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p-DİMETİLAMİNOBENZALDEHİD İLE SPEKTROFOTOMETRİK NOMİFENSİN HİDROJENMALEAT MİKTAR TAYİNİ

A SPECTROPHOTOMETRIC DETERMINATION OF NOMIFENSINE HYDROGENMALEATE USING p-DIMETHYLAMINOBENZALDEHYDE

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SUMMARY

A spectrophotometric method was developed for the determination of nomifensine hydrogenmaleate (NHM) alone and in capsules. The method is based on the Schiff's base formation between NHM and p-dimethylaminobenzaldehyde (p-DABA) in acidic and methanolic medium, with a maxium absorption at 425 nm.

The method gives a linear calibration graph over the concentration range of 2-8 µg/ml of NHM, with the relative standard deviation of 1.01 %.

ÖZET

Nomifensin hidrojenmaleatın (NHM) tek başına ve kapsüllerde miktar tayini için spektrofotometrik bir yöntem geliştirildi. Yöntem (NHM ve p-dimetilaminobenzaldehid (p-DABA) arasında, asitli ve metanollü ortamda, 425 nm de maksimum absorpsiyon gösteren bir Schiff bazı oluşmasına dayanmaktadır.

Yöntem, 2-8 µg/ml NHM konsantrasyon aralığında doğrusal bir ölçü eğrisi göstermektedir. Yöntemin bağıl standard sapması % 1.01'dir.

INTRODUCTION

NHM, 8-amino-1, 2, 3, 4 - tetrahydro -2- methyl -4- phenylisoquinoline hydrogenmaleate, is a psychotrop - antidepressant drug.

Some assay methods have been published for determination of the drug covering titrimetric (1), spectrophotometric (2-4), polarographic (5) and chromatographic (6, 7) procedures.

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The titrimetric method is based on nitritometric titration using metanil yellow as internal indicator (1).

Spectrophotometric methods are based on derivatisation with 1, 2-naphthoquinone -4- sulfonic acid sodium salt (2), ion pair extraction (3), and occurring a charge-transfer complex with iodine in chloroform phase (4).

No compendial method for the analysis of the drug is available.

p-DABA, known as Erlich reagent, is used for the detection of several functional groups containing primary amines (8). It forms yellow-orange coloured Schiff's bases in acidic medium with primary aromatic amines and this reaction forms the basis for analyses of amines by visible spectrophotometry (9-10).

This paper represents a spectrophotometric method for the determination of NHM and its capsules using p-DABA reagent in acidic-methanolic medium.

EXPERIMENTAL

Instrument

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

Reagents

All chemicals were of analytical reagent grade. NHM and its capsules were kindly supplied by Hoechst Company, İstanbul and other chemicals were from Merck, Darmstadt, W. Germany.

All aqueous solutions were prepared using distilled water.

Stock NHM solution : Dissolve 100 mg of NHM in 30 ml of warm methanol and dilute to 100 ml with water.

Standard NHM solutions : Dilute 1 - 4 ml aliquot of the stock solution to 50 ml with water.

Stock p-DABA solution : Dissolve 1.25 g of p-DABA in 25 ml of methanol.

Standard p-DABA solution : Transfer 4 ml of the stock solution into a 10 ml volumetric flask, add 1 ml of 3 N HCI and dilute to the mark with methanol.

Assay Procedure

Powder - Transfer 1.0 ml of the standard solution containing 20 - 80 µg/ml of NHM into a 10 ml volumetric flask. Add 2.0 ml of standard p-DABA solution and dilute to the mark with methanol. Mix and allow to stand for 20 min. at r.t. Measure the absorbance at 425 nm against a blank prepared similarly. Prepare a calibration graph by plotting absorbance versus NHM content (µg/ml), calculate the regression equation of the calibration curve by the method of least-squares.

Capsules - Empty the content of twenty capsules and distribute well. Transfer an accurately weighed portion of the powder equivalent to 50 mg of NHM into a 50 ml volumetric flask. Add 20 ml of warm methanol and allow to stand for 1 hr by shaking occasionally. Dilute to the volume with water. Mix well and filter through a dry filter-paper. After discarding the first 15 ml portion, dilute 3 ml of the filtrate to 50 ml in a volumetric flask.

Transfer 1 ml of the final solution containing 60 µg/ml of NHM into a 10 ml volumetric flask and proceed as described under "powder". Calculate the concentration by means of the regression equation.

RESULTS AND DISCUSSION

The Schiff's base formation between NHM and p-DABA was performed in acidic and methanolic medium. Absorption spectrum of the reaction product showed a maximum at 425 nm. Molar absorptivity at this wavelength was calculated as 3.06×10^4 l. mol^{-1} cm^{-1}.

Optimum conditions of the reaction were investigated

The reaction was repeated using different acid (hydrochloric, sulfuric, acetic acid) and alcohol (methanol, ethanol, propanol) solutions. Maximum colour development was achieved with hydrochloric acid and methanol.

Optimum concentration of hydrochloric acid was investigated using 1 N-12 N solutions and 3 N acid concentration was found to be

satisfactory (Table 1).

Table-1 : Effect of the HCI concentration on colour development (for 7 µg/ml of NHM conc.)

Normality of HCI	1N	2N	3N	4N	5N	6N
A	0.330	0.585	0.645	0.641	0.622	0.600

The time course of the reaction was observed at three different temperatures (r. t., 40°, 60°). Optimum results were obtained in 20 min standing period at r.t. after adding the reagent and the colour obtained was stable for at least 90 min.

Optimum amount of the standard p-DABA solution was found to be 2.0 ml (Table 2).

Table-2 : Effect of the amount of standard p-DABA solution on the reaction (for 5 µg/ml of NHM conc.)

Amount of p-DABA (ml)	1.0	1.25	1.50	1.75	2.00	2.25	2.50
A	0.385	0.410	0.428	0.445	0.450	0.448	0.450

Under the conditions described in experimental part, Beer's law was obeyed over the range of 2-8 µg/ml NHM concentration (Fig. 1). The regression equation for the straight line was

$$A = 0.0889\ C + 0.0039,\ r = 0.9999\ (n = 5).$$

Reproducibility of the method was calculated for 6 µg/ml of NHM concentration. The coefficient of variation is 0.46 % (n =6).

The proposed method was applied to the commercial capsules satisfactorily. For comparison, the capsules were also analysed according to the nitritometric titration method using starch external indicator (1). The results obtained were compared with each other statistically (Table 3).

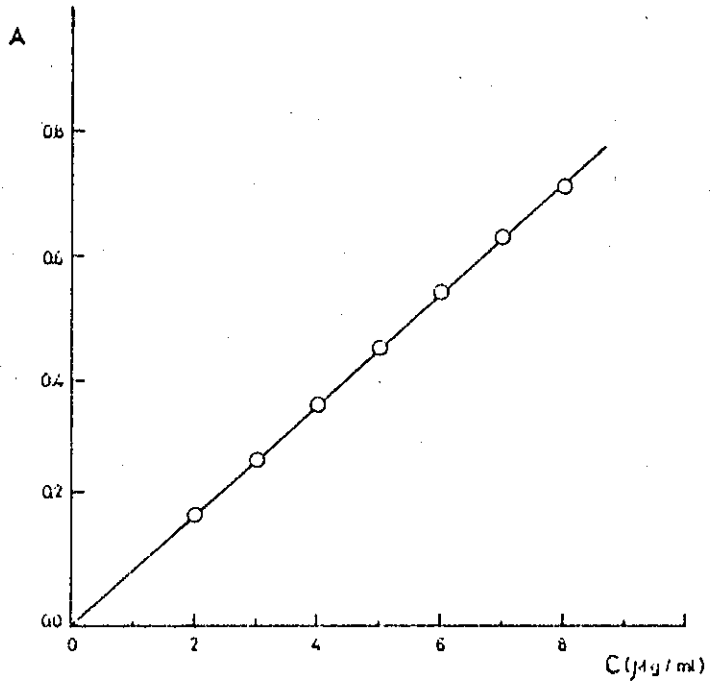

Fig-1: – Linear calibration graph, A = 0.0989 C + 0.0039, r = 0.9999

The results obtained indicates that the proposed method is precise, economic and suitable for routine analysis of NHM in capsules.

Table-3 : Determination of NHM in capsules (Label claim 50 mg NHM)

Statistical Values	Spectrophotometric Method	Titrimetric Method
$\bar{x}$	47.3 mg	48.1 g
s	0.48	0.69
$(s/\bar{x}).\ 100$	1.01 %	1.43 %
recovery	94.60 %	96.20 %
n	5	5
t test of significance	t = 1.90 (p = 0.05 t = 2.37)	
F test of variances	F = 2.07 (p = 0.05 F = 6.39)	

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