

Speciation, Preconcentration, and Determination of Iron(II) and (III) Using 1,10-Phenanthroline Immobilized on Alumina-Coated Magnetite Nanoparticles as a Solid Phase Extraction Sorbent in Pharmaceutical Products

Hossein Tavallali, Mohammad Ali Karimi, Gohar Deilamy-Rad

Abstract—The proposed method for speciation, preconcentration and determination of Fe(II) and Fe(III) in pharmaceutical products was developed using of alumina-coated magnetite nanoparticles ($\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs) as solid phase extraction (SPE) sorbent in magnetic mixed hemimicell solid phase extraction (MMHSPE) technique followed by flame atomic absorption spectrometry analysis. The procedure is based on complexation of Fe(II) with 1, 10-phenanthroline (OP) as complexing reagent for Fe(II) that immobilized on the modified $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs. The extraction and concentration process for pharmaceutical sample was carried out in a single step by mixing the extraction solvent, magnetic adsorbents under ultrasonic action. Then, the adsorbents were isolated from the complicated matrix easily with an external magnetic field. Fe(III) ions determined after facility reduced to Fe(II) by added a proper reduction agent to sample solutions. Compared with traditional methods, the MMHSPE method simplified the operation procedure and reduced the analysis time. Various influencing parameters on the speciation and preconcentration of trace iron, such as pH, sample volume, amount of sorbent, type and concentration of eluent, were studied. Under the optimized operating conditions, the preconcentration factor of the modified nano magnetite for Fe(II) 167 sample was obtained. The detection limits and linear range of this method for iron were 1.0 and 9.0 - 175 ng.mL^{-1} , respectively. Also the relative standard deviation for five replicate determinations of 30.00 ng.mL^{-1} Fe^{2+} was 2.3%.

Keywords—Alumina-coated magnetite nanoparticles, magnetic mixed hemimicell solid-phase extraction, Fe(II) and Fe(III), pharmaceutical sample.

I. INTRODUCTION

IRON is an essential nutritional element for all life forms, i.e. it is a cofactor in many enzymes and essential for oxygen transport and electron transfer. Although daily

requirements for iron are 8–18 mg for man and woman, respectively, it is potentially toxic in excess concentrations because of its pro-oxidant activity. Hence, its concentrations in body samples should be frequently controlled [1]. Although some food products contain iron, but, the nutritional value of a food of a given mineral depends not only on the mineral content, but also on its bioavailability for humans. In the case of iron, the effect that its solubility in water, oxidation state and extent of complex formation has on its bioavailability has been evaluated [2]. It is generally accepted that only soluble nonheme iron can be absorbed; thus, only a fraction of the soluble iron is available. So, it is well known that iron(II) is more available than iron(III), because the latter has a low solubility in the gut. However, iron(III) can be reduced to the more soluble iron(II) in the gut by the action of gastric hydrochloric acid and reducing agents, such as ascorbic acid [3]. Therefore, chemical speciation has gained an increasing interest in environmental and toxicological analyses. The most important reason, therefore, lies in the fact that the toxicity of an element, its biological availability and transport mechanisms highly depend on the chemical form in which it appears [4].

Recently, magnetic materials have received increasing attention. Magnetic materials as adsorbents have several advantages in comparison with traditional adsorbents. The separation process can be performed directly in crude samples containing suspended solid material without additional centrifugation or filtration, which makes separation easier and faster [5].

In this research, we used a new and rapid method of analyses by alumina-coated magnetite nanoparticles ($\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs) which were successfully synthesized, then modified by SDS in acidic media to form mixed hemimicelles and using OP as complexing reagent for Fe^{2+} . These new magnetic adsorbents were applied for an accurate, fast, and cheap method for the determination of the oxidation state and determination of iron (soluble, ferrous and ferric iron) in pharmaceutical sample based on MMHSPE technique assisted by ultrasonic action. Due to the high surface area and the excellent adsorption capacity of these nano-magnetic adsorbents, satisfactory separation recoveries of Fe(II) ions

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could be produced with only 0.05 g $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs without any matrix interferences. Moreover, the unique super paramagnetic property made these adsorbents separated from the matrix rapidly with an adsorptive magnet. Compared with

the conventional SPE methods, the proposed method still has advantages of simple operation procedures and short analysis time. This separation method shows great analytical potential in processing the complicated samples.

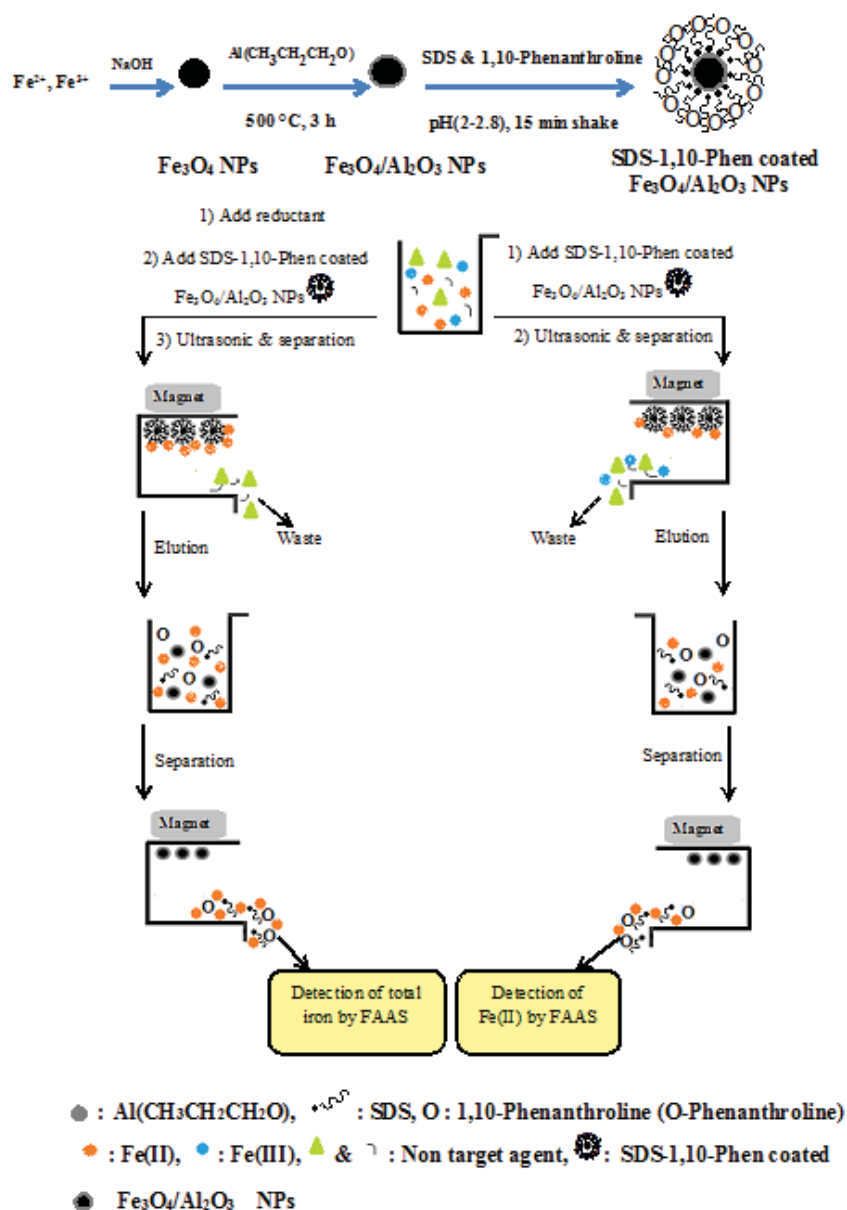


Fig. 1 Schematic illustration of the preparation of SDS-OP coated $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs and their application for speciation and pre-concentration of the analyte based on MHSPE

II. PROCEDURE

A. Preparation of Alumina-Coated Magnetite Nanoparticle

The Fe_3O_4 nanoparticles (Fe_3O_4 NPs) were prepared by chemical coprecipitation method [6]. Ferrous chloride (2.0 gr), ferric chloride (5.2 gr), and hydrochloric acid (12 mol.L^{-1}) (0.85 mL) were dissolved in 25 mL pure water. The mixture was added dropwise into 250 mL NaOH solution (1.5 mol.L^{-1}) under vigorous stirring with nitrogen gas passing continuously

through the solution during the reaction. After the reaction, the obtained Fe_3O_4 NPs precipitate was separated from the reaction medium under the magnetic field, and rinsed with 200 mL pure water four times. Then, the product was oven dried at 80°C .

The $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ nanoparticles ($\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs) were prepared according to [7] with minor modification. Aluminum isopropoxide (1.0 gr) was dissolved in ethanol (60 mL) to

form a clear solution. Fe_3O_4 NPs (0.1 g) were then dispersed in the freshly prepared solution for 5 min with the aid of ultrasonic action. A mixture of water and ethanol (1:5, v/v) was added dropwise to the suspension of Fe_3O_4 NPs with vigorous stirring. The mixture was stirred for half an hour after the addition. Subsequently, the suspension was standing for one hour before separating and washing with ethanol. After five cycles of separation/washing/redispersion with ethanol, the powder obtained was oven dried and calcined at 500°C for three hours. The magnetic property of Fe_3O_4 NPs and $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs was analyzed using a JDM-13 vibrating sample magnetometer. Both Fe_3O_4 nanoparticles and the $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ nanoparticles show super paramagnetic behavior at room temperature due to no hysteresis. The saturation magnetization (M_s) values of the Fe_3O_4 nanoparticles and the $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ nanoparticles 50.00 emu g^{-1} and 10.2 emu g^{-1} , respectively. It is noticed that the saturation magnetization of Fe_3O_4 nanoparticles is higher than that of $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ nanoparticles, because the surface of $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ nanoparticles is coated with a layer of nonmagnetic Al_2O_3 . However, the saturation magnetization for Fe_3O_4 NPs and $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs is sufficient for magnetic separation with an external magnetic field. A scanning electron microscopy (SEM) image of $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs, which illustrates the uniform size distribution of the nanospheres and to confirm that Al_2O_3 , SDS and OP are bonded to the Fe_3O_4 NPs, the characterizations were performed by FT-IR spectroscopy.

B. Speciation Procedure Based on Mixed Hemimicelles Solid-Phase Extraction (MHSPE) Procedures

0.05 gr $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ were prepared according to previous step, were added to 500 mL solution containing 80 mg SDS and 5 mL, 0.5% 1, OP solution in a 500 ml flask. The pH of solution was adjusted to 2-2.8 with 1 mol.L^{-1} HCl solutions, and then the flask was shaken mechanically for 15 min. subsequently, the nanoparticles that modified by surfactant and selective complexing reagent were isolated simply by placing a strong magnet. The target analyte a 500 mL of sample solution containing 80 ppb Fe(II) and Fe(III) were prepared and the pH value was adjusted to pH value was adjusted to 4.0 with acetate buffer solution was added into the SDS-OP coated $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs and then, the mixture was homogenized and the extraction was performed under ultrasonic action for 8 min. The ultrasonic extraction was performed at room temperature. Subsequently, the SDS-OP coated $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs were isolated by placing a strong magnet and the supernatant was poured away. The preconcentrated target analyte absorbed on SDS-OP coated $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs was eluted with ethanol ($3 \times 1 \text{ mL}$). The analytes in the effluent were determined by FAAS. The procedure is the same for Fe(III), except that 10 ml of $1\% \text{ mv}^{-1}$ of ascorbic acid was added to each conical flask, as reduction agent, in order to reduce Fe(III) into Fe(II) ions, before added samples solutions to sorbents were carry out. The eluate was used directly for further flame atomic spectrometry (FAAS) analysis (Fig. 1).

The procedure is the same for Fe(III), except that of

ascorbic acid, as reduction agent, was added to the analyte solution in order to reduce Fe(III) into Fe(II) ions.

C. Analysis of Pharmaceutical Products

Firstly, one tablet of each drug was individually placed in a 50 mL conical volumetric flask. 25 mL of deionized water and 1.0 mL of concentrated HCl (65% (v/v)) were added to the flask, heated on a hot plate for 30 min and then cooled to room temperature. The individual dissolved sample solutions were quantitatively transferred to 50 ml volumetric flasks. The speciation-preconcentration procedure given above was applied to the samples.

III. RESULT AND DISCUSSION

There are many factors affecting the recovery of Fe(II), so it is necessary to investigate the influence of these factors and to optimize the experimental conditions.

A. Characterization of the Adsorbent

To confirm that Al_2O_3 and OP are bonded to the Fe_3O_4 NPs, the characterizations were performed by FT-IR spectroscopy. By overlaying these FTIR spectra, the spectral similarities are observed. The broad feature in the range $3441\text{--}3220 \text{ cm}^{-1}$ was due to O–H stretch (ν_1), which corresponds to the hydroxyl groups attached by the hydrogen bonds to the iron oxide surface, and also the water molecules chemically adsorbed to the magnetic particle surface [8]. The transmittance waveband from 635 to 573 cm^{-1} , which corresponds to the metal–oxygen bonds, is considered as an indication of the ferrite formation.

Fig. 2 displays the SEM image of $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs, which illustrates the uniform size distribution of the nanospheres.

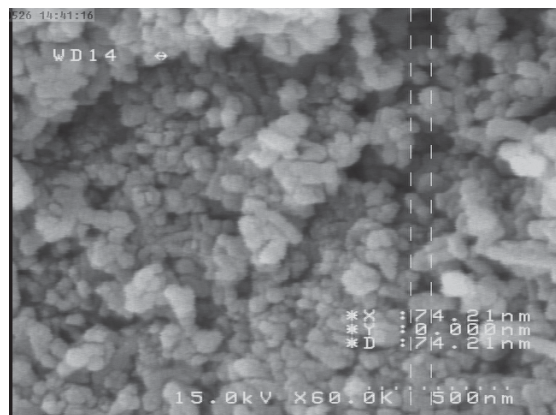


Fig. 2 SEM image of the proposed sorbent $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs

B. The Optimization of MSPE Conditions

In this study, one-variable-at-a-time optimization approach was used for the optimization of MSPE conditions. The optimization was carried out by the standard solutions. The parameters affecting the performance of the extraction, such as amount of magnetic adsorbents, chelating reagent and SDS, Effect of pH, extraction solvent, extraction time, sample volume and desorption condition, were investigated. When one parameter changed, the other parameters were fixed at

their optimized values.

C. Analytical Performance

Under the optimum experimental conditions, limit of detection ($S/N = 3$) was calculated to be 1.0 ng.mL^{-1} for Fe^{2+} . A good correlation coefficient was obtained and relative standard deviation (R.S.D.) for 10 replicate measurements of 60 ng.mL^{-1} Fe(II) was 0.9995 and 2.3%. The calibration curves were investigated from 9.0 up to 175 ng.mL^{-1} which were linear. As the amount of Fe(II) in the sample solution was measured after a final volume of nearly 3 mL, the solution was concentrated by a factor of 167.

D. Application of Purpose Method to Pharmaceutical Samples

In order to evaluate the analytical applicability of the proposed procedure, it was applied to determine the Fe(II) and Fe(III) species in pharmaceutical samples. Pharmaceutical samples were prepared from drugstore in Shiraz (Iran). The results are given in Table I.

TABLE I
TOTAL SOLUBLE IRON AND IRON(II) AND IRON(III) SOLUBLE IN THE
PHARMACEUTICAL SAMPLES EXPRESSED AS MG/1.0 G TABLET

pharmaceutical sample	Fe(II)	Fe(III) ^a	Total iron
Geriatric Pharmaton	6.1 ± 0.4^b	1.0 ± 0.4	7.1 ± 0.2
MULTI Daily	10.6 ± 0.3	1.2 ± 0.4	11.8 ± 0.2

^a Fe(III) content was calculated by difference, subtracting Fe(II) to total soluble iron.

^b Average of three measurements (\pm S.D.)

IV. CONCLUSIONS

The new and rapid separation method of analyses reported here is useful for measuring soluble iron, iron(II) and (III) in the pharmaceutical sample. In this research, modified magnetite NPs (SDS-OP coated $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs) were successfully synthesized and a new type of MMHSPE method assisted by ultrasound was proposed for speciation and preconcentration of iron(II) in pharmaceutical sample. Easy and low cost synthesis of sorbents compared with the commercial adsorbents and rapid extraction of Fe^{2+} , simple isolation of adsorbents from sample matrix by using external magnetic field without additional centrifugation or filtration after analyte adsorption, are some advantages of this work. On the other hand, these $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ NPs can be reused at least 20 times on average without the obvious decrease of recovery after wash/calcine procedures. Compared with the classical separation methods, it is obvious that the sample preparation used in the proposed method is simple and time-saving. So, MMHSPE provides a simple and fast speciation method with great potentiality in pretreatment of the complicated samples. This methodology also gives good accuracy, low limits of detection, and excellent precision on the target analytes, which show its potentiality in trace analysis in various samples with the complicated matrix.

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REFERENCES

- [1] S. B. Goldhaber, "Trace element risk assessment: essentiality vs. toxicity," *Regul. Toxicol. Pharm.*, vol. 38, pp. 232–242, 2003.
- [2] K. Lee, F. M. Clydesdale, "Iron sources for food fortification and their changes due to food processing," *CRC Cr. Rev. Food Sci.*, vol. 11, pp. 117–153, 1978.
- [3] A. Quinteros, R. Farre', M.J. Lagarda, "Optimization of iron speciation (soluble, ferrous and ferric) in beans, chickpeas and lentils Food Chemistry," *Food Chem.* vol. 75, pp. 365–370, 2001.
- [4] J.F. Van Staden, L.V. Mulaudzi, R.I. Stefan, "Speciation of Mn(II) and Mn(VII) by on-line spectrophotometric sequential injection analysis," *Anal. Chim. Acta*, vol. 499, pp. 129–137, 2003.
- [5] Z. Sabatková, M. Safariková, I. Safarik, "Magnetic ovalbumin and egg white aggregates as affinity adsorbents for lectins separation" *Biochem. Eng. J.*, vol. 40, pp. 542–545, 2008.
- [6] Z.F. Wang, H.S. Guo, Y.L. Yu, N.Y. He, "Synthesis and characterization of a novel magnetic carrier with its composition of Fe_3O_4 /carbon using hydrothermal reaction," *J. Magn. Magn. Mater.* vol. 302, pp. 397–404, 2006.
- [7] Y. Li, Y.C. Liu, J. Tang, H.Q. Lin, N. Yao, X.Z. Shen, C.H. Deng, P.Y. Yang, X.M. Zhang, " $\text{Fe}_3\text{O}_4/\text{Al}_2\text{O}_3$ magnetic core-shell microspheres for rapid and highly specific capture of phosphopeptides with mass spectrometry analysis," *J. Chromatogr. A*, vol. 1172, pp. 57–71, 2007.
- [8] D. Creanga, G. Calugaru, "Physical investigations of a ferrofluid based on hydrocarbons," *J. Magn. Magn. Mater.* vol. 289, pp. 81–83, 2006.