

NOMİFENSİN HİDROJENMALEAT'IN METOL-KROM (VI) BELİRTECİYLE SPEKTROFOTOMETRİK MİKTAR TAYİNİ

SPECTROPHOTOMETRIC ASSAY OF NOMIFENSINE HYDROGENMALEATE USING METOL-CHROMIUM (VI) REAGENT

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SUMMARY

A spectrophotometric method was developed for the determination of nomifensine hydrogenmaleate (NHM) and its capsules. The Method is based on oxydation of metol with potassium dichromate at pH 3 in the presence of NHM. The oxydation product has a maximum absorbance at 504 nm. The absorbance is linear over the concentration range of 10-50 µg/ml MHM and is stable for at least 90 min.

The method was applied to commercially available capsules. The results obtained were compared statistically with those obtained from the method of comparison. Relative standard deviation of the method is 0.86 %.

ÖZET

Nomifensin hidrojenmaleat (NHM) ve kapsüllerinin miktar tayini için spektrofotometrik bir yöntem geliştirildi. Yöntem metolün potasyum bikromat ile pH 3 de NHM eşliğinde oksidasyonuna dayanmaktadır. Oksidasyon ürünü 504 nm de maksimum absorpsiyon göstermektedir. Absorbans 10-50 µg/ml aralığında NHM konsantrasyonu ile doğru orantılıdır ve en az 90 dak. dayanıklıdır.

Yöntem piyasada bulunan kapsüllere uygulandı ve sonuçlar kıyas yönteminkilerle istatistik olarak kıyaslandı. Yöntemin bağıl standart sapması % 0.86 olarak hesaplandı.

INTRODUCTION

NHM, 8-amino-1,2,3,4-tetrahydro-2-methly-4-phenylisoquinoline hydrogenmaleate is used as a psychotrop-antidepressant drug. It has commercial capsules in the market.

Titrimetric (1), spectrophotometric (2-4), fluorometric (4), polarographic (5), gas (6,7) and high performance liquid (8,9) chromatographic methods have been published for the determination of NHM in both biological fluids and pharmaceutical preparations. No compendial method for assay of the drug is available.

Metol (p-N-methylaminophenol sulphate)-chromium (VI) reagent has been employed for visible spectrophotometric determination of several primary aromatic amines (10-12).

This paper describes a spectrophotometric method for the determination of NHM and its capsules using metol-chromium (VI) reagent in acidic medium.

EXPERIMENTAL

Instrument

A uv-visible double-beam spectrophotometer (Shimadzu UV-150-02) with 1 cm glass cells was used.

Reagents

All chemicals were reagent grade. NHM and its capsules were kindly supplied by Hoechst Company, İstanbul, Turkey; metol was purchased from Eastman, Kodak Co.N.Y., and other chemicals were from Merck, A.G. Darmstadt, W.Germany.

Distilled water was used for preparing all aqueous solutions.

Stok NHM solution: Dissolve 100 mg of NHM in 30 ml of warm methanol. Dilute to 100 ml with water (1 mg/ml).

Standart NHM solutions: Dilute 10-50 ml of the stock solution to 100 ml with water.

Metol: 0.16 % aqueous solution. Prepare fresh in every use and protect from the day-light.

Potassium dichromate: 0.01 M aqueous solution.

Buffer solutions: Prepare according to the reference No. 13.

Assay Procedure

Powder-1.0 ml of the standard solution containing 100-500 µg/ml NHM was transferred into a 10 ml volumetric flask containing 5 ml of pH 3 buffer, 1.25 ml of metol, and 1.0 ml of potassium dichromate solutions. The mixture was allowed to stand for 20 min at r.t. After dilution to the volume with water, absorbance was measured at 504 nm against a blank prepared similarly. A calibration graph of absorbance versus NHM content (µg/ml) was plotted. Regression equation of the calibration graph was calculated by the method of least-squares.

Capsules-Twenty capsules were emptied and distributed. An accurately weighed portion of the powder, equivalent to 50 mg of NHM, was transferred to a 50 ml volumetric flask. 20 ml of warm methanol was added and the mixture was shaken for 1 hr. It was diluted to the volume with water, mixed and filtered through a dry filter paper. 20 ml of the filtrate was diluted to 50 ml with water. 1.0 ml of the resulting solution was subjected to the procedure as described under "powder".

The amount of NHM in capsules was calculated by means of the regression equation obtained previously.

RESULTS AND DISCUSSION

Metol undergoes oxydation to p-N-methylquinone-imine with potassium dichromate in basic medium, but in acidic medium the reaction proceeds only in the presence of a primary aromatic amine and the intensity of the colour produced is directly proportional to the amine present (10). In this study NHM was taken as primary aromatic amine and the absorption spectrum showed a maximum at 504 nm.

Optimum conditions of the reaction were investigated.

400 µg/ml of NHM solutions were subjected to the procedure at different pH values between 1 and 7 (Table 1). pH 3 was selected as optimum value.

Table-1: Effect of pH on the reaction of NHM with metol-chromium (VI) reagent.

pH	1	2	3	4	5	6	7
A	0.129	0.558	0.604	0.520	0.265	0.108	0.091

Optimum concentrations of metol and potassium dichromate were investigated for 40 µg/ml of NHM, For this purpose two kinds of experiment were performed. In the first, metol concentration was changed while potassium dichromate concentration was hold constant and in the second, vica versa. 1.25 ml of metol and 1.0 ml of potassium dichromate solutions were found to be sufficient.

Maximum absorbance value for the same reaction mixture was achieved by adding the reagents in the order of pH 3 buffer-metol-potassium dichromate-NHM. Maximum colour development was obtained in 20 min standing peroid at r.t.after addition of the reagenets and it was stable at least 90 min. The day-light did not effected colour development while elevated temperatures caused decomposition.

Under the experimental conditions, a linear calibration curve was obtained between absorbance and NHM concentration over the range 10-50 µg/ml. The regression equation for the straight line is

$$A = 0.0147 C + 0.0042, r = 0.9999 (n = 5).$$

The method is sensitive. Calculated molar absorptivity is $5.3 \times 10^3 \text{ l.mol}^{-1} \cdot \text{cm}^{-1}$.

Precision of the method calculated by means of its reproducibility at 40 µg/ml level and expressed in terms of relative standard deviation is 0.93 % (n = 7).

The proposed method was tested with the commercial capsules. The capsules were also analysed according to the nitritometric titration method for comparison using starch as external indicator. The results obtained were compared statistically with each other (Table 2).

Table-2: Analysis of NHM in Capsules (Label Claim 50 mg NHM).

Statistical Values	Speetrophotometric Method	Titrimetric Method
\bar{x}	47.4 mg	48.2 mg
s	0.41	0.74
(s/ \bar{x}) .100	0.86 %	1.54 %
Recovery	94.80	96.40
n	5	5
t test of significance	t = 1.89 (p = 0.05)	t = 2.31)
F test of variances	F = 3.25 (p = 0.05)	F = 6.39)

Examination of the results indicates that the proposed method is precise, fast, and does not require any solvent other than water. So the method could be modified for automated analysis of NHM in dosage forms.

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