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Research Article

ANALYTICAL APPLICATION OF E.B.T IN SPECTRPHOTOMETRIC DETERMINATION OF ELETRIPTAN HYDROBROMIDE

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ABSTRACT

Objective: A simple and sensitive spectrophotometric method has been developed for the estimation of Eletriptan Hydrobomide (EHB).

Methods: The method is based on the formation of ion-association complex with EHB with acid dye, Eriochrome black T(EBT). The cationic form of the dye E.B.T involves in the formation of neutral coloured ion-association complex with negative charge (acid groups in the drug) which is extractable into chloroform and behaves as a single unit being held together by electrostatic attraction.

Results: The absorption maxima were found to be at λMax 510nm. The method obeys Beer's law within the limits 40-240µg/ml and gives reproducible results. Molar absorptivity value is obtained as 1.2116 x 105 L mol-1 cm-1 and recovery was found to be 99.806 to 99.742. Interferences of the other ingredients and excipients were not observed.

Conclusion: The proposed method can be used for the determination of EHB both in pure and pharmaceutical formulations.

Keywords: Eletriptan Hydrobomide (EHB), Ion- association Complex

INTRODUCTION

Eletriptan Hydrobromide, IUPAC Name is3-(1-methyl-2-pyrrolidinylmethyl)-5-(2-(phenylsulfonyl)ethyl-1H-indole hydrobromide**.** Eletriptan Hydrobromide is selective serotonin receptors against used to treat migraine headache EHB will only treat a headache that has already begun. It will not prevent headache or reduce the number of attacks. Electriptan Hydrobromide is a second generation triptan.The volume of distribution of eletriptan following IV administration is 138L plasma protein binding is moderate and approximately 85%.It is white crystalline powder firmly soluble in water and methanol.

Preparation of Standard drug solution

A 1mg/ml solution was prepared by dissolving 100mg of pure EHB in 100ml of water and further diluted to of 80µg/ml.

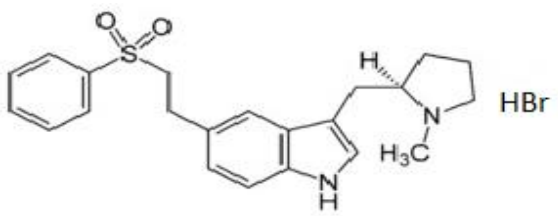


Fig.1: Chemical structure of EHB

Literature Survey on the analytical methods for EHB

A very few physico- chemical methods appeared in the literature for the determination of EHB in pharmaceutical formulations (less) and more for the plasma samples. The methods so far reported includes LC[1-4], TLC[5], HPLC[6-8] and spectro photometric(UV and visible)[9- 11]. The presence of hydrophilic substituents such as – OH or – COOH often prevents extraction of the complex into the organic phase. According to the same principle, basic dyes[12]can be used for the assay of acidic drugs. In the present paper, we describe one visible spectrophotometric method based on the Ion-Association Complex[13-16] with the acidic dye E.B.T, with EHB for its assay. Good number of methods were reported in the literature using E.B.T[17-22] . The RP-HPLC method reported in this study was validated in accordance with the International Conference on Harmonization (ICH) guideline[23-25].Application of ion association complex is reported using acidic dyes [26] and using EBT[27-28] as chromogenic reagent for the assay of drugs other than the drug selected by the author.

The analytically important functional groups of EHB were not properly exploited designing suitable spectrophotometric methods for the determination of the selected drug. The author made some attempts in developing visible spectrophotometric methods and succeeded in developing the method based on the reaction between the drug and acidic dyes namely EBT under specified experimental conditions. As the extraction spectrophotometric procedures are popular for their sensitivity and selectivity in the assay of drugs, the extractive spectrophotometric acid-dye technique was therefore, utilized in the present work for the estimation of EHB. The present paper describes one simple and sensitive extraction visible spectrophotometric method for the determination of EHB, based on its tendency to form chloroform extractable ion-associates with acidic dye EBT belonging to this category under experimental conditions by exploiting the basic nature of Nitrogen in tertiary amine of the drug molecule. According to the literature, it is the first time for EHB determination in bulk as well as formulations by visible spectrophotometry for this drug.

EXPERIMENTAL

Apparatus and chemicals: A Shimadzu UV-Visible spectrophotometer 1801 with1cm matched quartz cells was used for all spectral measurements. A Systronics digital pH meter mode-361was used for pH measurements. All the chemicals used were of analytical grade. EHB Pure drug was obtained as a gift sample from Genmed,Pfizer Canada Inc, Gd Eletriptan-40mg (Tablet-1) and Relpax 40 mg, (Tablet-2) were purchased from local market.

Preparation of Standard stock solution

The stock solution (1 mg/ml) of Eletriptan Hydrobromide (EHB) was prepared by dissolving 100 mg of it in 100 ml of millipore-distilled water. A portion of this stock solution was diluted stepwise with the distilled water to obtain the working standard EHB solution of concentrations 04-500 µg/L

Preparation of Sample solution

About 2 tablets of 20mg were pulverized and the powder equivalent to 40mg of EHB was weighed, dispersed in 25ml of alcohol, shaken well and filtered. The filtrate was evaporated to dryness and the residue was dissolved as under standard solution preparation.

Recommended procedure

Into a series of 25ml calibrated tubes, aliquots of standard EHB solution (1-6ml, 240µg/ml) were transferred and then solutions of 2ml methanol and 2ml of 0.1% Erichrome Black-T solution was added successively and the volume made to 15 ml by the addition of water and final volume made to 25 ml by the addition of chloroform. Thus the formed solution allowed to stand for clear separation of the two phases. The chloroform phase was transferred into test tube by separating funnel. The absorbance was measured at λmax 510 nm (Fig.4) against reagent blank prepared similarly. The content of the EHB was calculated from its calibration graph. Fig .5.

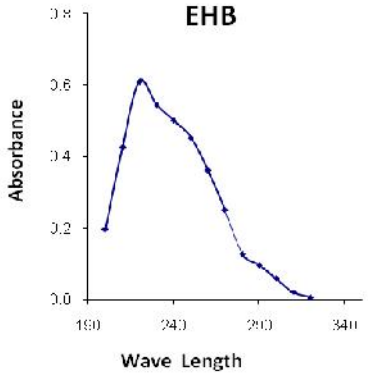


Fig.2: Absorption Spectra of EHB in Methanol (UV Reference method)

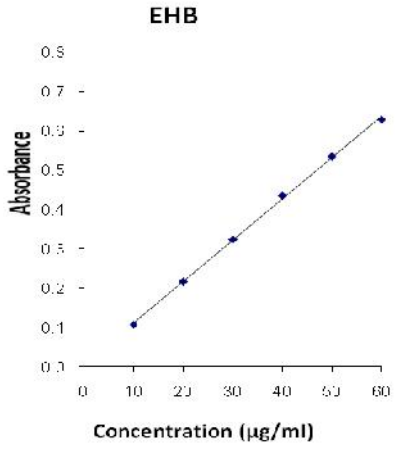


Fig. 3:Beer's Law plot of EHB in methanol (UV Reference method)

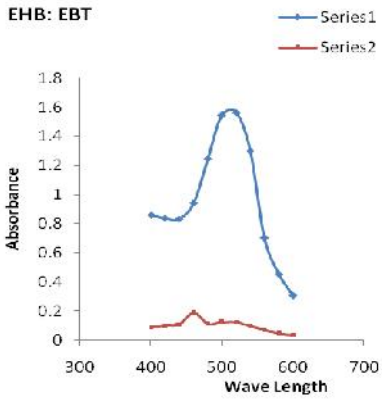


Fig.4: Absorption spectrum of EHB for EBT

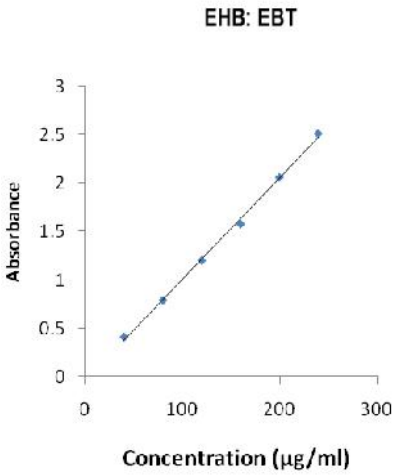


Fig.5: Beer·s law plot of EHB for EBT

For pharmaceutical formulations

The tablet powder equivalent to 100mg of EHB was extracted with 3x25 ml of chloroform and filtered. The combined filtrate was evaporated to dryness and the residue was dissolved in100ml of distilled water to achieve a concentration of 1mg/ml stock solution. The solution was further diluted step wise with distilled water to get working standard solutions and analysed under procedures described for bulk samples.

RESULTS AND DISCUSSION

In developing the method, a systematic study of the effects of various relevant parameters in the concerned were undertaken by varying one parameter at a time and controlling all other parameters to get maximum colour development, minimum blank colour, reproducibility and reasonable period of stability of final coloured species formed. The conditions so obtained were incorporated in the recommended procedures. The optical characteristics such as Beer'slimits, molar absorptivity, and sandell's sensitivity, regression analysis using the method of least squares was made to evaluate the slope(b),intercept(a),and correlation Co-efficient (r) for each system are presented in Table-1.The accuracy of the method is ascertained by comparing the results obtained for pharmaceutical formulations by the proposed methods and reference method by UV, developed in the laboratory using drug solutions , Stastically by the t-and f-tests and the results are summarized Table-2. Recoveries were determined by adding standard drug to the pre analysed pharmaceutical formulations. The ingredients usually present in pharmaceutical formulations did not interfere in the proposed method.

Table-1: Optical And Regression Charecteristics, Precision And Accuracy of Proposed Method

S.No	Parameter	Results
1	Wave length λ_{max} (nm)	510
2	Beer's law limits (µg ml^{-1})	40-240
4	Detection limits (µg ml^{-1})	10.2413
5	Molar absorptivity (1 mole cm^{-1})	1.2116×10^{5}
6	Sandell's sensitivity (µg cm^{-2} / 0.001 absorbance unit)	3.8247×10^{-3}
7	Regressionequation (Y = a + bC) Slope (b)	0.0105
8	Standard deviation of slope (S_b)	2.3010×10^{-4}
8	Intercept (a)	-0.0436
10	Standard deviation of intercept (S_a)	3.5844×10^{-2}
11	Standard error of estimation (S_e)	3.8503×10^{-2}
12	Correlation coefficient (r^2)	0.9981
13	Relative standard deviation (%)*	2.1809
14	% Range of error(Confidence Limits) 0.05 level*	2.2890
	% Range of error(Confidence Limits)0.01 level	3.5898
	% Error in bulk samples**	0.68

Table-2: Assay of EHB in Pharmaceutical Formulations

Sample	Amount taken (mg)	Amount found by proposed method	Reference Method	Percentage recovery by proposed method
Tablet I	40	39.60 ±0.025 F=2.44 t=0.50	39.92 ±0.016	99.806 ±0.025
Tablet II	40	39.78 ±0.024 F=1.36 t=0.77	39.88 ±0.028	99.742 ±0.089

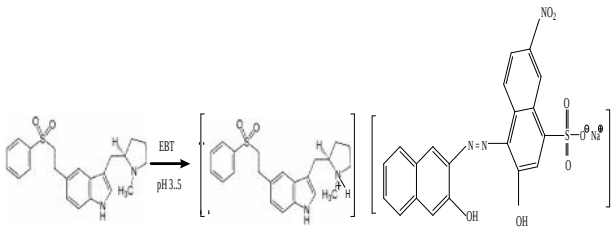
*: Average ± standard deviation of six determinations; the t- and F- values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limit t=2.57, F=5.05.

**: After adding 2 different amounts of the pure labeled to the pharmaceutical formulations, each value is an average of 3 determinations

Colored Species formation

EHB forms an ion association complex with a basic dye E.B.T, which is extractable into chloroform from aqueous phase. The cationic form of the dye E.B.T , involves in the formation of neutral coloured ion- association complex with negative charge acid group in the drug (scheme 1) which are extractable into chloroform behave as a single unit being held together by electrostatic attraction. It is supported by slope ratio method which was obtained as 1 : 1 .

Scheme1:



CONCLUSION

The proposed method by author is more superior compared to few visible spectro photometric methods reported so far mainly in terms of λmax value, ϵ max, stability of coloured species. It can be seen from the results presented above, that the proposed method has good sensitivity and λmax. Stastical analysis of the results (Table-1) shows that the proposed procedure has good precision and accuracy. Results of the analysis of pharmaceutical formulations (Table-2) reveal that the proposed method is suitable for their analysis with virtually no interference of the usual additives. The proposed method is simple, sensitive, and reliable and can be used for routine determination of EHB in bulk samples and pharmaceutical formulations depending upon the needs of the specific situation.

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