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VISIBLE SPECTROPHOTOMETRIC METHOD FOR DETERMINATION OF ELETRIPTAN HYDROBROMIDE IN PHARMACEUTICAL FORMULATION USING MARQUIS REAGENT

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ABSTRACT

A novel, simple, sensitive, precise and accurate visible spectrophotometric method has been developed and validated for the determination of Eletriptan hydrobromide in pharmaceutical formulation using marquis reagent. The absorption maximum of the drug was found to be 530 nm. The linearity was obtained in the concentration range of 2-12 µg/ml with correlation coefficient 0.998. The results of analysis for the method have been validated statistically and by recovery studies indicate the accuracy and precision of the method. The proposed method was simple, accurate, and precise hence can be applied for the analysis of Eletriptan in pharmaceutical tablet dosage form.

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INTRODUCTION

Eletriptan chemically known to be 3-[(-1–methylpyrrolidin–2-yl)methyl]–5-(2-phenylsulfonylethyl)-1H–indole (Fig.1).Migraine is described as neurovascular headache, and it is characterized by recurrent attacks of headache which typically last up to 72 hours. Simple analgesics and non steroidal anti-inflammatory drugs are effective if taken at the earliest signs of the attack. It is selective at 5-HT1B/1D receptor agonist; thought to be due to the agonist effects at the 5-HT1B/1D receptors located on intracranial blood vessels (including arteriovenous anastomoses) and sensory nerves of the trigeminal system that result in cranial vessel constriction and inhibition of proinflammatory neuropeptide release[1-3]. Literature Survey on the analytical methods for Eletriptan hydrobromide reveals various physico-chemical methods for estimation of eletriptan hydrobromide in biological fluids and pharmaceutical formulations and most of them are based on HPLC[4-9] and visible spectrophotometric methods[10-12] , plasma and saliva using automated sequential trace enrichment[13], TLC[14] , determination of eletriptan hydrobromide in plasma using liquid chromatography coupled with Tandem mass spectroscopy[15], determination of process related impurities in Eletriptan using UPLC method[16] , Capillary Electrophoresis. Only few visible spectrophotometric methods reported for estimation of eletriptan in pharmaceutical formulation but methods are not simple and have time consuming. So there is a scope to develop a visible spectrophotometric method for estimation of eletriptan, hence attempt has been made to develop a simple visible spectrophotometric method using marquis reagent for estimation of eletriptan in pharmaceutical formulation.

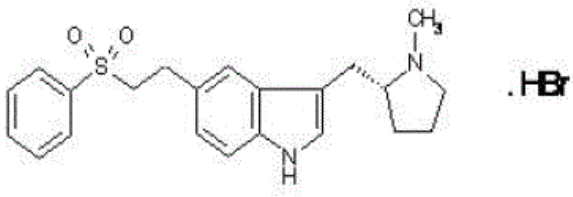

Fig. 1 : Chemical Structure of Eletriptan Hydrobromide.

MATERIALS AND METHODS

Instrumentation

A Elico double beam SL 210 UV-VIS spetrophotometer, model equipped with 10 mm quartz cells served for spectral and absorbance measurement.

MATERIALS AND REAGENTS

Pure form of Eletriptan Hydrobromide is obtained as gifted sample. RELPAX® Tablets containing each containing 20 mg of eletriptan hydrobromide was procured from local pharmacy. Methanol and distilled water is of E Merck Limited. Formaldehye, glacial acetic acid and con.H_2SO_4 is of SD Fine Chemicals Ltd, Mumbai.

Preparation of Marquis Reagent :

Reagent A : 8 to 10 drops of formaldehyde mixed with 10 ml of glacial acetic acid.
Reagent B : Concentrated H_2SO_4

Preparation of standard solution:

An accurately weighed 100 mg of eletriptan hydrobromide was dissolved in 100 ml of methanol to obtain a stock solution 1000 µg/ml and this stock solution was further diluted with methanol to get a working standard solution containing the concentration of 100 µg/ml of the drug.

Preparation of sample solution:

Twenty tablets were weighed accurately and powdered. Tablet powder equivalent to 10 mg of Eletriptan HBr was weighed and transferred to 100 ml volumetric flask separately. About 40 ml of methanol was added and sonicated for 20 minutes for complete solublisation of drug. The solution was filtered through whatman filter paper. The filtrate volume was made up to the mark with the same solvent resulting solution of 100 µg/ml concentration and suitably diluted to obtain the suitable concentration for analysis.

Determination of λ_{max}

The 1 ml of working standard solution of Eletriptan HBr (100 µg/mL) was taken in 25 ml calibrated tube. To this, 1 ml of reagent A and 10 ml of conc. H_2SO_4 were added successively and the volume was brought up to 20 ml with methanol and kept aside for 10 min for complete color development. After color development the volume was made up to the mark with methanol. In order to investigate the wavelength maximum, the above colored solution was scanned in the range of 400-800 nm by UV-Visible spectrophotometer against a reagent blank. From the absorption spectra, it was concluded that 530 nm is the most appropriate wavelength for analyzing Eletriptan HBr. Absorption spectrum for the method is shown in Figure 1.

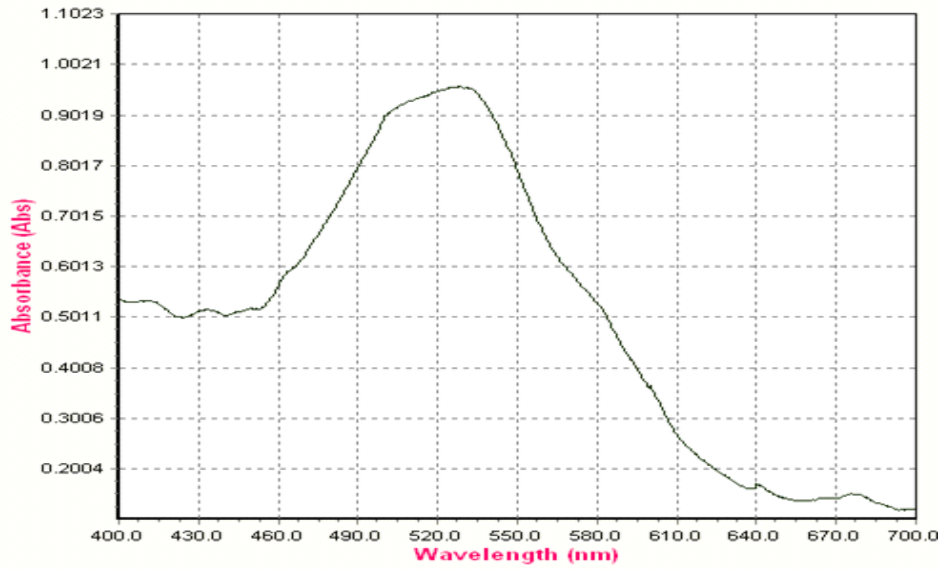

Fig. 2. Absorption spectra of Eletriptan HBr.

The optimum conditions for each method were established by varying one parameter at a time and keeping the others fixed and observing the effect produced on the absorbance of colored species and incorporated in the procedure. Also suitable concentration of reagents, their order of addition, as well as the time required to obtain maximum absorbance were observed. Linearity and stability of the colored complex were studied.

Procedure for Pharmaceutical Formulation

Twenty tablets were weighed accurately and powdered. Tablet powder equivalent to 10 mg of Eletriptan HBr was weighed and transferred to 100 ml volumetric flask separately. About 40 ml of methanol was added and sonicated for 20 minutes for complete solublisation of drug. The solution was filtered through whatman filter paper. The filtrate volume was made up to the mark with the same solvent resulting solution of 100 µg/ml concentration. From this 1 ml was transferred into 25 ml volumetric flask and to this, 1 ml of reagent A and 10 ml of conc H_2SO_4 were added successively and the volume was brought up to 20 ml with methanol and kept aside for 10 min for complete color development. After color development the volume was made up to the mark with methanol and absorbance of the resulting solution was measured at 530 nm.

Table: 1 Assay of marketed formulation.

Formulation	Amount of drug taken from tablet(mg)	Mean amount of drug found from tablet (mg)	% Mean Assay* ±%RSD
RELPAX® Tablets	20	20.03	100.15±0.4005

average of six determinations

RESULTS

Validation

The proposed method was validated according to International Conference on Harmonization (ICH) guideline[17].

Linearity and Range

Aliquots (0.5 – 3 ml) of Elitriptan HBr from standard stock solution (100 µg/ml) were transferred into a series of 25 ml calibrated volumetric flasks. To this, 1 ml of reagent A and 10 ml of conc. H_2SO_4 were added successively and the volume was brought up to 20 ml with methanol and kept aside for 10 min for complete color development. After color development the volume was made up to the mark with methanol to get the concentrations in the range of 2-12 µg/ml and absorbance of the resulting solutions was measured at 530 nm against reagent blank. The regression parameters were shown in Table 2.The calibration curve is shown in fig 3.

Table: 2 Optical Characteristics of Elitriptan Hydrobromide.

S.No.	Parameter	Values
1.	Absorption maxima (nm)	530
2.	Linearity range (µg/ml)	2-12
3.	Regression Equation(y=bx+c)	y=0.0416x+0.0038
4.	Slope(b)	0.0416
5.	Intercept(c)	0.0038
6.	Correlation Coefficient(r^2)	0.9987
7.	Molar Absorptivity(lit.mol^{-1} cm^{-1})	0.546414×10^4
8.	Sandell's Sensitivity(µg/cm^2/ 0.001 abs unit)	0.0177906

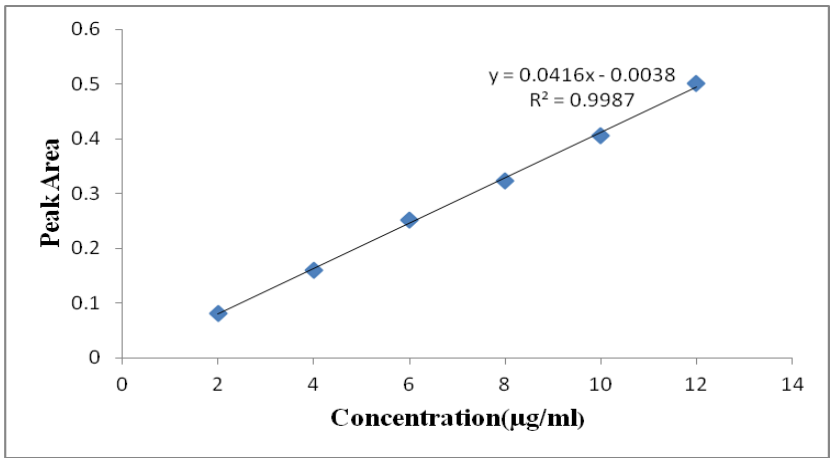

Fig. 3.Calibration curve of Elitriptan Hydrobromide.

PRECISION

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. The precision of analytical method was usually expressed as the standard deviation or relative standard deviation (coefficient of variation) of series of measurement. The precision of the method studied as system precision, interday and intraday precision (Table 3 and Table 4).

Table: 3 System Precision.

Amount taken (µg/ml)	(n=6)Repeatability ± S.D	(n=6)%RSD
8 µg/ml	99.66±0.405	0.406

Table: 4 Intraday and Interday Precision.

	Intraday		Interday	
Con. taken (µg/ml)	Con. found* (µg/ml)	%RSD	Con. found* (µg/ml)	%RSD
2	1.98	0.94	1.95	0.96
4	3.93	0.86	3.91	0.91
6	5.95	0.96	5.94	0.93

**average of three determinations*

ACCURACY

To assess the accuracy of the proposed method, recovery studies were carried out at three different levels i.e. 80 %, 100 % and 120 %. To the preanalysed sample solution a known amount of standard drug solution was added at three different levels, absorbance was recorded. Solutions were prepared in triplicates and accuracy was indicated by % recovery. (Table 5)

Table: 5 Accuracy.

S.No.	(%) level	Actual conc. (µg/ml)	Conc. Added (µg/ml)	Conc. found (µg/ml)	(n=3) %Recovery ±%RSD	%Mean Recovery ±%RSD
1.	80 %	4	3.2	3.17	99.16±0.161	
2.	100 %	4	4	3.98	99.72±0.206	99.57±0.171
3.	120 %	4	4.8	4.79	99.85±0.146	

ROBUSTNESS

The robustness of a method is its capacity to remain unaffected by small changes in conditions. To determine the robustness of the method, the experimental conditions were deliberately altered and assay was evaluated. The effect of detection wavelength was studied at ±2 nm. For changes of conditions, the sample was assayed in triplicates. When the effect of altering one set of conditions was tested, the other conditions were held constant at the optimum values. Assay for all deliberate changes of conditions should be within 98.0–102.0 % for the proposed method (Table 6).

Table: 6 Results from Robustness study.

Formulation	Amount of drug taken from tablet(mg)	At 528 nm (n=3)%assay±%RSD	At 532 nm (n=3)%assay±%RSD
RELPAX® Tablets	20	99.87±0.613	99.62±0.586

RUGGEDNESS

Ruggedness of the proposed method is determined by analysis of aliquots from homogeneous slot by two analysts using same operational and environmental conditions (Table 7).

Table: 7 Results for Ruggedness studies.

Formulation	Amount of drug taken from tablet(mg)	Analyst 1 (n=3)%assay±%RSD	Analyst 2 (n=3)%assay±%RSD
RELPAX® Tablets	20	100.01±0.732	99.92±0.457

DISCUSSION

The developed visible spectrophotometric method is based on reaction of Eletriptan with marquis reagent resulting in the formation of violet colored chromogen for which the absorption peak appears at 530 nm. Linearity of the method was observed in the concentration the range of 2-12 µg/ml. Statistical analysis of the calibration curve was done with correlation co-efficient (r^2 = 0.9987) shows the validity of beers law. The proposed method was applied to pharmaceutical formulation and percent amount of drug estimated was found in good agreement with the label claim. The excipients used in the pharmaceutical preparation do not interfere in this analysis. The recovery experiment was carried out at three different levels i.e., 80 %, 100 % and 120 %. The percentage recovery was found to be in the range 99.1-99.8 % indicates of accuracy of the method. The precision of the method was studied as system, intra-day and inter-day precision. The % RSD value < 1% indicates the precision of the method. Ruggedness of the proposed method was studied with the help of two analysts and robustness for the method was studied by variation in wavelength both of which show low values of % RSD indicates the ruggedness and robustness of the method.

CONCLUSION

The developed visible spectrophotometric method for the determination of Eletriptan was novel, simple, accurate, precise and sensitive. The method was validated as per the guidelines laid by ICH. The results of the validation tests were found to be satisfactory and therefore this method can be applied successfully to analyze the drug Eletriptan in its pharmaceutical dosage forms.

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