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Spectrophotometric determination of methoxamine using cerium(IV) in presence of sodium lauryl sulphate and rhodamine-B

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Abstract

A sensitive spectrophotometric assay has been developed for the determination of methoxamine in pure dosage form and in its pharmaceutical preparations. The method is based on the acidic oxidation of methoxamine with cerium(IV) in the micellar medium of sodium lauryl sulphate at 96°C. The reaction yields a water-soluble purple product which can be quantified spectrophotometrically at 505 nm. The calibration curve was linear between 1.0 and 20 μg ml^{-1} with a limit of detection 0.5 μg ml^{-1}. The molar absorptivity at 505 nm is 8.3×10^3 ℓmol^{-1} cm^{-1}. The method is simple and rapid since the product is measured directly in solution without extraction. © 1997 Elsevier Science B.V.

Keywords: Spectrophotometric assay; Methoxamine; Cerium; Sodium lauryl sulphate

1. Introduction

Methoxamine hydrochloride, I, 2-amino-1-(2,5-dimethoxyphenyl)propan-1-ol hydrochloride, is a sympathomimetic drug that, as such, has the properties of a vasoconstrictor. It is used primarily to raise the blood pressure of a patient whose blood pressure has dropped because of the induction of anaesthesia. The drug has also been useful in terminating episodes of paroxysmal supraventricular tachycardia [1,2].

A few chromatographic methods, including TLC [3–7], paper chromatography [4,8,9], GLC [5,10,11], GC-Mass [3] and HPLC [12], have been reported for the determination of methoxamine HCl. In the British Pharmacopoeia a UV method is recommended [13]. Recently, a rapid, selective and sensitive HPLC method for the qualitative and quantitative determination of methoxamine in rabbit plasma and in pharmaceutical formulations has been reported by us [14].

The present study describes an accurate, sensitive, more convenient and less time-consuming spectrophotometric method for the determination of methoxamine HCl in bulk drug and in its pharmaceutical preparations. The method is

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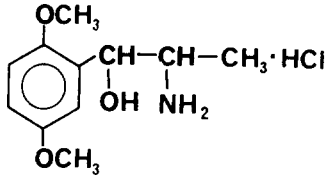
based on the acidic oxidation of methoxamine with cerium(IV) in the micellar medium of sodium lauryl sulphate at 96°C. The colored product is then quantified spectrophotometrically at 505 nm. The results obtained by applying this method are compared with those found using the official BP (1988) method. The influence of interferents is also studied.



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2. Experimental

2.1. Spectrophotometric system

All spectrophotometric measurements were made by using an LKB 4050 ultraviolet-visible spectrophotometer equipped with matched set of LKB 10 mm path length observation cells. The solutions were heated using a water-bath (GFL Gesellschaft Labortechnik, type 1023).

2.2. Chemicals and reagents

Chemicals used were of the highest purity available from their sources. Ceric ammonium nitrate from Fluka (Switzerland), Sodium lauryl sulphate from Winlab (Maidenhead, England), Rhodamine-B from Riedel-de Häen (Seelze, Germany), Methoxamine HCl (Lot. No. 19445) and Vasoxine® ampoules (Lot. No. H2959A) containing 20 mg ml^{-1} methoxamine HCl from Wellcome Foundation (London, England).

2.3. Preparation of the sample and standards

For the standard solutions of methoxamine HCl, a stock solution of the drug (1000 μg ml^{-1}) was prepared by dissolving an accurately weighed amount (0.1000 g) of methoxamine HCl in 100 ml of distilled water. This stock was diluted to a concentration of 50 μg ml^{-1} with distilled, deionized water and was used for preparation of the standard curves.

2.4. Assay of methoxamine HCL in Vasoxine® ampoules

The contents of three Vasoxine® ampoules (each containing 20 mg ml^{-1} methoxamine HCl) were pooled and a 1 ml aliquot (20 mg) from the mixture was pipetted and transferred to a 100 ml volumetric flask, and diluting to the mark with distilled, deionized water. No filtration or centrifugation was made as the sample solution was clear. From this solution a working final solution containing 10 μg ml^{-1} methoxamine HCl was prepared.

3. Procedure

An accurately measured volume of standard methoxamine HCl solution or sample solution is mixed with 1 ml of 0.10 mol ℓ^{-1} Ce(IV) solution. The mixture was then diluted with 10 ml distilled, deionized water and heated for 1 min in a water-bath set to a 96°C. After cooling the mixture, 1 ml of sodium lauryl sulphate (15 000 μg ml^{-1}) solution was pipetted and added gently to the mixture, followed by addition of 1 ml of 250 μg ml^{-1} rhodamine-B solution. The reactants were gently mixed and heated further for 5 min. The solution was then cooled to room temperature and diluted to 25 ml in a volumetric flask with distilled, deionized water. The absorbance was measured at 505 nm against a blank solution. The calibration curve was obtained by applying the same procedure, using standard methoxamine HCl solutions.

4. Results and discussion

4.1. Optimization of the procedure

The conditions for the production of analytically useful absorbance measurements from the cerium(IV) oxidation of methoxamine HCl were optimized so as to achieve maximum and repro-

ducible absorbance measurements. The cerium(IV) concentration and the nature and concentration of the acid present in the reaction solution have a marked influence on the analytical signal and were investigated in order to obtain the maximum absorbance reading. The effect of the cerium(IV) concentration at various sulphuric acid concentrations on 30 μg ml^{-1} of methoxamine. HCl is shown in Fig. 1. The results showed that the cerium(IV) and sulphuric acid concentrations as they were increasing the absorbance reading was increasing to give a maximum absorption up to 5×10^{-4} mol l^{-1} after which the signal started to decrease, the dilution efficiency is being the limiting factor. It was noticed that the sensitivity deteriorated when hydrochloric acid (forming turbide solution) and water (forming unstable product), were used instead of sulphuric acid. Therefore, sulphuric acid was the most suitable medium for the sensitive measurement of methoxamine. HCl, and Ce(IV) concentration of 5×10^{-4} mol ℓ^{-1}, was chosen for further studies.

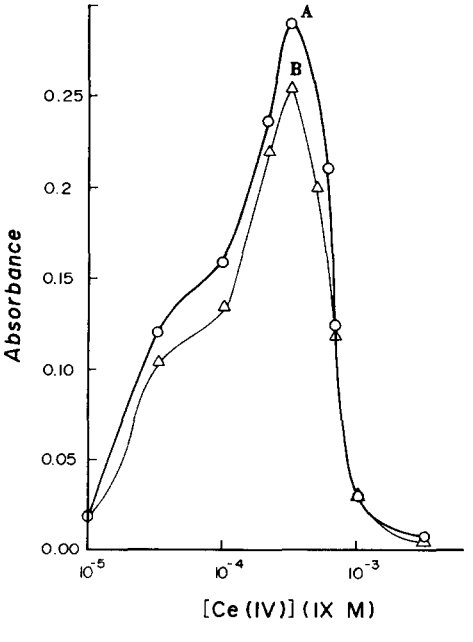

Fig. 1. Effect of Ce(IV) concentration (dissolved in two different sulphuric acid concentrations; (A) 1.0 mol l^{-1} and (B) 0.5 mol l^{-1}) on the absorbance measurements of methoxamine HCl (30 μg ml^{-1}).

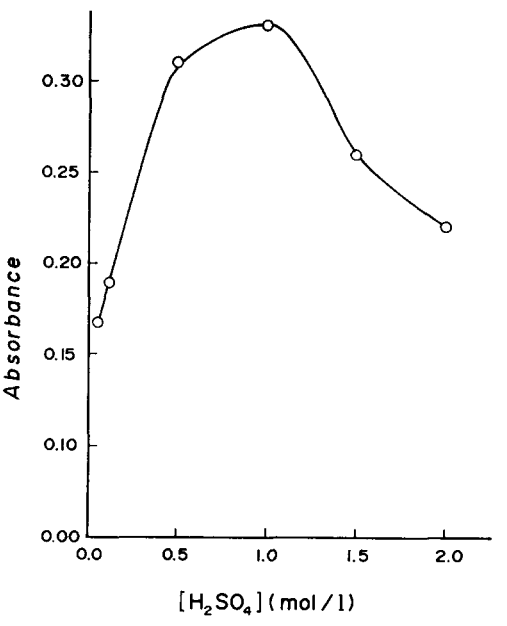

Fig. 2. Effect of H_2SO_4 concentration on the absorbance measurements of methoxamine HCl (40 μg ml^{-1}) in presence of Ce(IV) solution (5×10^{-4} mol ℓ^{-1}).

For a given concentration of 5×10^{-4} mol l^{-1}, a 1.0 mol ℓ^{-1}, H_2SO_4 concentration produced maximum absorbance from the methoxamine HCL (40 μg ml^{-1}) molecule (Fig. 2), hence this concentration was chosen for the analytical procedure.

Various types of surfactants (anionic, nonionic and cationic) were examined as potential enhancers for the reaction of methoxamine HCl with Ce(IV). It was observed that when 400 μg ml^{-1} solutions of these surfactants were used, cationic and nonionic surfactants like cetyltrimethylammonium bromide and Brij-35, respectively, had negative effects on the reaction rate leading to a smaller absorbance change. On the other hand, anionic surfactants, like sodium lauryl sulphate (SLS), were observed to increase absorbance and reaction rate. These results are summarized in Table 1. Therefore, sodium lauryl sulphate was used as the surfactant of choice, because it gave the largest increase in absorbance, indicating a faster reaction rate and a better sensitivity than other surfactants.

Table 1
The enhancement effect of surfactants on the absorbance

Surfactant	Average absorbance ($n = 3$)
No surfactant	0.28
Cetyltrimethylammonium bromide	0.20
Brij-35	0.25
Sodium lauryl sulphate	0.33

The influence of the concentration of SLS on the reaction of the drug with Ce(IV) was studied in the range 0–2000 μg ml^{-1} (Table 2). A 600 μg ml^{-1} SLS gave the greatest absorbance measurement and hence, this concentration was used subsequently.

Little attention has been directed to the application of some sensitizers for the color reactions of methoxamine HCl. Therefore, in this work, the use of some sensitizing compounds as a means for improving the colorimetric determination of methoxamine HCl is studied. Table 3 shows that rhodamine-B is a good sensitizer and was therefore used for subsequent studies. The optimum concentration range of rhodamine-B was 10–20 μg ml^{-1} (Fig. 3). A concentration of 10 μg ml^{-1} was chosen for further studies due to a negligible blank absorbance reading.

Table 2
The effect of SLS concentration on the absorbance of the reaction product of methoxamine HCl (40 μg ml^{-1}) with Ce(IV) (5×10^{-4} mol l^{-1})

SLS (μg ml^{-1})	Average absorbance ($n = 3$)
0	0.26
50	0.28
100	0.29
250	0.30
400	0.31
500	0.32
600	0.35
750	0.35
1000	0.35
2000	0.27
3000	0.27

Table 3
Effect of different sensitizers on the colorimetric determination of methoxamine HCl (20 μg ml^{-1}) in presence of Ce(IV) (5×10^{-4} mol l^{-1}) and SLS (600 μg ml^{-1})

Sensitizer (μg ml^{-1})	Average absorbance ($n = 3$)
None	0.107
Quinine	0.106
Fluorescein	0.128
Rhodamine-B	0.161

4.2. Calibration results

Under the selected experimental conditions described above, the calibration graph was linear in the 1.0–20.0 μg ml^{-1} methoxamine HCl range with a correlation coefficient of 0.9989 and a slope of 0.021. The detection limit, defined as the amount of the drug that gives a signal twice the background noise, was 0.5 μg ml^{-1} and the average standard deviation of 10 replicate analyses of 20 μg ml^{-1} methoxamine HCl was 1.8%.

4.3. Effect of interferents

In order to apply the suggested method for the analysis of a pharmaceutical dosage form, the influence of commonly used excipients and addi-

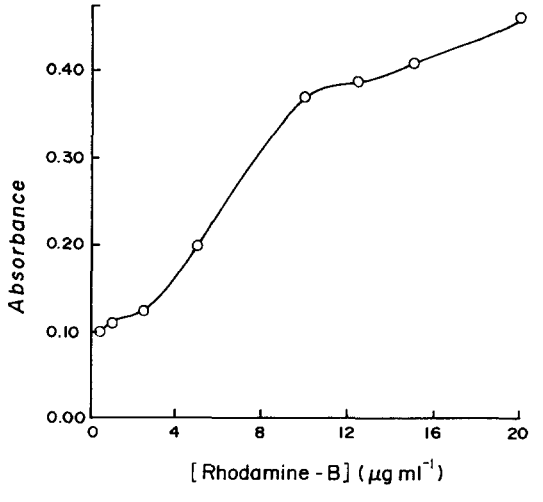

Fig. 3. Effect of rhodamine-B concentration on the colorimetric determination of methoxamine HCl (20 μg ml^{-1}) in presence of Ce(IV) (5×10^{-4} mol l^{-1}) and SLS (600 μg ml^{-1}).

Table 4
Effect of diverse components on the determination of methoxamine HCl (20 μg ml^{-1}) in presence of Ce(IV) 5×10^{-4} mol l^{-1}, SLS (600 μg ml^{-1}) and Rhodamine-B (10 μg ml^{-1})

Additive	Concentration (μg ml^{-1})	Recovery of methoxamine HCl (%)
D(+) Galactose	20	100
	200	102.6
D(+) Glucose	20	98.9
	200	100.7
Fructose	20	99.5
	200	103.2
Sucrose	20	100
	200	102.7
Starch	20	100
	200	99.8
Carbowax	20	100
	200	101.1
Magnesium stearate	20	100
	200	98.5

tives was investigated in the determination of 20 μg ml^{-1} methoxamine HCl solutions. Results obtained are shown in Table 4. Under the reaction conditions used, the foreign substances tested did not interfere with the proposed method.

4.4. Precision and accuracy of the method

The precision of the method was investigated by determining the percentage standard deviation for ten multiple analyses of a series of solutions containing 20 μg ml^{-1}. Such value was 1.8%.

The accuracy of determination was tested by applying the recommended procedure. The recoveries of the different amounts tested were determined from the standard reference graph and found to be satisfactory, as shown in Table 5.

4.5. Application

The proposed spectrophotometric method was applied for the determination of methoxamine HCl in a pharmaceutical dosage form of Vasoxine®. The results obtained for this procedure were

Table 5
Determination of methoxamine HCl (μg/ml) in presence of Ce(IV) 5×10^{-4} mol l^{-1}, SLS (600 μg ml^{-1}) and Rhodamine-B (10 μg ml^{-1})

Calculated	Found[a]	Error (%)
2	2.04	+2.00
4	3.95	−1.25
6	6.1	+1.67
8	7.89	−1.38
10	10.15	+1.5

[a]Average of three determinations.

evaluated against the British Pharmacopoeia (BP) procedure as shown in Table 6. The results are in good agreement with that obtained by the BP method. But the proposed method has the added advantage that the assay is performed at 505 nm in the visible region of the spectrum, away from ultraviolet-absorbing interferents that might be associated with a determination in biological samples.

5. Conclusion

The suggested method has the advantage of being simple, accurate and sensitive and may be considered for routine quality-control of methoxamine HCl formulations.

Table 6
Determination of methoxamine HCl

Methoxamine HCl taken (μg ml^{-1})	Recovery ± S.D.[a] (%)	
	Proposed procedure	BP
5	99.3 ± 0.8	99.2 ± 1.1
6.5	100.0 ± 1.5	99.8 ± 1.2
7	98.6 ± 2.1	101.3 ± 1.6
8.5	100.0 ± 0.6	98.8 ± 0.9
11	99.7 ± 1.1	100.0 ± 0.8
15	102.0 ± 0.9	100.0 ± 0.8

[a]Standard deviation calculated as a mean for three determinations.

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