

# A SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF PRAZOSIN HYDROCHLORIDE IN TABLETS

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## ABSTRACT

A rapid and sensitive analytical method was developed for the spectrophotometric assay of prazosin hydrochloride. The method is based on the formation of a coloured derivative between the drug and 1,2-naphthoquinone-4-sulfonic acid sodium salt (NQS). The reaction proceeds quantitatively at pH = 4.5 and 70 °C in 40 min. After the extraction of the derivative with chloroform: n-butanol (3:1), the absorbance was measured at 400 nm. The method was applied to commercially available tablets and the results were statistically compared with those obtained by an ultraviolet spectrophotometric and differential pulse polarographic methods using t- and F-tests.

## INTRODUCTION

Prazosin hydrochloride (**1**) is an antihypertensive agent in the quinazoline family /1/.

There are fluorimetric /2/, UV spectrophotometric /3/, potentiometric /4/ and differential pulse polarographic /5/ methods for the assay of the drug in the literature. The official USP XXII method uses a HPLC technique for the determination of **1** in capsules /6/. There is no conventional method for the tablets. HPLC is widely used for the assay of the drug in body fluids /7-9/. No spectrophotometric method has been developed in this regard. A simple, time saving and sensitive method for the assay of prazosin hydrochloride in pharmaceuticals is needed. This paper describes a spectrophotometric method

based on the reaction of prazosin hydrochloride with 1,2-naphthoquinone-4-sulfonic acid (NQS) via its amino group on the side chain attached to the 2-position of the dihydropyridine ring. NQS was previously reported to be a sensitive colour reagent for several primary and secondary amines /10-12/.

## EXPERIMENTAL

### Apparatus

A UNICAM UV2 UV/Visible spectrometer with 1 cm glass cells was used.

### Chemicals

Pharmaceutical grade prazosin hydrochloride was kindly received from Pfizer A.Ş Istanbul, Turkey, and Minipress tablets containing (1 mg prazosin hydrochloride/tablet) were purchased from the market. NQS and other chemicals were purchased from Merck, Darmstadt, Germany. All solvents were analytical reagent grade and water was distilled.

### Reagent solution

1% NQS solution in water was freshly prepared.

### Buffer solution

1.361g potassium dihydrogen orthophosphate was dissolved in 75 mL water and the solution pH adjusted to 4.5 with 0.1 M hydrochloric acid and diluted with water to 100 mL.

*Standard solutions:* A stock solution of 1 (1 mg/mL) was prepared using methanol. Standard solutions were obtained by diluting the stock solutions with methanol for the preparation of the calibration curve in the concentration range of 40-200 µg/mL.

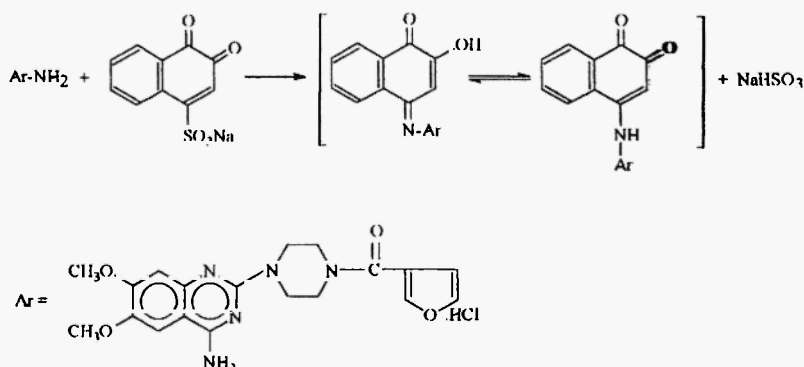
*Sample solution:* Thirty tablets were weighed and powdered. An accurately weighed portion of the powdered tablets, equivalent to about 5 mg of prazosin hydrochloride, was shaken mechanically with about 15 mL of methanol for 30 min and diluted to 25 mL with methanol, mixed and filtered.

## Assay Procedure

0.2 – 1.0 mL aliquots of standard solution and 3.0 mL of the sample solution were transferred into 20 mL glass stoppered centrifuge tubes. The volumes of standard solutions were completed to 1.0 mL and the volumes of sample solutions to 3.0 mL with methanol. 1.0 mL of buffer solution and 0.6 mL of NQS solution were added to each tube. The tubes were maintained at 70°C in a water bath for 40 min. After cooling to ambient temperature 5.0 mL of chloroform: n-butanol mixture (3:1) were added. The mixtures were vortexed for 1.0 min and filtered through 597 HY Rundfilter. The absorbances of the organic phases were measured at 400 nm against a blank solution. The amount of prazosin hydrochloride was calculated from the regression equation of the calibration curve obtained by standard solutions.

## RESULTS AND DISCUSSION

The reaction between prazosin hydrochloride and NQS (Scheme 1) is a simple condensation reaction with the elimination of  $\text{NaHSO}_3$  /13/.



**Scheme 1:** Reaction of prazosin hydrochloride (1) with NQS

The optimum conditions for the formation of yellow coloured chromophore were investigated as a function of pH and the type of the buffer, reaction temperature and time, the type of the extraction solvent and the reagent amount. The effect of pH was studied in the range of 1 – 5.5. The maximum absorbance value was obtained with pH 4.5 phosphate buffer (Table I). The reaction was very slow at room temperature, so the effect of

temperature and time on the reaction rate was examined in 60-80°C intervals (Table II).

The reaction was completed in 40 min at 70°C. The lability of prazosin hydrochloride-NQ in aqueous medium necessitated its extraction into the organic phase. Accordingly, chloroform, n-butanol, ethyl acetate, methylisobutyl ketone (IBMK), acetonitril, acetone and chloroform: n-butanol (1:1), chloroform: n-butanol (3:1), chloroform: n-butanol (1:3), n-butanol: ethyl acetate (2:1) solvent mixtures were tested as extraction solvents and the maximum absorbance value was obtained with chloroform: n-butanol (3:1) solvent mixture at 400 nm. The colour intensity of prazosin hydrochloride-NQ was stable for more than 48 hours in this solution.

**Table I**  
Effect of the pH on the reaction

	Chloride buffer			Acetate buffer			Phosphate buffer		
PH	1.0	1.5	2.0	2.5	3.5	4.5	4.0	4.5	5.5
Absorbance	0.073	0.142	0.411	0.308	–	0.380	0.598	0.695	–

**Table II**  
Effect of temperature and time on the reaction

Time (min)		10	20	30	40	50	60
Absorbance	60°C	0.629	0.629	0.633	0.633	0.633	0.824
	70°C	0.581	0.580	0.608	0.820	0.581	0.580
	80°C	0.597	0.598	0.590	0.590	0.568	0.568

The optimum amount of the reagent was determined by carrying out the reaction with  $4.76 \cdot 10^{-7}$  mole of prazosin hydrochloride and 0.2 – 1.0 mL of 1% NQS solution. 0.6 mL of 1% NQS solution was enough to complete the reaction (Table III).

**Table III**  
Effect of the amount of the reagent

Standard NQS Solution (mL) (1% w/v)	0.2	0.4	0.6	0.8	1
Absorbance	0.448	0.590	0.696	0.589	0.593

Under these conditions a linear relationship existed between absorbance (A) and prazosin hydrochloride concentration (C) over a 40 – 200  $\mu\text{g.mL}^{-1}$  range. The regression equation was

$$A = 3.56.10^{-3} C + 0.109 \quad (r = 0.9999)$$

The method was applied to the determination of prazosin hydrochloride in commercially available Minipress tablets and the results were compared with those obtained by UV-spectrophotometric method (since a pharmacopoeial method is not available) and differential pulse polarographic method /5/ (Table IV). There was no significant difference between the proposed method and reference methods.

**Table IV**  
Assay results of Minipress tablets (1 mg prazosin.HCl/tablet)

Statistical Values	Described method	Reference methods	
		Differential pulse polarographic method /5/	*UV-spectrophotometric method /3/
X	992.9	999.5	987.1
Recovery (%)	99.29	99.95	98.71
SD	14.7	15.3	10.6
SD%	1.48	1.53	1.07
N	5	5	5
t test of significance (p = 0.5, t = 2.31)		t = 0.62	t = 0.64
F test of significance (p = 0.05, F = 6.39)		F = 1.08	F = 1.92

\*  $\lambda_{\text{max}} = 330.4 \text{ nm}$  in methanol / 0.1 N  $\text{CH}_3\text{COOH}$  (7:3 v/v)

In conclusion, the method described in this paper is suitable for the routine assay of prazosin hydrochloride in pharmaceuticals. Although this is not as sensitive as chromatographic methods, it provides an alternative for the rapid and selective spectrophotometric determination in the UV region /3/. Spectrophotometric recordings at 400 nm showed no interference from the excipients of the tablet formulations. The procedure takes only 50 minutes and it does not require expensive solvents and reagents, whereas chromatographic methods do.

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