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Visible Spectrophotometric determination of Loratadine through oxidative coupling reaction in bulk and its pharmaceutical preparations

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Abstract: A simple, sensitive, highly accurate Visible Spectrophotometric method here been developed for the determination of Loratadine in bulk and tablet dosage form with MBTH as an oxidative coupling reagent. Method A and B are based on the oxidative coupling reaction of drug with MBTH in presence of ferric chloride Fe(III) and sodium periodate ($NaIO_4$) to form colored chromogens exhibiting λ_{max} at 624 and 630 nm respectively. Beer's law was obeyed in the concentration range of 2-10µg ml^{-1} and 5-25 µg ml^{-1} with molar absorptivity values of 8.153 x10^3 l mol^{-1} cm^{-1} & 9.397 x 10^3l mol^{-1} cm^{-1}, the slope, intercept, correlation coefficient were also calculated. The results of analysis for the two methods have been validated statistically and by recovery studies

Keywords: Loratadine, Visible Spectrophotometery, MBTH.

Introduction:

Loratadine is a derivative of azatadine and a second-generation histamine H1 receptor antagonist used in the treatment of allergic rhinitis and urticaria. Unlike most classical antihistamines (histamine H1 antagonists) it lacks central nervous system depressing effects such as drowsiness. IUPAC Name ethyl 4-{13-chloro-4-azatricyclo[9.4.0.0{3,8}]pentadeca-1(11),3,5,7,12,14-hexaen-2-ylidene}piperidine-1-carboxylate. Its molecular formula is $C_{22}H_{23}ClN_2O_2$ and its molecular weight is 382.883. The chemical structure is:

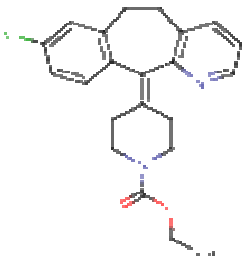


Figure: 1.01. Structure of Loratadine

Loratadine is a white to off white powder. It is practically soluble in water and slightly soluble in methanol and ethanol. It is official in USP[1], BP[2], IP[3]. It is non sedating peripheral histamine H1receptor antagonist. A literature survey reveals Spectrophotometric [4-5] and HPLC [6-13] methods.

The objectives of the work are to develop new spectrophotometric method for its estimation in bulk and tablet dosage form with good accuracy, simplicity, precision and economy. Hence the present work deals with the Spectrophotometric estimation of Loratadine using MBTH with ferric chloride Fe(III) and MBTH with sodium periodate ($NaIO_4$).

Experimental:

Materials and Methods

UV-Visible spectrophotometer: An ELICO SL-207 model, 2nm high resolution, double beam and 1cm length quartz coated optics, wavelength 190-1100nm, high stability, linearity; precision instrument was used for all the spectral measurements.

Reagents: All the chemicals and reagents were of analytical grade and the freshly prepared solutions were always used in the present investigation.

MBTH (3-methyl-2-benzothialinone hydrazone hydrochloride) **solution:** Prepared by dissolving 200 mg of MBTH in 100 ml distilled water.

Fe(III) solution: Prepared by dissolving 1.0 mg of anhydrous ferric chloride in 100 ml distilled water.

($NaIO_4$) solution: Prepared by dissolving 200 mg of sodium periodate in 100 ml distilled water.

Preparation of standard solution of Loratadine: Loratadine (100mg) was accurately weighed and dissolved in 20ml of distilled water, transferred to a standard 100ml volumetric flask. The final volume was made up to the mark with distilled water. The final concentration was brought to 100µg/mL with distilled water.

Recommended procedures:

Method-A: MBTH+ Fe(III)

Into a series of 25 ml calibrated tubes containing aliquots of standard LRD solution (0.5 – 2.5 ml), 0.5 ml of 0.2% MBTH solution was added and kept aside for 5 min. After that, 2.0 ml of Fe(III) solution was added and again kept aside for 10 min. The volume was made upto the mark with distilled water. The absorbance was measured at 630 nm against a similar reagent blank. The amount of LRD was deduced from its calibration curve.

Method B: MBTH+ $NaIO_4$

Aliquots of standard LRD solution (0.5 – 2.5 ml,) were transferred into a series of 10 ml calibrated tubes. To each of the above aliquots 1.0 ml of water and MBTH solution were added and mixed thoroughly and then the reaction kept aside for 15 min. After that 2.0 ml of sodium periodate was added, then the total solution was diluted with distilled water, shaken well and the absorbance of each colored species was measured after 10 minutes at 624 nm against a similar reagent blank. The amount of LRD was computed from its calibration graph.

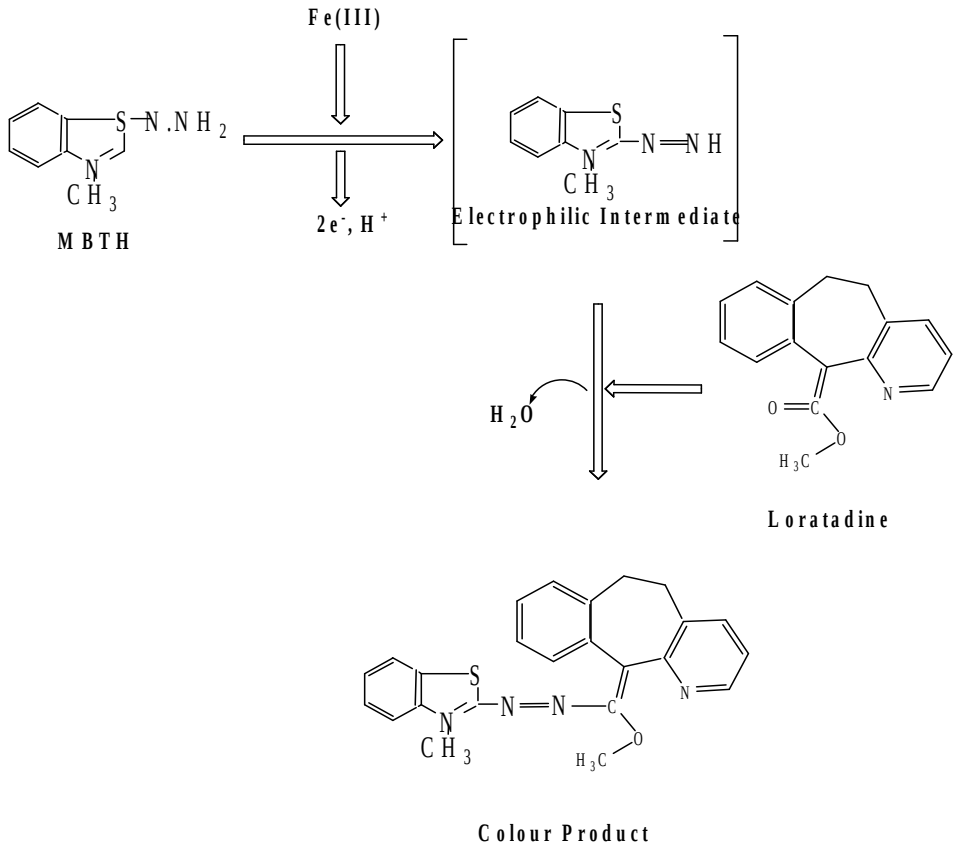
Procedure for the assay of Loratadine in pharmaceutical dosage forms:

Twenty tablets were weighed accurately and reduced to fine powder, drug equivalent to 100 mg of Loratadine taken in a 100 ml volumetric flask, sonicated for about 30 min, and the volume was made upto the mark with distilled water, filtered by using Whattmann-42 filter paper. The filtrate was quantitatively diluted with methanol to yield concentrations in the linear range of the assay of Loratadine.

Results and Discussion:

Loratadine LRD possesses different functional moieties such as primary amine, secondary amine, and keto group of varied reactivity. The methods (A&B) are based on the oxidative coupling reaction with MBTH in presence of Fe (III) & in the presence of $NaIO_4$ by concerning the reagents used for color development by exploiting appropriate functional groups in LRD and portable scheme of reactions is shown in Scheme-A and Scheme-B .The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar extinction coefficient, percent relative standard deviation and percent range of error were calculated (Figures 1&2) for the method and the results are summarized in Table 1. The accuracy of the methods was ascertained by comparing the results of the proposed methods with that of reported method (Table 2). In order to justify the reliability and suitability of proposed methods, known amounts of pure drug was added to its various pre analyzed dosage forms and were analyzed by the proposed method, which indicates that the proposed method can be successfully applied for the analysis of Loratadine in dosage forms. The additives and excipients usually present in pharmaceutical preparations did not interfere. Thus the proposed methods were simple, sensitive, accurate, reproducible and can be used for the routine analysis of Loratadine in bulk and in pharmaceutical dosage forms.

Scheme-A:



Scheme-B:

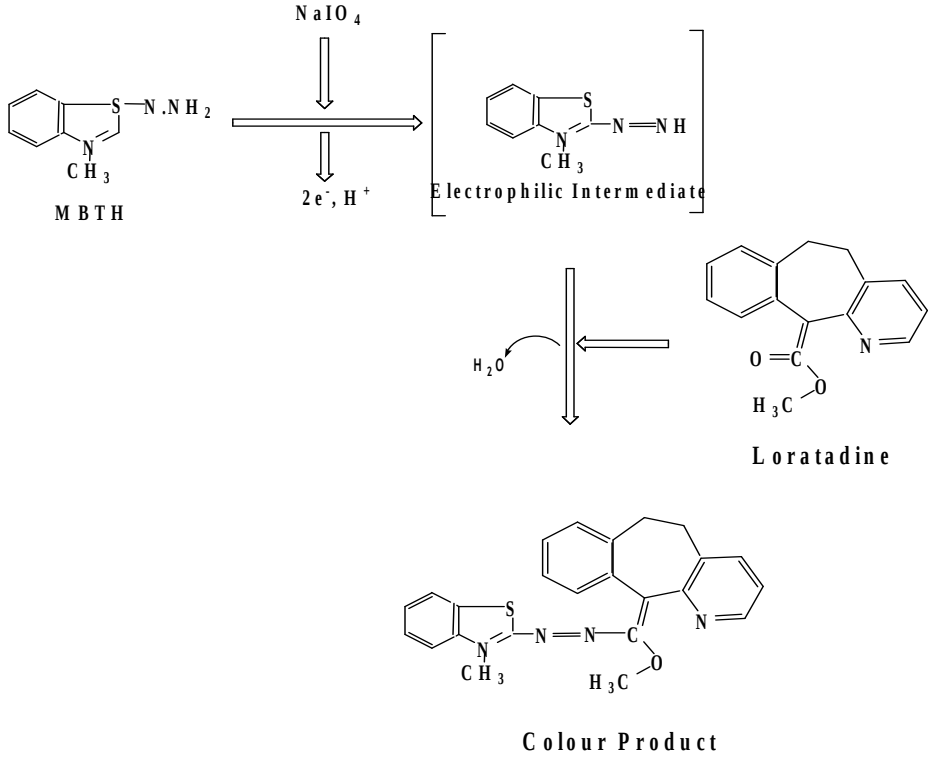


Fig. 1.02: Absorption spectrum of LRD with MBTH - NaIO4

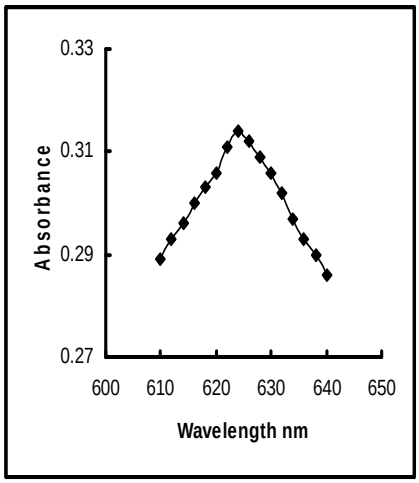


Fig. 1.03.: Absorption spectrum of LRD with MBTH - Fe(III)

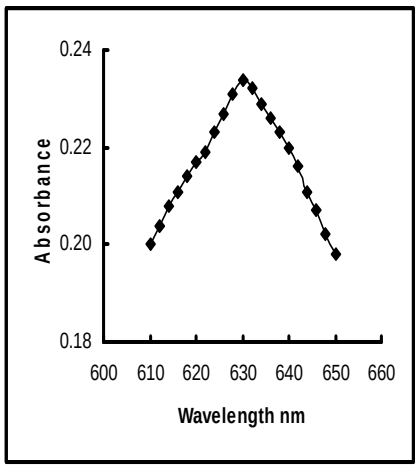


Fig. 1.04: Beer's Law plot of LRD with MBTH-- $NaIO_4$

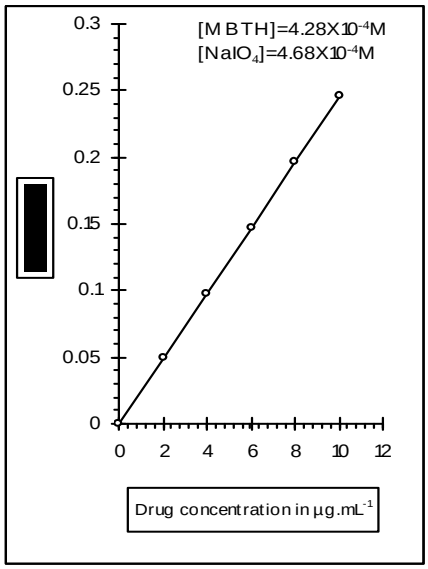


Fig. 1.05: Beer's Law plot of LRD with MBTH-Fe(III)

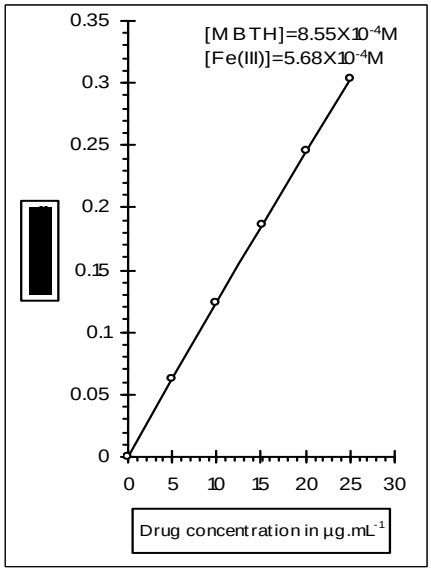


Table-1.01: Optical Characteristics, Precision, Accuracy of the methods proposed for the Determination of Loratadine

Parameter	**M_A**	**M_B**
λ_{max} (nm)	624	630
Beer's law limits (µg/mL)	2.0 – 10.0	5.0 – 25.0
Molar absorptivity (1 $mol^{-1}.cm^{-1}$)	8.153×10^3	9.397×10^3
Sandell's sensitivity (µg.cm^{-2}/0.001 absorbance unit)	0.0420	0.05376
Optimum photometric range (µg/mL)	2.0 – 8.0	5.0 – 20.0
Regression equation (Y=a+bc) ;Slope (b)	2.53×10^{-2}	1.91×10^{-2}
Standard deviation on slope (S_b)	4.62×10^{-3}	2.20×10^{-3}
Intercept (a)	1.0×10^{-3}	4.0×10^{-4}
Standard deviation on intercept (S_a)	0.003063	0.003689
Standard error on estimation (S_e)	0.002065	0.003517
Correlation coefficient (r)	0.9997	0.9998
Relative standard deviation (%)	1.449	0.485
% Range of error (confidence limits)		
0.05 level	0.217	0.181
0.01 level	0.361	0.301

Table -1.02: Determination of Loratadine in Pharmaceutical Formulations

Sample	Labelled amount (mg)	Amount found by proposed methods*		Ref. Method	% Recovery by proposed methods**	
		Method A	Method B		Method A	Method B
Tablet	10	10.2.2 ±0.17 F = 0.49 t = 0.59	10.6 ±0.14 F = 0.73 t = 0.27	10.8 ± 0.12	97.68 ± 0.03	97.56± 0.19

* Average ± standard deviation of six determinations, the t-and F-test values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limit, F = 5.05, t = 2.228

** Recovery of 10 mg added to the preanalysed pharmaceutical formulations (average of three determinations).

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