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PROKAİNAMİD HİDROKLORÜR'ÜN TABLETLERDE p-DİMETİLAMİNOBENZALDEHİD İLE SPEKTROFOTOMETRİK MİKTAR TAYİNİ

SPECTROPHOTOMETRIC DETERMINATION OF PROCAINAMIDE HYDROCHLORIDE IN TABLETS WITH p-DIMETHYLAMINOBENZALDEHYDE

Sıdıka SUNGUR* - Sezen İSLİMYELİ* - Sabiha MANAV YALÇIN*

SUMMARY

A spectrophotometric method for the determination of microgram level of procainamide hydrochloride in tablets was described. The method was based on the coloured Schiff's base formation between procainamide and p-dimethylaminobenzaldehyde. The reaction proceeded quantitatively in acidic and ethanolic medium at room temperature in twenty minutes. The absorption maximum was at 449 nm. A linear relationship existed between absorbance and concentration over the range of 1-4 mcg.ml^{-1} of procainamide hydrochloride . The results of the analysis of procainamide hydrochloride tablets so obtained correlated well with those obtained by the USP XVIII method at 95 % confidence level.

ÖZET

Mikrogram düzeyinde prokainamid hidroklorür'ün tabletlerde miktar tayini için spektrofotometrik bir yöntem tarif edildi. Yöntem, prokainamid hidroklorür ile p-dimetilaminobenzaldehid arasında renkli Schiff bazı oluşumuna dayanmaktadır. Reaksiyon asidli ve etanollü ortamda, oda sıcaklığında ve 20 dakikada kantitatif olarak oluşmaktadır. Absorpsiyon maksimumu 449 nm' dedir. Absorbans ile prokainamid hidroklorür konsantrasyonu arasında 1-4 mcg.ml^{-1} konsantrasyon aralığında doğrusal bir ilişki olduğu saptanmıştır. Prokainamid hidroklorür tabletlerinin analizinden elde edilen sonuçlar USP XVIII yöntemi ile elde edilen sonuçlar ile % 95 güven düzeyinde uygunluk göstermiştir.

INTRODUCTION

Procainamide hydrochloride, an antiarrhytmic drug causes a decrease in systematic arterial pressure. Methods for the quantitation of this drug include titrimetric, spectrophotometric, fluorometric and

* Yıldız Üniversitesi Fen-Edebiyat Fakültesi, Kimya Bölümü, Şişli / İSTANBUL.

chromatographic procedures (1). The USP (2), BP (3) and TF (4) methods for determination of procainamide hydrochloride in pharmaceuticals are time consuming, since they are based on a prior separation of the drug from the dosage form followed by diazotization titration of the compound with standard sodium nitrite at low temperature.

Spectrophotometric methods for the analysis of procainamide hydrochloride involving diazotization and coupling reaction with Bratton-Marshall reagent (5-7), Schiff's base formation with vanillin (8,9) and p-dimethylaminocinnamaldehyde (10), ionpair formation with acid dyes (11,12), the reaction with 1,2-naphthoquinone-4-sulphonic acid (13), metol-chromium (VI) (14) or 9-chloroacridine (15) are available in the literature.

p-Dimethylamino benzaldehyde (Ehrlich Reagent) has been employed as a colorimetric reagent for aromatic amines (16,17). It forms yellow-orange coloured Schiff's bases in acidic medium.

This paper describes a simple, time saving and sensitive spectrophotometric method for the determination of procainamide hydrochloride and its tablets using p-dimetylaminobenzaldehyde (p-DABA) reagent in acidic and ethanolic medium.

EXPERIMENTAL

Instrument

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

Chemicals

Procainamide hydrochloride and its tablets were kindly supplied by Fako İlaçları A.Ş., İstanbul. All chemicals were of analytical reagent grade. p-Dimethylaminobenzaldehyde and other chemicals were from Merck, Darmstadt, W.Germany.

Aqueous solutions were prepared using distilled water.

Solutions

Stock procainamide hydrochloride solution: 100 mg of procainamide hydrochloride was dissolved in water and diluted to 100 ml with the same solvent.

Standard procainamide hydrochloride solution: 1-4 ml aliquots of the stock solution were diluted to 100 ml with water (10-40 mcg.ml^{-1}).

p-DABA solution: 1 g of p-DABA was dissolved in 95% ethanol and diluted to 50 ml with the same solvent.

Acid solutions: 1 % aqueous hydrochloric and sulfuric acid solutions were prepared.

Assay Procedure

A 1 ml of standard procainamide hydrochloride solution (10-40 mcg procainamide hydrochloride) was transferred into a 10 ml calibrated flask. 1 ml of 1 % HCl solution, 1 ml of 95% ethanol and 2 ml of p-DABA solution were added and diluted to the volume with water. The mixture was mixed and allowed to stand for 20 min. at room temperature and the absorbance of the solution was read at 449 nm against a blank solution prepared similarly. Calibration curve was prepared by plotting absorbance values versus final concentrations of procainamide hydrochloride (mcg.ml^{-1}). Regression equation of the calibration curve was calculated by the method of least squares.

Procainamide hydrochloride tablets

A quantity of thoroughly mixed powder of the tablets equivalent to about 10 mg of procainamide hydrochloride was accurately weighed and transferred into a 100 ml calibrated flask. 50 ml of water was added and the mixture was shaken for 15 min. The volume was adjusted to 100 ml with water, mixed well and filtered through a dry filter-paper. The first 20 ml portion of the filtrate was discarded and 10 ml of filtrate was diluted to 100 ml with water in a calibrated flask. 3 ml of the final solution was pipetted into a 10 ml calibrated flask and the assay procedure for procainamide hydrochloride in tablets was calculated by means of the regression equation of the calibration curve.

RESULTS AND DİSCUSSION

The Schiff's base formation between procainamide hydroçhloride and p-DABA was performed in acidic and ethanolic medium. The absorption spectrum of the reaction product showed a maximum at 449 nm. Molar absorptivity at this wavelength was calculated as 4.6×10^4 $1.mol.^{-1}.cm^{-1}$.

The optimum conditions of the reaction were investigated. The effect of varying acid concentrations was studied and 1 ml of 1 % HCl solution was found to be sufficient to obtain maximum colour developlent. 1 ml of 95 % ethanol was required to prevent the precipitation of the excess p-DABA. Optimum amount of p-DABA solution was found to be 2 ml (Table 1). To determine the effect of temperature and reaction period, the time course of the reaction was observed at three different temperatures. Optimum results were obtained in 20 min. at room temperature. The absorbance remained constant for at least 60 min (Table 2).

Table-1: Effect of the amount of reagent on the reaction.

ml of p-DABA Solution	0.5	1.0	1.5	2.0	2.5	3.0
A	0.278	0.586	0.817	0.924	0.924	0.923

Table-2 : Changes in absorbance with time at room temperature.

Time (min)	5	10	15	20	25	30	40	50	60
A	0.886	0.809	0.918	0.921	0.923	0.924	0.924	0.924	0.924

Under the experimental conditions a linear relationship existed between absorbance and concentration over the 1-4 mcg. ml^{-1} concentraiton range. The regression equation for the straight line was

$$A = 0.1686\ C - 0.0009 \quad (r = 0.9999\ ;\ n=6)$$

Results obtained by applying the proposed spectrophotometric method to commercially avaible procainamide hydrochloride tablets were statictically compared with those obtained by the USP XVIII method (18) in terms of t-and F-tests of significance at 95% confidence level (Table 3).

Tables-3: Analysis of procainamide hydrocloride (250 mg) tablets.

Statistical Values	Proposed Method	USP XVIII Method
Mean (mg)	247.6	251.7
% recovery	99.04	100.68
Standard deviation	2.56	3.58
Relative standard deviation	1.03 %	1.53 %
n	6	6
Confidence limits	244.9-250.3	247.7-255.8
t test of significance	1.98	(p=0.05 t= 2.23)
F test of significance	2.26	(p=0.05 t=5.05)

The proposed method is simpler than the USP XVIII and TF 1974 titrimetric methods in that fewer manupulations are involved. Furthermore it is precise, fast, economic and suitable for routine anlysis of procainamide hydrocloride in tablets. It can be also used in the stability investigation of procainamide hydrochloride.

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