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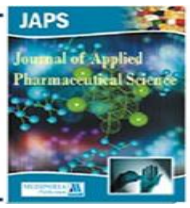

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Estimation of Naratriptan Hydrochloride in Bulk and Formulation by First Order Derivative UV-Spectrophotometric Methods

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ABSTRACT

Naratriptan Hydrochloride is a triptan drug used for the treatment of migraine headaches and is a selective 5-hydroxytryptamine 1 receptor subtype agonist. Two simple, precise and economical UV-Spectrophotometric methods have been developed for the determination of Naratriptan Hydrochloride in pharmaceutical dosage form. In Method I, zero order spectrum of Naratriptan Hydrochloride was derivatized into first order ($\Delta \lambda = 2$, scaling factor = 9) using UV-probe software and the amplitude of the trough was recorded at 232.2 nm. While in 'Method II', area under curve (AUC) of the first order derivative spectrum was selected between 294.20 – 299.00 nm. In Method I and II, Naratriptan Hydrochloride obeyed linearity in the concentration range of 10 - 60 µg/ml. The coefficient correlation (r^2) in Method I and II were found to be $r^2 = 0.999$ and $r^2 = 0.998$, respectively. The % amounts of Naratriptan Hydrochloride quantified by Method I and Method II was found to be 98.79 % and 99.43%. The developed methods were validated statistically and by recovery studies.

Keywords: Naratriptan Hydrochloride; First Order Derivative, Area under Curve technique.

INTRODUCTION

Naratriptan Hydrochloride, N-methyl-3- (1-methyl-4- piperidinyl)-1 *H*-indol-5-ethanesulfonamide is a selective 5-hydroxytryptamine 1 receptor subtype agonist used in the treatment of migraine headaches. A detailed literature survey for Naratriptan Hydrochloride revealed that several analytical methods such as electroscopy tandem mass spectrometry and liquid chromatography (LC) in human serum (Vishwanathan *et al.*, 2000; Dulery *et al.*, 1997) and RP-HPLC with tandem mass spectrometric detection method have been reported for the determination of Naratriptan Hydrochloride in human plasma and its application to bioequivalence study.(Reddy *et al.*,2011). Naratriptan Hydrochloride is official in United States Pharmacopeia (U.S.P. 29). In the present work, two simple 'first order derivative UV-Spectrophotometric methods' have been developed for the estimation of Naratriptan Hydrochloride by measuring 'Amplitude of trough' and 'Area under the curve (AUC)' at the selected wavelengths in bulk and in tablet formulation. Further, the validation of developed methods as per ICH guidelines (ICH, 2005).

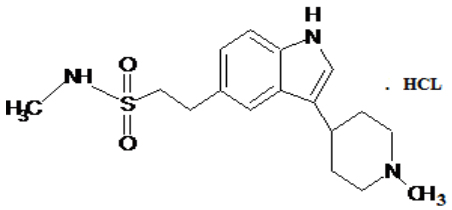

Fig. 1: Chemical structure of Naratriptan Hydrochloride.

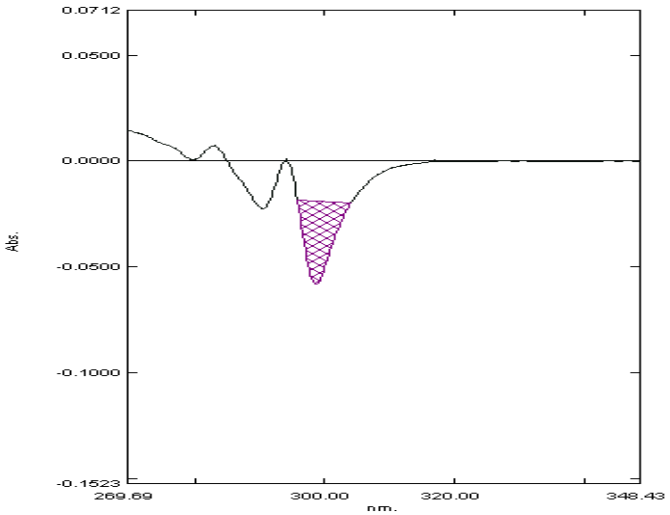

Fig. 2: First Order Derivative spectrum of Naratriptan Hydrochloride in Methanol showing AUC.

EXPERIMENTAL WORK

Material and Method

Naratriptan Hydrochloride working standard was obtained as gift from USV Ltd., India. The drug was used without further purification. Tablet (NARATREX 1) containing 1 mg of Naratriptan Hydrochloride was purchased from local market. Analytical grade solvents were used for the experiment.

Table. 1: Optical characteristics of Naratriptan Hydrochloride

Parameters	Method I	Method II
Beer-Lambert's range(µg/ml)	10 – 60	10 - 60
λ max(nm)/ wave length range (nm)	232.20	294.20 – 299.00
Slope	0.007	0.062
Intercept	0.056	0.013
Correlation coefficient	0.999	0.998

Instruments

UV-Visible double beam spectrophotometer (UV-2450, SHIMADZU Limited, Japan) with 1 cm matched quartz cells and electronic balance (Model Shimadzu AUX 120).

Preparationof Stock Standard Solutionand study of linearity

Stock standard solution was prepared by dissolving 10 mg of Naratriptan Hydrochloride in 100 mL methanol solution to obtain concentration of 100 µg/mL.

Method I (First Order UV-Spectrophotometric method)

Aliquots of stock solution were further diluted with methanol to obtain concentration in the range of 10- 60 µg/mL and scanned in the UV-region (400 nm – 200 nm). The zero order spectrum (λ max 223) was derivatized into first order spectrum (Δ λ = 2, scaling factor = 9) and amplitude of the trough was recorded at 232.2 nm.The linearity curve was plotted concentration *versus* amplitude of the trough.

Method II (First Order UV-Spectrophotometric using Area under Curve technique)

The AUC technique is applicable where there is no sharp peak or when broad spectra are obtained.

The solutions prepared for linearity study in Method I was scanned in the UV- region (400 nm – 200 nm). The AUC between two wavelengths 294.20 – 299.00 nm were chosen for study. The calibration curve was constructed by plotting concentration versus AUC.

Analysis of tablet formulation

Twenty tablets were accurately weighed and average weight determined. A quantity of powder drug equivalent to 1.0 mg of Naratriptan Hydrochloride was transferred to 25 ml volumetric flask containing 15 ml of methanol, shaken manually for 15 min; volume was adjusted to mark with same solvent and filtered through Whatmann filter paper No.41. This solution was scanned and as mentioned in Method I and Method II and the concentration of Naratriptan Hydrochloride was determined using respective linearity curves.

Accuracy of the methods

The accuracy of the proposed methods was determined by calculating mean % recovery performed at three different levels i. e. 80 %, 100% and 120%. To the pre-analyzed sample solution (20 µg/mL) in both method and a known amount of Naratriptan Hydrochloride bulk drug was added at 80% to 120% and the re-analyzed the Naratriptan Hydrochloride by proposed methods, the results are shown in **Table 2.**

Table. 2: Accuracy studies.

% Value	Initial Amount (µg/ml)	Added Amount (µg/ml)	% Recovery		% RSD (n=3)	
			Method I	Method II	Method I	Method II
80	20	16	99.86	99.34	0.95	1.15
100	20	20	100.21	100.03	1.05	1.25
120	20	24	102.11	101.75	1.12	1.15

n= number of determinations

RESULTS AND DISCUSSION

Methanol was chosen as solvent for dissolving Naratriptan Hydrochloride. In Method I and Method II, Naratriptan Hydrochloride obeyed linearity in the concentration range of 10-60 µg/ mL. The % amount of Naratriptan Hydrochloride estimated by Method I and II was found to be 98.79 % and 99.43 %. Results indicated that there was no interference from the excipients usually occurs in tablet formulation.

The developed methods were validated for accuracy, precision and ruggedness as per ICH guidelines.

The accuracy methods were studied as mean % recovery and found to be in the range of 99.86 – 102.11 (Method I) and 99.34 - 101.75 (Method II), respectively.

The precision of the methods was determined as repeatability, intra-day and inter-daystudy. Precision of methods was studied at the concentration of 20 µg/mL, 30 µg/mL, 40 µg/mL is shown in **Table 3** .The low value of % RSD (n=3) indicates high Precision of the method.

Table. 3: Precision:

Conc. (µg/ml)	% RSD			
	Intra-day (n = 3)		Inter-day (n = 3)	
	Method-I	Method- II	Method-I	Method- II
20	1.2	1.03	1.0	0.98
30	0.92	1.01	0.90	0.95
40	0.98	0.97	1.56	1.87

n= number of determinations

Sensitivity of method was estimated by determining LOD and LOQ; it was found to be 0.98 µg and 2.94 µg in 'Method I' and in 'Method II' 1.09 µg and 3.48 µg, respectively.

Ruggedness of the proposed methods was determined by analyzing sample solution of 20 µg/mL by two different analyst using similar operational and environmental conditions. The results are reported in **Table 4.** The low value of % RSD indicates that method is rugged.

Table 4: Ruggedness.

Analysts		Amount found [%]	% RSD [n = 3]
Method I	1	99.40	0.96
	2	99.28	0.91
Method II	1	97.75	0.84
	2	98.46	1.52

n= number of determinations

CONCLUSION

Both these developed UV-Spectrophotometric methods are simple, accurate and precise and can be used for routine analysis of Naratriptan Hydrochloride from its tablet formulation.

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