

Novel spectrophotometric methods for estimation of naratriptan in pharmaceutical dosage forms

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ABSTRACT

Naratriptan is a triptan drug. Two simple, sensitive and accurate spectrophotometric methods have been developed for the determination of Naratriptan in pure state and in its pharmaceutical dosage forms. The developed Method A, involves the formation of drug-picric acid complex in chloroform solution and it shows maximum absorption at λ_{\max} 400 nm; linearity in the range of 2.5-12.5 $\mu\text{g/mL}$. Method B is based on the formation of charge transfer complex formation of chloranilic acid with drug. The developed chromogen in Method B exhibits maximum absorption at λ_{\max} 525 nm and linearity in the range of 100-500 $\mu\text{g/mL}$. The results obtained were statistically evaluated and were found to be accurate and reproducible.

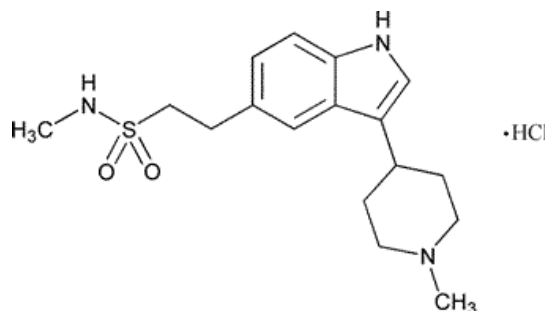
Key words: Naratriptan, spectrophotometric, pharmaceutical dosage forms.

INTRODUCTION

Naratriptan¹ 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.P², 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-HT₂₋₄ 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 migraine³ is generally attributed to its agonist activity at 5-HT_{1D/1B} receptors. The U.S. Food and drug Administration (FDA) approved Naratriptan on February 11, 1998⁴.

Literature reveals no colorimetry and HPLC methods reported for Naratriptan in dosage forms. Only a few analytical methods are reported in the literature for estimation of Naratriptan in pharmaceutical dosage forms and in biological fluids such as LC-MS^{5, 6}

In the present investigation, two simple, sensitive and accurate visible spectrophotometric methods have been developed for the estimation of Naratriptan in tablet dosage forms and in bulk drug. Method A shows λ_{\max} at 400 nm and linearity in the range of 2.5-12.5 $\mu\text{g/mL}$. Method B exhibits λ_{\max} at 525 nm and linearity in the range of 100-500 $\mu\text{g/mL}$.



Chemical structure of Naratriptan

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, 400 mg of picric acid was dissolved in 100 mL of chloroform.
- For Method B, 100 mg of chloranilic acid was dissolved in 20 mL of isopropyl alcohol, filtered and made up to 100 mL with chloroform.

Standard Preparation

For Method A, 10 mL of 100 $\mu\text{g/mL}$ of pure Naratriptan.Hcl standard solution prepared in water was transferred into a 150 mL separating funnel. To this 10 mL of 0.1% sodium hydroxide was added and kept aside to separate free base with continuous shaking. The free base was extracted with 20 mL chloroform thus the obtained chloroform layer is used for the development of chromogen.

For Method B, 100 mg of pure Naratriptan.Hcl was dissolved in 10 mL of water and transferred to 150 mL separating funnel. To this 10 mL of 0.1% sodium hydroxide was added drop wise with shaking. The free base was extracted with 20 mL of chloroform for three times and then made up to 100 mL with chloroform. This chloroform solution containing drug is used for color development.

Sample Preparation

Twenty tablets were taken and made into fine powder. The powder equivalent to average weight was taken and dissolved in 10 mL of water and transferred into a separating funnel, to this 10 mL of 0.1% sodium hydroxide was added and kept aside with continuous shaking. Then 20 mL of chloroform was added to extract the drug into chloroform. This was further diluted in respective concentrations required for Methods A and B so that linearity range can be obtained and further analysis was carried out as described under standard curve.

Procedure for estimation

Method A

Aliquots of standard solution containing 0.5-2.5 mL (2.5-12.5 $\mu\text{g/mL}$) were transferred to a series of 10 mL volumetric flasks. To this 1 mL of picric acid reagent was added and made up to volume with chloroform. The absorbance of the yellow colored chromogen species was measured at λ_{max} 400 nm against reagent blank. The amount of Naratriptan.Hcl in the sample solution was computed from the standard calibration curve.

Method B

Aliquots of standard solution containing 0.1-0.5 mL (100-500 $\mu\text{g/mL}$) were transferred to a series of 10 mL volumetric flasks. Now the volume in all the flasks is made up to 1 mL with chloroform, followed by addition of 1 mL of chloranilic acid reagent and made up to volume with acetonitrile. The absorbance of the purple colored species was measured at λ_{max} 525 nm against reagent blank. The amount of Naratriptan.Hcl in the sample solution was computed from the standard calibration curve.

RESULTS AND DISCUSSION

The developed Method A is based on the quantitative yellow colored complex formation of drug with picric acid reagent. Picric acid in chloroform solution will have very little or no color. When chloroform solution of drug is added to this picric acid reagent it develops intense yellow color due to the presence of cyclic tertiary nitrogen in Naratriptan. It was found that 2 mL of reagent is sufficient for producing maximum color intensity.

The proposed Method B is based on the drug which possesses cyclic tertiary nitrogen of aliphatic nature and function as electron donor and participates in charge transfer interaction with substituted quinines (chloranilic acid). The colored species formed due to the formation of radical cation.

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.

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 and reproducible and can

Table 1: Optical characteristics, regression data, Precision and accuracy of the proposed methods for Naratriptan

Parameter	Method A	Method B
λ_{\max} (nm)	400	525
Beer's law limits ($\mu\text{g/mL}$)	2.5-12.5	100-500
Molar absorptivity ($\text{Lit.mole}^{-1}.\text{cm}^{-1}$)	3.421×10^4	2.426×10^4
Detection limits ($\mu\text{g/mL}$)	0.2905	2.667
Sandell's Sensitivity ($\mu\text{g/cm}^2/0.001 \text{ abs. unit}$)	0.0242	0.813
Optimum photometric range	1.5-15.5	75-150
Regression equation ($Y=a+bc$) :Slope (b)	0.0408	0.00123
Standard deviation of slope (Sb)	4.33×10^{-3}	3.0×10^{-6}
Intercept (a)	0.0016	0.0009
Standard deviation of intercept (Sa)	0.0036	0.00099
Standard error of estimation (Se)	0.2906	2.667
Correlation coefficient (r)	0.9996	0.99998
% Relative standard deviation*	0.5029	0.5984
% Range of Error*(confidence limits)		
0.05 level	0.788	0.9851
0.01 level	0.5029	0.5984
% Error in bulk samples**	0.34	0.11

* Average of six determinations

** Average of three determinations

Table 2: Assay and recovery of Naratriptan in dosage forms

Method	Pharmaceutical Formulation	Labelled Amount (mg)	Proposed Method			% recovery by Proposed methods** \pm S.D
			Amount t found* (mg) \pm S.D	(value)	F (value)	
A	Brand-1	2.5	2.46 ± 0.082	0.165	2.534	100.8 ± 0.50
		1.0	1.04 ± 0.009	0.183	2.474	100.9 ± 0.61
B	Brand-11	2.5	2.52 ± 0.008	0.075	1.104	99.61 ± 1.01
		1.0	1.06 ± 0.011	0.984	1.985	99.38 ± 0.64

* Average \pm 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.

be used for the routine determination of Naratriptan in bulk and pharmaceutical dosage forms.

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