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DERIVATIVE SPECTROPHOTOMETRIC DETERMINATION OF NARATRIPTAN HYDROCHLORIDE IN PURE AND DOSAGE FORMS BY OXIDATIVE COUPLING AND CONDENSATION REACTIONS

G.Ramu[1, 2]
T. Vijaya Bhaskara Reddy[1]
C. Rambabu*[1]

[1]Department of Chemistry, Acharya Nagarjuna University, Nagarjuna Nagar, Guntur, AP-India, PIN: 522510
[2]Department of Chemistry, Sir C.R.Reddy P.G. College, Eluru, West Godavary AP-India, PIN: 534007

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ABSTRACT

Two simple and sensitive second order derivative visible spectrophotometric methods have been developed for the assay of naratriptan hydrochloride (NTT) in pure and dosage forms. Method-I was an oxidative coupling reaction using MBTH as oxidative coupler in the presence of strong oxidizing agent Ce (IV) and Method-II was condensation reaction with vanillin in concentrated sulphuric acid. The wavelength of maximum absorbance (630nm in Method-I and 570nm in Method-II) were determined from the absorption spectra of the colored product recorded as a function of wavelength against a regent blank. The molar absorptivity (in Method-I 6.03E+03and Method-II 7.42E+03 lt/mole/cm), Sandell's sensitivity (6.25E-02 for Method-I 5.56E-02 µg/cm^2 / 0.001 Abs for Method-II) and slope of the calibration curve (in Method-I 4.26E-06 and in Method-II 2.48E-05) for the proposed methods were calculated and found Method–II was more sensitive than in Method-I. The values of limit of detection and limit of quantification for Methods I and II were found to be 0.245, 0.210 and 0.815, 0.699 respectively. The correlation coefficient r=0.9999 in both methods indicate that there was a good correlation between absorbance and concentration. The two methods were found to be precise, accurate and linear in the range of concentration 2.5-40.0µg/ml. Pharmaceutical formulations were analyzed by the proposed methods and acceptable results were obtained therefore these methods can be adopted for the routine analysis of naratriptan hydrochloride in pure and dosage forms in any quality control laboratory.

Keywords: Naratriptan hydrochloride, derivative spectrophotometry, oxidative coupling, condensation and calibration plot and assay.

1. INTRODUCTION

Naratriptan hydrochloride is chemically known as *N*-methyl-3-(1-methyl-4-piperidinyl)-1*H*-indole-5-ethanesulfonamid mono hydrochloride. It is a novel second generation triptan antimigrane used for the treatment of the acute migraine attacks. The empirical formula is $C_{17}H_{25}N_3O_2S$•HCl, representing a molecular weight of 371.93 grams. Naratriptan hydrochloride is a white to pale yellow powder that is readily soluble in water. The molecular structure was presented in Fig.1. It is available in the market as naratrex (Sun Pharma), amerge (GlaxoSmithKline) of 1.0mg tablet and naramig (GlaxoSmithKline) 2.5mg tablet. Each amerge (naratriptan) tablet for oral administration contains 1.11 or 2.78 mg of naratriptan hydrochloride equivalent to 1 or 2.5 mg of naratriptan, respectively. Each tablet contains the inactive ingredients such as croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, triacetin and titanium dioxide, iron oxide yellow and indigo carmine aluminum lake (2.5-mg tablet only) for coloring.

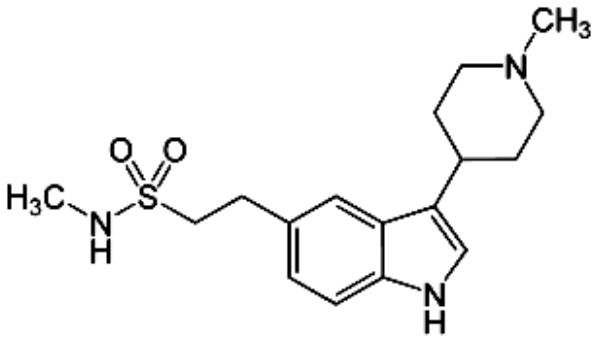

Fig.1: The molecular structure of Naratriptan hydrochloride

Dolery et al. [1] have developed a liquid chromatographic electro spray mass spectrometric method for the determination of naratriptan, sumatriptan in rabbit plasma.

Address for correspondence

Prof. C. Rambabu
E-mail: rbchintala@gmail.com

Vishwanathan and his co workers [2] have reported a LC-ESIMS/MS method for the determination of antimigran drugs such as naratriptan, sumatriptan, and rizatriptan in human serum. Manish Yadav et al [3] have reported a LC-ESI-MS/MS method for the quantification of naratriptan in human plasma. Balasekhara Reddy [4] et al. developed a HPLC tandem mass spectrometry method for the estimation of naratriptan in human plasma. Ramu et al developed an RP-HPLC method [5] for the assay of naratriptan hydrochloride in pharmaceutical formulations. Some UV-Visible spectrophotometric [6-10] methods and a volatametric method [11] were present in the literature to determine naratriptan in pharmaceutical formulations.

The aim of developing first and second order derivative spectrophotometric methods is to know about any kind of interferences that may occur in zero order spectra and to determine the amount of NTT on the basis of measuring derivative amplititudes. In the present investigation, the author has made some attempts to use some colored reactions such as oxidative coupling reaction (Method-I) using MBTH as oxidative coupler in the presence of strong oxidizing agent Ce(IV) and condensation reaction(Method-II) with vanillin in concentrated sulphuric acid to estimate the amount of naratriptan hydrochloride in pure and dosage forms.

2. EXPERIMENTAL

2.1 Instrumentation

UV-Visible Spectrophotometer:- Elico SL159 model,2nm high resolution, double beam, 1cm length quartz coated optics; Wavelength range190-1100nm ; High stability, linearity, precision instrument was used for all the spectral measurements.

2.2 Materials and Methods

All the chemicals, reagents and solvents used in the present investigation (MBTH-Fluka, Cerric Ammonium Sulphate-Merck, Vanillin-BDH and H_2SO_4 Merck) were analytical grade. Distilled water used for the analysis was prepared by double distillation in the laboratory. A gift sample of naratriptan hydrochloride was provided by Chandra Labs an Analytical Testing Laboratory Hyderabad and different dosage forms were obtained from the local pharmacy.

Preparation of standard drug solution: Accurately weighed amount of 100mg of reference naratriptan hydrochloride was transferred into a 100ml volumetric flask, dissolved in double distilled water and made up to the mark. Working standard solutions of concentration 250µg/ml for the Method-I and 200µg/ml for the Method-II were prepared by transferring 25.0ml and 20.0ml of the stock solution into two separate 100ml standard flasks and made up to the mark with double distilled water respectively.

Preparation of reagents: Analytical grade chemicals and reagents were used in the preparation of 3-Methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) solution (Fluka; 0.2%, 8.56 x 10^{-3}M) and Cerric ammonium sulphate (Ce (IV) solution (Merck, 1%, 9.35 x 10^{-3}M) for Method-I and vanillin solution (BDH, 0.2%, 1.31 x 10^{-2}M) for Method-II in double distilled water. The details of preparation of the reagents were as follows. Concentrated Sulfuric acid and methanol were used directly. *MBTH (Fluka; 0.2% w/v, 8.56 x 10^{-3}M):* About 200mg of MBTH was accurately weighed and dissolved in double distilled water. *Ce (IV) solution (Merck; 1% w/v , 9.35 x 10^{-3}M):* 1% Ce (IV) solution was prepared by dissolving accurately 1.0g of potassium dichromate in 100ml of distilled water. *H_2SO_4 solution (Qualigens; 2.3M v/v):* 6.38ml of 18M H_2SO_4 was added to 93.62ml distilled water slowly with continuous shaking and cooling. *Vanillin solution (BDH, 0.2% w/v, 1.31 x 10^{-2}M):* Prepared by dissolving accurately weighed 200mg of Vanillin in 100ml of CH_3OH.

2.3 Method Development

Optimum conditions necessary for rapid and quantitative formation of the colored product with maximum stability and sensitivity were established by varying the parameters one at a time, keeping the others fixed and observing the effect produced on the absorbance of the colored species. After a detailed study of the effects of various parameters involved in the optimization the following procedures are proposed for the assay of NTT by first and second order derivative spectrophotometry.

Method-I: Different aliquots of standard NTT working standard solution were transferred into a series of 25ml calibrated tubes, 0.5mL of MBTH solution was added and kept aside. After 5minutes, 2.0mL of Ce(IV) solution was added and kept aside for 10min. and the volume was made up to the mark with distilled water. The absorption spectra (Fig.2), first order derivative and second order derivative spectra (Fig.3, Fig.4) for each of the concentration of NTT were recorded over the wavelength range 550-750nm at different slit width against a regent blank under similar conditions. Calibration curves were constructed by plotting drug concentration against amplitudes of the derivative spectrum at 630nm and thus amount of NTT was deduced from the calibration curve (Fig.5).

Method-II: Into different 20ml graduated tubes, different amounts of NTT were transferred and the volume of the each tube was adjusted to 3.0ml with methanol. 2.0ml of vanillin ($1.31x10^{-1}$M) and 3.0ml of concentrated sulphuric acid were added to each tube and thoroughly shaken. Then the reaction mixture was adjusted to 10.0ml with methanol. The absorption (Fig.6) spectra, First order derivative and second order derivative spectra (Fig.7 and Fig.8) for each of the concentrations of NTT were recorded over the wavelength range 400-800nm against a solvent blank at different slit width ($\Delta\lambda$) and the calibration curve for derivative spectrophometry was constructed by plotting drug concentration verses the amplitudes of the derivative spectrum at 570nm and thus amount of NTT was deduced from the calibration curve (Fig.9).

2.4 Method Validation

Precision: The precision of each proposed method was ascertained from the amplitude values obtained for five replicates of a fixed amount of NTT in total sample solution. The standard deviation and percent relative standard deviation were calculated for the proposed methods and were presented in Table-1.

Accuracy: To determine the accuracy of each proposed method, different amounts of samples (75%, 100%, and 125%) of naratriptan HCl were taken and analyzed by the proposed method. The percent of recovery, standard deviation and percent of relative standard deviation were calculated. The results were recorded in Table-2 and Table-3

Linearity and Range: Calibration plots were plotted for second derivative amplitudes against concentration of the drug and found to be linear within the linearity limits 2.5-40.0 µg/ml for the Method-I and Method-II respectively. The slope, intercept, correlation coefficient were evaluated by the least square regression method. The correlation coefficient of the standard curves (n = 5) for the two methods was found to be greater than 0.999. This indicates that there was a good correlation between second derivative amplitudes and concentration of the drug. The values of correlation coefficient, slope and intercept were shown in Table-4

Limit of detection (LOD) and limit of quantization (LOQ): The limit of detection (LOD) and limit of quantitation (LOQ) were calculated from the formulae LOD=3.3s/b and LOQ=10s/b where s was the standard deviation of the intercept and b is the slope of the calibration curves (n=5).The results were presented in Table-4.

2.5 Analysis of Formulations

Ten tablets of naratriptan hydrochloride were accurately weighed and finely powdered in a mortar. An amount of tablet mass equivalent to 25mg was transferred to a 100mL volumetric flask and dissolved in water. The resulting solution was filtered and the percent of recovery was determined by adding different known amounts of the standard drug to equal amount of test sample, reagents were added and diluted to the same volume. The absorption values were measured for every solution and the results were plotted on a graph with the dependent variable (absorbance) on y-axis and the amount of the drug added on x-axis. Extrapolation of the straight line thus obtained to the point where the x-axis was cut provides a measure of drug in the test solution. Commercial formulations of naratriptan hydrochloride were successfully analyzed by the proposed methods. The values obtained by the proposed and reference methods for the formulations were compared statistically with F-test and t-test and found to be not different

significantly. The results were summarized in Table-5 and Table-6.

The effect of wide range of excipients and other active ingredients usually present in the formulations were investigated by the proposed methods under the optimum conditions. The commonly used excipients and other active ingredients usually present in the formulations do not interfere even if they were present in large amount than they usually exist.

3. RESULTS AND DISCUSSIONS

Derivative spectrophotometry was an analytical technique of good utility and offers background correction and better selectivity than normal spectrophotometry. Single or multi-components can be analyzed in the presence of broad, interfering background matrix absorption. Of course, for quantitative analytical purposes, only the amplitudes versus concentrations were measured. The ^{1}D and ^{2}D zero-crossing point of NTT for the proposed methods were found 630 method Method-I, 520 Method-II; and 585 and 670 nm Method-I and 535and 595nm Method-II respectively. The selection of the optimal wavelength was based on the fact that the absolute value of the total derivative spectrum at the selected wavelength has the best linear response to the analyte concentration. The ^{2}D spectrum shows better resolution and linearity than first order spectrum. Therefore the maximum amplitude of the second derivative curves were obtained at wavelength 630 nm and 570 nm for Method-I and Method-II respectively were chosen for the determination of naratriptan hydrochloride respectively.

Low percent of relative standard deviation values (0.738, 0.944) for the Method-I, Method-II respectively indicate that the developed methods were highly precise. The mean percent of recovery and percent of relative standard deviation were evaluated at 75%, 100% and 125% concentration levels and found to be 99.98, 99.70 and 100.05; 0.790, 0.610 and 0.7535 for Method-I.; 100.91, 100.13 and 100.11; 0.726, 0.486 and 0.655 for Method-II. Low % RSD values and high % Recovery values support for high accuracy of the methods.

4. CONCLUSIONS

The second order derivative spectrophotometric methods developed by the author were simple sensitive, selective, reproducible, and stable. The developed method could be readily adapted to routine quality control of NTT by ordinary laboratories.

5. ACKNOWLWDGEMENTS

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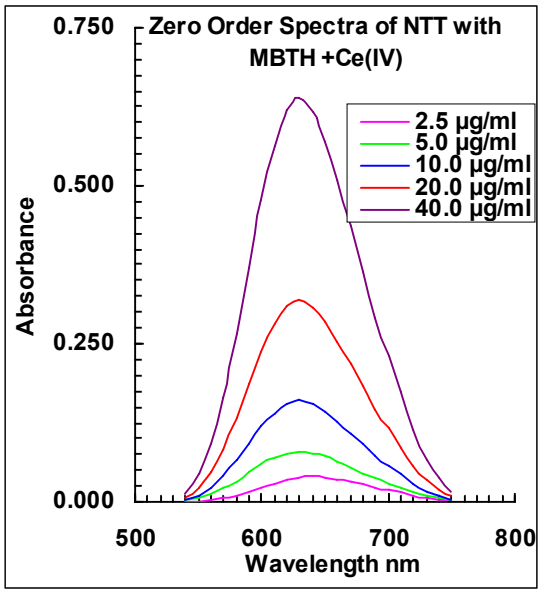

Fig.2: Absorption Spectra of NTT with MBTH+Ce(IV) Method-I

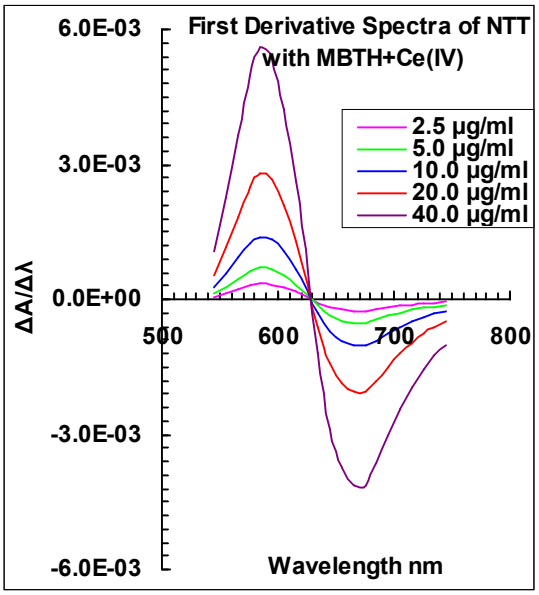

Fig.3: First Derivative Spectra of NTT with MBTH+Ce(IV) Method-I

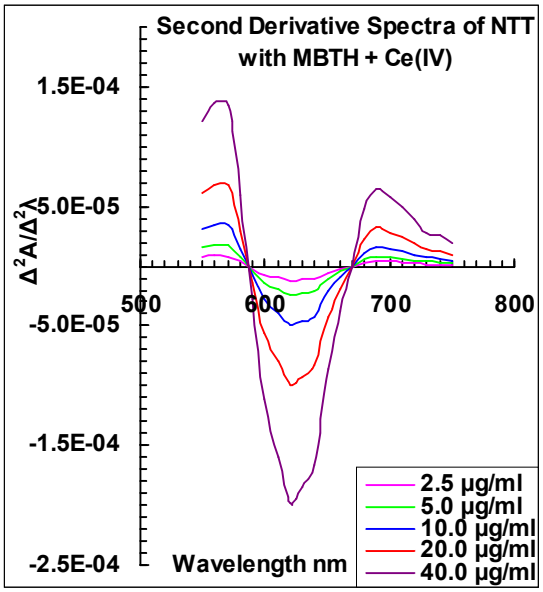

Fig.4: Second Derivative Spectra of NTT with MBTH+Ce(IV) Method-I

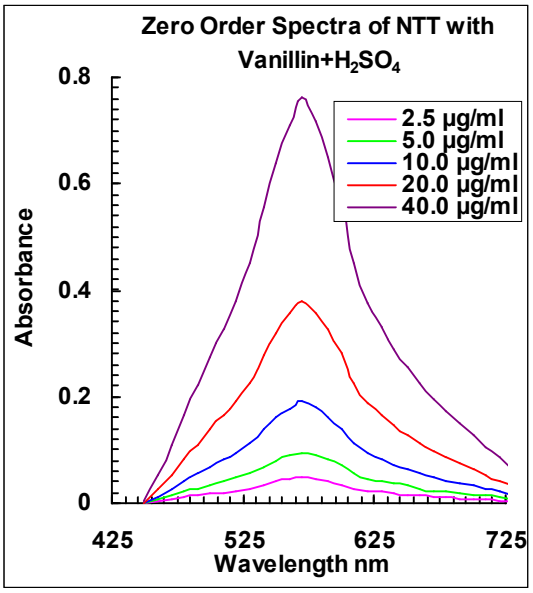

Fig. 6: Absorption Spectra of NTT with Vanillin+H_2SO_4 Method-II

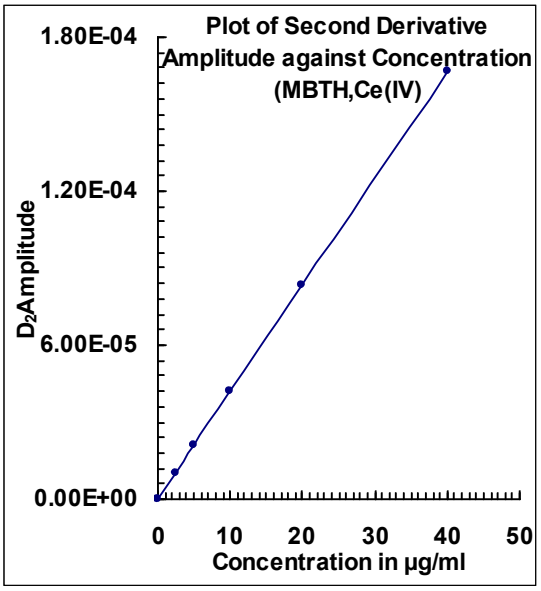

Fig.5 Linear Plot of Second Derivative Amplitude against Concentration of NTT Method-I

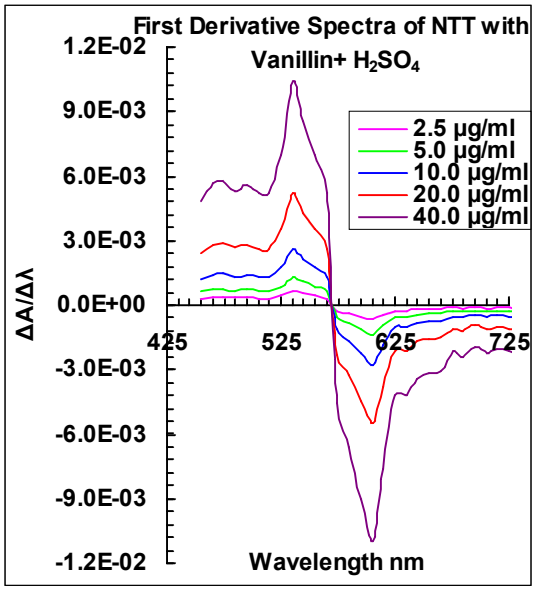

Fig.7: First Derivative Spectra of NTT with Vanillin+H_2SO_4 Method-II

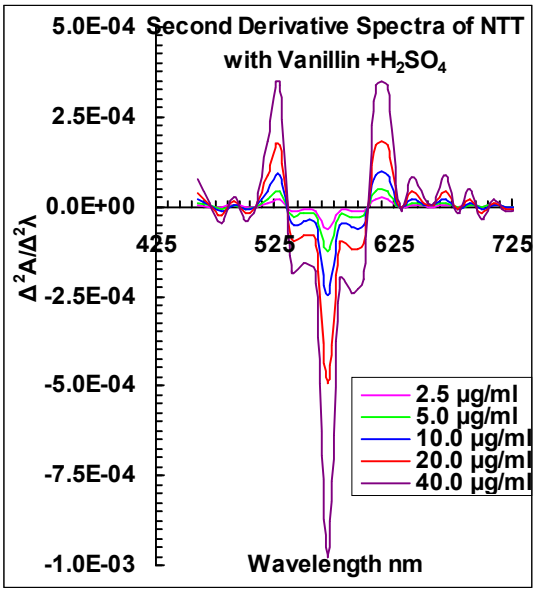

Fig.8: Second Derivative Spectra of NTT with Vanillin+H_2SO_4 Method-II

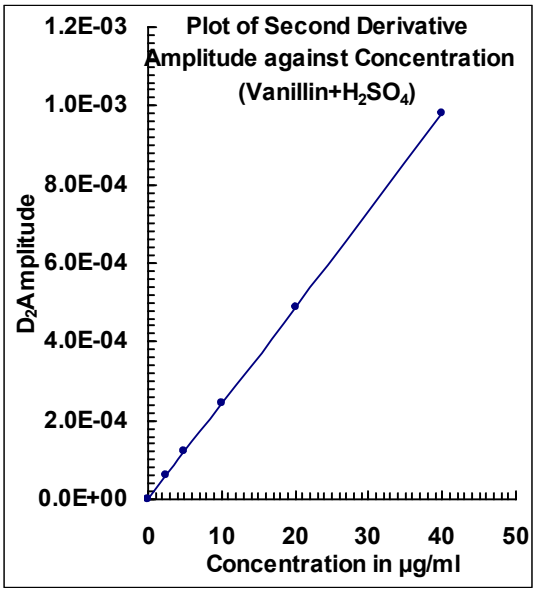

Fig.9: Linear Plot of Second Derivative Amplitude against Concentration of NTT Method-II

Table 1: Precision of the proposed methods

S. No	Name of the Parameter	Method-I	Method-II
1	Amount Taken (µg/ml)	10.00	10.00
2	Mean (n=5)(µg/ml)	10.03	9.99
3	Standard Deviation (S)	0.074	0.094
4	%Relative Standard Deviation	0.738	0.994
5	0.05 level confidence limit	0.412	0.142
6	%Recovery	100.30	99.90

Table 2: Accuracy of the Method-I

Concentration-1			Concentration-2			Concentration-3		
Taken µg/ml	Found µg/ml	%Recovery	Taken µg/ml	Found µg/ml	%Recovery	Taken µg/ml	Found µg/ml	%Recovery
7.5	7.44	99.20	10	9.94	99.4	12.5	12.55	100.4
7.5	7.53	100.40	10	9.96	99.6	12.5	12.65	101.2
7.5	7.53	100.43	10	10.04	100.4	12.5	12.43	99.44
7.5	7.56	100.80	10	9.89	98.9	12.5	12.43	99.44
7.5	7.43	99.07	10	10.02	100.2	12.5	12.47	99.76
Mean	7.498	99.98		9.97	99.7		12.51	100.048
SD	0.059			0.061			0.094	
%RSD	0.789			0.610			0.753	

Table 3: Accuracy of the Method-II

Concentration-1			Concentration-2			Concentration-3		
Taken µg/ml	**Found µg/ml**	**%Recovery**	**Taken µg/ml**	**Found µg/ml**	**%Recovery**	**Taken µg/ml**	**Found µg/ml**	**%Recovery**
7.5	7.64	101.87	10	10.08	100.80	12.5	12.56	100.48
7.5	7.53	100.40	10	10.02	100.20	12.5	12.42	99.36
7.5	7.55	100.67	10	9.95	99.50	12.5	12.43	99.44
7.5	7.61	101.47	10	9.98	99.87	12.5	12.59	100.72
7.5	7.51	100.13	10	10.03	100.30	12.5	12.57	100.56
Mean	7.57	100.90		10.01	100.13		12.51	100.11
SD	0.055			0.048			0.082	
%RSD	0.726			0.486			0.655	

Table 4: Linearity studies and regression parameters

S. No.	Name of the Parameter	Method-I	Method-II
1	Linearity Limits µg/ml	2.5-40.0	2.5-40.0
2	Slope (b)	4.26E-06	2.48E-05
3	Intercept(a)S	-5.78E-07	8.13E-07
4	Correlation Coefficient (r)	0.9999	0.9999
5	Limit of Detection (LOD) µg/ml	0.245	0.210
6	Limit of Quantification (LOQ) µg/ml	0.815	0.699

Table 5: Assay of NTT in pharmaceutical formulations

Brand	Amount of the drug mg				Percent of Recovery **	
	Taken	Found *			Proposed Method	Reference
		Method-I			Method-I	
Naratrex	2.5	Mean	2.498	%REC	99.94	100.4
		SD	±0.015	%RSD	±0.609	± 0.42
		F	2.102			
		t	0.133			
Naramig	2.5	Mean	2.498	%REC	99.92	99.6
		SD	±0.016	%RSD	±0.647	± 0.63
		F	2.371			
		t	0.053			
Naratrex	1.00	Mean	0.999	%REC	99.99	99.6
		SD	±0.012	%RSD	±1.18	± 0.63
		F	1.258			
		t	0.080			
Naramig	1.00	Mean	1.002	%REC	100.20	100.4
		SD	±0.008	%RSD	±0.786	± 0.42
		F	1.561			
		t	2.498		99.94	

Table 6: Assay of NTT in pharmaceutical formulations

Brand	Amount of the drug mg			Percent of Recovery **		
	Taken		Found *	Proposed Methods		Reference
			Method-II		Method-II	M_{Ref}
Naratrex	2.5	Mean	2.480	%REC	99.95	100.4
		SD	±0.02	%RSD	±0.805	± 0.42
		F	3.687			
		t	0.586			
Naramig	2.5	Mean	2.499	%REC	99.99	99.6
		SD	±0.013	%RSD	±0.538	± 0.63
		F	1.64			
		t	0.34			
Naratrex	1.00	Mean	1.004	%REC	100.42	99.6
		SD	±0.009	%RSD	±0.857	± 0.63
		F	1.672			
		t	0.863			
Naramig	1.00	Mean	1.000	%REC	100.01	100.4
		SD	±0.002	%RSD	±0.161	± 0.42
		F	2.023			
		t	0.056			

**Average of six determinations are considered, AVG=Average, SD=Standard deviation, F=F-test value, t=t-test value; Theoretical values at 0.05 level of confidence limit F=5.05, t=1.812.*
***%REC=% of Recovery, %RSD=%of Relative standard deviation; Recovery of 10.0mg added to the preanalyzed formulations (Average of six determinations)*

REFERENCES

1. Dulery B D, Petty M H, Schoun J, David M, Huebert N D. "A method using a liquid chromatographic-electrospray mass spectrometric assay for the determination of antimigraine compounds. Preliminary Pharmacokinetics of MDL 74,721 Sumatriptan and Naratriptan, in rabbit. *J.Pharm.Biomed.Anal*, 15, (1997), 1009-1020.
2. Vishwanathan K, Bartlett MG, Stewart JT. "Determination of antimigraine compounds rizatriptan, zolmitriptan, naratriptan and sumatriptan in human serum by liquid chromatography/electrospray tandem mass spectrometry". *Rapid Commun.Mass Spectrom*, 14,(2000), 168-172.
3. Manish Yadav, Chirag Patel, Mahendra Patel, Ajay Gupta, "Sensitive and rapid determination of Naratriptan, a second generation Antimigrane drug in human plasma by LC-ESI-MS/MS. Application to a bioequivalence study". *Journal of Chromatographic Science*, 49, (2011), 101-107.
4. Balasekhara Reddy Challa,Bahlul Zayed Shtaiway Awen, Babu Rao Chandu, Rihana Praveen Shaik., "Method development and validation of for naratriptan determination in human plasma by HPLC with tandem mass spectrophotometry detection and itsapplications to bioequivalence". *Brazilian Journal of Pharmaceutical Science*, 47,(2011),13-22.
5. Ramu.G, Biksham Babu.A, Sravan Kumar.M, Rambabu.C, Assay of naratriptan hydrochloride in pharmaceutical formulations by RP-HPLC method, *Journal of Pharmacy Research*.5(5), (2012,), 2627-2630.
6. Sreelakshmi A, Devala Rao G, Sudhakara Sai Babu G. Novel Spectrophotometric methods for the estimation of naratriptan in Pharmaceutical dosage form. *Biosciences Biotechnology Research Asia,* 57, 6(2), (2006), 243-249.
7. Kumara Swamy.G, J.V.L.N. Sheshagiri Rao,: Spectrophotometric determination of naratriptan in bulk and pharmaceutical dosage form", *Indo American Journal of Pharmaceutical Research*, 1(4), (2011), 253-256.

8. Desi ReddyR.B, Charitha.A, Naga Sowjanya.G, Sravan Kumar.G, Gananadhamu.S, Krishna Kishore.G, Krishna Chaitanya.K, Spectrophotometeric estimation of naratriptan hydrochloride with iron reagents, *Journal of Global Trends in Pharmaceutical Sciences*, 4(2), (2013),1107-1110.
9. Ramesh .C, Reddy.G., Nagarjuna, Narayana .T.V., Rao K.V.S. Prasada, Rao B. Ganaga, Assay of Naratriptan Hydrochloride in Bulk and Its Pharmaceutical Formulations by Extraction Spectrophotometry, *Research Journal of Pharmacy and Technology,4(5), (2011), 747-451.*
10. Borse, Jayshri S. Shirkhedkar, Atul A., Estimation of Naratriptan Hydrochloride in Bulk and Formulation by First Order Derivative UVSpectrophotometric Methods, *Journal of Applied Pharmaceutical Science*; 2(6),(2012), 227-231.
11. Velasco-Aguirre C, Alvarez-Lueje A. Volatametric behaviour of Naratriptan and its determination.*Talanta*,82(2), (2010),796-802.