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Spectrophotometric determination of methoxamine hydrochloride using NQS and brucine metaperiodate

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ABSTRACT

*Two simple and sensitive extractive visible spectro photometric methods (A and B) for the assay of Methoxamine hydrochloride (**MHC**), in pure and pharmaceutical formulations, The method-A is based on the condensation reaction of MHC reduced with sodium 1,2-naphthaquinone-4-sulfonate (NQS) in an alkaline medium to form an orange-red colored Schiff's base of maximum absorption peak (λmax) at 445 nm,The method-B is based on the formation coloured complexes with the dimethoxy benzene nucleus of brucine is attacked by Per Iodate with the formation of o-quinone (bruciquinone) which in turn undergoes nucleophilic attack on the most electron rich position of the coupler i.e., proton bearing amino group (primary amine), to give 1-mono substituted bruciquinone derivative. The reaction mechanism in both methods were discussed. The absorbance of colored complex is gound at 520nm. Beer's law is obeyed in the concentration range 5-30 µg/Ml,50-500 µg/Ml, the molar absorptivity values are1.9652 x $10^{5,}$ 1.4797 x 10^{4}L/mol.cm, Sandell sensitivity are1.2605 x 10^{-3},1.6741x10^{-2}ng/cm2 (For methods A&B).The methods proposed gave reproducible results with the percentage recoveries in the formulations found to be 99.800 to 99.772 (Method A) and 99.812 to 99.749 (Method B).*

Keywords: Spectrophotometry; NQS; bruciquinone,Per Iodate, Pharmaceutical formulations**.**

INTRODUCTION

Methoxamine hydrochloride (**Fig.1**), 2-amino-1-(2,5-dimethoxyphenyl)propan-1-ol, is relatively selective α_1-adrenoreceptor agonist producing an increasing in peripheral vascular resistance[1,2]. MHC is a potent sympathomimetic that increases both systolic and diastolic blood pressure. It is used in the treatment of some hypotensive patients, particularly those with paroxysmal atrial tachycardia (arrhythmia) and acts almost exclusively on alpha-adrenergic receptors. Press or action is due primarily to direct peripheral vasoconstriction, leading to a rise in blood pressure. The resulting vagal reflux accounts for the sinus bradycadia observed, which is throughout to be responsible for terminating arrhymias. Literature survey reveals few analytical methods were reported for the determination of MHC in biological fluids by HPLC with fluorescence detection[3,4]**.** Spectrophotometric method analysis[5,6]. The analytical useful functional groups in MHC have not been fully exploited for designing suitable visible spectrophotometric methods and so still offer a scope to develop more visible spectrophotometric methods with better sensitivity, precision and accuracy. The author has made some attempts in this direction and succeeded in developing two methods based on nucleophilic substitution[7-10]and oxidative coupling reaction[11,12]. The present paper describes two simple and sensitive extraction visible spectro photometric methods for the

determination of MHC based on the substitution[13-16] reaction with NQS in (Method-A) and oxidative coupling[17,18] with Brucine/IO_4^- in (Method-B). The methods have extended pharmaceutical formulations as well. Upon thorough survey of literature there is no single method available for the estimation by visible spectrophotometry which is far simpler and economical and less time consuming as compared to above mentioned methods. .

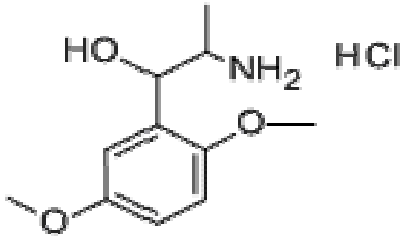


Fig.1.Chemical Structure of Methoxamine hydrochloride

MATERIALS AND METHODS

Instruments Used
A Schimadzu UV-Visible spectrophotometer 1801 with 1 cm matched quartz cells was used for all spectral and absorbance measurements. A Systronics digital pH meter 361 was used for pH measurements.

Reagents :
All the chemicals used were of analytical grade andthe solutions were prepared in triply distilled water.

Method- A:
1.NQS solution(Loba, 0.5%, 1.93 x 10^{-2} M)
2.NaOH solution(E-Merck, 20%, 5M)

Method- B:
1.Brucine Aqueous solution of (E-Merck,0.2%,5.0 x 10^{-3} M in 0.16 M sulphuric acid)
2.Sodium meta periodate (0.2 %,9.35x10^{-3}M)
3.Sulphuric acid (0.16M)

A standard Drug solution
The stock solution (1 mg/ml) of Methoxamine Hrdrochloride (MHC) was prepared by dissolving 100 mg of it in 100 ml of millipore-distilled water. A portion of this stock solution was diluted stepwise with the distilled water to obtain the working standard MHC solution of concentrations 4-500 µg/ml.

Procedure of Assay of MHC in formulations
An accurately weighed amount of formulation (injection powder) equivalent to 100 mg of drug was dissolved in 20 ml of distilled water, shaken well and filtered. The filtrate was further diluted to 100 ml with distilled water to get 1 mg/ml solution of drug in formulations.

One ml of this solution was furthered diluted to 25 ml to get 40 µg/m*l* solution. The absorbance of the solution was determined λ_{max} 270 nm (**Fig.2**). The quantity of the drug was computed from the Beer's law plot (**Fig.3**) of the standard drug in distilled water ,the results obtained were tabulated in **Table-2**

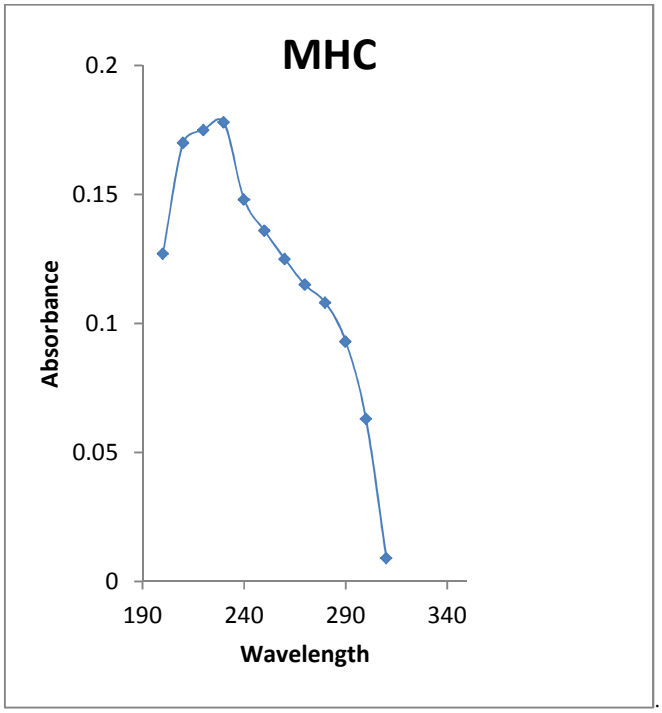


Fig.2. Absorption Spectra of MHC in Methanol (UV reference method)

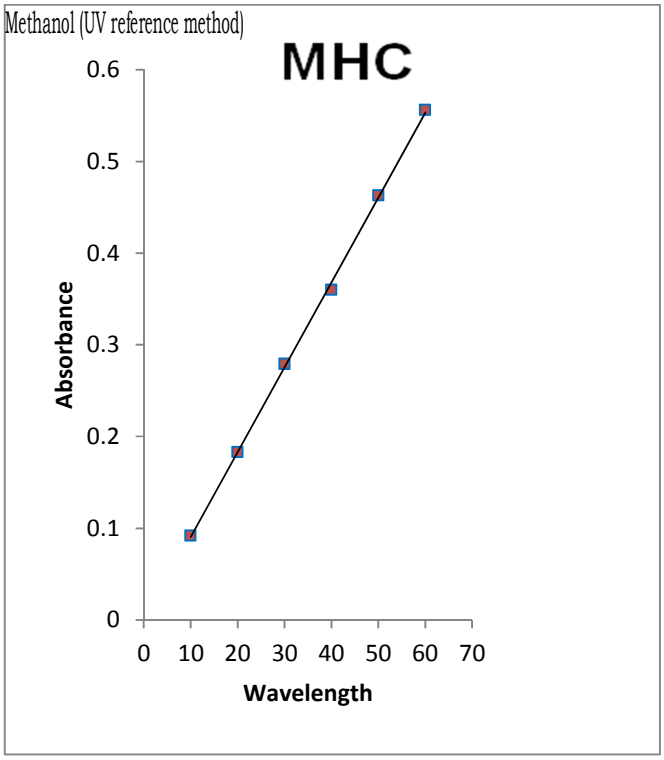


Fig.3 Beer's law plot of MHC in Methanol (UV reference method)

Sample Solution:
An accurately weighed amount of formulation (injection powder) equivalent to 100 mg of drug was dissolved in 20 ml of distilled water, shaken well and filtered. The filtrate was further diluted to 100 ml with distilled water to get 1 mg/ml solution of drug in formulations. One ml of this solution was furthered diluted to 25 ml to get 40 µg/ml solution.

Assay Procedures:
After systematic and detailed study of the various parameters involved, as described under results and discussion in this chapter, the following procedures were recommended for the determination of MHC in bulk samples.

Method -A:
Aliquots of standard MHC solution (0.1-0.6 ml, 30 µg/ml) were placed into a series of 20 ml test tubes. Then 1ml of NQS and 1.0 ml of NaOH solutions were added to each tube and kept aside for 2 min. at lab temperature. The solutions were made up to the mark with distilled water. The absorbance was measured at λ_{max} 445nm (**Fig.4**) against a reagent blank prepared simultaneously. The amount of MHC in a sample was obtained from the Beer-Lambert's plot (**Fig.5**).

Method -B:
Into a series of 20 ml calibrated tubes, aliquots of standard MHC solution (0.1-0.6 ml, 300 µg/ml) were taken. Then 3.0 ml of Brucine solution and 1.5 ml of IO_4^- solution were added successively. The flasks were kept aside for 2 min. and then 2.0 ml of sulphuric acid was added and then heated the contents on boiling water bath for 15 min. The flasks were cooled to room temperature and made up to the mark with distilled water. The absorbance of the coloured species was measured after 5 min at λ_{max} 520 nm (**Fig.6**) against the reagent blank. The amount of MHC was computed from its calibration graph (**Fig.7**

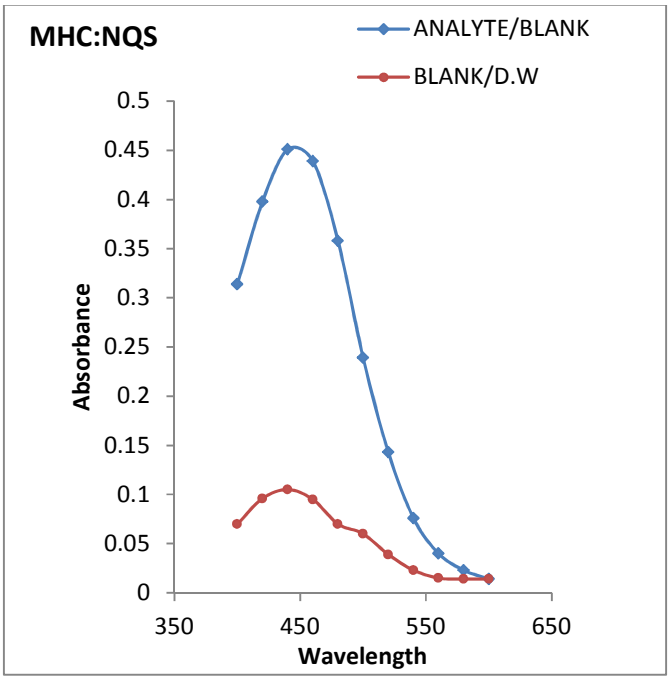


Fig.4 Absorption spectra of MHC: NQS

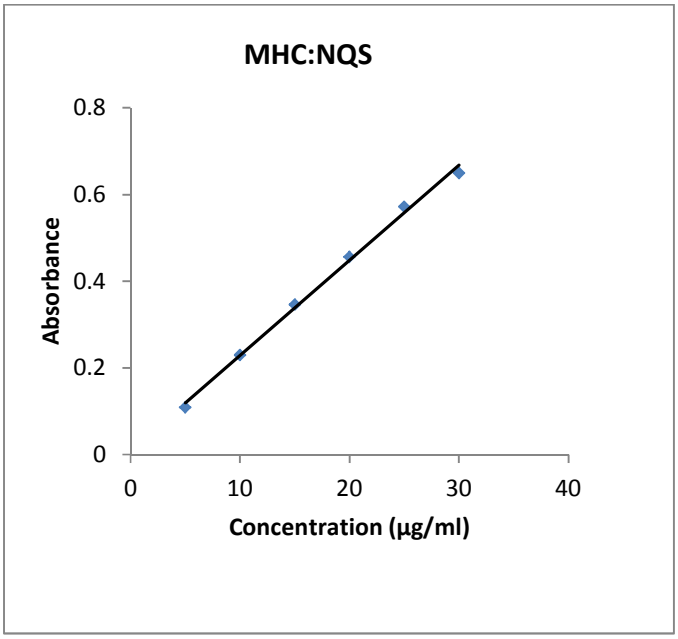


Fig.5 Beer's plot of MHC: NQS

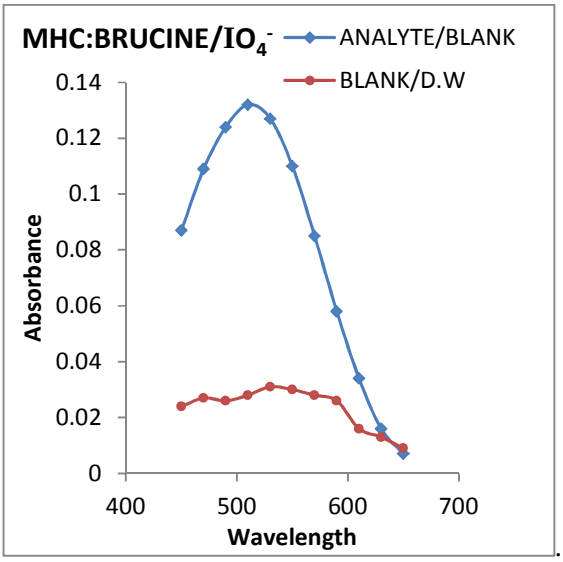


Fig.6 Absorption spectra of MHC: BRUCINE/IO_4^-

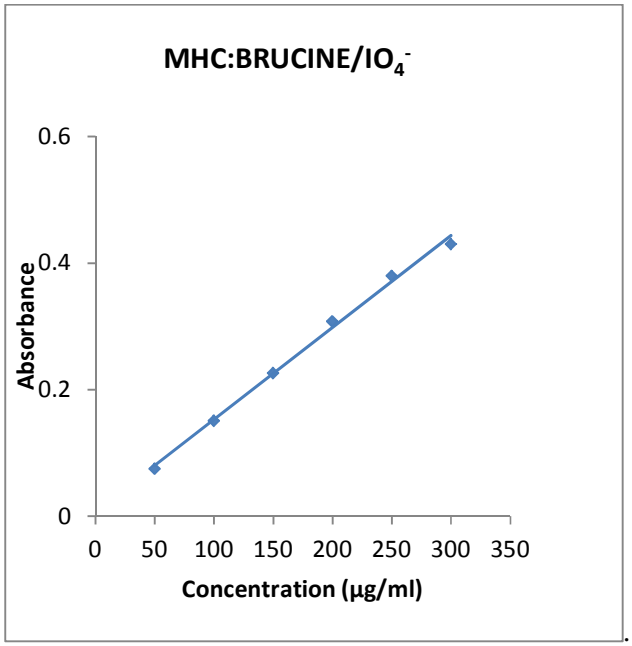
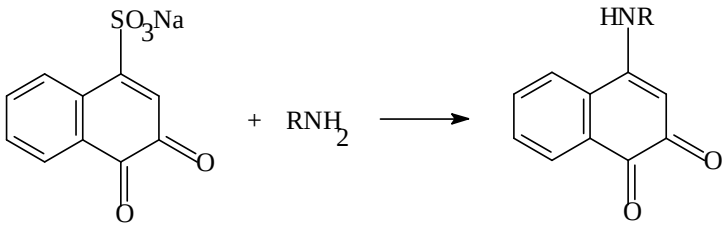


Fig.7 Beer's plot of MHC: BRUCINE/IO_4^-

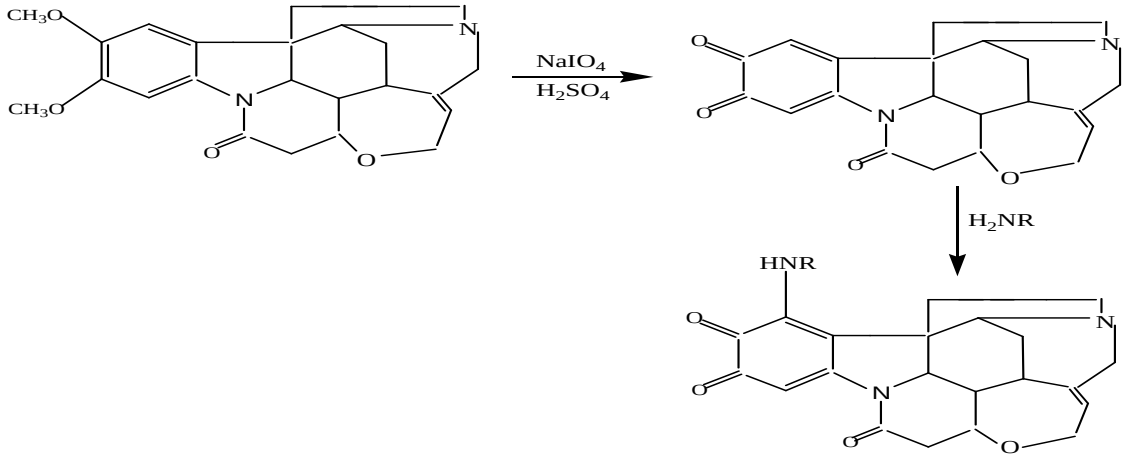
Recovery studies:
As an additional demonstration of accuracy, recovery experiments were carried out by adding known amounts of drug to the already analysed formulation. The results are presented in **Table.2**.

CHEMISTRY OF COLOURED SPECIES:
Method -A:
In this method, the presence of primary amino group in MHC permits the development of new spectrophotometric method for its determination through the formation of coloured nucleophilic substitution reaction product with NQS. The reactions of MHC with NQS are represented in the **scheme.1**

Scheme .1



Method- B:
The dimethoxy benzene nucleus of brucine is attacked by IO_4^- with the formation of o-quinone (bruciquinone) which in turn undergoes nucleophilic attack on the most electron rich position of the coupler i.e., proton bearing amino group (primary amine), to give 1-mono substituted bruciquinone derivative. The reactions of MHC with brucine in the presence of IO_4^- are described in the **scheme.2**



scheme.2

RESULTS AND DISCUSSION

In developing the proposed methods, a systematic study of the effects of various relevant parameters in the methods concerned were undertaken by varying one parameter at a time and controlling all other parameters to get maximum color development, minimum blank color, reproducibility and the responsible period of stability of final colored species formed. In order to test whether the colored species formed (or diminished) in the above methods adhere to Beer-Lambert's plot, the absorbance at appropriate wavelength of a set of solutions containing different amounts of MHC and specified amounts of reagents (as described in the recommended procedures of each method) were noted against appropriate reagent blanks or distilled water. Least square regression analysis was carried out for the slope, intercept and correlation coefficient. Beer-Lambert's limits, molar absorptivity and Sandell's sensitivity for MHC with each one of the mentioned reagents were calculated. The precision of each one of the two proposed visible spectrophotometric methods were ascertained separately from the absorbance values obtained by actual determination of eight replicates of a fixed amount of MHC in the final dilution. The present relative standard deviation and percent range of errors (at 0.05 and 0.01 confidence limits) were calculated for the proposed methods are presented in the Table.1. The values obtained by the proposed and reference method (UV) for pharmaceutical formulations were compared statistically by the t-and F- test were given inTable.2 and found not to differ significantly. Recovery experiments indicated the absence of interference from the commonly encountered pharmaceutical excipients present in pharmaceutical formulations. The proposed methods are found to be simple, sentsitive and accurate and can be used for the routine quality control analysis of MHC in bulk and samples and pharmaceutical formulations.

Table:1 Optical and Regression characteristics, precision and accuracyof the proposed methods for EHB

S.No	Parameter	Method-A	Method-B
1	Wave length λ_{max} (nm)	445	520
2	Beer's law limits (µg ml^{-1})	5-30	50-300
3	Detection limits (µg ml^{-1})	0.5191	6.1576
4	Molar absorptivity (1 mole cm^{-1})	1.9652×10^{5}	1.4797×10^{4}
5	Sandell's sensitivity(µg cm^{-2} / 0.001 absorbance unit)	1.2605×10^{-3}	1.6741×10^{-2}
6	Regressionequation (Y = a + bC) Slope (b)	0.0399	0.003
7	Standard deviation of slope (S_b)	3.5456×10^{-4}	3.1622×10^{-5}
8	Intercept (a)	0.0035	0.0048
9	Standard deviation of intercept (S_a)	6.9041×10^{-3}	6.1576×10^{-3}
10	Standard error of estimation (S_e)	7.4161×10^{-3}	6.6143×10^{-3}
11	Correlation coefficient (r^2)	0.9997	0.9997
12	Relative standard deviation (%)*	0.5701	0.4981
13	% Range of error(Confidence Limits) 0.05 level*	0.5984	0.5228
14	% Range of error(Confidence Limits)0.01 level	0.9851	0.8199
15	% Error in bulk samples**	0.1	0.105

: Average of six determinations considered: Average of three determinations*

Table:2 Assay and recovery of EHB in Pharmaceutical Formulations

Sample	Amount taken (mg)	Amount found by proposed methods		Reference Methods	Percentage recovery by proposed methods	
		Method-A	Method-B		Method-A	Method-B
Tablet-I	20mg	19.85 ±0.015 F=1.147 t=1.58	19.95 ±0.012 F=1.361 t=1.45	19.95 ±0.014	99.800 ±0.284	99.875 ±0.041
Tablet-II	20mg	19.84 ±0.014 F=1.147 t=1.70	19.93 ±0.018 F=1.44 t=1.50	19.92 ±0.015	99.772 ±0.068	99.749 ±0.110

** 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 formulations, each value is an average of 3 determinations.*

CONCLUSION

The proposed methods are simple, sensitive, accurate and economical for routine analysis of MHC in bulk and its pharmaceutical formulations. Based on molar absorptivity data and Beer's law range, it may be concluded that among the proposed methods, method B is more sensitive than method A

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