacin and piroxicam in pure and pharmaceutical formulations, J. Pharm. Biomed. Anal. 2002;29(5):859-864.
18. Mostafa S, El-Sadek M, Alla EA. Spectrophotometric determination of ciprofloxacin, enrofloxacin and perfloxacin through charge transfer complex formation, J. Pharm. Biomed. Anal. 2002;27:133-142.
19. Rizk M, Belal F, Ibrahim F, Ahmed S, Sheribah ZA. Derivative spectrophotometric analysis of 4-quinolone antibacterials in formulations and spiked biological fluids by their Cu(II) complexes. J. AOAC Int. 2001;84(2):368-375.
20. Vella J, Busuttil F, Bartolo NS, Sammut C, Ferrito V, Serracino-Inglott A, Azzopardi LM, LaFerla G. A simple HPLC-UV method for the determination of ciprofloxacin in human plasma, Journal of Chromatography B. 2016;989:80-85.
21. Muchohi SN, Thuo N, Karisa J, Muturi A, Kokwaro GO, Maitland K. Determination of ciprofloxacin in human plasma using high-performance liquid chromatography coupled with fluorescence detection: Application to a population pharmacokinetics study in children with severe malnutrition, Journal of Chromatography B. 2011;879:146-152.
22. Watabe S, Yokoyama Y, Nakazawa K, Shinozaki K, Hiraoka R, Takeshita K, Suzuki Y. Simultaneous measurement of pazufloxacin, ciprofloxacin and levofloxacin in human serum by high-performance liquid chromatography with fluorescence detection. Journal of Chromatography B. 2010;878:1555-1561.
23. Navalo´n A, Ballesteros O, Blanc R, V´ılchez JL. Determination of ciprofloxacin in human urine and serum samples by solid-phase spectrofluorimetry. Talanta. 2002;52:845-852.
24. Lee HB, Peart TE, Svoboda ML. Determination of ofloxacin, norfloxacin and ciprofloxacin in sewage by selective solid-phase extraction, liquid chromatography with fluorescence detection, and liquid chromatography-tandem mass spectrometry. Journal of Chromatography A. 2007;1139:45-52.
25. Herna´ndez M, Aguilar C, Borrull F, Calull M. Determination of ciprofloxacin, enrofloxacin and flumequine in pig plasma samples by capillary isotachophoresis-capillary zone electrophoresis, J. Chromatogr. B Anal. Technol. Biomed. Life Sci. 2002;772(1):163-172.
26. Fierens C, Hillaert S, Van den Bossche W. The qualitative and quantitative determination of quinolones of first and second generation by capillary electrophoresis. J. Pharm. Biomed. Anal. 2000;22(5):763-772.

27. Schmitt-Kopplin Ph, Burhenne J, Freitag D, Spiteller M, Kettrup A. Development of capillary electrophoresis methods for the analysis of fluoroquinolones and application to the study of the influence of humic substances on their photodegradation in aqueous-phase. J. Chromatogr. A. 1999;837(1-2):253-265.
28. Barro´n D, Jimenez-Lozano E, Cano J, Barbosa J. Determination of residues of enrofloxacin and its metabolite ciprofloxacin in biological materials by capillary electrophoresis. J. Chromatogr. B. 2001;759:73-79.
29. Rusu A, Tóth G, Szőcs L, Kökösi J, Kraszni M, Gyéresi Á, Noszál B. Triprotic site-specific acid-base equilibria and related properties of fluoroquinolone antibacterials. Journal of Pharmaceutical and Biomedical Analysis. 2012;66:50-57.
30. Herrera-Herrera AV, Ravelo-Pérez LM, Hernández-Borges J, Afonso MM, Palenzuela JA, Rodríguez-Delgado MÁ. Oxidized multi-walled carbon nanotubes for the dispersive solid-phase extraction of quinolone antibiotics from water samples using capillary electrophoresis and large volume sample stacking with polarity switching. Journal of Chromatography A. 2011; 1218:5352-5361.
31. Santana-Viera S, Montesdeoca-Esponda S, Sosa-Ferrera Z, Santana-Rodríguez JJ. Cytostatic drugs in environmental samples: An update on the extraction and determination procedures. TrAC Trends in Analytical Chemistry. 2016;80:373-386.
32. Lombardo-Agüí M, García-Campaña AM, Gámiz-Gracia L, Cruces Blanco C. Laser induced fluorescence coupled to capillary electrophoresis for the determination of fluoroquinolones in foods of animal origin using molecularly imprinted polymers. Journal of Chromatography A. 2010;1217:2237-2242.
33. Snitkoff GG, Grabe DW, Holt R, Bailie GR. Development of an immunoassay for monitoring the levels of ciprofloxacin in patient samples. J. Immunoassay. 1998;19(4):227-238.
34. Brás Gomes FBM, Riedstra S, Ferreira JPM. Development of an immunoassay for ciprofloxacin based on phage-displayed antibody fragments. Journal of Immunological Methods. 2010;358:17-22.
35. Sultan SM, Suliman FO. Flow injection spectrophotometric determination of the antibiotic ciprofloxacin in drug formulations. Analyst. 1992;117(9):1523-1526.
36. Suliman FO, Sultan SM. Sequential injection technique employed for stoichiometric studies, optimisation and quantitative determination of some fluoroquinolone antibiotics complexed with iron(III) in sulfuric acid media. Talanta. 1996;43(4):559-568.
37. Attia KAM, Nassar MWI, El-Zeiny MB, Serag A. Stability-indicating methods for the analysis of ciprofloxacin in the presence of its acid induced degradation product: A comparative study. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2016;159:219-222.
38. Kohli MR, Yamaguchi M, Setzer FC, Karabucak B. Spectrophotometric Analysis of Coronal Tooth Discoloration Induced by Various Bioceramic Cements and Other Endodontic Materials. Journal of Endodontics. 2015;41:1862-1866.
39. Aly FA, Al-Tamimi SA, Alwarthan AA. Chemiluminiscence determination of some fluoroquinolone derivatives in pharmaceutical formulations and biological fluids using [Ru (bipy)32+]-Ce(IV) system. Talanta. 2001;53:885-893.
40. Burkhead MS, Wang H, Fallet M, Gross EM. Electrogenerated chemiluminescence: An oxidative-reductive mechanism between quinolone antibiotics and tris(2,2′-bipyridyl)ruthenium(II). Analytica Chimica Acta. 2008;613:152-162.
41. Auger J, Boulay R, Jaillais B, Delion-Vancassel S. Analysis of biogenic amines by solid-phase microextraction and high-performance liquid chromatography with electrochemical detection. J. Chromatogr. A. 2000;870:395.
42. Afkhami A, Saber-Tehrani M, Bagheri H, Madrakian T. Flame atomic absorption spectrometric determination of trace amounts of Pb(II) and Cr(III) in biological, food and environmental samples after preconcentration by modified nano-alumina. Microchim Acta. 2011;172:125-136.
43. Afkhami A, Saber-Tehrani M, Bagheri H, Madrakian T. Simultaneous removal of heavymetal ions in wastewater samples using nano-alumina modified with 2,4-dinitrophenylhydrazine. J Hazard Mater. 2010;181:836-844.
44. Huang CZ, Hu B. Silica-coated magnetic nanoparticles modified with γ-mercaptopropyltrimethoxysilane for fast and selective solid-phase extraction of trace amounts of Cd, Cu, Hg and Pb in environmental and biological samples prior to their determination by inductively coupled plasma mass spectrometry. Spectrochim Acta B. 2008;63:437-444.
45. Afkhami A, Norooz-Asl R. Removal, preconcentration and determination of Mo(VI) from water and wastewater samples using maghemite nanoparticles. Colloids Surf A. 2009;346:52-57.
46. Afkhami A, Moosavi R. Adsorptive removal of Congo red, a carcinogenic textile dye, from aqueous solutions by maghemite nanoparticles. J Hazard Mater. 2010;174:398-403.

47. Afkhami A, Moosavi R, Madrakian T. Preconcentration and spectrophotometric determination of low concentrations of malachite green and leuco-malachite green in water samples by high-performance solid-phase extraction using maghemite nanoparticles. Talanta. 2010;82:785-789.
48. White BR, Stackhouse BT, Holcombe JA. Magnetic γ-Fe2O3 nanoparticles-coated with poly-l-cysteine for chelation of As(III), Cu(II), Cd(II), Ni(II), Pb(II) and Zn(II). J Hazard Mater. 2009;161:848-853.
49. Wang YX, Gupta K, Li JR, Yuan B, Yang JCE, Fu ML. Novel chalcogenide based magnetic adsorbent KMS-1/L-Cystein/Fe3O4 for the facile removal of ciprofloxacin from aqueous solution, Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2018;538:378-386.
50. Kariminia S, Shamsipur A, Shamsipur M. Analytical characteristics and application of novel chitosan-coated magnetic nanoparticles as an efficient drug delivery system for ciprofloxacin. Enhanced drug release kinetics by low-frequency ultrasounds. Journal of Pharmaceutical and Biomedical Analysis. 2016;129:450-457.
51. Dhal S, Mohanty A, Yadav I, Uvanesh K, Kulanthaivel S, Banerjee I, Pal K, Giri S. Magnetic nanoparticle incorporated oleogel as iontophoretic drug delivery system. Colloids and Surfaces B: Biointerfaces. 2017;157:118-129.
52. Danalıoğlu ST, Bayazit ŞS, Kerkez Ö, Alhogbi BG, Abdel Salam M. Removal of ciprofloxacin from aqueous solution using humic acid and levulinic acid-coated Fe3O4 nanoparticles. Chemical Engineering Research and Design. 2017;123:259-267.
53. Manbohi A, Ahmadi SH. In-tube magnetic solid-phase microextraction of some fluoroquinolones based on the use of sodium dodecyl sulfate coated Fe3O4 nanoparticles packed tube. Analytica Chimica Acta. 2015;885:114-121.
54. Tang Y, Liu H, Gao J, Liu X, Gao X, Lu X, Fang G, Wang J, Li J. Upconversion particle@Fe3O4@molecularly imprinted polymer with controllable shell thickness as high-performance fluorescent probe for sensing quinolones. Talanta. 2018;181:95-103.
55. Okaikue-Woodi FEK, Kelch SE, Schmidt MP, Enid Martinez C, Youngman RE, Aristilde L. Structures and mechanisms in clay nanopore trapping of structurally-different fluoroquinolone antimicrobials. Journal of Colloid and Interface Science; 2018;513:367-378.
56. Fan R, Chen XH, Gui Z, Liu L, Chen XY. A new simple hydrothermal preparation of nanocrystalline magnetite Fe_3O_4. Mater Res Bull. 2001;36:497-502.
57. Zhang DE, Tong ZW, Li SZ, Zhang XB, Ying AL. Fabrication and characterization of hollow Fe3O4 nanospheres in a microemulsion. Mater Lett. 2008;62:4053-4055.
58. Jiang WQ, Yang HC, Yang SY, Horng HE, Hung JC, Chen YC et al. Preparation and properties of superparamagnetic nanoparticles with narrow size distribution and biocompatible. J Magn Magn Mater. 2004;283:210-214.
59. Yu LQ, Zheng LJ, Yang JX. Study of preparation and properties on magnetization and stability for ferromagnetic fluids. Mater Chem Phys. 2000;66:6-9.
60. Khollam YB, Dhage SR, Potdar HS, Deshpande SB, Bakare PP, Kulkarni SD, Date SK. Microwave hydrothermal preparation of submicron-sized spherical magnetite (Fe_3O_4) powders. Mater Lett. 2002;56:571-577.
61. Wang SZ, Xin HW, Qian YT. Preparation of nanocrystalline Fe_3O_4 by γ-ray radiation. Mater Lett. 1997;33:113-116.
62. Afkhami A, Saber-Tehrani M, Bagheri H. Modified maghemite nanoparticles as an efficient adsorbent for removing some cationic dyes from aqueous solution. Desalination. 2010;263:240-248.
63. Saxena R, Singh AK, Rathore DPS. Salicylic acid functionalized polystyrene sorbent amberlite XAD-2. Synthesis and applications as a preconcentrator in the determination of zinc(II) and lead(II) by using atomic absorption spectrometry. Analyst. 1995;120:403-405.
64. Boussetta S, Branger C, Margaillan A, Boudenne JL, Coulomb B. Salicylic acid and derivatives anchored on poly(styrene-co-divinylbenzene) resin and membrane via a diazo bridge: Synthesis, characterisation and application to metal extraction. React Funct Polym. 2008;68:775-786.
65. Xu Q, Yin P, Zhao G, Yin G, Qu R. Synthesis and characterization of silica gel microspheres encapsulated by salicyclic acid functionalized polystyrene and its adsorption of transition metal ions from aqueous solutions. Cent Eur J Chem. 2010;8:214-222.
66. Liu XQ, Ma ZY, Xing JM, Liu HZ. Preparation and characterization of amino-silane modified superparamagnetic silica nanospheres. J Magn Magn Mater. 2004;270:1-6.
67. Shishehbore MR, Afkhami A, Bagheri H. Salicylic acid functionalized silica-coated magnetite nanoparticles for solid-phase extraction and preconcentration of some heavy metal ions from various real samples. Chemistry Central Journal. 2011;1:5-41.