

Fast Removal of Citalopram Drug from Waste Water Using Magnetic Nanoparticles Modified with Sodium Dodecyl Sulfate Followed by UV-Spectrometry

M. Khoeini Sharifabadi¹, M. Saber Tehrani¹, A. Mehdinia², P. Abroomand Azar¹,
S. Waqif Husain^{1,*}

¹Department of Chemistry, Science and Research Branch, Islamic Azad University, Tehran, Iran

²Department of Marine Science, Iranian National Institute for Oceanography, Tehran, Iran

(Received: 3 March 2013

Accepted: 17 May 2013)

ABSTRACT: A simple and sensitive, solid-phase extraction method for the removal of Citalopram drug from waste water has been developed by using magnetic nanoparticles modified with surfactant sodium dodecyl sulfate. These magnetic nanoparticles have shown great adsorptive tendency towards Citalopram drug. The effect of different parameters influencing the extraction efficiency of this drug were investigated and optimized including the pH, amount of the surfactant, contact time and temperature. The extracts were analyzed by ultraviolet spectrophotometry at 239nm. Under these conditions, the related standard deviation (RSD %) of the method at two concentrations (5 and 50 $\mu\text{g}\cdot\text{mL}^{-1}$) was in the range of (3.14–3.75) % (n = 8). The calibration curve was linear in the range of 2-100 $\mu\text{g}\cdot\text{mL}^{-1}$ of Citalopram drug with a correlation coefficient of >0.99.

KEYWORDS: Fe₃O₄ magnetic nanoparticles, Citalopram hydrobromide, Waste water, Solid-phase micro extraction, UV- spectrometry.

INTRODUCTION

Citalopram(1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile) (CIT) with pKa=9.78 is a bicyclic phthalate compound with a selective serotonin reuptake inhibitor(SSRI) and is used for treatment of central nervous system (CNS) abnormalities such as anxiety, obsessive-compulsive disorders, various phobias (agoraphobia and social phobia) borderline personality disorder[1]. For treatment of major depression, two classes of anti-depressants are frequently used: a) tricyclic anti-depressants (TCA_s) and: b) selective serotonin reuptake inhibitors (SSRI_s) [2]. The SSRI_s differ from the TCA_s in their chemical structure and in their mechanism of action

(metabolism and pharmacokinetics). When pharmacological profile of TCA_s and SSRI_s is compared, SSRI_s have a different, and better tolerated adverse effect profile than TCA_s [3] and toxicity of the SSRI_s is comparatively low, but there have been case reports of deaths in which CIT was strongly suspected as causative agents [4, 5]. CIT drug's cardiac toxicity has aroused concern [6, 7] and some reports have shown that combination of SSRI_s with other drugs have led to humans death [8, 11].

In pharmacopoeias limit test and in some poisons regulations it is described that no more than 10ppm of one product will appear in another product (basis for heavy metals in starting materials).

Corresponding Author: S. WaqifHusain, Department of Chemistry, Science and Research Branch, Islamic Azad University, Tehran, Iran. E-mail: syedwaqifhusain@yahoo.com

Therefore elimination of pervious product from tank is necessary. On the other hand, the important sources of water pollutant are effluents from the pharmaceutical factory, therefore, it is necessary to develop an efficient method for the removal of drugs residual in waste waters [12]. Some of the extraction methods for this drug such as liquid-liquid extraction (LLE), solid phase extraction (SPE) and solid phase micro extraction (SPME) were reported [13, 21]. However, these methods are laborious, time consuming and need excessive amount of hazardous and expensive organic solvents. Therefore for routine analysis of numerous samples, these methods are not suitable. Solid phase extraction (SPE) for high extraction efficiency, low consumption of organic solvent, low extraction time for sample preparation and easy operation is the preferred pre-concentration method [22, 25].

Recently magnetic nanoparticles have been developed with interesting properties such as high chemical stability and biocompatibility [26]. These particles have some advantages including: small size, high surface area to volume ratio, high magnetic properties and effective ability for binding. For separation of MNP_s from solution no centrifugation or filtration is required, but by use of an external magnetic field they are separated easily. For preparation of these particles different methods such as co-precipitation, micro emulsion, thermal decomposition and hydrothermal synthesis have been used. Among these methods, co-precipitation is a facile and convenient method. Pure magnetic particles tend to agglomerate in order to reduce their surface energy, thus to prevent this phenomenon, modification of the NP surface is required. However, these nanometer sized metal oxides are not target-selective, therefore to overcome this limitation modification of these magnetic nanoparticles is necessary [27, 32]. Due to high surface area of these magnetic-nanoparticles, speedy removal of the analyte takes place from the matrix. The adsorption of drugs on these particles coated with

anionic surfactant is due to formation of hemimicelles leading to the specific interaction between weakly positive charge on drug's molecule and the coated anionic surfactant.

In this work we reported a simple and sensitive method using magnetic nanoparticles modified by surfactant sodium dodecyl sulfate for the pre-concentration and removal of Citalopram drug from waste water samples.

MATERIALS AND METHOD

Chemicals including ferric chloride ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$), ferrous chloride ($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$) hydrochloric acid (HCl), sodium hydroxide (NaOH), methanol and sodium dodecyl sulfate (SDS) were of analytical grades from E.Merck (Darmstadt, Germany). All aqueous solutions were prepared using doubly distilled water. The water was purified on a mili-Q-ultrapure water purification system obtained from Milipore (Milford MA, USA). CIT was obtained from Darou pakhsh Pharmaceuticals (Tehran, Iran) and waste waters were obtained from Darou pakhsh Pharmaceutical Factory.

Instruments

The spectrophotometric measurements were made at 239nm using Varian Cary 100 (USA) spectrophotometer equipped with 1.0cm quartz cell and D₂ lamp. Transmission electron microscope (TEM) was from Philips EM 208 (Voltage 100 KV). pH-meter model 713 from Metrohm (Swiss) the stirrer from IKA (USA). For magnetic separations a strong magnet of NdFeB (10×5×4 cm) was used.

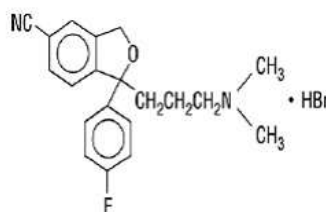


Figure 1. The Citalopramhydrobromide Drug.

Preparation of standard solutions and real sample

Stock solution of CIT was prepared in methanol with concentration of 100 mg.mL^{-1} and stored in dark glass/bottle at 4°C . Waste water samples were collected from effluent of Darou pakhsh Paharmaceutical factory and filtered with millipore filter before extraction. The working solution was prepared by spiking the drug in the waste water. The calibration curve for this drug was achieved by simple linear regression of drug's absorbance versus its concentration, and the concentration of drug in real samples was calculated based on the obtained calibration curve.

Synthesis and Characterization of $\text{Fe}_3\text{O}_4\text{NP}_s$

Fe_3O_4 nanoparticles were prepared by the chemical co-precipitation method as following:

10.4gr of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 4gr of $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ and 1.7 ml of HCl (12 mol.L^{-1}) were dissolved in 50 ml of deionized and degassed (with ultrasonic) water. This solution mixture was added drop wise to a beaker containing 500ml of $1.5 \text{ mol.L}^{-1} \text{NaOH}$ solutions (which was heated to 80°C) under nitrogen gas for 30 min with vigorous stirring by a stirrer (1000 rpm) to prevent the oxidation of Fe^{2+} ions [33].

During this whole process, the temperature of the solution was maintained at 80°C and nitrogen gas was used to prevent the intrusion of oxygen. After completion of the reaction, the obtained $\text{Fe}_3\text{O}_4 \text{NP}_s$ precipitate was separated from the reaction medium using a magnet and washed with 500ml deionized water four times. Finally, the obtained MNP_s were re-suspended in 500ml of the degassed deionized water. The pH of obtained suspension was 11.0 and the suspension of prepared MNP_s was stable up to one month. The synthesized MNP_s were characterized using transmission electron microscopy (TEM) and is shown in Figure 2. As it can be seen the particles diameter is lower than 50nm.

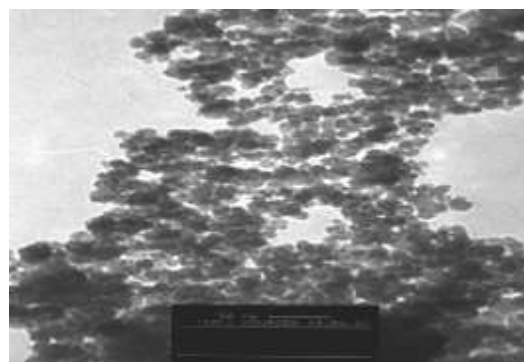


Figure 2. TEM image of the synthesized MNP_s , (magnification 160000).

Extraction Procedure

Optimization studies were carried out according to the following procedure: 20 ml of aqueous solution of the CIT drug (10 mg.L^{-1}) was added in a 50ml beaker, then 1ml of MNP_s suspension (containing 10mg of $\text{Fe}_3\text{O}_4 \text{NP}_s$) was added to the solution and the pH was adjusted to 3.0, then 0.5ml of SDS (10 mg.mL^{-1}) was added to it. The mixture was stirred for 5min to enhance the drug's adsorption efficiency. Using a strong magnet placed at the bottom of the beaker, $\text{Fe}_3\text{O}_4 \text{NP}_s$ were separated quickly from sample solution.

The magnet was removed and the supernatant was separated. The CIT concentration in the supernatant clear solution was determined by a UV Spectrophotometer at 239nm against blank. The following equation was applied to calculate the CIT removal efficiency: CIT removal efficiency

$$(\%) = \left(\frac{C_0 - C_r}{C_0} \right) \times 100$$

where C_0 and C_r are the initial and residual concentrations of the CIT in the solution (mg.L^{-1}) respectively.

RESULTS AND DISCUSSION*Effect of pH*

pH is one of the prime factors influencing the adsorption behaviour of mixed hemimicelles system. The isoelectric point at $\text{pH}=6.5$ (pH_{pzc}) for the Fe_3O_4

nanoparticles was reported earlier [34, 36]. When the pH was below the pH_{pzc} , Fe_3O_4 NP_s surface was positive and the anion surfactant can be sorbed to the Fe_3O_4 NP_s surface to form mixed hemimicelles. In this

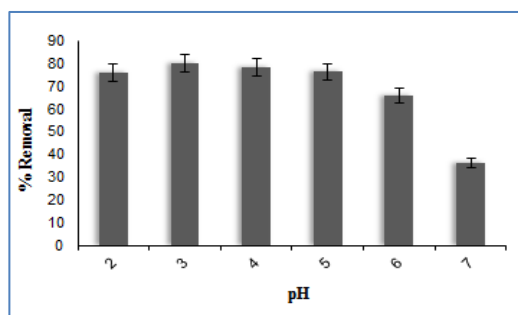


Figure 3. The adsorption performance of CIT as a function of samples pH.

Influence of SDS concentration

To modify the surface of MNP_s , SDS was added to the solution and by coating different amounts of SDS on the surface of nanoparticles, adsorption of CIT drug was investigated on it. Admicelles were formed on surface of NP_s by increasing the surfactant concentration. The results show that increasing the SDS amount, leads to the formation of SDS aggregates (hemimicelles, mixed hemimicelles or admicelles), and the adsorption amount of the drug increases remarkably. Maximum adsorption was obtained when SDS amount was 5mg in the mixture. At higher amounts of SDS, the adsorption of the drug was decreased; it may be due to the formation of SDS aggregates in the solution which can compete with formation of SDS aggregates on the surface of Fe_3O_4 . The results of the effect of SDS amount on adsorption of CIT is shown in Figure 4.

study, the effect of pH between 2 to 7 was examined. The absorption performance of the drug is illustrated in Figure 3. Results show that the best pH for these studies was 3.0. Therefore this pH was selected

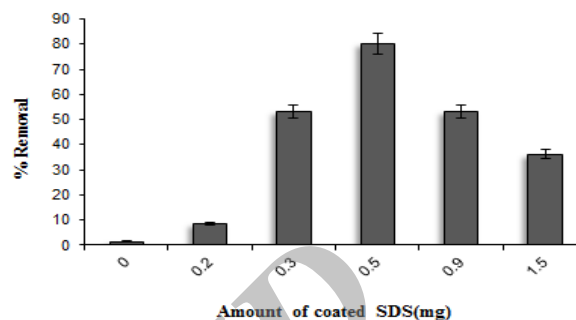


Figure 4. Adsorption efficiency of SDS-coated MNP_s as a function of the amount of SDS added.

Effect of ionic strength and contact time

The effect of ionic strength on the adsorption of CIT was investigated by addition of NaCl in the range of 0–10% (W/V). It is found that it has no effect on adsorption of CIT drug. Results of contact time indicate that the adsorption of CIT increases with contact time up to 10min, and after that maximum removal is achieved. Therefore, 10 min was the optimum contact time.

Effect of solution temperature

The effect of temperature on the adsorption of CIT was investigated in the range of 25 to 50°C. It is observed that that increasing the temperature has no effect on adsorption of CIT on the adsorbent.

Analytical application and performance

Under the optimum conditions described above, quantitative parameters, such as linear range, correlation coefficient, limit of detection and precision were evaluated. The calibration curve was linear in the range of 2 to 100 $\mu g \cdot mL^{-1}$. For a sample volume of 20ml the calibration equation was $A = 0.002 C + 0.004$ ($R_2 = 0.996$). Where A is the absorbance of the extract at 239 nm and C is the concentration of CIT in the sample solution in $\mu g \cdot mL^{-1}$. The precision of the analytical method was studied using eight replicate experiments containing each 5 and 50 $\mu g \cdot mL^{-1}$, and the

relative standard deviations (RSD) were 3.14% and 3.75%, respectively. The accuracy of the method was evaluated by the recovery test carried out with spiked waste water samples.

Analysis of CIT in waste water samples

In order to validate the developed method, it was applied to a number of waste waters samples (n=8). The water samples were analysed before and after spiking $10\mu\text{g}\cdot\text{mL}^{-1}$ of CIT under optimized conditions. The results are recorded in Table1.

Table 1.Determination of CIT in waste water samples.

Waste water sample	CIT	RSD	n
Real Sample	$9.65\mu\text{g}\cdot\text{mL}^{-1}$	2.47%	8
Real Sample (Spiked with CIT. $10\mu\text{g}\cdot\text{mL}^{-1}$)	$22.15\mu\text{g}\cdot\text{mL}^{-1}$	3.16%	8

n = number of samples measured

CONCLUSION

A novel SPE method based on SDS-coated Fe_3O_4 NP_s mixed hemimicelles with high adsorption capacity, acceptable sensitivity, simple synthesis, rapid, inexpensive, using little amount of nanoparticles and harmless to environment, has been developed for the removal and determination of trace amounts of Citalopram drug in waste water streams.

REFERENCES

- Baumann P., Rochat B., 1995. Comparative Pharmacokinetics of selective serotonin reuptake inhibitors: a look behind the mirror. *International Clinical Psychopharmacology*.10: 15-21.
- Mourilhe P., Stokes P.E., 1998. Risk and benefits of selective reuptake inhibitors in the treatment of depression.*Drug Safety*. 18:57-82.
- Kasper S., Hoflich G., Scholl H.P., Moller H.J., 1994. Safety and antidepressant efficacy of Selective serotonin reuptake inhibitors. *Journal of Clinical Pharmacology*. 9:1-12.
- Worm K., Dragsholt C., Simonsen K., Kringsholm B., 1998. Citalopram concentrations in samples from autopsies and living persons. *International Journal of Legal Medicin*. 111:188-190.
- Ostrom M., Eriksson A., Thorson J., Spigest O., 1996. Fatal overdose with citalopram.*Lancet*.348:339-340.
- Howland R.H., 2011. A critical evaluation of the Cardiac Toxicity of Citalopram.*Psychology & Society Journal*. 49:13-16.
- Cooke M.J., Waring W.S., 2013. Citalopram and cardiac Toxicity.*Eur. Journal of Clinical Pharmacology*.69:755-760.
- Singer P.P., Jones G.R., 1997. An uncommon fatality due to moclobemide and paroxetine.*Journal of Analytical Toxicology*.21:518-520.
- Neuvonen P.J., Pohjola-Sintonen S., Tacke U., Vuori E., 1993. Five fatal cases of Serotonin Syndrome after moclobemide-citalopram or moclobemid clomipramine over dose. *Lancet*. 342:1419-1420.
- Sternbach H., 1991. The serotonin syndrome.*American Journal of Psychiatry*. 148:703-713.
- Ferslew K.E., Hagarorn A.N., Harlan G.C., Mccor Mick W.F., 1998. A fatal drug interaction between clozapine and fluoxetine. *Journal of Forensic Sciences*. 43:1082-1085.
- Mak S.Y., Chen D.H., 2004. Fast adsorption of methylene blue on polyacrylic acid-bound iron oxide magnetic nano particles. *Dyes and Pigments*. 6:93-98.
- Macek J., Ptacek P., Klima J., 2001. Rapid determination of citalopram in human plasma by High performance liquid chromatography.*Journal of Chromatography B*. 755: 279-285.
- Pistos C., Panderi I., 2004. Liquid chromatography positive ion electrospray mass spectrometry method for the quantification of citalopram in human plasma. *Journal of Chromatography B*. 810: 235-244.
- Kristoffersen L., Bugge A., Lundanes E., Slordal L., 1999. Simultaneous determination of Citalopram fluoxetine, paroxetine and their metabolites in plasma

and whole blood by high performance liquid chromatography with ultraviolet and fluorescence detection. *Journal of Chromatography B*. 734: 229-246.

16. Molander P., Thomassen A., Kristoffersen L., Greibrokk T., Lundanes E., 2001. Simultaneous determination of citalopram, fluoxetine, paroxetine and their metabolites in plasma by temperature programmed packed capillary liquid chromatography with on-column focusing of large injection volumes. *Journal of Chromatography B*. 766: 71-87.

17. Juan H., Zhiling Z., Huande L., 2005. Simultaneous determination of fluoxetine, citalopram, paroxetine, venlafaxine in plasma by high performance liquid chromatography-electro spray ionization mass spectrometry. *Journal of Chromatography B*. 820: 33-39.

18. Meng Q.H., Gauthier D., 2005. Simultaneous analysis of citalopram and desmethyl citalopram by liquid chromatography with fluorescence detection after solid phase extraction. *Clinical Biochemistry Journal*. 38: 282-285.

19. Wille S.M.R., Maudens, K.E., Van-Peteghem C.H., 2005. Development of a solid phase extraction for 13 (new) generation antidepressants and their active metabolites for gas chromatographic-mass spectrometric analysis. *Journal of Chromatography A*. 1098:19-29.

20. BerzasNevado J.J., VillasenorLierena M.J., GuiberteauCabanillas C., Rodriguez Robledo V., 2006. Screening of citalopram, fluoxetine and their metabolites in human urine samples by gas chromatography-mass spectrometry. A global robustness/ruggedness study. *Journal of Chromatography A*. 1123:130-133.

21. Bagheri H., Khalilian F., Babanezhad E., Eshaghi A., 2008. Solvent microextraction with back Extraction combined with liquid chromatography-fluorescence detection for the determination of citalopram in human plasma. *Analytical Chemical Acta*. 610: 211-216.

22. Parham H., Pourreza N., Rahbar N., 2009. Solid phase extraction of lead and cadmium using Solid sulfur as a new metal extractor prior to determination by flame atomic absorption spectrometry. *Journal of Hazardous Materials*. 163:588-592.

23. Ngeontae W., Aeungmaitrepirom W., Tuntulani T., 2007. Modified silica gel with amino thioamidoanthraquinone for solid phase extraction and pre-concentration of Pb(II), Cu(II), Ni(II), Co(II) and Cd(II). *Talanta*. 71:1075-1082.

24. Maier M., Fritz H., Gerster M., Schewitz J., 1998. Quantitative analysis of modified antisense oligonucleotides in biological fluids using cationic nanoparticles for solid phase extraction. *Journal of Analytical Chemistry*. 70: 2197-2204.

25. Song Y., Zhao S., Tchounwou P.B., Liu Y.M., 2007. A nanoparticle based solid phase extraction method for liquid chromatography-electrospray ionization-tandem mass spectrometric analysis. *Journal of Chromatography A*. 1166: 79-84.

26. Sun Y.K., Ma M., Zhang Y., Gu N., 2004. Synthesis of nanometer-size magnetite particles From Magnetite. *Colloids and Surfaces A*. 245:15-19.

27. Jing T., Du H., Dai Q., Xia H., Niu J., Hao Q., Mei S., Zhou Y., 2010. Magnetic molecularly Imprinted nanoparticles for recognition of lysozyme. *Biosensors & Bioelectronics*. 26: 301-306.

28. Chen L.G., Liu, J., Zeng, Q.L., Wang, H., Yu, A.M., Zhang, A.M., 2009. Preparation of magnetic molecularly imprinted antibiotics from egg and tissue samples. *Journal of Chromatography A*. 1216: 3710-3719.

29. Mehdinia A., BaradaranKayyal T., Jabbari A., OvaisazizZanjani M., Ziaei E., 2013. Magnetic molecularly imprinted nanoparticles based on grafting polymerization for selective detection of 4-nitrophenol in aqueous sample. *Journal of Chromatography A*. 1283:82-88.

30. Faraji M., Yamini Y., Rezaee M., 2010. Extraction of trace amounts of mercury with sodium dodecyl sulphate-coated magnetite nanoparticles and its

determination by flow injection inductively coupled plasma–optical emission spectrometry. *Talanta* .81: 831-836.

31. Lu A.H., Salabas E.L., Schuth F., 2007. Magnetic nanoparticles: synthesis, protection, functionalization and application. *Angewandte Chemie International Edition* .46:1222-1246.

32. Afkhami A., Saber-Tehrani M., Bagheri H., 2010. Simultaneous removal of heavy metal ions in waste waters samples using nano–alumina modified with 2, 4 – dinitrophenyl hydrazine. *Journal of Hazardous Materials*. 181: 836-844.

33. Faraji M., Yamini Y., Saleh A., Rezaee M., Ghambarian M., Hassani R., 2010. A nanoparticle-based solid phase extraction procedure followed by flow injection inductively coupled plasma-optical emission spectrometry to determine some heavy metal ions in water samples. *Analytical Chemistry* .69:172-177.

34. Parham H., Rahba N., 2009. Solid phase extraction spectrophotometric determination of Salicylic acid using magnetic iron oxide nanoparticles as extractor. *Journal of Pharmaceutical and Biomedical Analysis*. 50: 58-63.

35. Holsen T.M., Taylor E.R., Seo Y.C., Anderson P.R., 1991. Removal of sparingly soluble organic chemical from aqueous solutions with surfactant–coated ferrihydrite. *Journal of Environmental Science and Technology* .25: 585-589.

36. Zhao X., Shi Y., Cai Y., Mou S., 2008. Cetyltrimethyl ammonium bromide coated magnetic nanoparticles for the preconcentration of phenolic compound from environmental water samples. *Journal of Environmental Science and Technology*. 42: 1201-1206.

Archive of SID

Archive of SID