



## **NEW SPECTROPHOTOMETRIC METHODS FOR ESTIMATION 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 formation of colored species on binding of the drug with the ligand, 1, 10-phenanthroline followed by ferric chloride and ortho phosphoric acid. The developed chromogen in Method A shows maximum absorption at  $\lambda_{\max}$  510 nm and linearity in the range of 1-6  $\mu\text{g/mL}$ . Method B is based on the reaction between drug and 2, 2'-Bipyridyl with ferric chloride and ortho phosphoric acid to form a colored chromogen and it shows maximum absorption at  $\lambda_{\max}$  520 nm and linearity in the range of 20-80  $\mu\text{g/mL}$ . Method C is based on oxidation of the drug in the presence of ferric chloride followed by complex formation with bathophenanthroline. The developed chromogen in Method C shows maximum absorption at  $\lambda_{\max}$  620 nm and linearity in the range of 1-5  $\mu\text{g/mL}$ . The results obtained were statistically evaluated and were found to be accurate and reproducible.

**Key words:** Naratriptan, Spectrophotometric

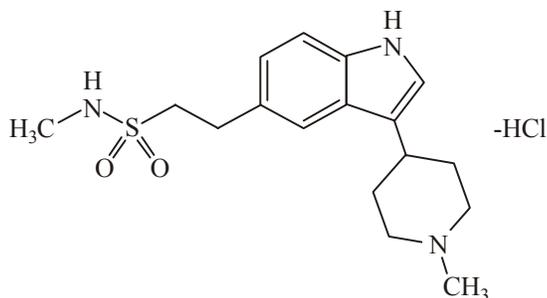
### **INTRODUCTION**

Naratriptan<sup>1</sup> is an antimigraine drug<sup>2, 3</sup>. Chemically, it is N-methyl-2-[3-(1-methyl piperidin-4-yl)-1H-indol-5-yl] ethane sulfonamide. Naratriptan binds with high affinity to 5-HT<sub>1D</sub> and 5-HT<sub>1B</sub> receptors and has no significant affinity or pharmacological activity at 5-HT<sub>2,4</sub> receptor subtypes or at adrenergic  $\alpha_1$ ,  $\alpha_2$  or  $\beta$ ; dopaminergic D1 or D2; muscarinic; or benzodiazepine receptors. The therapeutic activity of naratriptan in migraine is generally attributed to its agonist activity at 5-H<sub>1D/1B</sub> receptors.

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Literature reveals that no colorimetry and HPLC methods have been reported for naratriptan in dosage forms. Only a few articles relating to its therapeutics have made an attempt to develop new analytical methods for the estimation of drug in dosage forms based on the functional groups. In the present investigation, three 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  $\lambda_{\max}$  at 510 nm and linearity in the range of 1-6  $\mu\text{g/mL}$ . Method B exhibits  $\lambda_{\max}$  at 520 nm and linearity in the range of 20-80  $\mu\text{g/mL}$ . Method C shows  $\lambda_{\max}$  at 620 nm and linearity in the range of 1-5  $\mu\text{g/mL}$ .



**Chemical structure of naratriptan**

## EXPERIMENTAL

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

### Reagents preparation

For method A, 198 mg of 1, 10-phenanthroline<sup>4-7</sup> was dissolved in 100 mL of 0.1N hydrochloric acid. 162 mg of anhydrous ferric chloride was dissolved in 100 mL of distilled water. 33.3 mL of above stock solution was further diluted to 100 mL with distilled water. 1.3 mL of orthophosphoric acid was diluted to 100 mL with distilled water.

For method B, 156 mg of 2, 2'-bipyridyl was dissolved in 100 mL of 0.1N hydrochloric acid. 162 mg of anhydrous ferric chloride was dissolved in 100 mL of distilled water. 33.3 mL of above stock solution was further diluted to 100 mL with distilled water. 1.3 mL of orthophosphoric acid is diluted to 100 mL with distilled water.

For method C, 332 mg of bathophenanthroline was dissolved in 100 mL of 0.1N

hydrochloric acid. 162 mg of anhydrous ferric chloride was dissolved in 100 mL of distilled water. 33.3 mL of above stock solution was further diluted to 100 mL with distilled water. 1.3 mL of orthophosphoric acid was diluted to 100 mL with distilled water.

### **Standard preparation**

About 100 mg of pure drug naratriptan was accurately weighed and dissolved in 100 mL of water. This stock solution was used as such for method B. The stock solution was further diluted with water to get the working standard solution of concentration 100 µg/mL for methods A and C.

### **Sample preparation**

Twenty tablets of naratriptan were weighed and powdered. A quantity of tablet powder equivalent to 10 mg of naratriptan was accurately weighed and transferred into a 100 mL volumetric flask containing distilled water. 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 water. 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:** Into a series of 10 mL volumetric flasks, aliquots of standard naratriptan solution (100 µg/mL) containing from 1.0 to 6.0 µg were transferred. To each flask, 1.0 mL of 0.003 M ferric chloride was added. Then 1.0 mL of 1, 10-phenanthroline was added to all flasks and the volumes in all volumetric flasks were equalized with water. The contents were gently boiled for 30 minutes. The solutions were cooled and 2.0 mL of orthophosphoric acid was added to all and final volume was brought to 10 mL with water. Absorbances were measured at 510 nm against the reagent blank. The amount of naratriptan present in the sample solution was computed from calibration curve.

**Method B:** Into a series of 10 mL volumetric flasks, aliquots of standard naratriptan solution (100 µg/mL) containing 20.0 to 80.0 µg were transferred. To each flask, 1.0 mL of 0.003 M ferric chloride was added. Then 1.0 mL of 2, 2'-bipyridyl was added to all the flasks and the volumes in all volumetric flasks were equalized with water. The contents were gently boiled for 50 minutes. The solutions were cooled and 2.0 mL of orthophosphoric acid was added to all and final volume was brought to 10 mL with water. Absorbances were measured at 520 nm against the reagent blank. The amount of naratriptan present in the sample solution was computed from calibration curve.

**Method C:** Into a series of 10 mL volumetric flasks, aliquots of standard naratriptan solution (1000  $\mu\text{g/mL}$ ) containing 1.0 to 5.0  $\mu\text{g}$  were transferred. To each flask, 1.0 mL of 0.003 M ferric chloride was added. Then 1.0 mL of bathophenanthroline was added to all the flasks and the volume in all volumetric flasks were equalized with water. The contents were gently boiled for 10 minutes. The solutions were cooled and 2.0 mL of orthophosphoric acid was added to all and final volume was brought to 10 mL with water. Absorbances were measured at 620 nm against the reagent blank. The amount of naratriptan present in the sample solution was computed from calibration curve.

## RESULTS AND DISCUSSION

The developed Methods A, B and C are based on the reducing property of naratriptan due to the presence of functional moieties vulnerable to oxidation selectively with oxidizing agents such as Fe (III) under controlled experimental conditions. When treated with known excess of oxidant, giving products of oxidation besides unreacted oxidant. The reduced form of Fe (III) i.e. Fe (II)<sup>8</sup> has a tendency to give colored complex on treatment with 1, 10-phenanthroline (Method A), 2, 2'-bipyridyl (Method B) and bathophenanthroline (Method 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 are 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.

**Table 1: Optical characteristics, regression data, precision and accuracy of the proposed methods for naratriptan**

Parameter	Method A	Method B	Method C
$\lambda_{\text{max}}$ (nm)	510	520	620
Beer's law limits ( $\mu\text{g/mL}$ )	1-6	20-80	1-5
Molar absorptivity (Lit. $\text{mole}^{-1}.\text{cm}^{-1}$ )	$4.946 \times 10^4$	$3.589 \times 10^3$	$7.085 \times 10^4$

Cont...

Parameter	Method A	Method B	Method C
Detection limits ( $\mu\text{g/mL}$ )	0.087	0.576	0.145
Sandell's Sensitivity ( $\mu\text{g/cm}^2/0.001$ abs. unit)	0.00752	0.1036	0.00525
Optimum photometric range	0.5-6.5	15-90	0.5-7
Regression equation ( $Y = a + bc$ ) :			
Slope (b)	0.13318	0.0097	0.1857
Standard deviation of slope (Sb)	$9.75 \times 10^{-3}$	$3.36 \times 10^{-5}$	$2.7 \times 10^{-2}$
Intercept (a)	-0.00054	-0.0018	0.0077
Standard deviation of intercept (Sa)	0.00352	0.0017	0.00813
Standard error of estimation (Se)	0.0052	0.0024	0.0112
Correlation coefficient (r)	0.9997	0.9999	0.9992
% Relative standard deviation*	0.335	0.363	0.306
% Range of error* (confidence limits)			
0.05 level	0.352	0.382	0.321
0.01 level	0.552	0.596	0.503
% Error in bulk samples**	0.05	0.92	0.45
*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 and 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**

Method	Pharmaceutical Formulation	Labelled Amount (mg)	Proposed method			% Recovery by proposed methods ** $\pm$ S.D
			Amount found* (mg) $\pm$ S.D	t (value)	F (value)	
A	Brand-I	2.5	2.53 $\pm$ 0.015	0.617	1.874	100.2 $\pm$ 0.54
		1.0	0.95 $\pm$ 0.010	0.821	2.206	99.81 $\pm$ 1.01
B	Brand-II	2.5	2.41 $\pm$ 0.008	0.401	2.638	99.92 $\pm$ 1.04
		1.0	1.03 $\pm$ 0.011	0.527	1.526	100.3 $\pm$ 0.69
C	Brand-I	2.5	2.55 $\pm$ 0.012	0.396	2.540	100.2 $\pm$ 1.01
		1.0	0.99 $\pm$ 0.017	0.262	2.175	99.82 $\pm$ 0.75

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.

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