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An Isocratic Reverse Phase Hplc Method Development For The Determination Of Eletritan Hydrobromide In Pure And Pharmaceutical Formulations

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Abstract: An isocratic reverse phase high performance liquid chromatographic method has been developed for the determination of eletriptan hydrobromide in pure pharmaceutical formulations. The separation of eletriptan hydrobromide in the recommended method was based on a Water Alliance E2695 HPLC system equipped with 2487 UV dual wavelength absorbance detector and a binary pump using a zorbax SB C18 column (150 x 4.6 mm, 5µm). A mixture of ammonium acetate buffer of pH 3.5±0.05 and 80% acetonitrile in water in the ratio 80:20 v/v are chosen as mobile phase and allowed to flow a rate of 1.0 ml/min. for 25min. Detection of the component was carried out at 220 nm using UV detector. The retention time of eletriptan hydrobromide was found to be 10.548 min. The calibration curve was found to be linear over the concentration range of 20-70 µg/ml. The proposed method was validated as per ICH guide lines and was found to be applicable for the determination of Eletriptan hydrobromide in pharmaceutical formulations. The developed method was found to be simple, sensitive and selective.
Key Words: Eletriptan hydrobromide, Isocratic, HPLC, Validation.

INTRODUCTION

Eletriptan hydrobromide is a second generation triptan drug intended for treatment of migraine headaches. Its mode of action is believed to reduce swelling of the blood vessels surrounding the brain. This swelling is associated with the head pain of a migraine attack. eletriptan blocks the release of substances from nerve endings that cause more pain and other symptoms like nausea, and sensitivity to light and sound. It is thought that these actions contribute to relief of symptoms by eletriptan. It is used as an abortive medication, blocking a migraine attack which is already in progress. It is sold in the US and Canada under the brand name relpax and in several other countries under the brand name relert. Each replax Tablet for oral administration contains 24.2 or 48.5 mg of eletriptan hydrobromide equivalent to 20 mg or 40 mg of eletriptan, respectively. Eletriptan was approved by the U.S. Food and Drug Administration 2002 for the acute treatment of migraine with or without aura in adults[1-3]. Eletriptan is chemically designated as (*R*)-3-[(1-Methyl-2-pyrrolidinyl) methyl]-5-[2-(phenyl sulfonyl) ethyl]-1*H*-indole mono hydrobromide. The empirical formula is $C_{22}H_{26}N_2O_2S.HBr$, representing a molecular weight of 463.40. It is a white to light pale colored powder that is readily soluble in water. The literature survey revealed only a few HPLC [4-7] and one LC-MS technique[8] and some spectrophotometric[9-10] and spectropfluorimetric [11] methods have been reported for the determination of eletriptan hydrobromide. The chemical structure of the drug is presented in Fig.1.

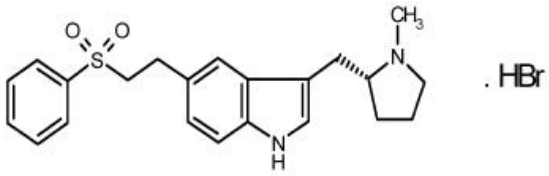

Fig.1 The chemical structure of the eletriptan hydrobromide

EXPERIMENTAL

Materials and Methods

Water Alliance E2695 HPLC system of binary pump equipped with 2487 UV dual wavelength absorbance detector was employed for analysis. Ammonium acetate and acetic acid (Sd.Fine) and HPLC grade acetonitrile (Merck) were used. 0.01M ammonium acetate in water of pH to 3.5 adjusting with acetic acid is used as solvent-A and acetonitrile: water in the ratio 80:20 v/v was used as solvent-B. A diluent was prepared by mixing solvent A and solvent B in the ratio 50:50 v/v and used for sample preparations. Pure sample of eletriptan hydrobromide was gifted by Matrix Laboratories Hyderabad and the formulations were purchased from local pharmaceutical. Commercially available formulations were procured from local market. Primary stock solution of eletriptan hydrobromide (1000 µg/ml) was prepared with the diluent solution. Working standard solution of 40.0 µg/ml and calibration solutions of concentration range 20-70 µg/ml were prepared and used in the analysis. The chromatographic separation was carried out on a zorbax SB C18 column (150 x 4.6 mm, 5µm) using a mobile phase (80:20 v/v) of acetate buffer and 80% acetonitrile in water at a flow rate of 1.0 ml/min. with UV detection at 220 nm under isocratic conditions at ambient temperature. 20 µl aliquot of each solution was injected automatically onto the column in duplicate and the chromatograms were recorded. Calibration graph was constructed by plotting the mean peak area verses drug concentration. The amount of drug content in different formulations were determined by making them into a fine powder and weighing the powder an amount equivalent to 100 mg of eletriptan hydrobromide transferred into a 100 ml volumetric flask. The contents of the flask were made up to volume with diluent and filtered through a 0.45µ membrane filter. The filtrate was suitably diluted with the solvent in order to obtain test solutions in the range of concentration.

Validation

The developed method was validated as per ICH guidelines for the parameters like specificity, linearity, precision, accuracy, regression characteristics, limit of detection and limit of quantification. Specificity was evaluated by preparing an analytical placebo (40.0µg/ml) and was confirmed that the signal measured was caused by only by the analyte. The system suitability parameters were presented in **Table-1. A typical chromatogram was presented in Fig.2**. Linearity parameters of proposed method were calculated by analyzing different concentration solutions each twice, a plot was drawn between the concentration of the drug and the average peak area and the results were are presented in Table 2. Precision of the method was evaluated in terms of intra-day (repeatability) and interday (intermediate) precision. Repeatability was checked by analyzing three different concentration levels and percent relative standard deviation were calculated and are presented in Table 3. The drug content in the formulations was quantified using the proposed method. The amount of Eletriptan hydrobromide obtained in formulation is shown in the Table 4. Limit of detection and limit of quantification were calculated by the proposed method, which were based on the standard deviation of the response and the slope of the calibration curve.

Table 1. System suitability parameters of proposed method

S.No.	Parameter	Value of the parameter
1	Retention time (min.)	10.548
2	Theoretical plates	11313
3	Tailing factor	1.10

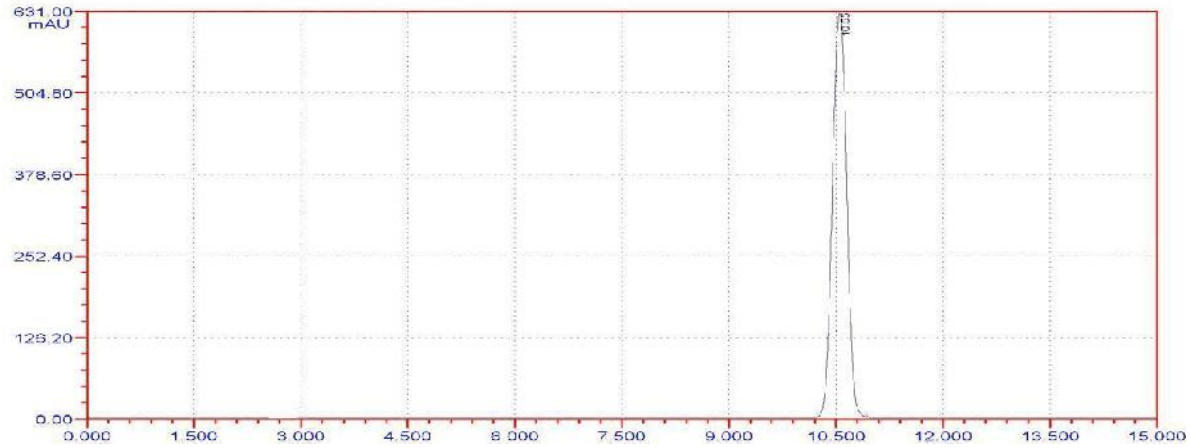

Fig.2 A typical chromatogram of Eletriptan Hydrobromide (40µg/ml)

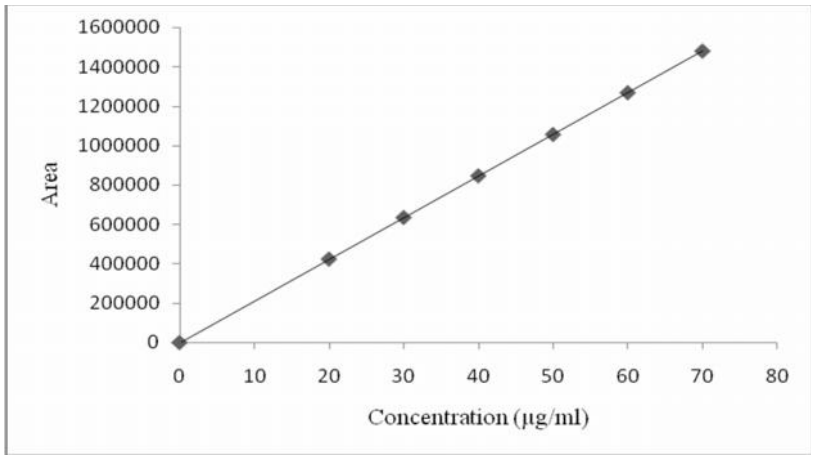

Fig.3 Calibration plot of Eletriptan Hydrobromide

Table 2. Linearity parameters of proposed method

S.No.	Parameter	Value of the parameter
1	Wave length (nm)	220
5	Calibration range (µg/ml)	20-70
6	Slope	21133.02
7	Intercept	1192.97
8	Correlation coefficient	0.9999
9	Limit of detection	0.0755
10	Limit of quantification	0.2515

Table 3. Intra and inter day precision of proposed method

Concentration of Drug (µg/ml)	Intra-day precision (% RSD)	Inter-day precision (% RSD)
20.0	0.4538	0.7842
30.0	0.6452	0.9656
40.0	0.5124	0.6438

Table 4. Assay of Eletriptan Hydrobromide in tablet dosage forms

Type of Formulation	Labeled amount mg/tablet	Amount found (mg)	%Recovery ±% RSD
Tablet-1	20.0	19.94 ± 0.1833	97.0±0.9193
Tablet-2	40.0	39.96 ± 0.151	99.9±0.3779

RESULTS AND DISCUSSION

The aim of the present investigation was to develop a sensitive, precise and accurate high performance liquid chromatographic method for the determination of Eletriptan hydrobromide in pharmaceutical formulations. The system suitability parameters such as tailing factor (1.1) and number of theoretical plates (11313) are found to be within the limits and the retention time of the component was found to be 1.055min. A typical chromatogram for the standard was presented in Fig.2. The intra-day precision or inter-day precision of a method was expressed in terms of statistical parameters such as standard deviation and %RSD, calculated for five replicate measurements and found to be less than 2.0. Inter-day precision of the method was determined by carrying out the experiment on different days using same instrument and same column under similar chromatographic conditions. The proposed method was linear in the range of concentration 20-70µg/ml with correlation coefficient 0.9999 (Fig.3). The correlation coefficient, slope and intercept were presented in Table-2. The accuracy of the method was determined from recovery experiments. The recovery studies were carried out at three different concentration levels. The mean percentage recovery of the drug was found to be 99.2% and the results were presented in Table-4.

CONCLUSIONS

The main objective of developing the method is to increase the sensitivity, precision and recovery of the drug. The proposed isocratic RP-HPLC was found to be precise and accurate as indicated by repeatability and recovery studies. Recovery studies were found to be within the limits. The developed method can be used as an alternative method for routine analysis in quality control.

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