International Journal of Recent Research and Review, Vol. III, September 2012

ISSN 2277 – 8322

Voltammetric Assay of Antiviral Drug Nitazoxanide in Bulk Form, Human Breast Milk and Urine Sample

Hemlata Sharma[1], K K Jhankal[2], Ramlal Saini[3], D. K. Sharma[4]

Department of Chemistry, University of Rajasthan, Jaipur, India

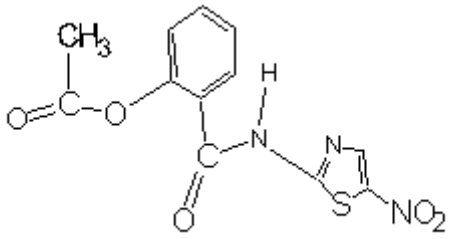
Email: hema.1611@yahoo.co.in

Abstract **- Dynamic Voltammetric methods have been employed for the fast and inexpensive determination of Nitazoxanide drug. Cyclic voltammetric Square wave cathodic adsorptive stripping voltammetry (SW-CAdSV) and Differential pulse cathodic adsorptive stripping voltammetry (DP-CAdSV) methods have been developed for the determination of antiparasitic nitazoxanide drug in bulk form, human breast milk and urine samples, based on its electrochemical reduction at a glassy carbon electrode(GCS). The Phosphate buffer of pH 7.0 was found to be reasonable as a supporting electrolyte for assay of the drug. A systemic study of the experimental parameters that affect the stripping response was carried out and experimental conditions were optimized.**

Keywords- Nitazoxanide, Square wave cathodic adsorptive stripping voltammetry, cyclic voltammetry, electron-transfer coefficient (α), diffusion coefficient (D).

I. INTRODUCTION

Nitazoxanide [2-(5-nitro-1, 3-thiazol-2-ylcarbamoyl) phenyl acetate] is prescribed for treatment of diseases caused by *Giardia -intestinalis* and *Cryptosporidium* like diarrhea, chronic hepatitis B, rotavirus disease, and immune-compromised patients, including those with AIDS or HIV infection. The drug shows activity against numerous intestinal protozoa, helminthes and anaerobic bacteria [1-5]. The drug represents a significant advance in the treatment of intestinal parasitical infections worldwide. The monitoring of the drug is important for quality assurance in preparations and for obtaining optimum therapeutic concentrations, while minimizing the risk of toxicity [6-8].



As a well established and useful drug it has generated significant analytical interest, several methods have been described for its determination in pharmaceutical formulations or biological fluids. The main methods employed are based on spectrophotometry [9,10] chromatography and HPLC [11-16]. Although the selectivity and the detection limit have been improved in these methods, these are rather time-consuming methods and require large number of complicated steps to follow on for analysis. For this purpose, the desirable technique for the analysis of drugs should be rapid, simple, low cost, and of high sensitivity in analysis [17-21]. In all available electrochemical methods, stripping analysis is an extremely sensitive technique that utilizes a bulk electrolyte step to preconcentrate the analyte from the sample solution into or onto the working electrode. Nitazoxanide molecule has electroactive groups so electro analytical methods have been developed for the determination of Nitazoxanide. Therefore, this approach was investigated for the quantitative determination of Nitazoxanide. Electrochemical methods have shown remarkable

advantage in analysis of drugs in pharmaceutical formulation. A survey of the literature reveals that electrochemical techniques have demonstrated large applicability in studies of electrodic reaction mechanisms of pharmaceutical compounds. Electrochemical techniques are time-saving, quantitative, and qualitative with improved sensitivity over other available methods. Application of voltammetric methods to the estimation of very important pharmaceuticals such as Nitazoxanide is also required due to the availability of simple and handy size equipment [22-25].

The analytical problems described here for this determination are of considerable value to analytical chemistry. In the present paper, electrochemical behavior of Nitazoxanide has been reported by employing cathodic adsorptive stripping voltammetry (CAdSV) and Cyclic voltammetry (CV).

II. EXPERIMENTAL

A. Reagent and Material

Nitazoxanide was kindly provided by Ind-Swift Limited India and was used without further purification. A stock standard solution of bulk Nitazoxanide (1×10^{-3} mol L^{-1}) was prepared in N, N- Dimethyl formamide (DMF) and stored at 4°C until assay. One tablet of Nitazoxanide was weighed and ground to a homogeneous fine powder in a mortar. A portion of the finely ground material equivalent to 100mg of Nitazoxanide accurately weighed and transferred into a 10 ml calibrated flask containing 8 ml DMF. The content of the flask was sonicated for about 10 min and then made up to volume with DMF. The solution was next filtered through a 0.45 µm milli-pore filter (Watman filter paper). The Working solutions (1×10^{-9} to1×10^{-4} mol L^{-1}) bulk Nitazoxanide were prepared daily by appropriate dilution of the standard solution of bulk Nitazoxanide with DMF just before use. A series Phosphate buffer of pH values 2 to 11 was prepared and used as a supporting electrolyte.

Apparatus Required:

Model 1230A [SR 400] electrochemical analyzer (CHI Instrument, USA) was employed for electrochemical techniques, with a totally automated attached to a PC with proper CHI 100W version 2.3 software for total control of the experiments and data acquisition and treatment. A three-electrode cell system was used with activated glassy carbon electrode (ø = 3 mm, CHI) as working electrode, Ag/AgCl (3 M KCl) as the reference electrode and a platinum wire as the auxiliary electrode. A magnetic stirrer (CAT.NO-1250-2 LAB-LINE INSTRUMENT, INC. USA) and a stirring bar provided the convective transport during the preconcentration step. A digital pH-meter (CHINO- DB-1011) was used for measuring the pH values of the investigated solutions. The digital pH meter was fitted with a glass electrode and a saturated calomel electrode as the reference, which was previously standardized with buffers of known pH.

B. Pre Treatment of The Glassy Carbon Electrode

The glassy carbon working electrode was polished to a mirror finish using a CHI polishing kit with alumina paste and thoroughly washed with double distilled water before measurements.

III. PROCEDURE

10 mL of the total solution containing Phosphate buffer of pH 7 and the appropriate concentration of the analyte (bulk Nitazoxanide) were transferred into the electrochemical cell, through which a pure nitrogen stream was passed for 10 min to remove the oxygen gas before measurements. Voltammograms were recorded by scanning the potential towards the negative direction using Cathodic Adsorptive square wave potential-waveform. Quantification of Nitazoxanide was performed by means of both calibration curve and standard addition methods. The reversibility of the reduction process was investigated by using CV.

IV. ANALYSIS OF SPIKED URINE & BREAST MILK SAMPLES

Drug-free human breast milk, obtained from healthy volunteers (after obtaining their written consent) was centrifuged (4000 rpm) for 30 min at room temperature, and separated sample were stored frozen until assay. An aliquot of breast milk sample was fortified with Nitazoxanide dissolved in DMF to achieve a final concentration of 1x 10^{-3} M. Acetonitrile removes breast milk proteins effectively. After vortexing for 30sec., the mixture was then centrifuged for 10 min at 4000 rpm in order to eliminate breast milk protein residues. Appropriate volumes of this sample were transferred into the voltammetric cell and diluted up to the volume with phosphate buffer at pH 7 and subsequently analyzed according to the recommended in the general analytical procedure. A blank experiment was carried out adopting the above procedure. An aliquot of human urine sample was collected and analyzed as breast milk sample.

V. RESULTS AND DISCUSSION

The electrochemical behavior of nitazoxanide was studied by cyclic voltammetric, and cathodic adsorptive stripping voltammetric techniques on GCE. In both electrochemical methods Nitazoxanide gave one well defined reduction peak in aqueous solution, which is attributed to the reduction of the NO_2 group.

A. Cyclic Voltammetric Behavior

Nitazoxanide exhibited one distinct and well-defined cathodic peak in the potential range 0.0 to -1.0 V, at all the concentrations (fig.-1). No peak could be observed in the anodic direction of the reverse scans, suggesting the irreversible nature of the electrode process.

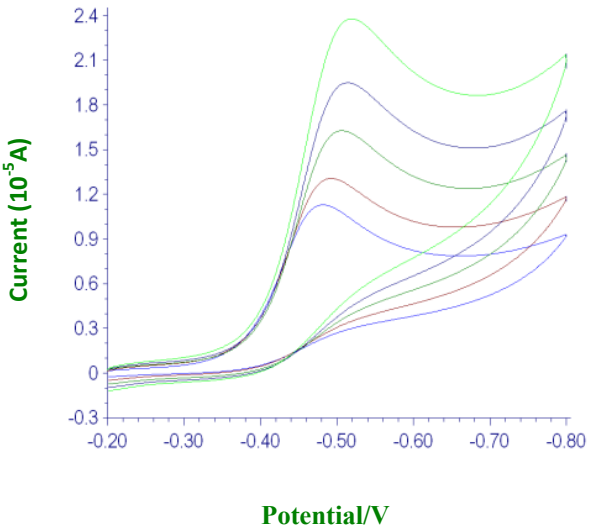


Fig.1 Cyclic voltammograms of 1×10^{-6} mol L^{-1}Nitazoxanide in phosphate buffer at different scan rates: (a) 50 mV^{-1} (b)100 mV^{-1} (c)200 mV^{-1} (d) 300 mV^{-1} (e) 400mV^{-1}

B. Stripping Voltammetric Studies

Stripping voltammetric methods were optimized for trace determination of Nitazoxanide by square wave potential-waveforms. Stripping voltammograms of bulk in the Phosphate buffer (pH 2 to 11) recorded by square wave voltammetry following its preconcentration onto the GCE by adsorptive accumulation for 15 sec. exhibited a well-defined single irreversible cathodic peak with a better enhanced peak current magnitude at pH 7. Therefore, a Phosphate buffer of pH 7 was chosen as a supporting electrolyte in the rest of study.

C. (Dp-Cadsv) Method

The optimum operational conditions of pulse-height scan rate and preconcentration parameters for determination of bulk Nitazoxanide applying differential pulse cathodic adsorptive stripping voltammetry (DP-CAdSV) at the GCE were identified. This was carried out by recording voltammograms of 1×10^{-8} mol L^{-1} bulk Nitazoxanide in the Phosphate buffer of pH 7.0 (fig.2) applying the described DP-CAdSV method.

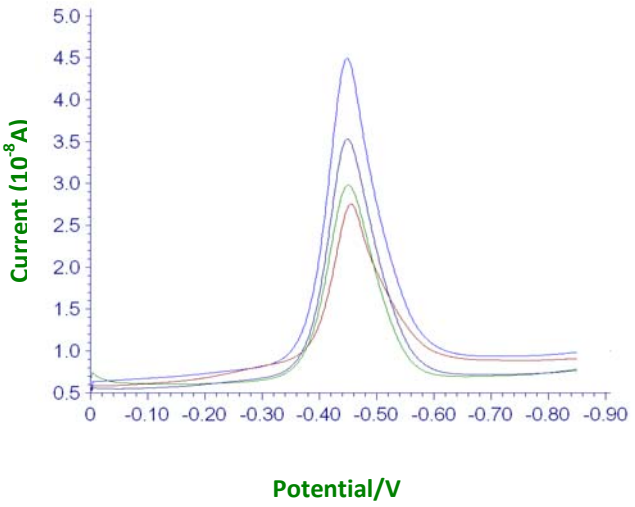


Fig. 2 The DPCAdS voltammograms for increased concentrations of nitazoxanide in bulk forms: (1) 5x10^{-9} (2) 7x10^{-9} (3) 9x10^{-9}(4) 12x10^{-9}mol L^{-1}; Eacc. = 0.0 V, tacc. = 15 s, pulse amplitude 50 mV, pulse width 30 ms, and ΔE=10 mV and Phosphate buffer (9mL) of pH 7.

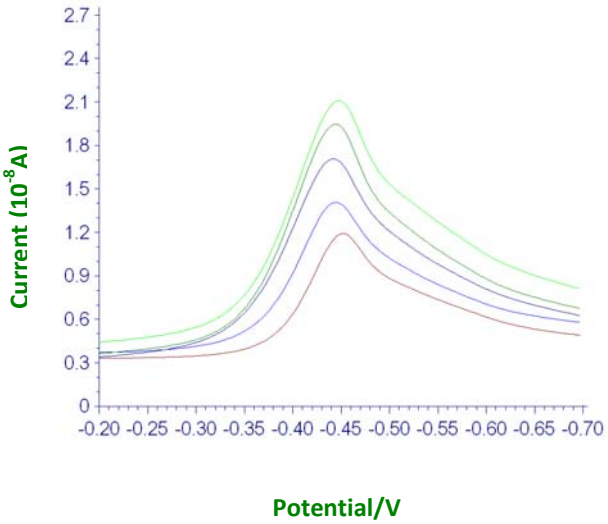


Fig. 3 SW-CAdS voltammograms of nitazoxanide in phosphate buffer in different concentrations: (a)1×10^{-9} mol l^{-1} (b)1.5×10^{-9}mol l^{-1}(c) 2×10^{-9} mol l^{-1} (d)2.5×10^{-9} mol l^{-1} (e)3×10^{-9} mol l^{-1}.

D. (Sw-Cadsv) Method

Optimum operational conditions of both preconcentration and pulse-parameters for determination of bulk nitazoxanide applying square wave cathodic adsorptive stripping voltammetry (SW-CAdSV) were identified. SW-CAdS voltammograms of various concentrations of nitazoxanide were recorded under the optimal operational conditions (fig.3) applying the described SW-CAdSV method.

VI. VALIDATION OF THE PROCEDURE

Validation of the proposed procedure for assay of the drug at trace levels was examined via evaluation of the limit of detection (LOD), limit of quantization (LOQ), reproducibility, recovery, selectivity, robustness and ruggedness.

A. LOD and LOQ

The Limits of detection (LOD) and quantification (LOQ) of Nitazoxanide were calculated using the equations [32-34]:

$$LOD= 3s/b$$

$$LOQ=10s/b$$

Where s is the standard deviation of the intercept and b is the slope of the calibration curve. Reproducibility, accuracy and precision of results applying the described stripping voltammetric methods were examined by performing five replicate analyses of standard solutions of bulk Nitazoxanide. A LOD of 1.878x10^{-10} mol L^{-1} and a LOQ of 6.262 x10^{-10} mol L^{-1} bulk were achieved (Table-I) applying the described DP-CAdSV method. A LOD of 1.078x10^{-10} mol L^{-1} and a LOQ of 3.595x10^{-10} mol L^{-1} bulk Nitazoxanide were achieved (Table - I) applying the described SW-CAdSV method. The obtained results confirmed the reliability of the described stripping voltammetric methods for assay of Nitazoxanide.

B. Linerity

The applicability of the proposed SWCAdSV and DPCAdSV procedures as analytical methods for the determination of Nitazoxanide was examined by measuring the stripping peak current as a function of concentration of the bulk drug at least three times under

the optimized operational parameters. The calibration plot of the peak current versus the concentration was found to be linear over the range $1x10^{-9}$ to $1x10^{-8}$ mol L^{-1} in for the stripping voltammetric process. The linear regression equation (fig.4 and5) is expressed as

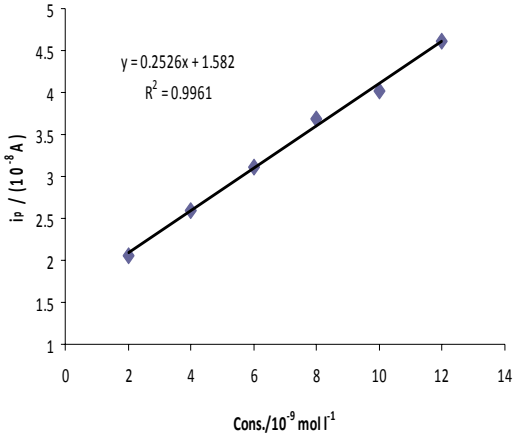


Fig.. 4 Plot of i_p versus concentration from DPCAdS voltammograms in Fig.. 2for Nitazoxanide in bulk forms.

DPCAdSV:

i_{pc} (10^{-8} A) = $0.2526x10^{-8}$ (mol L^{-1}) + 1.5852; r^2 = 0.9961

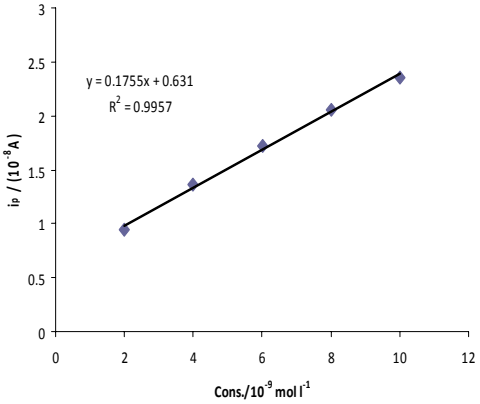


Fig. 5 Plot of i_p versus concentration from SWCAdS voltammograms in Fig.3 for Nitazoxanide in bulk forms

SWCAdSV:

i_{pc} (10^{-8}A) = 0.1755 $x10^{-8}$ (mol L^{-1}) +0.631; r^2 = 0.999

The regression plots showed that there is a linear dependence of the current intensity on the concentration in both DPCAdSV and SWCAdSV modes over the range, as given in Table - I. The table also shows the detection limits and the results of the statistical analysis of the experimental data such as slopes, intercept, the correlation coefficients obtained by the linear least-squares treatment of the results, along with the standard deviation (SD) of the intercept (Sa) on the ordinate. The good linearity of the calibration graphs and the negligible scatter of the experimental points are clearly evident by the values of the correlation coefficient and SD. The specificity of the method was investigated by observing any interference encountered from the excipients of the tablets mass. It is shown that, in the proposed method, co-administered drugs did not interfere.

C. Specificity

Specificity is the ability of the method to measure the analyte response in the presence of all the potential impurities. The specificity of the optimized procedure for estimation of Nitazoxanide was examined in the presence of excipients which were added to dosage form. Samples containing $1x10^{-9}$ mol L^{-1} bulk and different concentrations of the excipient under evaluation were analyzed by means of the proposed procedure. The obtained mean percentage recoveries (%R) and the relative standard deviations (%RSD) based on the average of five replicate measurements 97.5(0.5) to 100.5 (1.60) for SWCAdSV and 98.25(1.2) to 100.5(1.13) for DPCAdSV showed no significant interference from excipients. Thus the proposed procedure can be considered specific.

D. Repeatability

The repeatability was examined by performing five replicate measurements for $1x10^{-9}$ mL^{-1} bulk drug followed preconcentration for 200 s under the same operational conditions (Table - II). Percentage recoveries (%R) of 97.5, 99, 98.25, 98.9, 99 and 100.5

were achieved with a mean value of 98.86 and (%RSD) of 1.006, which indicates repeatability and high precision of for SW-CAdSV. Percentage recoveries (%R) of 98.25, 98.83, 99.25, 100.25 and 100.5 were achieved with a mean value of 99.33 and (%RSD) of 0.878, which indicates repeatability and high precision of for DP-CAdSV.

E. Roubstness

The robustness was examined by evaluating the influence of small variation of some of the most important procedure variables including preconcentration potential (E_{acc}) and preconcentration time (t_{acc}). The obtained result provided an indication of the reliability of the proposed procedure for the assay of Nitazoxanide and hence it can be considered robust. The obtained mean percentage recoveries based on the average of five replicate measurements were not significantly affected within the studied range of variations of some operational parameters and consequently the proposed procedure can be considered robust.

F. Precision And Stability

The intraday and interday precision of the proposed procedure was estimated by analyzing $1x10^{-9}$mol L^{-1} Nitazoxanide solutions five times in successive days using SWCAdSV and DPCAdSV. The percentage recoveries based on the average of five separate determinations are given in Table - II. The results confirmed both the good precision of the proposed procedure and the stability of the drug's solution.

G. Ruggedness

The ruggedness test of the analytical assay method is defined as the degree of reproducibility of assay results obtained by the successful applications of the assay over time and multiple laboratories and analysts. Two analysts, analyzed the same standard with SWCAdSV and DPCAdSV methods using the same instrument. The methods were found to be rugged with the results of variation coefficients 0.915 and 1.0% for SWCAdSV, 0.958 and 1.3% for DPCAdSV methods for first and second analysts, respectively. The results show no statistical differences between different analysts.

VII. ASSAY OF NITAZOXANIDE IN SPIKED HUMAN URINE

Nitazoxanide in spiked human urine was successfully analyzed by the described voltammetric methods (DPCAdSV and SW-CAdSV) without the necessity for extraction of the drug prior to the analysis. Representative DPCAdSV and SW-CAdS voltammograms of Nitazoxanide in spiked human urine recorded under the optimum operational conditions of the described stripping voltammetric methods are shown in Figures 6 and 7 respectively. No interfering peaks were observed in the blank human urine sample within the studied potential range. Linear variations of the peak current (i_p) with concentration of Nitazoxanide in spiked human urine were obtained within the concentration ranges of 1×10^{-9} to 1×10^{-8}mol L^{-1} DP-CAdSV and SW-CAdSV following the regression equations:

DPCAdSV:

$$i_{pc}\ (10^{-8}\ A) = 0.3137x10^{-8}\ (\text{mol } L^{-1}) + 0.2173$$

$$r^2 = 0.9965$$

SW-CAdSV:

$$i_{pc}\ (10^{-8}\ A) = 0.1547x10^{-8}\ (\text{mol } L^{-1}) + 0.7042\ ;$$

$$r^2 = 0.9985$$

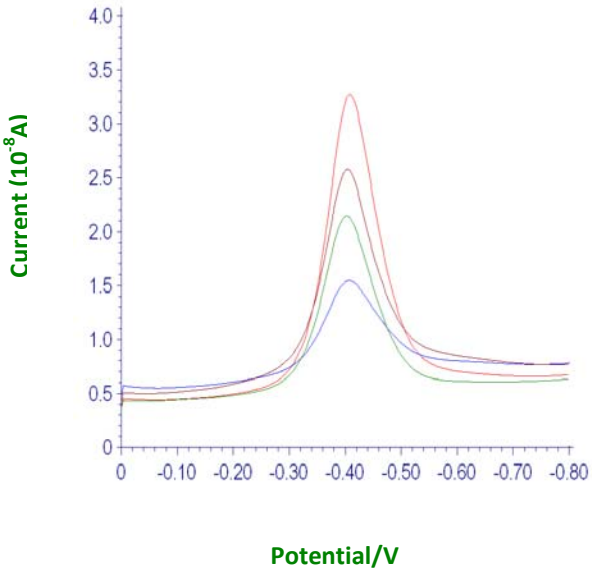


Fig. 6 The DPCAdS voltammograms for increased concentrations (mol L^{-1}) of nitazoxanidespiked urine samples: (1) 3x10^{-9} (2) 7x10^{-9} (3) 9x10^{-9} (4) 12x10^{-9}; Eacc. = 0.0 V, tacc.=15 s, pulse amplitude 50 mV, pulse width 30 ms, and ΔE=10 mV and Phosphate buffer(9mL) of pH 7. Eacc. = 0.0 V, tacc. = 15 s, pulse amplitude 50 mV, pulse width 30 ms, and ΔE=10 mV and Phosphate buffer(9mL) of pH 7.

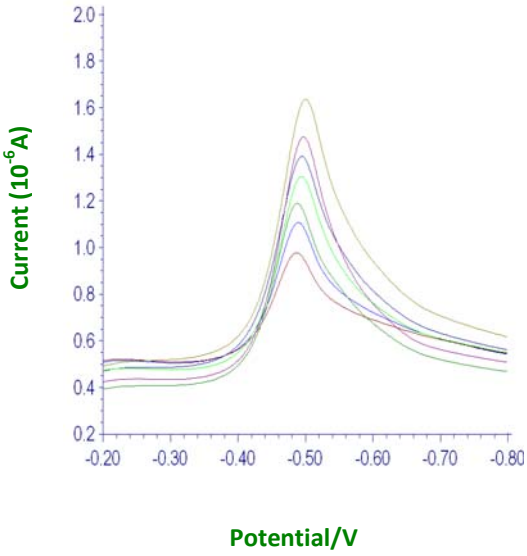


Fig. 7 The SWCAdS voltammograms for increased concentrations (mol L^{-1}) of nitazoxanide spiked in urine samples: (1) 1x10^{-9} (2) 3x10^{-9} (3) 5x10^{-6} (4) 7x10^{-9} (5) 9x10^{-9} (6)1.5x10^{-9} (7) 2x10^{-9}; Eacc.=0.0 V, tacc.=15 s, a=50 mV, f=20 Hz, ΔE=10 mV and Phosphate buffer (9mL)of pH 7.

Detection limits of 2.078×10^{-10} and 1.365×10^{-10} mol L^{-1} and quantitation limits of 4.551×10^{-10} and 6.926×10^{-10} mol L^{-1} Nitazoxanide were achieved by the described DP-CAdSV and SW-CAdSV methods (Table - I) respectively. Mean percentage recoveries and rela standard deviations of 99.11 ± 0.94 (DP-CAdSV) 99.33 ± 1.758 (SW-CAdSV) were achieved based replicate measurements of 1×10^{-8} mol L^{-1} Nitazoxa (Table - III) in spiked human urine. These res confirmed the reliability of the described strip voltammetric methods for assay of Nitazoxanide in human urine.

VII. ASSAY OF NITAZOXANIDE IN SPIKED HUMAN BREAST MILK

Nitazoxanide in spiked human breast milk was successfully analyzed by the described voltammetric methods (SW-CAdSV and DPCAdSV) without the necessity for extraction of the drug prior to the analysis. Representative DPCAdSV and SW-CAdS voltammograms of Nitazoxanide in spiked human breast milk recorded under the optimum operational conditions of the described stripping voltammetric method is shown in Figures 8 and 9 respectively. No interfering peaks were observed in the blank human breast milk within the studied potential range. Linear variations of the peak current (i_p) with concentration of in spiked human breast milk were obtained within the concentration ranges of 1×10^{-8} to1×10^{-9} mol L^{-1} SW-CAdSV and DPCAdSV following the regression equations:

DPCAdSV:

i_{pc} (10^{-8} A) = 0.999x10^{-8} (mol L^{-1}) + 0.0571 ;

r^2 = 0.9999

SW-CAdSV:

i_{pc} (10^{-8} A) = 0.1525x10^{-8} (mol L^{-1}) + 0.3057 ;

r^2 = 0.9993

LOD for Nitazoxanide in spiked human breast milk using 0.601×10^{-10} mol L^{-1} (SWCAdSV) and 0.718×10^{-10} mol L^{-1}(DP-CAdSV) were calculated. LOQ for same solution 2.00×10^{-10} mol L^{-1}(SWCAdSV) and 2.393×10^{-10} mol L^{-1}(DP-CAdSV) were calculated (Table- I). Mean percentage recoveries and relative standard deviations of 100.47±1.116 (DP-CAdSV) and 99.49 ± 1.227 (SW-CAdSV) were achieved based on replicate measurements of 2×10^{-9} mol L^{-1} (Table- III) Nitazoxanide in spiked human breast milk. These results confirmed the reliability of the described stripping voltammetric methods for assay of Nitazoxanide in human breast milk.

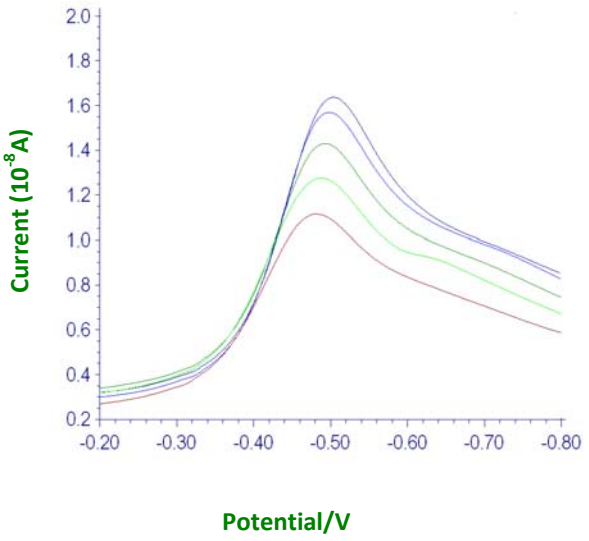


Fig. 8 The DPCAdS voltammograms for increased concentrations of nitazoxanide in human breast milk: (1) $4x10^{-9}$ (2) $6x10^{-9}$ (3) $8x10^{-9}$ (4) $10x10^{-9}$ (5) $11x10^{-9}$(mol L^{-1}) Eacc. = 0.0 V, tacc. = 15 s, pulse amplitude 50 mV, pulse width 30 ms, and ΔE=10 mV and Phosphate buffer (9mL) of pH 7

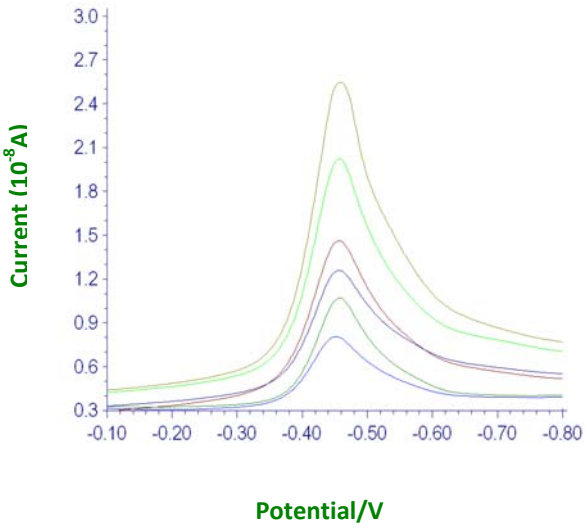


Fig. 9 The SW-CAdS voltammograms of nitazoxanide in human breast milk in different concentrations: (a) 1×10^{-9} mol L^{-1} (b)4×10^{-9}mol L^{-1} (c) 6×10^{-9} mol L^{-1} (d)8×10^{-9} mol L^{-1} (e)12×10^{-9} mol L^{-1} (f)15×10^{-9} mol L^{-1}

VIII. CONCLUSION

A fully validated, sensitive, selective, fast and low-cost, cathodic adsorptive stripping square wave voltammetry procedure was developed for trace determination of nitazoxanide in bulk. The electro-reduction of nitazoxanide at the GCE in buffered solution was studied. . The results obtained show that the above-described methods are useful not only for nitazoxanide determination in conventional electrolytes, but also in more complex matrices such as dosage forms, Breast milk and urine samples. The principal advantages of DP-CAdSV and SW-CAdSV techniques over the other techniques are that they may be applied directly to the analysis of pharmaceutical dosage forms and biological samples without the need for separation or complex sample preparation, since there was no interference from the excipients and endogenous substances The achieved limits of quantitation (LOQ) by means of the described stripping voltammetric methods are low as well as they offer good possibilities for determination of drug in low-dosage pharmaceutical preparations and in real plasma samples.

IX. ACKNOWLEDGMENT

Authors are thankful to the University Grants Commission (U.G.C.), New Delhi, India for financial support for this work and lupin India ltd. for providing drug nitazoxanide sample.

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Table I : Regression Data of The Calibration Lines for Quantitative Determination of Nitazoxanide by Dpcadsv And Swcadsv in Supporting Electrolyte, Breast Milk and Urine Sample

Techniques	DPCAdSV			SWCAdSV		
	Supporting electrolyte	**Breast milk**	**Urine**	**Supporting electrolyte**	**Breast milk**	**Urine**
Linearity range (mol L^{-1})	$1x10^{-9}$ - $1x10^{-8}$	$1x10^{-9}$ $1x10^{-8}$	$1x10^{-9}$ - $1x10^{-8}$	$1x10^{-9}$ - $1x10^{-8}$	$1x10^{-9}$ - $1x10^{-8}$	$1x10^{-9}$ -$1x10^{-8}$
Slope (A/M)	$0.2526x10^{-8}$	$0.313x10^{-8}$	$0.999 x10^{-8}$	$0.175 x10^{-8}$	$0.154 x10^{-8}$	$0.152 x10^{-8}$
Intercept (nA)	1.582	0.2173	0.0571	0.631	0.7042	0.3057
Correlation Coefficient (r^2)	0.9961	0.9965	0.9999	0.9957	0.9985	0.9993
t-test	0.2865	0.36	0.35	0.2931	0.32	0.31
Variance ratio (F)	0.958	0.92	0.93	0.915	0.932	0.91
LOD (M)	$1.878 x10^{-10}$	$2.078x10^{-10}$	$0.718x10^{-10}$	$1.078 x10^{-10}$	$1.365 x10^{-10}$	$0.601x10^{-10}$
LOQ (M)	$6.262 x10^{-10}$	$6.926x10^{-10}$	$2.393x10^{-10}$	$3.595 x10^{-10}$	$4.551x10^{-10}$	$2.004x10^{-10}$
Repeatability of peak current (RSD%)	0.82	0.88	0.74	0.75	0.77	0.81
Repeatability of peak potential (RSD%)	0.66	0.69	0.82	0.71	0.63	0.72
Reproducibility of peak current (RSD%)	0.73	0.84	0.78	0.78	0.87	0.83
Reproducibility of peak potential (RSD%)	0.79	0.85	0.89	0.84	0.72	0.79

Table II: Assay Results of Tablets and Mean Recoveries in Spiked Tablets

	SWCAdSV	**DPCAdSV**
Labeled claim (mg)	300	300
Amount found (mg)	295.2	303.6
R.S.D. %	1.006	0.878
Bias %	1.6	-1.2
Added (mg)	20.0	20.0
Found (mg)	19.7 7	19.86
n	5	5
Recovery %	98.86	99.33
R.S.D. % of Recovery	1.32	1.25
Bias %	0.15	0.65

Table III : Application of SWCAdSV and DPCAdSV Methods to Determination of Nitazoxinide in Spiked Human Breast Milk and Urine Samples

Techniques	**Medium**	**Added cons.**	**Found cons.**	**n**	**Average recovery%**	**RSD%**	**Bias %**
DPCAdSV	Breast milk	$2x10^{-9}$	$2.009x10^{-9}$	5	100.47	1.116	0.75
SWCAdSV	Breast milk	$2x10^{-9}$	$2.009x10^{-9}$	5	99.49	1.227	0.5
DPCAdSV	urine	$2x10^{-9}$	$1.982x10^{-9}$	5	99.11	0.94	-0.65
SWCAdSV	Urine	$2x10^{-9}$	$1.986x10^{-9}$	5	99.33	1.758	-0.25