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The Influence of Green Surface Modification of Magnetite Nanoparticles on the Tolid Phase Extraction Tramadol Followed by High Performance Liquid Chromatography–Diode Array Aetection

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Abstract
In this paper, a new rapid and sensitive method based on sodium dodecyl sulfate modified Fe3O4@α–Linolenic acid nanocomposite combined with high-performance liquid chromatography-photo diode array detection (HPLC–PDA) has been proposed for the extraction and determination of tramadol (TRA) in water samples. The Fe3O4@α–Linolenic acid NPs were synthesized and then characterized by Fourier transform-infrared spectroscopy (FT−IR), scanning electron microscopy (SEM) and X-ray diffraction (XRD). The main factors influencing extraction and desorption efficiency were optimized. Under optimum conditions, the method was successfully applied to the determination of TRA in the environmental samples and good linearity in the range of 0.1–500ng.mL^{-1}(R^2> 0.99) obtained. The detection limit (LOD) and relative standard deviation (RSD) were0.074ng.mL^{-1} and 2.89 %(n=5) respectively. Finally, the proposed method was successfully applied with the relative recoveries percentages from 94–103.97% for the extraction and determination of tramadol in aqueous samples.

Keywords
Tramadol; Magnetic Nanoparticle; Solid Phase Extraction; HPLC-DAD.

1. INTRODUCTION

Tramadol (TRA);2-[(dimethylamino)methyl]-1-(3-methoxyphenyl) cyclohexanol, is an opioid pain medication that used as an centrally acting analgesic(Fig. 1). It has been shown that a synthetic analogue of codeine and this analgesic rapidly metabolized by the cytochrome P450 enzyme system in the liver [1, 2]. It acts as an opiate agonist with μ-opioid receptor agonist activity. After oral administration, TRA demonstrates 65-70% bioavailability and approximately 30% of the main drug is defecated unchanged in the urine [3]. It is an effective an algetic that has been used since 1997 to severe pain, widely prescribed with no clinically relevant cardiovascular or respiratory depressant activity [4]. Side effects of TRA include nausea, dizziness, drowsiness, drymouth, constipation, low blood pressure, sweating and confusion [5].

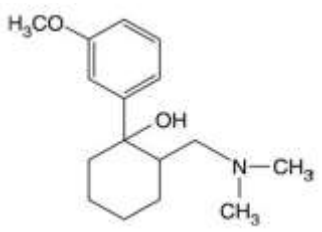

Fig. 1. Chemical structure of Tramadol**.**

The methods described for the determination of tramadol involve liquid chromatography (LC) with ultraviolet [6,7], fluorescence [8,9], or diode array detectors [10,11]. GC-MS and LC-MS [12-15], Capillary gas chromatography [16], electrochemical methods [17,18] etc.

Among these methods HPLC–PDA has been considered as the specific method due to the performance and strong separation ability of TRA in biological fluids and wastewater samples [19, 20].

Solid-phase extraction (SPE) is most popular techniques widely used for the extraction/preconcentration of trace amounts of drugs in various environmental samples due to factors such as easily use, time saving and simplicity and it is the most accepted sample pretreatment method today [21-24]. Lately, nanoparticles, particularly magnetic nanoparticles (MNPs), have been evolved as a new type of solid phase extraction sorbent material. Magnetic nanoparticle based solid phase extraction (MNSPE), a magnetic field is used to isolate analytes in solution without the need for filtration or centrifugation [25, 26].Among the available adsorbents, iron oxides have been extensively used as adsorbent in MNSPE because of their super para-magnetism, high surface area to volume ratio, biocompatibility, high magnetic

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saturation, low toxicity, simple preparation process and low price. The magnetite nanoparticles are very much susceptible to air oxidation and are easily aggregated in aqueous systems.

Recent research indicated that Linoleic acid has high affinity to Fe3O4 nanoparticles, and sorption of α–Linolenic acid on the Fe3O4 nanoparticles enhanced the stability of nano-dispersions by preventing their aggregation [27]. Numerous in natural aqueous systems, α–Linolenic acid has a Structure of alkyl and aromatic units that attach with carboxylic acid and phenolic hydroxyl functional groups [28-30]. In this study, a simple, eco-friendly and low-cost magnetic sorbent material prepared by SDS-coated Fe3O4@α–Linolenic acid NPs was developed for the removal of TRA from wastewater samples. The physical and chemical characterization of the synthesized SDS-coated Fe3O4@α–Linolenic acid NPs was conducted, and under the optimized conditions, MNPs modified provided surfactant free extracts and were shown to be efficient as a SPE sorbent for the preconcentration TRA from water samples. To the best of our knowledge, SDS-coated Fe3O4@ α–Linolenic acid has not been employed yet for the extraction and determination of TRA drug.

In the present work, sodium dodecyl sulfate-coated Fe3O4@α–Linolenic acid nanocomposites were synthesized and employed as sorbent in SPE of tramadol from water samples and its determination by HPLC-DAD has been used because of its admissible sensitivity as well as its relative low cost. Various factors that influence extraction performance including adsorption and desorption conditions were optimized.

2. EXPERIMENTAL

2.1. Apparatus

HPLC analysis consisted of a Shimadzu (Tokyo, Japan) LC-6AVP pump, SPD-M10AVP diode array detector (DAD), a Rheodyne model 7725i injector with a 20μL loop was used to inject the samples. The chromatographic system was composed of an isocratic Waters pump, a Waters 2996 photodiode array detector and an online degasser. Chromatographic separation was attained on an ACE 5μm, C18 4.6mm×250mm column. The mobile phase was a mixture of water–acetonitrile (30/70, v/v) with a flow rate of 1.0 ml min^{-1} and PDA detection wavelength used for quantification. The retention time for methanol as a solvent was 2.2min, and retention time for TRA was 7.2 min.

A Metrohm model 713 pH-meter (Herisau, Switzerland) with combined glass electrode was used for pH measurements. And Fourier-transform infrared (FT-IR) spectroscopy (Perkin–Elmer model Spectrum GX) was applied for studying the surface of synthesized Fe3O4 nanoparticles in the frequency range of 4000–400 cm^{-1} by the homogeneous mixed powder of the sample and KBr. A permanent magnet of Nd Fe B (10×5×4cm), model N48, with the magnetic field of 1.4 T was used for sorbent collection and magnetic decantation. X-ray powder diffraction (XRD) measurements were performed using a Bruker diffractometer model D8 Advance (Germany) with monochromatized Cu Kα radiation (λ= 1.5406 Å).The morphology of synthesized Fe3O4@α–Linolenic acid NPs was characterized with scanning electron microscope (LEO 1450VP SEM).

2.2. Reagents and materials

Ferrous sulfate(FeSO4, 99%), ferric chloride (FeCl3, 99%), Sodium Hydroxide(NaOH), sodium dodecyl sulfate(SDS), HPLC-grade acetonitrile, methanol, acetone, ethanol, chloroform, acetonitrile, hydrochloric acid and NaCl were all purchased from Merck(Darmstadt, Germany). flaxseed oil (fatty acid) was received from Zaradand pharmaceutical (Yasooj, Iran). Double distilled water (DDW) was used throughout. Distilled waterMilli-Q system using Distiller was prepared on a daily basis. All glassware were soaked in a mixture of dilutenitric acid and sulfuric acid for overnight and then rinsed again five times with deionized water and dried in hot air oven. Tramadol was obtained from Daroo Pakhsh pharmaceutical Co. (Tehran, Iran) and used without further purification.

2.3. Preparation of standard solutions and real samples

The TRA stock solution tramadol monthly prepared at concentration of 1000 mg L^{-1} in methanol and kept at 4 °C. Working standard solutions of different TRA in the appropriate concentrations were prepared daily with dilution of the stock standard solution with deionized water.

The calibration graph was constructed in the range of 0.1–500 $ng.mL^{-1}$ for TRA. the water samples were filtered and adjusted to pH 7 with the addition of NaOH or HCl solutions (0.1 M). Tap water samples were collected freshly from our laboratory (Bojnord, Iran). River water was collected from the Besh Ghardash River in Bojnord, north Khorasan, Iran. Standard addition method was applied for the measurement of TRA in all of the real samples.

2.4. Synthesis of α–Linolenic acid-Fe3O4NPs

Fe3O4nanoparticles were synthesized by the chemically co-precipitation method [31]. Typically, 100 ml of 0.4 $mol.L^{-1}FeCl_3$ and 100ml

of 0.2 mol.L^{-1} $FeSO_4$ were mixed and dissolved in deionized water and degassed (with ultrasonic). Then 2 mol.L^{-1} of sodium hydroxide was added into the above solution and the pH value was maintained between10-11 with continuous stirring using a magnetic stirrer (600 rpm) for1 hour and a dark precipitation was formed. Then 5 ml of flaxseed oil (α–Linolenic acid) was taken and heated to 80ºC in hot air oven and nitrogen gas was used to prevent the intrusion of oxygen. After achievement of the reaction, the precipitated Fe3O4 NPs was separated from the supernatant by magnetic field and washed successively with double distilled water (DDW)(3×50mL), methanol(3×50 mL), DDW(5×50 mL) and then filtered. Finally, α–Linolenic acid-Fe3O4NP*s* was dried in vacuum at 150ºC for 12 hour and grinded to fine powder. The obtained MNPs were stable up to one month.

2.5. Extraction Procedure

Extraction procedure was accomplished according to the following steps: (1) 20mL TRA solution in distilled water(10ng.mL^{-1}) was transferred to a glass vial,(2) 10mg of Fe3O4@α–Linolenic acid NPs was added to the TRA solution and the pH was adjusted to 3.0, (3) 0.5mL of the SDS 10mg$mL^{-1}$was added and the mixture was shaken for 5 min to enhance the TRA adsorption efficiency,(4) by use of a strong magnet with 1.4 Tesla (10×5×4cm) Fe3O4NPs placed at the bottom of the beaker was separated quickly from sample solution and the supernatant was decanted, (5) Finally the TRA was desorbed with 50μL methanol from MNPs and 40 µL of this solution was injected into the HPLC system for analysis. The Schematic presentation of TRA removal mechanism by SDS-coated Fe_3O_4@α–Linolenic acid NPs that was used in this research, have been shown in Fig. 2.

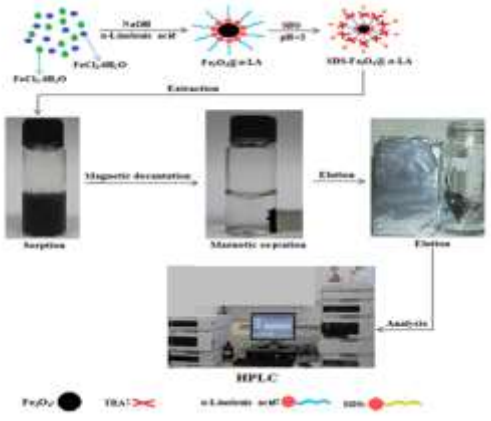

Fig. 2. Schematic presentation of TRA removal mechanism by SDS-coated Fe_3O_4@α–Linolenic acid NPs.

3. RESULT AND DISCUSSION

3.1. Characterization Fe3O4@α–Linolenic acid NPs

The existence of α–Linolenic acid on the surface of iron oxide particles was examined by infrared spectroscopy. The dried nanoparticles were mixed and pressed together with KBr. The presence of absorption peaks in the region of wavenumbers 550-630 cm^{-1} corresponding to the Fe-O vibration which confirmed the successful synthesis of Fe3O4 nanoparticles. The peak 3442cm-1 was related to the vibration of OH vibrations, indicating that the surface of Fe3O4 nanoparticles was covered with hydroxyl groups. The peaks at 1706 cm-1 and 1631 cm-1 were due to the overlapping of the absorption bands of the carboxyl groups (COO-) and double bond of α–Linolenic acid and Fe atoms. It was indicated that the α–Linolenic acid was absorbed on the surface of magnetite particles. So, α–Linolenic acid existed as a carboxyl group when it chemically interacted with the Fe3O4 nanoparticles. The interaction between carboxyl groups and metal atoms can be such as monodentate, bridging bidentate, chelating bidentate, and ionic. Therefore, these interactions specially the bridging bidentate interactions, where the covalent bonds and may be attributed to the COO-group and Fe interaction [32].

The other peaks observed in the region of 882 cm^{-1} - 1366 cm^{-1} were due to additional compounds (Polyphenols, Peroxides, Polycyclic Aromatic Hydrocarbons (PAHs), vitamin K and vitamin E) present in the oils [31]. The FTIR Spectra of synthesized Fe3O4@α–Linolenic acid NPs that was used in this research has been shown in Fig. 3.

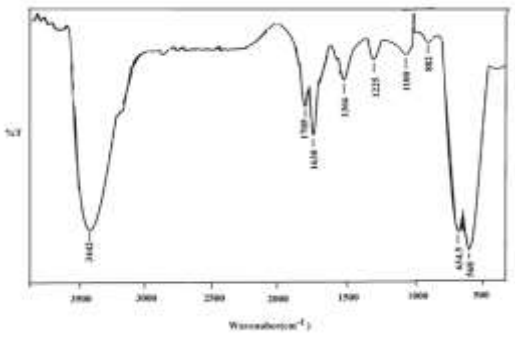

Fig.3. FT-IR spectrum of: Fe_3O_4@α–Linolenic acid NPs.

The size and morphology of the fabricated sorbent were examined through a scanning electron180 microscope (SEM). The SEM images of Fe3O4@α–Linolenic acidNPs were shown in Fig. 4. It was clear of MNPs had a good dispersion and the size of most products was

about 48nm. Also, the nanoparticles were spherical particles with a smooth and uniform surface morphology and had consistent size. The prepared Fe3O4 NPs were stabilized against agglomeration by a monolayer of α–Linolenic acid.

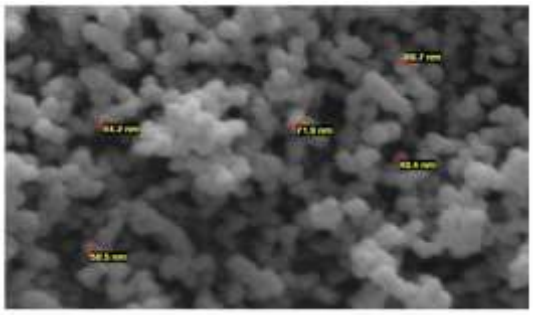

Fig.4. The scanning electron microscopy (SEM) of: Fe_3O_4@α–Linolenic acidNPs**.**

XRD analyses confirmed that the synthesized nanoparticles were Magnetite(Fe3O4) as shown in Fig. 5. Six characteristic peaks were marked by their indices (2 2 0), (3 1 1), (4 0 0), (4 2 2), (5 1 1) and (4 4 0) were observed for both samples reveal that the resultant nanoparticles were Fe3O4 with inverse-spinel structure [31]. No other characteristic peaks corresponding to the impurities of the Fe3O4@α–Linolenic acid NPs. In the pattern of XRD diffraction, the broad nature of the diffraction bands indicated that SPIONs have small particle sizes. The particle average crystallite size can also be quantitatively evaluated from the XRD data using the Scherrer formula: $D= k\lambda/ \beta\cos\theta$, where D is the average crystallite size, λ is the X-ray wavelength, β is the full-width at half maximum, and θ is the diffraction angle. Here is a constant equal to 0.94 for spherical shape. the particle size of the flaxseed oil stabilized Fe3O4 nanoparticles is 20-40 nm.

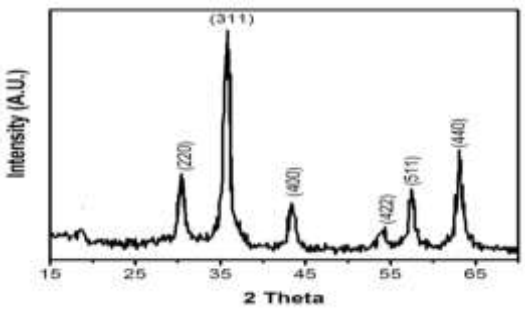

Fig.5. The X-ray diffraction (XRD) of: Fe_3O_4@α–Linolenic acidNPs.

3.2. Optimization method

3.2.1. Effect of sample pH

The charge density of sorbent surface is a key factor that affects the adsorption of analytes and it fluctuates with pH. Moreover, pH is one of the factors influencing the adsorption behavior of the system due to the change of the charge density on the MNPs surface [33-35]. The surface charge of Fe3O4 NPs is neutral at pH_{pzc}, which is about 7 [36]. But in the presence of Linolenic acid, pH_{pzc} is different from the bare Fe3O4 NPs and is lower than 7. Below the pH_{pzc}, the surface charge of the sorbent (Fe3O4@α–Linolenic acid NPs) is positive and an electrostatic repulsion can occur between the cationic forms of the basic analyte (TRA) and the sorbent's particles. Charge of the surface of MNPs is positive in the acidic condition, consequently an anionic surfactant such as SDS can be adsorbed onto surface. Therefore, cationic form of TRA can interact with negative charge head group of SDS (via ion-pair formation) and interact through hydrophobic interaction with carbon chain of SDS and α–Linolenic acid. The effect of pH on the adsorption of drug was considered over a pH range of 2–10 for Fe3O4@α–Linolenic acid NPs. The adsorption behavior of TRA is explained in Fig. 6a.The results show that maximum adsorption occurs in the pH 3.Thus, the extraction study at pH <3 was not executive because of inconsistency of the MNPs resulting from the dissolution of magnetite nanoparticles in acidic conditions and leaching, oxidizing and reduction of SDS ion adsorption, due to protonation of their sulfate groups.

3.2.2. Effect of the amount of SDS on adsorption of TRA

SDS has a most important factor in the extraction mechanism of the TRA. The results showed that adsorption amount of TRA increased remarkably by amount of SDS. So, to evaluate the surfactant effect, five amounts of SDS within the range of 5-25 mg were tested. In the optimum pH(acidic pH), TRA is adsorbed via negative head group of SDS and TRA is adsorbed through hydrophobic chain of SDS and α–Linolenic acid on the surface of NPs. Maximum adsorption was obtained when SDS amount was 10 mg. When SDS amount was above 10 mg, the adsorption of TRA decreased slowly, which may be credited to the formation of SDS micelles in the bulk of aqueous solution and the micelles caused TRA to restructure into the solution over again. Based on the results, 10 mg of SDS was added into the solution in the later experiments.

3.2.3. Effect of the adsorbent amount and extraction time

In order to study the effect of the adsorbent amount on the extraction efficiency, different amounts of sorbent within the range of 10–30 mg were added to the solution. The obtained results

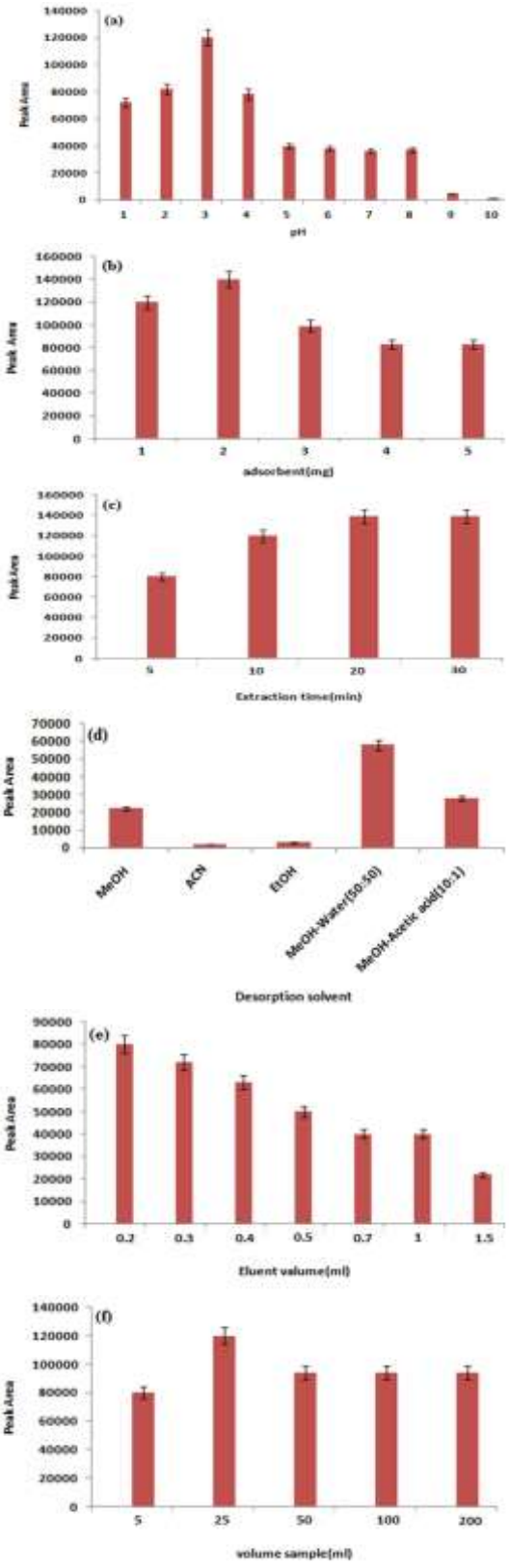

Fig.6. The Optimization of experimental conditionson the extraction efficiency of tramadol: (a)Effect of sample pH; (b) Effect of the adsorbent amount;(c) Effect ofextraction time;(d) Effect of eluent solvent; (e) Effect ofeluent's volume;(f) Effect of sample.

showed that the best extraction efficiency of drugs could be obtained using 10 mg of sorbent(in 25.0 mL of the feed solution). The obtained results showed that by increasing the adsorbent amounts up to 10mg; due to the increase of accessible sites, extraction recovery slowly increased, and then remained constant. Therefore satisfactory results can be obtained by lower amounts of nano-sized sorbents.

Also, the effect of the extraction time on the adsorption of TRA was investigated in the range of 5–30 min. Based on the obtained results, adsorption of TRA increased to 20 min and then remained constant. Therefore, extraction time of 20 min was applied in the following MSPE procedure.

3.2.4. Selection of proper eluent

After extraction, the analyte should be desorbed using an eluent solvent from the sorbent. Thus, desorption of TRA from the SDS-coated Fe3O4@α–Linolenic acidNPs was studied using different water miscible organic solvents, i.e. methanol, acetonitrile, ethanol, methanol-acetic acid(10:1), methanol-water(50:50). Between the different eluents, desorption capability of methanol-water (50:50) was found to be higher than the other solvents. This can be explained by suitable solubility of TRA in methanol-water.

3.2.5. Effect of eluent's volume and desorption time

The effect of volume of the eluent on desorption efficiency was studied in the range of 0.2–1.5mL. Based on the obtained results when the volume of eluent increased, peak areas decreased because of dilution effect. Therefore, 0.2mL of the methanol-water(50:50) was selected as the optimal volume. Also, the effect of desorption time was also examined in the range of 1–10 min. The results showed that adsorption of analyte increased to 5 min and then remained constant. Therefore, the time of 5 min appeared to be the optimum value for desorption of analyte.

3.2.6. Effect of sample volume

Sample volume is a major factor affecting extraction efficiency. To achieve better extraction efficiency with shorter operational time, sample volume was evaluated by extracting the drug from 5– 200mL aqueous solutions spiked with fixed 5ppm of TRA. According to the optimal conditions, the recoveries for TRA were still above 90% with sample volumes up to 25 mL.

3.3. Evaluation of analytical performance

Under the optimal experimental conditions mentioned above, quality features of the proposed

method were evaluated such as limit of detection (LOD) and quantification (LOQ), regression equations, correlation of determination (r^2), dynamic linear ranges (DLRs) and preconcentration factor (PF) were obtained. The calibration curve was obtained by plotting the peak areas of TRA against the concentration of the drugs in the aqueous sample. A broad dynamic linear range (DLR) with good determination coefficient (r^2> 0.99) was obtained. The LOD and LOQ were calculated based on the standard deviation of the response and the slope of calibration curve from the following equations: LOD = $3.3S_b/m$, LOQ =$10S_b/m$ where S_b is the standard deviation for five blank measurements and m is the slope of calibration curve [37]. In this study, the LOD and LOQ values were 0.074 and 0.1 $ng.mL^{-1}$, respectively. The results are summarized in Table 1.

The preconcentration factor, calculated as the chromatogram peak area after extraction of 10ng/mL of analyte was divided by the peak area before extraction under the same conditions was 134. In order to assess the repeatability of the method, three replicate determinations were carried out at concentration of 10ng/mL and the relative standard deviation (RSD) was calculated 2.89%.

Table 1. Figures of merit of the proposed method for the determination and extraction of TRA.

Analyte	DLR ($ng.mL^{-1}$)	LOD ($ng.mL^{-1}$)	LOQ ($ng.mL^{-1}$)	R^2	PF[a]	RSD[b]% (n=3)
TRA	0.1-500	0.74	0.1	0.994	134	2.89

a) Relative recovery (%)= (The found amount in the spiked sample - The found amount in the sample/The added amount) × 100

b) ND: not detected

3.4. Real sample analysis

To evaluate the applicability and investigate matrix effects of the proposed method, waste water ,Besh Ghardash river water and tap water samples were analyzed. The results are listed in Table 2.

Un-spiked water samples and water samples spiked with TRA at the concentration level 10ng/mL were analyzed by the proposed method (n = 3) for TRA. The results showed that recovery ranged between 94 and 103 with RSD values between 1.2% and 5.195%. Also Fig. 7 shows the HPLC chromatograms obtained from before and after spiking wastewater samples at the spiked levelwith the SDS-coated Fe3O4@α–Linolenic acid NPs.

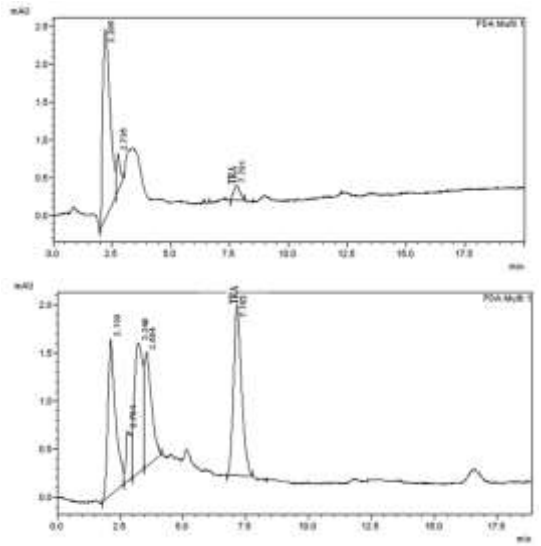

Fig. 7. HPLC Chromatograms of TRA in water samples (a) before spike, (b) after spiked with 10 ng mL^{-1} of TRA

3.5. Comparison with other related methods

Table 3 compares the figures of merit of the proposed method and several other methods for the extraction and determination of TRA water samples [38-41].In comparison with the other conventional sample preparation methods, the developed method has the merits of considerable wider linear dynamic range, lower detection limit, rapid extraction dynamics, short extraction time and small amount of organic solvent.

4. CONCLUSION

In this paper, for the first time, procedure based on SDS-coated Fe3O4@α–Linolenic acid NPs sorbents combined with HPLC has been developed to extract TRA in real water samples. Due to the use of MNPs sorbent the mentioned method is easy and time-saving. Also MNPs offer has the merits of considerable short analysis time, wide linearity, good separation efficiency , elevated pre-concentration, notable precision and high sensitivity.

Additionally, this technique was positively used to examine TRA in real water samples giving good qualitative and quantitative results. Based on the obtained results, the proposed method has a great analytical potential in preconcentration of the drug without any matrix interference in real samples.

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Table 2. Determination of TRA in different real water samples.

Sample	Cinitial ($ng.mL^{-1}$)	Cadded ($ng.mL^{-1}$)	Cfound ($ng.mL^{-1}$)	Relative recovery[a]%	RSD
River water	NDb	10	9.95± 0.2	99.5	2.01
		60	60.33±2.5	100.5	4.14
Tap water	ND	10	10.4±0.3	104	2.88
		60	58.2±0.7	97	1.2
Wastewater	5.1	10	15.7±0.66	103.97	4.2
		60	56.4±2.93	94	5.195

a) Relative recovery (%)= (The found amount in the spiked sample - The found amount in the sample/The added amount) × 100

b) ND: not detected

Table 3. Comparison of the proposed method with other reported methods for TRA determination.

Method	Sample	LOD ($ng.mL^{-1}$)	Ref.	
SPE/HPLC	Plasma	50	[37]	SPE-
GC-MS	Hair	10	[38]	HS-
SPME[a]/GC-MS	Plasma	0.2	[39]	MMIPNPs
Urine	1.5	[40]	MNPs-SPE/HPLC-PDA	Waste
water	0.07	Proposed method		

a) Head space-solid phase microextraction.

REFERENCES

[1] S.R. Abel. Tramadol: An Alternative Analgesic to Traditional Opioids and NSAIDs. *J. Pharmaceut. Care Pain Symptom Contr.* 3(2010) 5-29.

[2] W. M. Sweileh. N.Y. Shraim. S.H. Zyoud. S. W. Al-Jabi. Worldwide research productivity on tramadol: a bibliometric analysis. *Springer Plus* 5 (2016) 1108.

[3] N.Neskovic, D. Mandic, S.M.Skiljic, G.Kristek, H. Vinkovic, B.Mraovic, Z.Debeljak and S. Kvolik. Different pharmacokinetics of Tramadol, O-Demethyltramadol and N-Demethyltramadol in postoperative surgical patients from those observed in medical patients. Front. *Pharmaco*l. 12 (2021) 656748.

[4] C.R.Fulton. Y.Zang.Z. Desta. M.B.Rosenman. A.M. Holmes.B.S. Decker. et al. Drug-gene and drug-drug interactions associated with tramadol and codeine therapy in the ingeenious trial. Pharmacogenomics 20 (2019) 397–408.

[5] S.Grond.A. Sablotzki. Clinical pharmacology of tramadol. Clin. Pharmacokinet. 43 (2004) 879–923.

[6] S.H. Gan. R. Ismail. Validation of a high-performance liquid chromatography method for tramadol and o-desmethyltramadol in human plasma using solid-phase extraction. J. Chromatogr. B Biomed. Appl 759 (2001) 325-335.

[7] S.H. Gan. R. Ismail. W.W. Adnan and Z. Wan. Method development and validation of a high-performance liquid chromatographic method for tramadol in human plasma using liquid–liquid extraction. J. Chromatogr. B 772 (2002) 123-129.

[8] H. Ebrahimzadeh. Y. Yamini. A. Sedighi And M.R. Rouini. Determination of tramadol in human plasma and urine samples using liquid phase microextraction with back extraction combined with high performance liquid chromatography. J. Chromatogr. B 863 (2008) 229-234.

[9] Y. Gu. J.P. Fawcett. Improved HPLC method for the simultaneous determination of tramadol and O-desmethyltramadol in human plasma. *J. Chromatogr. B* 821 (2005) 240-243.

[10] Q. Tao. D.J. Stone. M.R. Borenstein. V. Jean-Bart. E.E. Codd. T.P. Coogan and R.B. Raffa. Gas chromatographic method using nitrogen–phosphorus detection for the measurement of tramadol and its O-desmethyl metabolite in plasma and brain tissue of mice and rats. *J. Chromatogr. B* Biomed. Appl 763 (2001) 165-171.

[11] Y. Gu. J.P. Fawcett. Improved HPLC method for the simultaneous determination of tramadol and O-desmethyltramadol in human plasma. *J. Chromatogr*. B 821 (2005) 240-243.

[12] P.S. Cheng. C.H. Lee. C. Liu and C.S. Chien. Simultaneous determination of ketamine, tramadol, methadone, and their metabolites in urine by gas chromatography-mass spectrometry. *J. Anal. Toxicol.* 32 (2008) 253-259.

[13] L. Chytil. M. Štícha. O. Matoušková. F Perlík and O. Slanař. Enatiomeric determination of tramadol and O-desmethyltramadol in human urine by gas chromatography–mass spectrometry. *J. Chromatogr. B* 877 (2009) 1937-1942.

[14] Y.F. Sha. S. Shen and G.L. Duan. Rapid determination of tramadol in human plasma by headspace solid-phase microextraction and capillary gas chromatography–mass spectrometry. *J. Pharm. Biomed. Anal*. 37 (2005) 143-147.

[15] T. Zhu. L. Ding. X. Guo. L. Yang and A. Wen. Simultaneous determination of tramadol and acetaminophen in human plasma by LC–ESI–MS. *Chromatographia* 66 (2007) 171-178.

[16] E.C.Y. Chan and P.C. Ho. Enantiomeric separation of tramadol hydrochloride and its metabolites by cyclodextrin-mediated capillary zone electrophoresis. J. Chromatogr. *B Biomed. Appl*. 707 (1998) 287-294.

[17] M. Valle. J.M. Pavon. R. Calvo. M.A. Campanero and I.F. Troconiz. Simultaneous determination of tramadol and its major active metabolite O-demethyltramadol by high-performance liquid chromatography with electrochemical detection. *J. Chromatogr. B Biomed. Appl*. 724 (1999) 83-89.

[18] P. Norouzi. R. Dinarvand. M. Reza Ganjali and A. Sadat Emami Meibodi. Application of Adsorptive Stripping Voltammetry for the Nano-Level Detection of Tramadol in Biological Fluids and Tablets Using Fast Fourier Transform Continuous Cyclic Voltammetry at an Au Microelectrode in a Flowing System. *Anal. Lett.* 40 (2007) 2252-2270.

[19] F. Ghorbani-Bidkorbeh. S. Shahrokhian. A. Mohammadi and R. Dinarvand. Simultaneous voltammetric determination of tramadol and acetaminophen using carbon nanoparticles modified glassy carbon electrode. Electrochim. *Acta*. 55 (2010) 2752-2759.

[20] A.A.Y El-Sayed. K.M. Mohamed. M.A. Hilal. S.A. Mohamed. K.E. Aboul-Hagag and A.Y. Nasser. Development and validation of high-performance liquid chromatography-diode array detector method for the determination of tramadol in human saliva. *J Chromatograph Separat Techniq* 114 (2011).

[21] M. Javanbakht. A.M. Attaran. M.H. Namjumanesh. M. Esfandyari-Manesh and B. Akbari-Adergani. Solid-phase extraction of tramadol from plasma and urine samples using a novel water-compatible molecularly imprinted polymer. *J. Chromatogr. B* 878 (2010) 1700-1706.

[22] Z. Lin. W. Cheng. Y. Li. Z. Liu. X. Chen and C. Huang. A novel superparamagnetic surface molecularly imprinted nanoparticle adopting dummy template: An efficient solid-phase extraction adsorbent for bisphenol *A. Anal. Chim. Acta* 720 (2012) 71-76.

[23] Z. Es'haghi and E. Esmaeili-Shahri. Sol–gel-derived magnetic SiO_2/TiO_2 nanocomposite reinforced hollow fiber-solid phase microextraction for enrichment of non-steroidal anti-inflammatory drugs from human hair prior to high performance liquid chromatography. *J. Chromatogr. B* 973 (2014) 142-151.

[24] A.A. Asgharinezhad. N. Mollazadeh. H. Ebrahimzadeh F. Mirbabaei and N. Shekari. Magnetic nanoparticles based dispersive micro-solid-phase extraction as a novel technique for coextraction of acidic and basic drugs from biological fluids and waste water. *J. Chromatogr. A* 1338 (2014) 1-8.

[25] M. Faraji. Y. Yamini and M. Rezaee M. Extraction of trace amounts of mercury with sodium dodecyle sulphate-coated magnetite nanoparticles and its determination by flow injection inductively coupled plasma-optical emission spectrometry. *Talanta* 81 (2010) 831-836.

[26] A.A. Atia. A.M. Donia and W.A. Al-Amrani. Adsorption/desorption behavior of acid orange 10 on magnetic silica modified with amine groups. *Chem. Eng. J*. 150 (2009) 55-62.

[27] J.L. Gong. B. Wang. G.M. Zeng. C.P. Yang. C.G. Niu. Q.Y. Niu and Y. Liang. Removal of cationic dyes from aqueous solution using magnetic multi-wall carbon nanotube nanocomposite as adsorbent. *J. Hazard. Mater*. 164 (2009) 1517-1522.

[28] M. Amelio. Chemical-physical characteristics of olive oils, *ONAOO*-2003, (2003) 2-5.

[29] E. Tripoli. M. Giammanco. G. Tabacchi. D. Di Majo. S. Giammanco and M. La Guardia. The phenolic compounds of olive oil: structure, biological activity and beneficial effects on human health. *Nutr. Res. Rev*. 18 (2005) 98-112.

[30] G.M. Ebaid. F.R. Seiva. K.K. Rocha. G.A. Souza and E.L. Novelli. Effects of olive oil and its minor phenolic constituents on obesity-induced cardiac metabolic changes. *Nutr. J.* 9 (2010) 1-9.

[31] K.L. Palanisamy, V. Devabharathi, N.M. Sundaram, The utility of magnetic iron oxide nanoparticles stabilized by carrier oils in removal of heavy metals from waste water. *Int. J. Res. Appl*. 1 (4) (2013) 15-22.

[32] F. C. Nalle, R. Wahid, I. O. Wulandari, A. Sabarudin. Synthesis and Characterization of Magnetic Fe3O4 Nanoparticles Using Oleic Acid as Stabilizing Agent. *Rasayan J. Chem*. 12 (2019) 14-21.

[33] B. Zargar. H. Parham. A. Hatamie. Modified iron oxide nanoparticles as solid phase extractor for spectrophotometeric determination and separation of basic fuchsin. *Talanta* 77 (2009) 1328-1331.
[34] L. Sun. C. Zhang. L. Chen. J. Liu. H. Jin. H. Xu and L. Ding. Preparation of alumina-coated magnetite nanoparticle for extraction of trimethoprim from environmental water samples based on mixed hemimicelles solid-phase extraction. *Anal. Chim. Acta* 638 (2009) 162-168.
[35] M. Faraji. Y. Yamini. A. Saleh. M. Rezaee. M. Ghambarian and R. A. Hassani. 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. *Anal. Chim. Acta* 659 (2010) 172-177.
[36] F. Xie. X. Lin. X. Wu. Z. Xie. Solid phase extraction of lead (II), copper (II), cadmium (II) and nickel (II) using gallic acid-modified silica gel prior to determination by flame atomic absorption spectrometry. *Talanta* 74 (2008) 836-843.
[37] Y. Cai. Z. Yan. M. Nguyen Van. L. Wang and Q. Cai. Magnetic solid phase extraction and gas chromatography–mass spectrometrical analysis of sixteen polycyclic aromatic hydrocarbons. *J. Chromatogr. A* 1406 (2015) 40-47.
[38] S.H. Gan and R. Ismail. Validation of a high-performance liquid chromatography method for tramadol and o-desmethyltramadol in human plasma using solid-phase extraction. *J. Chromatogr. B Biomed. Appl.* 759 (2001) 325-335.
[39] C. Moore. S. Rana and C. Coulter. Determination of meperidine, tramadol and oxycodone in human oral fluid using solid phase extraction and gas chromatography–mass spectrometry. *J. Chromatogr. B* 850 (2007) 370-375.
[40] Y.F. Sha. S. Shen and G.L. Duan. Rapid determination of tramadol in human plasma by headspace solid-phase microextraction and capillary gas chromatography–mass spectrometry. *J. Pharm. Biomed. Anal*. 37 (2005) 143-147.
[41] T. Madrakian. A. Afkhami. H. Mahmood-Kashani and M. Ahmadi M. Superparamagnetic surface molecularly imprinted nanoparticles for sensitive solid-phase extraction of tramadol from urine samples. *Talanta* 105 (2013) 255-261.

تأثیر اصلاح سبز سطح نانوذرات مگنتیت برای استخراج فاز جامد ترامادول و به دنبال آن کروماتوگرافی مایع با عملکرد بالا با تشخیص آرایه دیودی

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چکیده

در این مقاله، یک روش جدید سریع و حساس مبتنی بر نانوکامپوزیت Fe_3O_4 @ α-لینولنیک اسید روکش دار با سدیم دودسیل سولفات همراه با کروماتوگرافی مایع با عملکرد بالا -آشکارساز آرایه دیودی (HPLC-PDA) برای استخراج و تعیین ترامادول (TRA) در نمونه های آب ارایه شده است. نانوذرات Fe_3O_4 @ α-لینولنیک اسید توسط طیف سنجی مادون قرمز تبدیل فوریه (FT-IR) ، میکروسکوپ الکترونی روبشی (SEM) و پراش اشعه ایکس (XRD) مشخص یابی شد. عوامل اصلی موثر بر استخراج و واجذب بهینه سازی شدند. در شرایط مطلوب ، روش با موفقیت برای تعیین TRA در نمونه های محیطی اعمال شد و خطی بودن خوب در محدوده ۰,۱-۵۰۰ نانوگرم بر میلی لیتر ($R2> 0.99$) بدست آمد. حد تشخیص (LOD) و انحراف استاندارد نسبی (RSD) به ترتیب ۰,۰۷۴نانوگرم بر میلی لیتر و ۲,۸۹٪ بود. سرانجام، روش پیشنهادی برای استخراج و تعیین ترامادول در نمونه های آبی با درصد بازیابی نسبی از ۹۴ تا ۱۰۳,۹۷٪ با موفقیت اعمال شد.

واژه‌های کلیدی

ترامادول؛ نانو ذره مغناطیسی؛ استخراج فاز جامد؛ HPLC-DAD .