Materials Science and Engineering C 31 (2011) 230–237

Contents lists available at ScienceDirect

Materials Science and Engineering C

journal homepage: www.elsevier.com/locate/msec

Voltammetric behaviour of nitroxazepine in solubilized system and biological fluids

Rajeev Jain *, Jahangir Ahmad Rather, Ashish Dwivedi

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

ARTICLE INFO

Article history:
Received 15 April 2010
Received in revised form 27 July 2010
Accepted 1 September 2010
Available online 7 September 2010

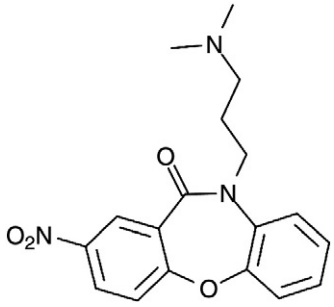
Keywords:
Nitroxazepine (Nitrox)
Solubilized system
Adsorptive stripping voltammetry
HMDE
Pharmaceutical formulation
Biological fluids

ABSTRACT

This study reports the development and validation of sensitive and selective assay method for the determination of the antidepressant drug in solubilized system and biological fluids. Solubilized system of different surfactants including cationic, anionic and non-ionic influences the electrochemical response of drug. Addition of cationic surfactant cetrimide to the solution containing drug enhances the peak current signal while anionic and non-ionic showed an opposite effect. The current signal due to reduction process was function of concentration of nitroxazepine, pH, type of surfactant and preconcentration time at the electrode surface. The reduction process is irreversible and adsorption controlled at HMDE. Various chemical and instrumental parameters affecting the monitored electroanalytical response were investigated and optimized for niroxazepine hydrochloride determination. The proposed SWCAdSV and DPCAdSV methods are linear over the concentration range 2.0×10^{-7}– 5.0×10^{-9} mol/L and 6.1×10^{-7}– 1.0×10^{-8} mol/L with detection limit of 1.62×10^{-10} mo/L and 1.4×10^{-9} mo/L respectively. The method shows good sensitivity, selectivity, accuracy and precision that makes it very suitable for determination of nitroxazepine in pharmaceutical formulation and biological fluids.

1. Introduction

Nitroxazepine hydrochloride (scheme 1) is a new psychoactive tricyclic antidepressant drug commonly used for treatment of depression and nocturnal enuresis. The antidepressant activity of nitroxazepine hydrochloride is similar to that of other tricyclic antidepressants like imipramine. The mechanism of action involves inhibition of both exogenously administered and endogenously released noradrenaline [1] (Scheme 1).



Scheme 1.

The monitoring of such compounds is of great importance for quality control and clinical laboratories. To date only few analytical methods have been reported for the estimation of nitroxazepine hydrochloride; they include polarographic analysis [2] and high-performance liquid chromatography [3]. The chromatographic methods are although accurate; however they are time consuming, expensive, solvent usage interference and require skilled personals and therefore are unsuitable for online or field monitoring. New pharmaceutical preparations and biosample analysis requires fast and specific method for the determination of nitroxazepine hydrochloride. Therefore a novel technique for the determination of nitroxazepine hydrochloride is still needed to be developed. The versatility of electrochemical techniques and the low detection limits as well as its low acquitisition costs made them widely applied in various fields especially in the determination of biological/chemical materials which posses electroactive groups. Electrochemical methods have been proved to be sensitive and reliable for the determination of numerous electroactive drug components [4–9]. The electroanalytical techniques proved to be useful both for the analysis of pharmaceutical formulation of drugs and in biological fluids. The advantages of electrochemical techniques in the analysis of drugs are their simplicity, low cost and relatively short analysis time as compared to other routine analytical techniques.

Reviewing the literature neither adsorptive stripping nor squarewave voltammetric method for the assay and quantification of nitroxazepine hydrochloride are reported. Hence the current electroanalytical research aimed to study the voltammetric behaviour of nitroxazepine and its interfacial adsorptive accumulation onto the hanging mercury dropping electrode (HMDE). Based on the results

* Corresponding author. Tel.: +91 751 2442766; fax: +91 751 2346209.
E-mail address: rajeevjain54@yahoo.co.in (R. Jain).

0928-4931/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.msec.2010.09.001

obtained a sensitive, simple and low cost SW and DPV-AdSV procedures were developed in solubilized system for the determination of nitroxazepine hydrochloride in pharmaceutical formulation and in biological fluids. There are certain advantages associated with this method such as more dissolution, high selectivity and no interference from other active compounds present in commercial dosage form. The development of meaningful dissolution procedure for drug products with limited water solubility has been a great challenge to analyst [10]. It has been seen that surfactant play a very important role in electrode reactions not only in solubilizing organic compounds, but also providing specific orientation of the molecules at the electrode interface [11,12].

The aggregates of surfactants such as micelles, liquid crystalline vesicles etc., which could enhance the stabilized content and the control of release behaviour of drugs are widely studied as drug delivery systems [13,14]. The use of surfactants as drug carriers make necessary to study the interaction of drugs with micellar systems. Micellar effects may be of many kinds including electrostatic, surface interactions, hydrophobic forces and partition between the micelle and the water phase. In addition micellar systems are considered to be primitive model systems for biological membranes [15]. Effects of surfactant on solubility and dissolution rate of poorly soluble drugs are well characterized [16]. Surfactants heavily influence the electrochemical processes of electroactive species [17,18] and thus are widely used in electronalytical chemistry to improve the sensitivity and selectivity [19–22]. Adsorption of surfactants on electrodes and solubilization of electroactive compounds in micellar aggregates might significantly change the redox potential, charge transfer coefficients and diffusion coefficients that enhances the electroanalytical response and hence lowers the detection limit [23,24].

In the present study, the effect of the changing the charge of the surfactant used namely anionic, non-ionic and cationic, its concentrations with the solution pH and concentration of analyte on the voltammetric response of this drug has been studied with improved sensitivity at HMDE. Thus the main objective of the present work is to develop an electrochemical method for the determination of nitroxazepine hydrochloride utilizing enhancement effect of solubilized system.

2. Experimental

2.1. Materials and methods

Nitroxazepine hydrochloride (99% purity) was obtained from Novartis India Ltd. Mumbai, India and was used as received. Tablets containing nitroxazepine hydrochloride (*Sintamil*) labeled 75 mg was obtained from commercial sources. KCl (0.1 mol/L) solution was prepared in double distilled water and used as supporting electrolyte. A stock solution of nitroxazepine hydrochloride (1.0×0^{-4} mol/L) was prepared in DMF (Dimethylformamide), cetrimide, sodium dodecyl sulphate (SDS) and in Tween 20. The solutions for recording voltammograms were prepared by mixing appropriate volume of stock solution, buffers and 0.1 mol/L KCl. All chemicals used are of analytical reagent grade quality and were employed without further purification.

2.2. Procedure

2.2.1. Sintamil tablet solution

Ten Tablets were weighed and the average mass per tablet was determined. A portion of the finely grounded material equivalent to 75 mg of nitroxazepine hydrochloride was accurately weighed and transferred into the 100 mL calibrated flask containing 70 mL surfactant solution. The content of the flask was sonicated for about 15 minutes and then made up to the volume with the surfactant solution. An aliquot of the solution was then analyzed according to the proposed voltammetric procedure.

2.2.2. Serum and plasma analysis

Drug-free human blood obtained from healthy volunteers (after having obtained their written consent) was centrifuged at 5000 rpm for 30 min at room temperature and separated serum and plasma samples were stored under refrigeration until assay. Then separated serum and plasma were treated with 1.0 mL of acetonitrile as protein denaturing and precipitating agent. After vortexing for 30 s, the mixture was then centrifuged for 10 min at 5000 rpm in order to eliminate serum and plasma protein residues and supernatant was taken carefully. An aliquot of serum and plasma sample was fortified with nitroxazepine hydrochloride dissolved in cetrimide to achieve a final concentration of 1.0×10^{-4} mol/L. Appropriate volumes of this supernatant were transferred into the volumetric flask and diluted up to the volume with phosphate buffer of pH 10.0. Then the protein-free spiked serum and plasma containing drug were analyzed according to the proposed stripping voltammetric procedure.

2.3. Instrumentation

Electrochemical measurements were performed using a μ-AUTOLAB TYPE III (Eco- Chemie B.V., Utrecht, The Netherlands) potentiostat-galvanostat with 757VA computrace software. The utilized electrodes were hanging mercury drop electrode (HMDE) as working electrode, Ag/AgCl (3.0 mol/L KCl) as reference electrode and a graphite rod as auxiliary electrode. Controlled potential coulometric experiments were carried out using an electrochemical cell i.e., Autolab Potentiostat/Galvanostat PGSTAT Metrohm 663 VA stand with GPES 4.2 (General Purpose Electrochemical Software) software. Coulometric experiments were performed by the potentiostatic mode using Pt foil with large surface area as working electrode and a Pt wire as the counter electrode. All the solutions examined by electrochemical technique and were purged for 10 min with purified nitrogen gas after which a continuous stream of nitrogen was passed over the solutions during the measurements. All pH-metric measurements were made on a Decible DB-1011 digital pH meter fitted with a glass electrode and a saturated calomel electrode as reference, which was previously standardized with buffers of known pH.

3. Results and Discussion

The electrochemical behaviour of nitroxazepine hydrochloride on HMDE was studied by using cyclic voltammetry (CV), differential pulse cathodic adsorptive stripping voltammetry (DPCAdSV) and squarewave cathodic adsorptive stripping voltammetry (SWCAdSV). In all electrochemical methods nitroxazepine hydrochloride gave one well defined reduction peak in DMF and cetrimide which is attributed to the reduction of $-NO_2$ group at mercury electrode.

3.1. Nitroxazepine behaviour in solubilized system

The influence of different solubilized system of surfactants including cationic (cetrimide), anionic (SDS) and neutral (Tween-20) on the reduction of nitroxazepine hydrochloride were explored by the proposed voltammetric procedure and the specific values of I_{pc} and E_{pc} were summarized in Table 1. On comparing the voltammetric

Table 1
Electrochemical parameters of nitroxazepine hydrochloride in solubilized Systems.

Electrolyte (Buffer pH 10.0)	[a]E_{pc} /V (vs. Ag/AgCl)	[b]I_{pc}/μA
1.2×10^{-7} mol/L Nitroxazepine hydrochloride + 8.14×10^{-4} mol/L Tween 20	0.41	0.41
1.2×10^{-7} mol/L Nitroxazepine hydrochloride + 2.43×10^{-3} mol/L Cetrimide	0.52	0.46
1.2×10^{-7} mol/L Nitroxazepine hydrochloride + 3.46×10^{-3} mol/ L Sodium Dodecyl Sulphate	0.48	0.28
1.2×10^{-7} mol/L Nitroxazepine hydrochloride + 1.36×10^{-2} mol/L DMF	0.49	0.30

[a] Cathodic peak potential.
[b] Cathodic peak current.