

A Spectrophotometric Method for the Determination of Prazosin Hydrochloride in Tablets

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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-sulphonic acid sodium salt (NQS). The reaction proceeds quantitatively at pH 4.5 and 70°C for 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 ultraviolet spectrophotometric and differential pulse polarographic methods using t- and F-tests.

Key Words: Prazosin hydrochloride, Spectrophotometry, Tablets.

Introduction

Prazosin (**1**) 1-(4-amino-6,7-dimethoxy-2-quiazolinyl)-4-(2-furanylcarbonyl) piperazine is an antihypertensive and a potent vasodilatory agent² in the quinazoline family and also has been found to be value in the treatment of heart failure³. The drug and its formulations are official in the British Pharmacopoeia⁴ and United States Pharmacopoeia⁵.

There are fluorimetric⁶, UV spectrophotometric^{7,8}, GLC⁹, TLC¹⁰, voltametric^{11,12}, and differential pulse polarographic^{13–15} methods in the literature for the assay of the drug. The official USP XXII method uses a HPLC technique for the determination of **1** in capsules⁵. There is no conventional method for the tablets. HPLC is widely used for the assay of the drug in body fluids^{16–18} and biological samples¹⁹. There is only one visible-range spectrophotometric method²⁰ in the literature, and so a simple, time-saving and sensitive method for the assay of prazosin hydrochloride in pharmaceuticals and bulk sample formulations is needed. This paper describes a spectrophotometric method based on the reaction of prazosin hydrochloride with 1,2-naphthoquinone-4-sulphonic 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^{21–23}.

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Experimental

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

Chemicals: Pharmaceutical grade prazosin hydrochloride was kindly provided by Pfizer A.Ş. İstanbul, Turkey, and Minipress tablets containing 1 mg prazosin hydrochloride/tablet were purchased. 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: 1.361 g 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 40-200 µg/mL.

Standard solution for UV-Spectrophotometric method: Stock solution containing 150 µg/mL of **1** was prepared in 0.1 N CH₃COOH: Methanol (30:70). Standard solutions (6-30 µg/mL concentration range) for the preparation of the calibration curve were obtained by diluting the stock solution appropriately.

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, and mixed and filtered.

Assay Procedure

Visible range spectrophotometric method

Into 20 mL glass stoppered centrifuge tubes were transferred 0.2-1.0 mL aliquots of standard solution and 3.0 mL of the sample solution. The volumes of standard solutions were completed to 1.0 mL and the volumes of sample solutions to 3.0 mL with methanol. Then 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) was added. The mixtures were vortexed for 1 min and filtered through a 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.

UV-Spectrophotometric method (Reference method)

Thirty tablets were weighted and powdered. To a quantity of powder containing the equivalent of 5 mg of **1** was added 20-25 mL 0.1 N CH₃COOH: methanol (30:70) and transferred to a 50 mL volumetric flask. The flask was agitated for 30 min and filled with the above mixture. The solution was filtered and the filtrate was used in the UV-spectrophotometric determination after appropriate dilution. The absorption spectrum of the diluted solution was recorded between 250 and 400 nm. The absorbance of the solution was measured at λ_{max} of 330.4 nm. The content of **1** was calculated from the corresponding calibration graph.

Results and Discussion

The reaction between prazosin hydrochloride and NQS (Scheme) is a simple condensation reaction with the elimination of NaHSO_3^{24} .

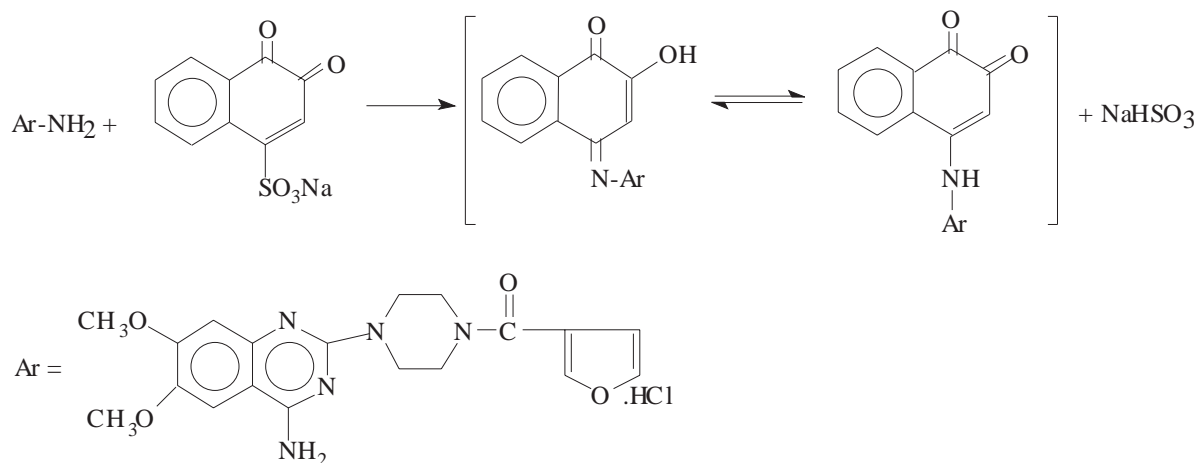


Table 1. Effect of the pH on the reaction

	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	-

The optimum conditions for the formation of yellow 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 1-5.5 because of several primary and secondary amines give condensation reaction in the pH range 2-4.5. The maximum absorbance value was obtained with pH 4.5 phosphate buffer (Table 1). The reaction was very slow at room temperature, and so the effect of temperature and time on the reaction rate was examined in 60-80°C interval (Table 2).

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. Therefore chloroform, n-butanol, ethyl acetate, methylisobutyl ketone (IBMK), acetonitril, and acetone, and chloroform:n-butanol (1:1), chloroform:n-butanol (3:1), chloroform:n-butanol (1:3), and n-butanol:ethyl acetate (2:1) solvent mixtures were tested as extraction solvents and the maximum absorbance value was obtained with the chloroform:n-butanol (3:1) solvent mixture at 400 nm. The colour intensity of prazosin hydrochloride-NQ was stable for more than 48 h in this solution.

Table 2. Effect of temperature and time on the reaction

Time(min)		10	20	30	40	50	60
	60°C	0.629	0.629	0.633	0.633	0.633	0.824
Absorbance	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 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 3). The absorption spectrum of the coloured product produced by the suggested procedure is shown in the Figure.

Table 3. Effect of the Amount of the Reagent

Standard NQS					
Solution (mL)	0.2	0.4	0.6	0.8	1
(1% w/v)					
Absorbance	0.448	0.59	0.696	0.589	0.593

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

$$A = 3.56 \cdot 10^{-3} C + 0.109 \quad (r = 0.9999)$$

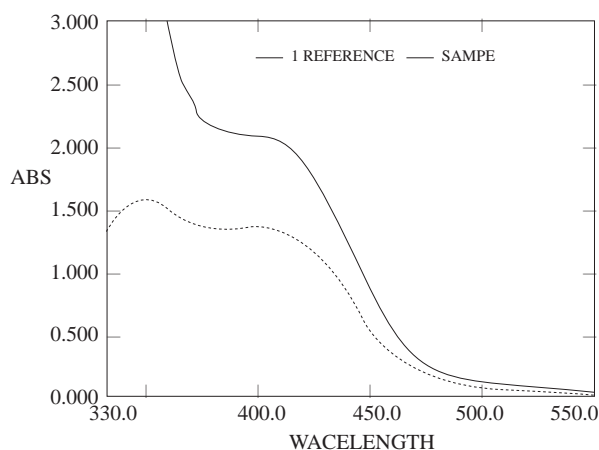


Figure. Absorption spectra of Prazosin HCl- NQS derivative (—) and its reagent blank (- - -).

The method was applied to the determination of prazosine hydrochloride in commercially available Minipress tablets and the results were compared with those obtained by UV-spectrophotometry (this method was developed by Pfizer A.Ş.) and the differential pulse polarographic method¹³ (Table 4). There was no significant difference between the proposed method and the reference methods.

In conclusion, the method described in this paper is suitable for the routine assay of prazosine hydrochloride in pharmaceuticals. Although not as sensitive as chromatographic methods, it is an alternative for the rapid and selective spectrophotometric determination in the UV region⁷. The commonly used excipients and additives in prazosin hydrochloride tablets such as talc (up to a 250-fold m/m excess compared with PRH), starch (200-fold), boric acid (150-fold), stearic acid (60-fold) and propyl paraben (5-fold) did not interfere in the method.

The proposed method has higher a λ_{max} value and sensitivity. This is a decisive advantage since the interference from the associated ingredients will be less at higher wavelengths than at lower wavelengths.

The results in Table 4 show that the proposed method can be applied for the analysis of pharmaceutical preparations with considerable precision, accuracy and sensitivity. The procedure takes only 50 min and does not require expensive solvents and reagents whereas chromatographic methods do.

Table 4. Assay Results of Minipress Tablets (1 mg prazosin.HCl/tablet)

Statistical Values	Described Method	Reference Methods	
		Differential Pulse Polarographic Method ¹³	*UV-Spectrophotometric Method ⁷
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 = 0.05, 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

* λ_{\max} = 330.4 nm in methanol / 0.1 N CH₃ COOH (7:3 v/v)

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