Journal of Pharmaceutical Analysis 2012;2(6):443–449

Contents lists available at ScienceDirect

Journal of Pharmaceutical Analysis

www.elsevier.com/locate/jpa
www.sciencedirect.com

ORIGINAL ARTICLE

Cathodic adsorptive stripping voltammetry of an anti-emetic agent Granisetron in pharmaceutical formulation and biological matrix

Rajeev Jain*, Ramkishor Sharma

School of Studies in Chemistry, Jiwaji University, Gwalior 474011, India

Received 27 November 2011; accepted 10 March 2012
Available online 18 March 2012

KEYWORDS

Granisetron;
Human plasma;
Solid-phase extraction;
Pharmaceutical formulation;
Voltammetry;
Hanging mercury drop electrode

Abstract Granisetron showed one well-defined reduction peak at Hanging Mercury Drop Electrode (HMDE) in the potential range from −1.3 to −1.5 V due to reduction of C=N bond. Solid-phase extraction technique was employed for extraction of Granisetron from spiked human plasma. Granisetron showed peak current enhancement of 4.45% at square-wave voltammetry and 5.33% at cyclic voltammetry as compared with the non stripping techniques. The proposed voltammetric method allowed quantification of Granisetron in pharmaceutical formulation over the target concentration range of 50–200 ng/mL with detection limit 13.63 ng/mL, whereas in human plasma 50–225 ng/mL with detection limit 11.75 ng/mL.

1. Introduction

Nausea and vomiting are two of the most severe side effects of cytotoxic chemotherapy or radiotherapy and prolonged vomiting may also induce severe complications [1]. Granisetron (endo-1-methyl-*N*-[9-methyl-9-azabicyclo (3.3.1) non-3-yl]-1H-indazole-3-carboxamide) (Fig. 1) is a highly selective 5-hydroxytryptamine 3 (5-HT3) receptor antagonist, and is considered to be a potent anti-emetic agent in the control of chemotherapy-induced nausea and vomiting. Its main effect is to reduce the activity of the vagus nerve, which is a nerve that activates the vomiting center in medulla oblongata [2]. Granisetron is a well-tolerated drug, and breaks down slowly, staying in the body for a long time. It is broken down by the liver's cytochrome P450 system and removed from the body by the liver and kidneys. Its metabolism involves N-demethylation and aromatic ring oxidation followed by conjugation.

However, higher dose and prolonged exposure of drug may cause some mild and long-term side effects in a subset of patients. Therefore, it is necessary to establish fast and sensitive analytical

*Corresponding author. Tel.: +91 0751 2442766; fax: +91 0751 2346209.
E-mail address: rajeevjain54@yahoo.co.in (R. Jain).

Peer review under responsibility of Institute of Materia Medica, Chinese Academy of Medical Sciences and Chinese Pharmaceutical Association.

Production and hosting by Elsevier

2095-1779 © 2012 Xi'an Jiaotong University. Production and hosting by Elsevier B.V. Open access under CC BY-NC-ND license.
10.1016/j.jpha.2012.03.005

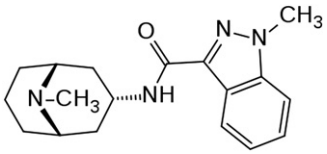

Figure 1 Chemical structure of Granisetron.

method for detection and quantification of Granisetron in biological matrix for clinical, toxicological and pharmacological studies. The widespread use of this compound also requires analytical method to assay the drug in pharmaceutical formulations and doses form. Several techniques have been explored for determination of Granisetron in pharmaceutical formulation and biological fluids such as high-performance liquid chromatography [3–6], potentiometric liquid membrane sensor [7], high performance thin layer chromatography [8] and liquid chromatography tandem mass spectrometry [9–11]. Although spectrophotometry and chromatography are the most commonly employed techniques, but the demand of expensive and sophisticated instrumentation, highly skilled personnel and time consuming extraction purification approaches prior to final analysis restrict their use in routine analysis. Since the last decade, electroanalytical techniques have been widely used in the field of pharmaceutical analysis [12–18]. These techniques have been found more selective, inexpensive, time saving and do not require time consuming purification steps after extraction, when compared with other analytical techniques [3–11]. However, no electroanalytical methods have yet been reported for the quantification of Granisetron in pharmaceutical formulation and human plasma. This work describes an analytical method with acceptable analytical characteristic of suitability and reliability for detection and quantification of Granisetron in pharmaceutical formulation and human plasma.

2. Experimental

2.1. Reagents and chemicals

Granisetron hydrochloride standard (99.20%) was kindly provided by Veeda Clinical Research Pvt. Ltd., Ahmedabad (India). Tablets containing Granisetron hydrochloride (*Graniforce*®, 1 mg/Tab) manufactured by Discovery Mankind were obtained from commercial source. Ultra pure water was obtained from Milli-Q purification system (Millipore Corp., Milford, MA, USA) and used throughout the studies. Phosphate buffer in the pH range 2.0–12.0 was prepared in ultra pure water and used without filtration. All chemicals used were of analytical reagent grade and employed without further purification. Drug free human blood plasma lots anti-coagulated with sodium heparin were procured from Radha Swami blood bank, Gwalior, India. These plasma lots were preserved at −20 °C in freezer and used after gentle thawing at room temperature.

2.2. Instrumentation and electroanalytical methods

Electrochemical measurements were performed using a μ Autolab Type III potentiostat-galvanostat (Eco-Chemie B.V., Utrecht, The Netherlands) with 757 VA computrace software. The electrodes utilized in the study were Hanging Mercury Drop Electrode (HMDE) as a working electrode, platinum wire as an auxiliary electrode and Ag/AgCl (3 M KCl) as a reference electrode. All pH measurements were performed on Decible DB-1011 digital pH meter fitted with a glass electrode as a working and saturated calomel electrode as a reference, which was previously standardized with buffer solutions of known pH. The electrochemical behavior of Granisetron hydrochloride was studied using square-wave cathodic adsorptive stripping voltammetry (SWCAdSV) and cyclic voltammetry. The voltammetric experiments were carried out at room temperature using 0.2 M phosphate buffer as supporting electrolyte. For electrochemical measurement a volume of phosphate buffer 9.9 mL and 0.1 mL analyte solution was added to the electrochemical cell and purged with pure nitrogen for 25 s. The required accumulation potential (E_{acc}) was applied to the working electrode for a selected accumulation time (t_{acc}), while the solution was stirred continuously at 2200 rpm. The stirring was stopped and after equilibrium time of 10 s, a negative-going potential scan was initiated using the parameters those are reported in Section 3.4.

2.3. Preparation of standard and test solutions

Standard stock solution of Granisetron hydrochloride (500 μg/mL) was prepared in methanol and further diluted with phosphate buffer to achieve a final concentration (100 ng/mL) in the working range. Ten tablets of Granisetron (*Graniforce*®, 1 mg/Tab) were ground to fine powder and mixed well. Sufficient amount of powder equivalent to 5 mg of Granisetron was taken for preparation of a stock solution (500 μg/mL) into 10 mL volumetric flask and the volume was made up to mark with methanol. This solution was vortexed and sonicated for 5 min to dissolve all contents of tablets properly. Clear supernatant liquid was withdrawn and diluted with phosphate buffer for preparation of test solutions in the calibration range. Stock and test solutions were stored at 2–8 °C in refrigerator until analysis.

2.4. Preparation of plasma calibration and quality control samples

Standard stock solution of Granisetron (1 mg/mL) was prepared by dissolving pure compound in methanol. Intermediate solutions were prepared from stock solution using a mixture of methanol/water (50:50, v/v) as a diluent. Working solutions were prepared from intermediate solutions using the same diluent, at proposed concentration levels of 0.50–2.25 μg/mL. Plasma calibration and quality control (QC) samples were prepared by 10% spiking of respective working solutions in blank plasma. The final methanol content of all calibrators and quality control samples was less than 5%.

2.5. Extraction techniques

Solid-phase extraction (SPE) technique was used to extract Granisetron from spiked human plasma samples. A volume of 0.5 mL each of calibrator and quality control samples was transferred to 1.5 mL pre-labeled rivals. Then 0.2 mL phosphate buffer (pH 2.5) was added to each sample, vortexed for 1 min and centrifuged at 4800 rpm for 5 min. SPE was performed using oasis mixed mode cation-exchanger (*MCX*) cartridges (30 mg/cc), a vacuum manifold device and a vacuum source. SPE cartridges were conditioned with 1 mL of methanol and equilibrated with 1 mL of phosphate buffer (pH 7.0).

Specimen samples were individually transferred to solid-phase cartridges and passed through the beds at a constant flow rate of 1 mL/min. The cartridges were washed with 1 mL of water to remove excess of matrix contents and allowed to dry for 30 s. The analyte was eluted with 1 mL of methanol and analyzed using square-wave and cyclic voltammetry.

3. Results and discussion

3.1. Effect of pH and electrolytes

The shape and characteristics of voltammograms depend on various electrolytes and pH of the medium. Therefore, effects of various electrolyte solutions such as phosphate, acetate, borate, Britton–Robinson and potassium chloride (KCl) on redox behavior of Granisetron were examined. Granisetron showed electroactivity in phosphate buffer solution. The effect of pH on the reduction peak current was also studied in pH range of 2.5–12.0 at constant concentration. With the rise in pH the peak current increased up to pH 6.5, after then redox peak current began to decrease due to pH dependence of half wave potential which indicates the involvement of protons in the electrode process and finally dislocated in alkaline pH due to lower number of available protons. Thus, phosphate buffer (pH 6.5) was selected for the study purpose. With the rise in pH peak potential was also shifted towards more negative potential, which indicated the existence of a protonation reaction coupled with the Granisetron hydrochloride electrode process. The linear dependence of peak potential on pH can be expressed by the following expression:

$$E_p(\text{mV}) = -4.5437\text{pH} - 120.2707; r = 0.9750 \quad (1)$$

3.2. Cyclic voltammetric behavior

Investigation of CV at different scan rates (υ, mV/s) can provide information involving electrochemical mechanism. Granisetron exhibited one well-defined cathodic peak in the potential range from -1.3 to -1.5 V (vs. Ag/AgCl) at all concentration levels. The absence of any oxidation peak in the anodic side of the reverse scan indicated that the reduction is totally irreversible. The influence of scan rate (υ, mV/s) on the peak current (I_p, A) was studied in the range of 25–200 mV/s, resulting in a linear relationship ($r = 0.9946$, $n = 8$) between I_p and υ with a slope of 0.0128. It was found that peak current increased with increasing scan rate (Fig. 2) and peak potential shifted toward more negative potential. The dependence of peak current and peak potential on scan rate can be expressed by following expressions:

$$I_p(\mu\text{A}) = 0.0128\upsilon(\text{mV/s}) + 0.2146; r = 0.9946 \quad (2)$$

$$E_p(\text{mV}) = -0.0009\upsilon(\text{mV/s}) - 1.4761; r = 0.9967 \quad (3)$$

3.3. Square wave cathodic adsorptive stripping voltammetry (SWCAdSV)

Different parameters affecting the adsorptive stripping response of Granisetron in phosphate buffer medium at the HMDE were examined to achieve a high sensitivity for their detection and quantification. These parameters included various experimental and instrumental variables such as accumulation time (t_{acc}), accumulation potential (E_{acc}), frequency (f), scan increment (Δs), pulse amplitude (ΔE_{sw}) etc.

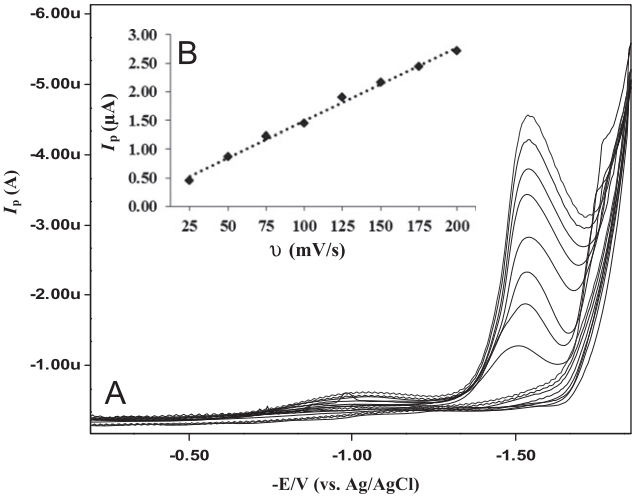

Figure 2 Cyclic voltammograms of Granisetron (100 ng/mL) at scan rate 25–200 mV/s (A) and plot of scan rate (υ, mV/s) vs. peak current (I_p, µA) (B).

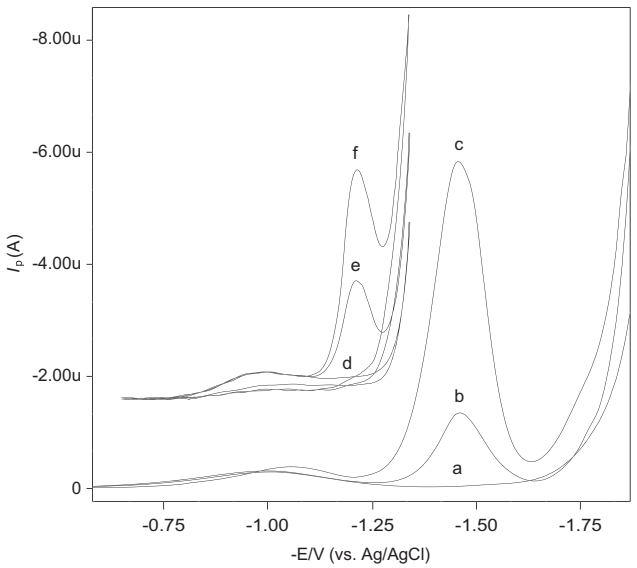

Figure 3 Square-wave voltammograms of Granisetron (175 ng/mL) at t_{acc} 0.0 s (curve b), t_{acc} 50 s (curve c) and cyclic voltammograms at t_{acc} 0.0 s (curve e), t_{acc} 50 s (curve f) and blank (curves a & d).

3.3.1. Effect of accumulation time

The analyte accumulation at the working electrode is a crucial step to achieve a high sensitivity for an electroanalytical quantitative method. Cathodic adsorptive stripping voltammetric peak height of Granisetron depends on the t_{acc}, suggesting an effective adsorption on the HMDE surface. The peak current increased linearly up to t_{acc} 50 s after those peak current remained constant due to saturated adsorption of Granisetron on the

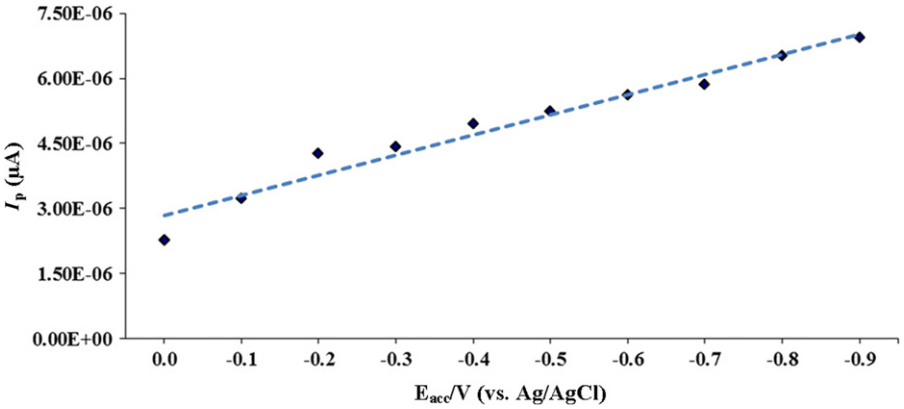

Figure 4 The plot of E_{acc}/V vs. peak current (I_p) of Granisetron (100 ng/mL) in the potential range from 0.0V to −0.9 V (vs. Ag/AgCl).

HMDE surface. The electroanalytical response of Granisetron stripping analysis was advantageous over that observed at non stripping techniques. At t_{acc} 50 s, Granisetron showed peak current enhancement of 4.45% at square-wave voltammetry (Fig. 3, curve c) and 5.33% at cyclic voltammetry (Fig. 3, curve f) as compared with the non stripping techniques (Fig. 3, curves b and e). Hence t_{acc} 50 s was selected as an optimum for the study purpose.

3.3.2. *Effect of accumulation potential*

The influence of E_{acc} on the peak current of Granisetron was also examined over the potential range from −0.1 to −0.9 V (vs. Ag/AgCl). Peak current increased linearly with increasing E_{acc} (Fig. 4). At more negative E_{acc} peak current increased due to strongly adsorption of Granisetron at the HMDE. Maximum peak current was achieved at E_{acc} −0.9 V, which can be expressed by following expression:

$$I_p(\mu A) = -4.1800E_{acc}(V) + 3.1333; r = 0.9753 \quad (4)$$

3.3.3. *Effect of frequency, scan increment and pulse amplitude*

Frequency was varied from the 10 Hz to 90 Hz with Δs 10 mV/s, ΔE_{sw} 50 mV/s and t_{acc} 50 s. Peak current increased linearly with frequency, but frequency 50 Hz was chosen to improve the sensitivity without any distortion of the peak or the baseline. Effect of the Δs on adsorptive cathodic peak current of Granisetron was studied; enhancement of the peak current achieved on the Δs 2–20 mV/s. When using Δs 20 mV/s higher current was observed and a distortion and enlargement of the peak occurred. This peak distortion makes difficult to measure the peak current accurately. The Δs 10 mV/s presented a better voltammetric peak, that is why used in the present study. The cathodic peak current for Granisetron was evaluated as a function of the ΔE_{sw} 15–50 mV/s in the conditions described above. The peak current increased linearly with increasing ΔE_{sw}. At ΔE_{sw} 50 mV/s peak current was found to be sharper and defined; hence ΔE_{sw} 50 mV/s was fixed for the study purpose.

3.4. *Method validation*

Validation of the proposed method to assay of Granisetron hydrochloride in human matrix and drug product was done as per USFDA and ICH guidelines [19,20]. The proposed method was validated using the following criteria: system suitability, specificity, recovery, linearity, reproducibility and ruggedness.

3.4.1. *System suitability*

The aim of the system suitability experiment is to ensure that the performance of the analytical system (including instrument, reagents, electrodes and analysts) is adequate for the intended analysis. After optimization of operational parameters system suitability experiment was performed. Six replicate readings of Granisetron (100 ng/mL) were taken by individually sample preparation. Relative standard deviation 1.24% was obtained using data generated from six replicate readings, indicating that the analytical system is adequate for the intended analysis.

3.4.2. *Specificity*

Specificity is the ability of the analytical method to measure the analyte in the presence of other interferences with acceptable accuracy and precision. The specificity of the assay procedure for estimation of Granisetron hydrochloride was evaluated in the presence of different concentrations of various inactive ingredients (excipients) of tablet like lactose monohydrate, microcrystalline cellulose, hydroxypropylmethyl cellulose, opadry ys-1r-7003, sodium starch glycollate, magnesium stearate. Interferences were not found at the reduction potential of Granisetron hydrochloride. The response of the analyte in the presence of excipients was also compared with the response of the pure Granisetron. It was found that assay result does not change. Thus, the proposed procedure can be considered specific.

3.4.3. *Recovery*

Formulation product recovery experiment was carried out at three different concentration levels in six replicates. The effects of various tablets inactive ingredients on recovery were also studied. For this known concentration of excipient solutions were mixed with definite amount of pre-analyzed formulations of the drug and the mixtures were analyzed as before. It was noticed that none of these interfered in the determination at the levels normally found in dosage forms. The results of recovery study were found to be quantitative, which are listed in Table 1.

Absolute recovery (in spiked human plasma) was performed by comparing extracted quality control (QC) samples of three different concentration levels, LQC (75 ng/mL), MQC (125 ng/mL) and HQC (200 ng/mL) in six replicates with unextracted samples of the same levels. The results indicated that

the mean recovery of Granisetron from human plasma was 58.69% (Table 1), which was enough for determination of Granisetron precisely in human matrix.

3.4.4. *Linearity*

The relationship between the reduction peak current (I_p, μA) and the concentration of Granisetron (ng/mL) was examined by SWCAdSV at HMDE surface. The reduction peak current was proportional to the Granisetron concentration. An excellent linearity was observed over a wide concentration range of 50–200 ng/mL (seven concentration levels). The calibration plot resulted in a straight line, which can be expressed by following expression:

$$I_p(\mu A) = 0.0310(ng/mL) - 0.0150; r = 0.9953 \quad (5)$$

Limit of detection (LOD) and limit of quantification (LOQ) estimated as 3S/m and 10S/m were found to be 13.63 ng/mL and 41.29 ng/mL respectively. Where, "*S*" is the standard deviation and "*m*" is the slope of the calibration curve. In aqueous solution, accuracy of all calibration standards was within 85–115%, except LLOQ, where it was 80–120% of the theoretical value (Table 2). The analytical characteristics for standard linearity and related validation parameters were also calculated and are summarized in Table 3. Representative square-wave cathodic adsorptive voltammograms and plot of concentration (μg/mL) vs. peak current (I_p, μA) are shown in Fig. 5.

Table 1 Recovery of Granisetron from human matrix and pharmaceutical formulation.

Recovery level	Human matrix	Formulation
Recovery level-1 [LQC][a] (%)	58.67	98.70
Recovery level-2 [MQC][a] (%)	58.80	98.94
Recovery level-3 [HQC][a] (%)	58.59	99.07
Mean recovery (%)	58.69	98.90
CV of mean recovery (%)	0.18	0.19
RSD (%)	0.106	0.188

[a]Recovery at each level represents the average of six observations ($n=6$).

Table 2 Accuracy of standard linearity and extracted plasma calibration curve of Granisetron.

Calibration standard	Accuracy (%)	
	Aqueous	Plasma
CS-01	88.58	83.20
CS-02	104.22	103.07
CS-03	107.19	107.80
CS-04	104.59	103.84
CS-05	105.44	102.53
CS-06	103.47	102.74
CS-07	99.08	99.40
CS-08	–	99.47

3.4.5. *Reproducibility and ruggedness*

For quantification of analyte, the developed analytical method should be reproducible and rugged. The high sensitivity of the adsorptive voltammetry is accompanied by reproducibility. The reproducibility was evaluated from six repeated measurements of the electrochemical signal of Granisetron standard solution (100 ng/mL). The precision of the developed method in terms of the relative standard deviation (% RSD) was 1.17%.

Ruggedness of the voltammetric method was verified by analyzing six samples of a Granisetron standard solution (100 ng/mL) by two different analysts by SWCAdSV method using the same instrument on different days. Overall RSD value 1.63% was obtained between the two sets of data, proving the ruggedness of the proposed method.

3.5. *Analytical applications of the proposed methodology*

3.5.1. *Biological matrix analysis*

This validated method was successfully applied to the determination of Granisetron in spiked human plasma using solid-phase as an extraction technique. An excellent calibration curve was observed over a wide concentration range of 50–225 ng/mL with a correlation coefficient (r) of 0.9966. The calibration plot resulted in a straight line, $I_p(\mu A) = 0.0099$ (ng/mL)+0.0885. The LOD and LOQ were found to be 11.75 and 35.61 ng/mL respectively, indicating that the level of Granisetron in human

Table 3 Square-wave voltammetric method validation parameters for standard linearity and extracted plasma calibration curve.

Parameters	Aqueous linearity	Plasma calibration curve
Slope	0.0310	0.0099
Standard deviation	0.0010	0.0002
Intercept	−0.0150	0.0885
Standard deviation	0.1280	0.0353
Correlation coefficient	0.9953	0.9966
Standard error of estimation	0.1258	0.0384
Sum of squares of regression	16.8175	2.5757
Sum of squares of residuals	0.0791	0.0088
Limit of detection (ng/mL)	13.63	11.75
Limit of quantification (ng/mL)	41.29	35.61

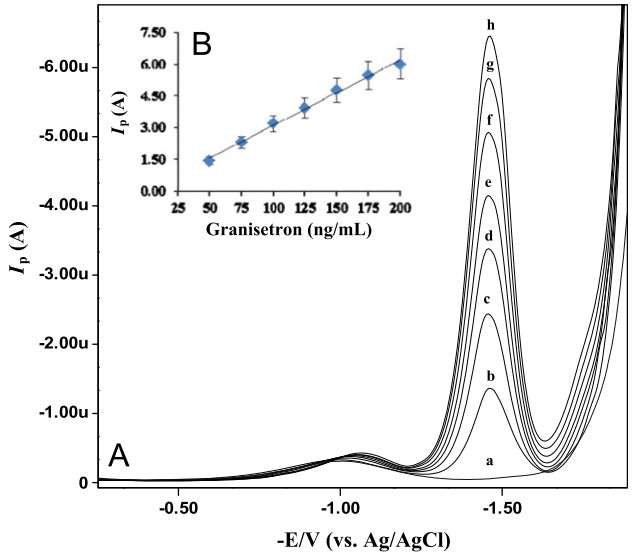

Figure 5 Square-wave voltammograms of standard solution of Granisetron at concentration levels, 50–200 ng/mL (A, curves b–h), blank solution (A, curve a) and plot of concentration vs. peak current (B).

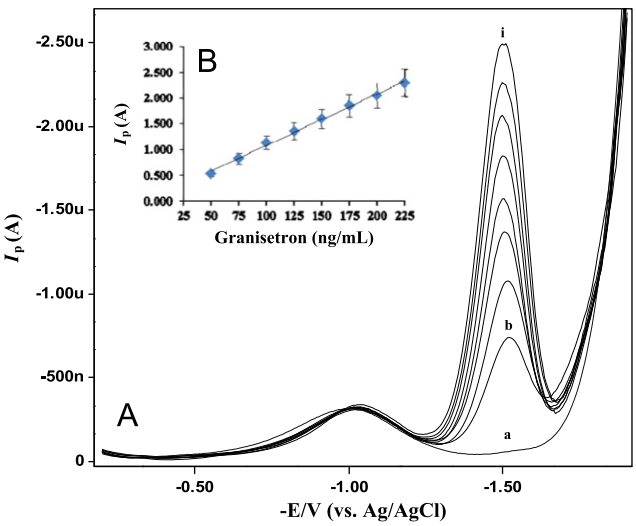

Figure 6 Square-wave voltammograms of Granisetron at concentration levels, 50–225 ng/mL (A, curves b–i), blank solution (A, curve a) and plot of concentration vs. peak current (B), extracted from human plasma through SPE.

matrix can be determined precisely. Representative SWCAdS voltammograms of different concentrations of Granisetron spiked in human plasma are depicted in Fig. 6A (curves b–i); its calibration curve is depicted in Fig. 6B. No interfering peaks were observed in the blank plasma samples within the studied potential range (Fig. 6A, curve a). The results indicated that the analytical method is accurate, as the accuracy was within the acceptance criteria of ±15% except LLOQ where it was ±20% of their nominal value (Table 2); whereas precision was also within the acceptance criteria (15%) at all concentration levels of the theoretical value. Various statistical parameters for linear regression equation were also calculated and are listed in Table 3.

3.5.2. *Pharmaceutical formulation analysis*

The optimized procedure was successfully applied to the determination of Granisetron hydrochloride in drug product (commercial dosage form, tablet *Graniforce*®). There was no need for filtration of tablets extracts from un-dissolved excipients; just dilution of an aliquot from the supernatant layer with the supporting electrolyte was required before measurement. Voltammograms of Granisetron hydrochloride in phosphate buffer exhibit well defined cathodic peak. The current was mainly adsorption-controlled and proportional to the concentration. The good linearity of the calibration graph and the negligible scatter of the experimental points are clearly evident by the correlation coefficients. The mean recovery of Granisetron found to be 98.90% proved the applicability of the proposed method (Table 1). The assay results obtained by the proposed method are listed in Table 4, indicating that method could be applied to the determination of Granisetron in drug product. Therefore, the proposed procedure may be applicable for analysis of this and other similar formulation products containing Granisetron.

4. Conclusion

The electrochemical reduction of Granisetron under the conditions described in this work is an irreversible process controlled by adsorption. Solid-phase extraction technique was employed for the extraction of Granisetron from human plasma. This method does not require sophisticated instrumentation and large setup for toxicological and pharmacokinetic studies. The proposed method does not required additional step like, evaporation after extraction of analyte from biological matrix.

The high percentage of recovery showed that the compounds was completely extracted from tablet formulation and the results indicated that the proposed method is sensitive, accurate, precise and cost effective as well as time saving

Table 4 Determination of Granisetron in tablets (*Graniforce*®) and human plasma by the proposed voltammetric methods.

Formulation products				Plasma samples			
Amount added (ng)	Amount[a] found (ng)	Accuracy (%)	CV (%)	Amount added (ng)	Amount[a] found (ng)	Accuracy (%)	CV (%)
75	74.14	98.85	1.33	75	73.24	97.65	1.83
125	123.99	99.19	1.05	125	123.77	99.02	1.50
175	173.55	99.17	1.29	200	198.10	99.05	1.59

[a]Amount found represents the average of six observations (n=6).

for routine analysis in quality control, assay of Granisetron in pharmaceutical formulation, doses form and pure form. Thus, this method can be adopted for routine analysis in quality control and research and development laboratories.

Acknowledgments

The authors are thankful to Veeda Clinical Research Pvt. Ltd., Ahmedabad (India), kindly providing the standard of Granisetron.

References

[1] V. Gebbia, G. Cannata, A. Testa, et al., Ondansetron versus Granisetron in the prevention of chemotherapy-induced nausea and vomiting, Cancer 74 (1994) 1945–1952.
[2] N.D. Kumar, S.A. Raju, S.B. Shirsand, et al., Formulation design of novel fast dissolving tablets using low and high compressible saccharides, Int. J. Pharm. Tech. Res. 1 (2009) 1585–1588.
[3] V.K. Boppana, Simultaneous determination of granisetron and its 7-hydroxyl metabolite in human plasma by reversed-phase high-performance liquid chromatography utilizing fluorescence and electrochemical detection, J. Chromatogr. A 692 (1995) 195–202.
[4] F. Pinguet, F. Bressolle, P. Martel, et al., High-performance liquid chromatographic determination of granisetron in human plasma, J. Chromatogr. B Biomed. Appl. 675 (1996) 99–105.
[5] C.T. Huang, K.C. Chen, C.F. Chen, et al., Simultaneous measurement of blood and brain microdialysates of granisetron in rat by high-performance liquid chromatography with fluorescence detection, J. Chromatogr. B 716 (1998) 251–255.
[6] I. Hewala, H. El-Fatatre, E. Emam, et al., Development and application of a validated stability-indicating HPLC method for simultaneous determination of granisetron hydrochloride, benzyl alcohol and their main degradation products in parenteral dosage forms, Talanta 82 (2010) 184–195.
[7] M.R. Ganjali, F. Aboufazeli, F. Faridbod, et al., Granisetron potentiometric sensor based on computational study, chemistry today, Focus on Pharm. Anal. 28 (2010) 4–9.
[8] S.L. Prabu, P. Selvamani, S. Latha, HPTLC method for quantitative determination of granisetron hydrochloride in bulk drug and in tablets, Lat. Am. J. Pharm. 29 (2010) 1455–1458.
[9] V.K. Boppana, C. Miller-Stein, W.H. Schaefer, Direct plasma liquid chromatographic-tandem mass spectrometric analysis of granisetron and its 7-hydroxy metabolite utilizing internal surface reversed-phase guard columns and automated column switching devices, J. Chromatogr. B Biomed. Appl. 678 (1996) 227—236.
[10] Y. Jiang, M. Lin, G. Fan, et al., Rapid determination of granisetron in human plasma by liquid chromatography coupled to tandem mass spectrometry and its application to bioequivalence study, J. Pharm. Biomed. Anal. 42 (2006) 464–473.
[11] R.V.S. Nirogi, V.N. Kandikere, M. Shukla, et al., Quantification of granisetron in human plasma by liquid chromatography coupled to electrospray tandem mass spectrometry, Biomed. Chromatogr. 20 (2006) 888–897.
[12] R. Jain, J.A. Rather, A. Dwivedi, et al., Highly sensitive and selective voltammetric sensor fullerene modified glassy carbon electrode for determination of cifitizoxime in solubilized system, Electroanalysis 22 (2010) 2600–2606.
[13] R. Jain, R.K. Yadav, A. Dwivedi, Square-Wave adsorptive stripping voltammetric behaviour of entacapone at HMDE and its determination in the presence of surfactant, Colloids Surf. A Physicochem. Eng. Asp. 359 (2010) 25–30.
[14] R. Jain, V.K. Gupta, N. Jadon, et al., Voltammetric determination of cefixime in pharmaceuticals and biological fluids, Anal. Biochem. 407 (2010) 79–88.
[15] R. Jain, V.K. Gupta, N. Jadon, et al., Determination of pyridostigmine bromide in bulk, pharmaceutical formulation and biological fluid, J. Electroanal. Chem. 648 (2010) 20–27.
[16] R. Jain, R.K. Yadav, Voltammetric assay of anti-anginal drug nicorandil in different solvents, Drug Test. Anal. 3 (2011) 171–175.
[17] R. Jain, J.A. Rather, Voltammetric determination of antibacterial drug gemifloxacin in solubilized systems at multi-walled carbon nanotubes modified glassy carbon electrode, Colloids Surf. B Biointerfaces 83 (2011) 340–346.
[18] R. Jain, J.A. Rather, Stripping voltammetry of in solubilized system and biological fluids, Colloids Surf. A Physicochem. Eng. Asp. 378 (2011) 27–33.
[19] Guidance for Industry, Bioanalytical method validation food and drug administration, Center for drug evaluation and research (CDER) (2001) 1–22.
[20] ICH topic Q2(R), Validation of analytical procedure: methodology, ICH Harmonized Tripartite Guidelines 4 (2005) 1–13.