ISSN: 0970-020 X; CODEN: OJCHEG
Oriental Journal of Chemistry
2011, Vol. 27, No. (1): Pg. 313-316

http://www.orientjchem.org

New Spectrophotometric Methods for the Determination of Naratriptan Hydrochloride in Bulk and its Pharmaceutical Formulations

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(Received: January 14, 2011; Accepted: February 18, 2011)

ABSTRACT

Three simple sensitive and reproducible visible spectrophotometric methods (A, B, and C) for the determination of Naratriptan hydrochloride (NTP) in bulk samples and pharmaceutical formulations are described. Method A is based on the formation of colored co-ordination complex with cobalt thiocyanate (CTC). Method B is based on the formation of colored species with citric acid - acetic anhydride (CiA-Ac_2O). Method C based on the formation of colored molecular complex involving NTP and sodium nitroprusside (SNP) in the presence of hydroxylamine mono hydrochloride (HA). Regression analysis of Beer's law plots showed good concentration ranges 5-35, 2-10 and 10-60 µg mL^{-1} for methods A, B and C respectively. The applicability of the methods was examined by analyzing tablets of NTP.

Key words: Naratriptan hydrochloride, CiA-Ac_2O, SNP, HA, CTC, Spectrophotometry.

INTRODUCTION

Naratriptan hydrochloride (NTP) [N-methyl-3-(-1-methyl-4-piperidinyl)-1H-indole-5-ethanesulfonamide monohydrochloride] is a selective 5-hydroxytryptamine receptor subtype agonist. It is available in tablet form for oral administration. And it is used for the treatment of migraine. The reported analytical procedures for the estimation of NTP in bulk samples and in unit dosage forms are based on sophisticated HPLC[1-3], GLC[4], and LC-MS[5, 6]. No visible spectrophotometric method has been reported for the assay of NTP in literature. This paper describes three visible spectrophotometric procedures by exploiting the property of tertiary nitrogen in drug, molecular

complex formation with CTC (method A), internal salt formation with CiA-Ac_2O (method B), and, formation of colored molecular complex involving NTP and SNP in the presence of hydroxylamine mono hydrochloride (HA) (method C).

MATERIAL AND METHODS

Preparation of solutions

A 1 mg/ml solution was prepared by dissolving 50 mg of pure NTP in 50 ml of distilled water and this stock solution further diluted with distilled water to give the working standard solution for method A and C (200 µg.mL^{-1}). For method C the stock solution (1mg mL^{-1}) of NTP was prepared by dissolving 100 mg of it initially in 10 ml of DMF, followed by dilution to 100 ml with dioxane. This stock solution was further diluted stepwise with dioxane to obtain the working standard solution of concentration of 80 µg mL^{-1}.

Reagents

All the chemicals and reagents were of analytical grade and the solutions were prepared in triply distilled water. Cobalt thiocyanate (CTC, 2.50 x 10^{-1}M) (method A) solution was prepared by dissolving 7.25 g of cobalt nitrate and 3.8 g of ammonium thiocyanate in 100 mL of distilled water and the solution was saturated with sodium chloride. Citric Acid- acetic anhydride solution (BDH, 6.245x10^{-1}M) was prepared by dissolving 12 g of citric acid monohydrate (BDH) in 5 mL of anhydrous methanol and diluting upto 100 mL with acetic anhydride (BDH) for method B. Aqueous solutions of sodium nitroprusside (SNP) (E. Merck, 1. 67 x 10^{-1} M) and NH_2OH (Fluka, 7.09 x 10^{-1} M) and Na_2CO_3 (Loba, 9.43 x 10^{-1} M) were prepared for method C.

Tablet solutions

An accurately weighed amount of tablet powder equivalent to 50 mg of NTP was extracted with chloroform and filtered. The combined filtrate was evaporated to dryness and the residue was dissolved and prepared in the same way as under standard preparation and analyzed.

Instruments

A Milton Roy Spectronic 1201 and Systronics 106 digital spectrophotometer with 1 cm matched quartz cells were used for the spectral and absorbance measurements. An Elico LI-120 digital pH meter was used for pH measurements.

Recommended procedures

Method A

Into a series of 125 mL separating funnels, containing aliquots of standard NTP (0.5 – 2.5 ml, 200 µg mL^{-1}) solution, 2.0 ml of buffer (pH 2.0) and 5.0 mL of cobalt thiocyanate solutions were added. The total volume of aqueous phase in each separating funnel was brought to 15 mL with distilled water. A 10 mL portion of nitrobenzene was added to each funnel and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the separated nitrobenzene layer was measured after 10 min at 620 nm against a reagent blank. The amount of drug was deduced from it's calibration curve.

Method B

Aliquots of standard chloroformic NTP solution (0.5 – 2.5ml, 80 µg mL^{-1}) were transferred into a series of 25 mL graduated tubes and gently evaporated on a boiling water-bath to dryness. Ten ml of citric acid -acetic anhydride reagent was added to each tube. The tubes were placed in a boiling water-bath and heated for 30 min. The solution in each tube was made upto the mark with Ac_2O. The absorbance of the colored solutions was measured at 580 nm after 15 min. against a reagent blank prepared in a similar way. The amount of drug was deduced from its calibration curve.

Method C

Aliquots of standard drug solution, 200 µg/ml, ranging from 1.0-3.0 ml were transferred into a series of calibrated tubes and the volume in each tube was brought to 3.0 ml with distilled water one ml of SNP and 2.0 ml of hydroxyl amine (HA) solutions were successively added to each tube and shaken for 2 min. Then 1.0 ml of sodium carbonate solution was added and shaken for 15-25 min. Then contents were diluted to 25 ml with distilled water and the absorbance measured after 10 min. at 580 nm (NTP) against the reagent blank. The amount of drug was computed from its calibration graph.

Table 1: Optical characteristics, precision and accuracy of the proposed methods of NTP

Parameters	Method A	Method B	Method C
λ_{max} (nm)	620	580	580
Beer's Law limits (μg.ml^{-1})	10-50	4-20	8-30
Molar absorptivity (l mol^{-1}cm^{-1})	5.198x10^{-3}	1.521^{-4}	6.825^{-3}
Sandell's sensitivity (μg/cm^2/0.001 absorbance unit)	0.072	0.025	0.054
Regression Equation (y = a + bc)			
Slope (b)	0.01396	0.04083	0.01863
Intercept (a)	0.0001	-0.00030	-0.00480
Correlation coefficient (r)	0.9999	0.9999	0.9999
Relative Standard Deviation (%)*	0.3550	0.182	0.2420
% of range error (confidence limit)(i) 0.05 level	0.297	0.153	0.202
(ii) 0.01 level	0.439	0.226	0.299
% error in bulk sample **	0.134	0.211	0.204

*Average of six determinations considered. **Average of three determinations.

Table 2: Determination of NTP in pharmaceutical formulations

Formulations	Labelled amount	Amount found by Proposed Methods**			Reference Δ method	%Recovery by Proposed methods***		
	(mg)	Method A	Method B	Method C		Method A	Method B	Method C
Tablet I	1	1.00± 0.006 F=1.56 t=0.67	1.00± 0.007 F=2.18 t=0.64	1.00± 0.006 F=1.39 t=0.67	0.99± 0.005	100.14± 0.67	100.16± 0.79	100.13± 0.63
Tablet II	1	1.00± 0.009 F=1.60 T=0.74	1.00± 0.011 F=2.23 t=0.88	1.00± 0.009 F=1.41 t=0.64	1.00± 0.007	100.55± 0.96	100.65± 1.13	100.52± 0.90
Tablet III	2..5	2.49 ±0.83 F=1.43 t=1.71	2.51 ± 1.08 F= 2.39 t= 1.25	2.51 ±0.34 F=1.46 t=0.86	2.50 ±0.698	99.6 ±0.33	100.3 ±0.51	99.7 ±0.74
Tablet IV	2.5	2.48 ±1.96 F=1.21 t=1.29	2.51 ± 2.09 F= 1.39 t= 0.56	2.49 ±0.65 F=1.58 t=0.49	2.49 ±1.776	99.3 ±0.78	99.5 ±0.77	99.6 ±0.26

* Two different batches of syrup or tablets from a pharmaceutical company.

**Average ± standard deviation of six determinations; the t- and F- values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limit, t = 2.57, F = 5.05.

***After adding 3 different amounts of the pure labeled to the pharmaceutical formulation, each value is an average of 3 determinations.

Ā Reference method (NTP)

RESULTS AND DISCUSSION

The optimum conditions for the color development of methods 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.

The optical characteristics such as Beer's law limits, molar absorptivity and Sandell's sensitivity for the methods are given in Table 1. The precision of the method was found by measuring absorbance of six replicate samples containing known amounts of the drugs and the results obtained are incorporated in Table 1. Regression analysis using the method of least squares was made to evaluate the slope (b), intercept (a) and correlation coefficient (r) for each method and is presented in Table 1. The accuracy of the methods was ascertained by comparing the results by proposed and reference methods (UV)[1] statistically by the t- and F- tests (Table 2). This comparison shows that there is no significant difference between the results of proposed methods and those of the reference ones. The similarity of the results is obvious evidence that during the application of these methods, the additives and excipients that are usually present in tablets do not interfere in the assay of proposed methods. As an additional check of accuracy of the proposed methods, recovery experiments were performed by adding a fixed amount of the drug to the pre-analyzed formulations. The amount of drug found, the % recovery was calculated in the usual way.

Interference studies

NTP exists in its pharmaceutical formulations either singly or in combination with other active ingredients. Results of the analysis of the former type reveal that the proposed methods are suitable for their analysis with virtually no interference of the usual additives.

CONCLUSIONS

The proposed methods are applicable for the assay of drug (NTP) and have the advantage of wider range under Beer's law limits. The decreasing order of sensitivity and λ_{max} among the proposed methods are B>C>A and A>B=C respectively. The proposed methods are simple, selective and can be used in the routine determination of NTP in bulk samples and formulations with reasonable precision and accuracy.

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