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Electrochemical Determination of Ebastine in Tablet Dosage Forms at Hanging Mercury Drop Electrode

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Abstract: The electrochemical behaviour of ebastine was studied at hanging mercury drop electrode using cyclic voltammetry and differential pulse voltammetry. The molecule shows a single, well defined reduction peak due to the reduction of carbonyl group. The voltammetric conditions were optimized with respect to maximum peak signals. The linearity between the peak signal and the concentration of ebastine over the concentration range of 2.0×10^{-8} M – 1.0×10^{-7} M was established .The detection and quantitation limits were found to be 0.48×10^{-8} M and 1.60×10^{-8} M respectively. The developed method was employed for the determination of ebastine in tablet dosage forms.
Key words: Ebastine; Hanging mercury drop electrode; Stripping voltammetry; Tablet dosage forms.

INTRODUCTION

Ebastine belongs to the class of second generation antihistamines used for the treatment of allergic rhinitis and chronic idiopathic urticaria. Its IUPAC name is 4-(4-benzhydryloxy-1-piperidyl)-1-(4-tert-butylphenyl)butan-1-one and its structure is given by Figure 1. Ebastine is reported to be effective in the treatment of allergic rhinitis with out adverse cardiac effects[1]. The allergic mechanism of the drug and its main metabolites along with their effect on inflammation mediators are also reported[2]. The drug is found to have prompt action with long lasting effect for daily-once administered in children[3]. Based on comparative clinical studies, the efficacy of the drug is demonstrated for the treatment of allergic disorders[4-5]. A number of chromatographic methods are developed for the determination of ebastine in biological samples[6-7] and in tablet formulations[8-11]. Analytical methods based on UV-Vis spectrophotometry and RP-HPLC are recently developed for the determination of ebastine in presence of phenylephrine in tablet dosage forms[12-13]. Voltammetric techniques offer simple, rapid and cost effective methods for the assay of pharmaceutical in a variety of matrices[14].The present report focusses on the development of stripping voltammetric method for the determination of ebastine in tablet formulations. The method developed can be directly adopted for the regular quality control studies of the drug under investigation.

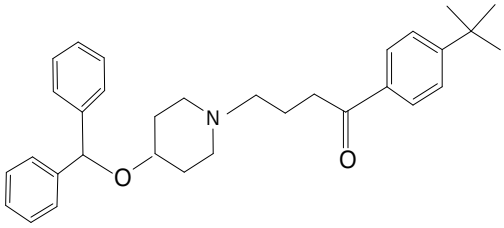

Figure 1: Structure of Ebastine

EXPERIMENTAL

Materials and Methods

Electrochemical measurements were performed by Metrohm E-506 polarecord (Herisau, Switzerland) in combination with Metrohm 663VA stand and with 612 VA scanner. A three electrode system consisting of hanging mercury drop electrode (HMDE) as a working electrode, an Ag/AgCl/KCl_{sat} as a reference electrode and Pt wire as a counter electrode was employed. An Elico LI-120 pH meter was used for the determination of pH of the buffer solutions.

Ebastine was obtained from Micro Labs (Bangalore, India). Erostin (10 mg) tablets were procured from local pharmacy. Britton- Robinson (BR) buffer of pH range 2-12 was obtained by using acetic, phosphoric and boric acid of 0.04 M each and the pH of the solution was adjusted using 0.2 M NaOH solution**.** All the chemicals and solvents used were of analytical reagent grade obtained from Merck (Mumbai, India)

Voltammetric determination of ebastine at HMDE

A stock solution of ebastine of concentration 1.0 $x10^{-3}$ M was prepared by dissolving an appropriate amount of ebastine in methanol. A working standard of conc. 1 X 10^{-6} M was prepared from the stock solution by dilution with double distilled water. 1.0 mL of standard solution and 9.0 mL of BR buffer of pH 4.0 was placed in the electrolytic cell and purged with nitrogen gas for 15 minutes. The potential of the electrode was scanned from -1.2 to -1.5 V vs. Ag/AgCl. Ebastine exhibited maximum peak current at –1.35 V in BR buffer of pH 4.0. The voltammogram of the blank was also recorded under similar conditions (Figure 2).

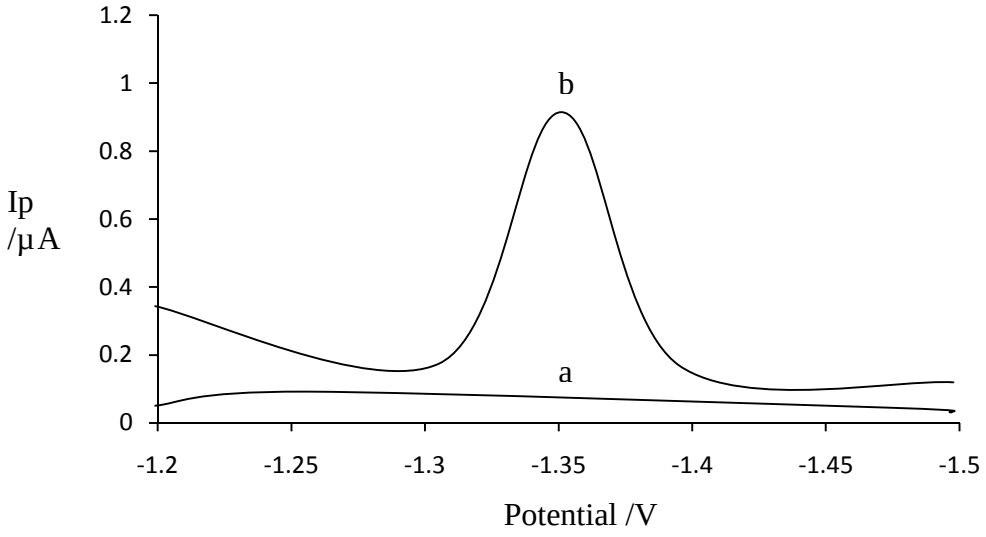

Figure 2: Differential Pulse Adsorptive Stripping Voltammogram of a) Blank and b) ebastine of Concentration 1 X 10^{-6} M at hanging mercury drop electrode (HMDE) in BR Buffer of pH 4.0.

Cyclic voltammetric study of ebastine

An aliquot of standard solution of ebastine of concentration $1.0x10^{-6}$ M and 9.0 ml of BR buffer of pH 4.0 was taken in the cell and purged with nitrogen gas for 15 minutes. The potential of HMDE was cycled between -1.2 V to -1.5 V vs. Ag/AgCl at a scan rate of 100 mV/s. A single, irreversible, well defined peak was obtained at -1.35 V for ebastine due to the $2e^-$ reduction of the carbonyl group attached to phenyl ring. No anodic peak was present in the reverse scan indicating that the reaction is irreversible. The cyclic voltammograms of the ebastine of concentration 1.0×10^{-6} M and blank signal were registered under similar conditions (Figure 3). The reduction mechanism of ebastine was given in Figure 4. Millicoulometric studies indicated that the number of electrons involved in the reduction reaction were 2.

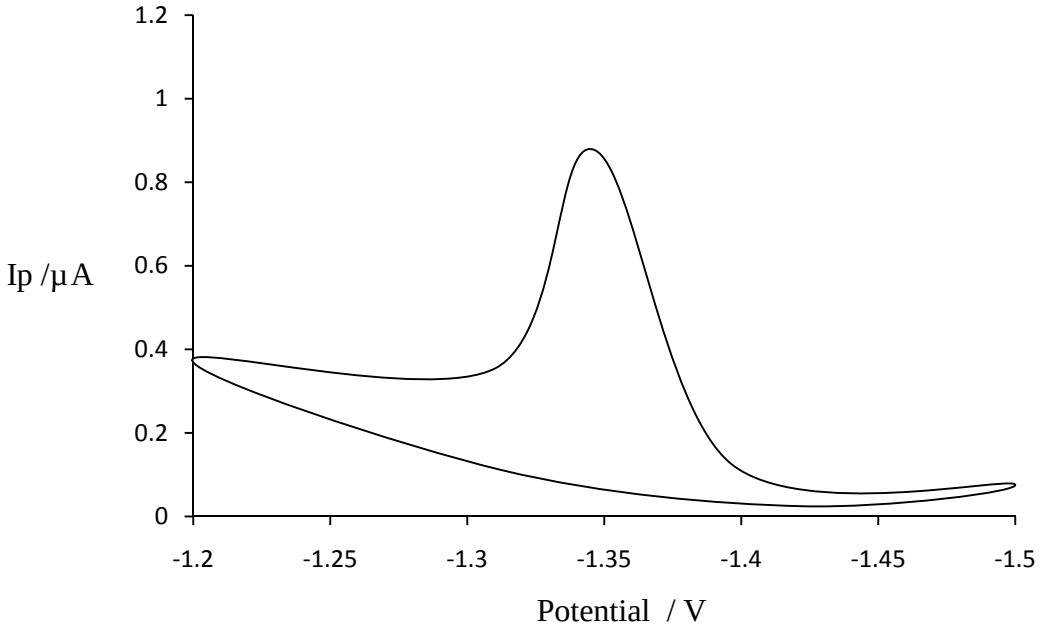

Figure 3: Cyclic voltammograms of ebastine of concentration 1.0×10^{-6} M using HMDE in BR buffer of pH 4.0

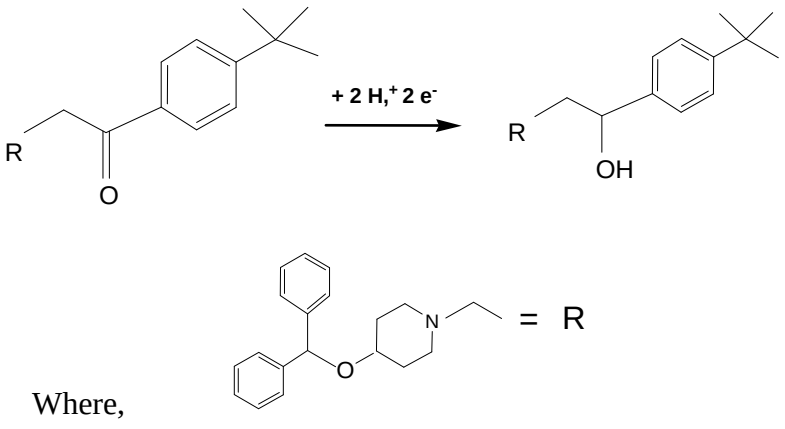

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Figure 4: Electrochemical reduction mechanism of ebastine

RESULTS AND DISCUSSION

Effect of voltammetric parameters

An increase in pH shifts the peak potential to negative value indicating the involvement of protons in the reduction reaction. Over the pH range 2-10, the maximum peak signal was obtained at 4.0 (Figure 5). The optimum accumulation time and accumulation potentials were obtained as 80s and -1.0 V vs. Ag/AgCl respectively. The influence of scan rate on the peak signal was studied over the range 20 -200 mV/s. The I_p vs. $v^{1/2}$ plot gives a straight line with equation I_p (µA) = 0.0903 $v^{1/2}$ (mV/s) - 0.2477 with R^2 = 0.9855. Hence the reduction reaction is diffusion-controlled.

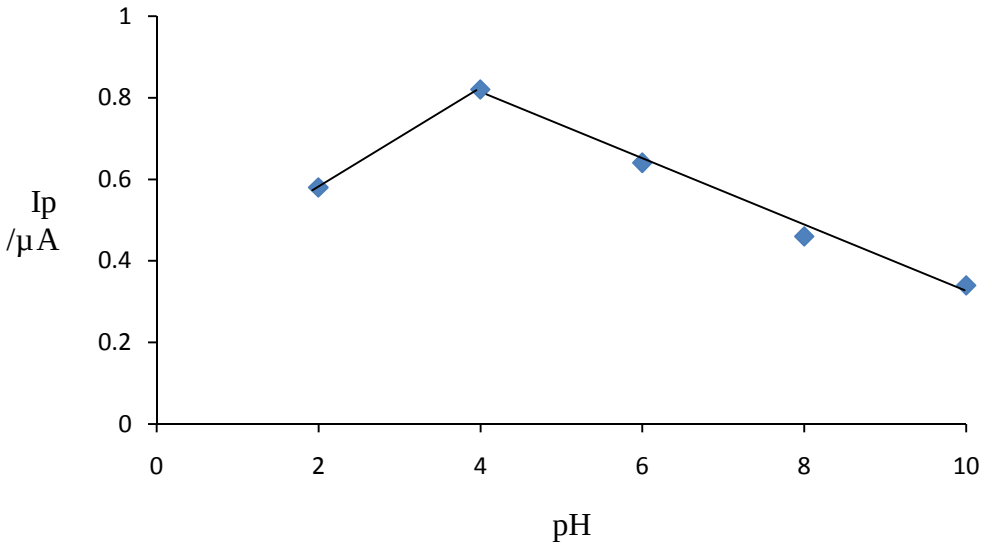

Figure 5: Effect of pH on the peak current of ebastine (1.0 X 10^{-6} M)

Application of voltammetric method to ebastine tablet dosage forms

Five tablets of Erostin (10 mg) were pulverized and a weighed portion taken in 1000 mL volumetric flask and dissolved in 50 ml methanol was added. It was made upto the mark with double distilled water. A series of working standards of concentration range 100-500 ng/mL were prepared using accurately weighed portion of the powdered tablets. Five replicate determinations were carried out for each concentration level using the developed methods. The average recoveries (%R) along with relative standard deviation (%RSD) values were presented in Table1.

Table 1. Voltammetric assay of ebastine tablets

Sample	Amount taken (ng/mL)	Amount found* (ng/mL)	% Recovery	% RSD
Erostin	100	99.34	99.34	0.68
	200	198.52	99.26	0.54
	300	294.63	98.21	0.62
	400	393.54	98.37	0.75

* No. of determinations = 5

Calibration plot

A calibration plot was obtained between peak signal and the concentration of ebastine over the range 2.0 x 10^{-8} M – 1.0 x10^{-7} M. The peak current increases linearly with the concentration of ebastine. The linear regression equation was given by Ip(µA) =2.25 C (µM) + 0.223 with R^2 = 0.9985. The limits of detection and limits of quantitation were calculated as 0.48 x 10^{-8} M and 1.60 x 10^{-8} M respectively.

Specificity of the procedure

The developed procedure was applied for the determination of bulk drug ebastine of concentration 1.0 x 10^{-6} M in the absence of excipients and in tablet formulation in the presence of excipients. Five replicate determinations were carried out in each case using the proposed method. The mean recoveries (%R) and relative standard deviation (%RSD) were given by 98.8 ± 1.12 % to 99.6 ± 1.04 % (without excipients) and 98.1 ± 1.20 % to 99.6 ± 1.16 % (with excipients) with no significant difference. Hence the procedure could be considered as specific.

Robustness of the determination

The effect of incremental changes in voltammetric parameters such as pH, accumulation potential and accumulation time and scan rate on the sensitivity of the method was found to be quite low. The results suggest that the procedure was robust in nature**.**

Precision of the method

The inter-day and intra-day precision was established by determining the bulk drug of conc.1.0 x 10^{-6} M on five successive days and five times on a single day using the protocol developed**.** The mean recoveries (%R) and relative standard deviation (%RSD) values are 99.4 (%R) and 1.13 (%RSD) for inter-day and 99.6 (%R) and 1.08 (%RSD) for intra-day measurements. The results suggest that the method is highly precise.

CONCLUSION

The electrochemical reduction of ebastine at hanging mercury drop electrode was studied and a method was developed for its determination in pharmaceutical formulation. The procedure developed is simple, rapid, selective, cost-effective one with out sample pre-treatment and extraction steps. The lower detection limits indicate that the method is quite sensitive. The application of the present method for the determination of ebastine and its metabolites is currently being considered in our laboratory.

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