NOVEL VISIBLE SPECTROPHOTOMETRIC METHODS FOR DETERMINATION OF NARATRIPTAN IN PHARMACEUTICAL FORMULATIONS

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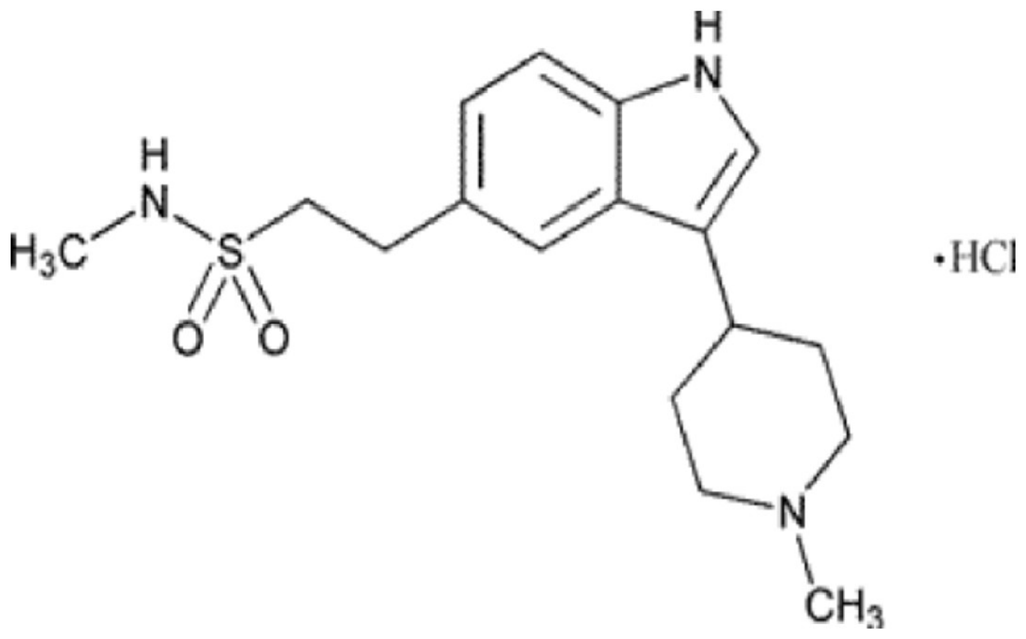
ABSTRACT

Naratriptan is a triptan drug. Three simple, sensitive and accurate spectrophotometric methods have been developed for the determination of Naratriptan in pure state and in its pharmaceutical formulations. The developed Method A is based on the condensation reaction between the drug and P-Dimethyl amino benzaldehyde. The developed chromogen in Method A shows maximum absorption at λ_{max} 580 nm and Linearity in the range of 2.5-12.5 µg/ml. Method B involves formation of colored species of the drug with P-Dimethyl amino cinnamaldehyde and it exhibits maximum absorption at λ_{max} 610 nm; Linearity in the range of 2-8 µg/ml. Method C is based on the condensation of the drug with vanillin and the developed chromogen shows maximum absorption at λ_{max} 550 nm; Linearity in the range of 2-10 µg/ml. The results obtained were statistically evaluated and were found to be accurate and reproducible.

Key words: Naratriptan, Spectrophotometric.

1.INTRODUCTION

Naratriptan(Bandari Suresh,2008) is an antimigraine drug. Chemically it is N-methyl-2-[3-(1-methyl piperidin-4-yl)-1H-indol-5-yl] ethane sulfonamide. It is an indole derivative and is official in U.S.P ,2007. Naratriptan binds with high affinity to 5-HT_{1D} and 5-HT_{1B} receptors and has no significant affinity or pharmacological activity at 5-HT_{2-4} receptor subtypes or at adrenergic α_1, α_2 or β; dopaminergic D1 or D2; muscarinic; or benzodiazepine receptors. The therapeutic activity of Naratriptan in migraine(Beata Duszynka,2001) is generally attributed to its agonist activity at 5-$H_{1D/1B}$ receptors. The U.S. Food and drug Administration (FDA) approved Naratriptan on February 11, 1998(Douglas). Literature reveals no colorimetry and HPLC methods reported for Naratriptan in pharmaceutical formulations. Only a few analytical methods are reported in the literature for estimation of Naratriptan in pharmaceutical formulations and in biological fluids such as LC-MS(Karthick Viswanathan,1999;Dulery,1997) . In the present investigation, three simple, sensitive and accurate visible spectrophotometric methods have been developed for the determination of Naratriptan in pharmaceutical formulations. Method A shows λ_{max} at 580 nm and Linearity in the range of 2.5-12.5 µg/ml. Method B exhibits λ_{max} at 610 nm and Linearity in the range of 2-8 µg/ml. Method C shows λ_{max} at 550 nm and Linearity in the range of 2-10 µg/ml.



Chemical structure of Naratriptan

2.EXPERIMENTAL

Spectral and absorbance measurements were made on systronics Double beam UV-Visible spectrophotometer model 2201 with 1cm matched quartz cells. Naratriptan was procured from a local pharmaceutical industry. All other reagents used were of analytical grade.

Reagents Preparation

For Method A, 125 mg of P-dimethyl amino benzaldehyde was dissolved in mixture of 65 ml of sulphuric acid and 35 ml of methanol. To this 0.05 ml of ferric chloride was added.

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For Method B, 200 mg of P-dimethyl amino cinnamaldehyde was dissolved in 100 ml of methanol.

For Method C, 125 mg of vanillin was dissolved in a cooled mixture of 65 ml of conc.sulphuric acid and 35 ml of water. To this 0.05 ml of ferric chloride solution was added.

Standard preparation

Naratriptan.Hcl standard stock solution (1 mg/ml) was prepared by dissolving 100 mg of drug in methanol and made up to volume with methanol in 100 ml volumetric flask. From this stock solution, working standard solution (100 µg/mL) was prepared with methanol for Methods A, B and C.

Sample preparation

Twenty tablets of Naratriptan were weighed and powdered. A quantity of tablet powder equivalent to 100 mg of Naratriptan was accurately weighed and transferred into a 100 ml volumetric flask containing methanol. The solution was sonicated for extracting the drug for about 15 minutes, filtered through a cotton wool and the filtrate was made up to volume with methanol. Then it was appropriately diluted with the same solvent and used for Methods A, B and C. Working sample solutions were prepared and the procedure described under bulk samples was followed.

Procedure for estimation

Method A: To a series of 10 ml volumetric flasks, methanolic Naratriptan standard solution (100 µg/ml) ranging from 2.5-12.5 µg was transferred and the volume in each volumetric flask was adjusted to 3.0 ml with methanol. Then 1.0 ml of P-dimethyl amino benzaldehyde was added. To all flasks 3.0 ml of conc.sulphuric acid was added and remaining volume was made up to the mark with methanol. Absorbance was measured at 580 nm against the corresponding reagent blank. The amount of Naratriptan present in the given sample solution was computed from corresponding calibration curve.

Method B: To a series of 10 ml volumetric flasks, methanolic Naratriptan standard solution (100µg/ml) ranging from 2-8 µg was transferred and the volume in each volumetric flask was adjusted to 3.0 ml with methanol. Then 1.0 ml of P-dimethyl amino cinnamaldehyde was added. To all flasks 2.0 ml of conc.sulphuric acid was added and the remaining volume was made up to the mark with methanol. Absorbance was measured at 610 nm against the corresponding reagent blank. The amount of Naratriptan present in the given sample solution was computed from corresponding calibration curve.

Method C: To a series of 10 ml volumetric flasks, methanolic Naratriptan standard solution (100 µg/ml) ranging from 2-10 µg was transferred and the volume in each volumetric flask was adjusted to 3.0 ml with methanol. Then 1.0 ml of vanillin was added. To all flasks 2.0 ml of conc.sulphuric acid was added and remaining volume was made up to the mark with methanol. Absorbance was measured at 550 nm against the corresponding reagent blank. The amount of Naratriptan present in the given sample solution was computed from corresponding calibration curve.

3.RESULTS AND DISCUSSION

The developed Methods A, B and C are based on the Naratriptan containing indole nucleus undergoes condensation reaction with aromatic aldehydes P-dimethyl amino benzaldehyde (Method A), P-dimethyl amino cinnamaldehyde (Method B) and vanillin (Method C) forming Schiff's bases to give colored species. It was found that 1.0 ml of the reagent was sufficient for producing maximum color intensity for Methods A, B and C.

The interference studies revealed that the common excipients usually present in the dosage forms do not interfere in the proposed method.

The optical characteristics and validation parameters were given in Table 1. To evaluate the accuracy and reproducibility of the method, known amounts of the pure drug was added to the previously analyzed pharmaceutical formulations and the mixture were reanalyzed by the proposed methods and the recoveries (average of six determinations) were given in Table 2.

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Table -1

Optical characteristics, regression data, Precision and accuracy of the proposed methods for Naratriptan

Parameter	Method A	Method B	Method C
λ_{max} (nm)	580	610	550
Beer's law limits (µg/ml)	2.5-12.5	2-8	2-10
Molar absorptivity (Lit.mole^{-1}.cm^{-1})	1.498 x 10^4	3.421 x 10^4	2.426 x 10^4
Detection limits (µg/ml)	0.16191	0.054	0.0935
Sandell's Sensitivity (µg/cm^2/0.001 abs. unit)	0.0248	0.0108	0.0153
Optimum photometric range	1.5-9.5	2.5-10.5	1-12
Regression equation (Y=a+bc) :Slope (b)	0.0407	0.0913	0.0652
Standard deviation of slope (Sb)	1.91 x 10^{-3}	2.96 x 10^{-3}	2.98 x 10^{-3}
Intercept (a)	-0.0013	0.00032	-0.0017
Standard deviation of intercept (Sa)	1.98 x 10^{-2}	0.0015	0.00184
Standard error of estimation (Se)	0.0031	0.0021	0.00286
Correlation coefficient (r)	0.99986	0.9999	0.9998
% Relative standard deviation*	0.5754	0.6606	0.625
% Range of Error*(confidence limits) 0.05 level 0.01 level	 0.604 0.947	 0.6934 1.087	 0.6563 1.0293
% Error in bulk samples**	0.21	0.34	0.11

* Average of six determinations
** Average of three determinations

The values obtained for the determination of Naratriptan in several pharmaceutical formulations (tablets) and bulk drug by the proposed and reference methods were compared (Table 2). The results indicate that the proposed methods are simple, sensitive, accurate, reproducible and can be used for the routine determination of Naratriptan in bulk and pharmaceutical formulations.

TABLE 2

Assay and recovery of Naratriptan in dosage forms

Pharmaceutical Formulation	Labelled Amount (mg)	Proposed Method			% recovery by Proposed Methods ** ± S.D
		Amount found* (mg) ± S.D	t (value)	F (value)	
Brand-1	2.5	2.45 ± 0.015	0.617	1.874	100.2 ± 0.54
	1.0	0.95 ± 0.010	0.821	2.206	99.81 ± 1.01
Brand-11	2.5	2.54 ± 0.008	0.401	2.638	99.92 ± 1.04
	1.0	1.05 ± 0.011	0.527	1.526	100.3 ± 0.69
Brand-1	2.5	2.48 ± 0.012	0.396	2.540	100.2 ± 1.01
	1.0	0.92 ± 0.017	0.262	2.175	99.82 ± 0.75

* Average ± Standard deviation of six determinations, the t and F values refer to comparison of the proposed method with reference method.
Theoretical values at 95 % confidence limits t = 2.571 and F = 5.05
** Average of five determinations.

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