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REVERSE PHASE HPLC METHOD FOR THE ANALYSIS OF ALFUZOSIN HYDROCHLORIDE IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

A simple, rapid and reproducible high performance reversed phase liquid chromatographic method has been developed for the estimation of alfuzosin hydrochloride in bulk drug samples and pharmaceutical dosage forms using RP C-18 column. The mobile phase consists of buffer (pH 3.8) and acetonitrile in the ratio 650 : 350 (v/v), respectively, and was pumped at 1.0 mL/min at 30°C. The detection was carried out at 244 nm and the calibration curve was linear in the range of 0.02 to 20 μg/mL. The method was statistically validated for its linearity, precision and accuracy. The intra- and inter-day variation was found to be less than 1% showing high precision of the assay method. Parameters of validation obtained prove the accuracy of the method and its applicability for the determination of alfuzosin hydrochloride in tablet formulations.

Key words : Alfuzosin hydrochloride, RP-HPLC

INTRODUCTION

Alfuzosin hydrochloride[1] is chemically N-{3-[4-amino-6,7-dimethoxy quinazolin-2-yl(methyl)amino]propyl} tetrahydro-2-furamide hydrochlroide, is used in the Benign Prostatic Hyperplasia (BPH) to relive symptoms of urinary obstruction. It is a α-adreno receptor blocker with actions similar to prozosin[2]. Alfuzosin hydrochloride is a quinazoline derivative. It competitively and selectively binds to the postrynaptic α_1-adrenergic receptors in the lower urinary tract[3-8]. It is not official in any pharmacopoeia. Literature survey reveals that spectrophotometric methods[9] and one HPLC method[10] have been reported for its quantitative estimation in bulk drug and pharmaceutical dosage forms. The aim of present work is to develop a simple, rapid, precise and accurate reversed-phase HPLC method for the determination of alfuzosin hydrochloride in bulk drug samples or in pharmaceutical dosage forms.

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EXPERIMENTAL

Instrumentation

Quantitative HPLC was performed on a gradient high pressure liquid chromatograph (Shimadzu HPLC Class VP series) with two LC-10AT VP pumps, variable wavelength progra mmable UV/VIS detector SPD-10A VP, CTO-10AS VP column oven (Shimadzu), SCL-10A VP system controller (Shimadzu), a disposable guard column LC-18 (Pelliguard)^{TM}, LC-18, 2 cm, Supelco, Inc., Bellefonte, A and RP C-18 column (150 mm x 4.6 mm I.D., particle size 5 μm) was used. The HPLC system was equipped with the software Class – VP series version 6.01 (Shimadzu).

Chromatographic conditions

The contents of the mobile phase were buffer solution and acetonitrile in the ratio 650 : 350. The contents of mobile phase were filtered before use through 0.45 μm membrane filter. Buffer was prepared by dissolving 6.0 g of sodium dihydrogen phosphate in 1000 mL of water and the pH was adjusted to 3.80 with 10% H_3PO_4. The flow rate of the mobile phase was maintained of 1.0 mL/min. The column temperature was maintained at 30°C and the detection was carried out by UV-detector at 244 nm. The run time was set at 15 min and the volume of the injection loop was 20 μl. Prior to injection of the drug solutions, the column was equilibrated for at least 30 min with the mobile phase flowing through the system. The data were acquired, stored and analysed with the software class VP series version-6.01 (Shimadzu).

Procedure

About 100 mg of alfuzosin was accurately weighed and dissolved in acetonitrile so as to give 1 mg/mL solution. Subsequent dilutions of this solution were made with mobile phase to get concentrations of 0.02 to 20 μg/mL of alfuzosin. The standard solutions prepared as above were injected five times into the column at a flow rate of 1.0 mL/min. The peak areas of the drug concentrations were calculated. The regression of the drug concentration over the peak areas was obtained. This regression equation was used to estimate the amount of alfuzosin in pharmaceutical dosage forms (tablets).

Alfuzosin solutions containing 6 μg/mL, 12 μg/mL and 20 μg/mL were subjected to the proposed reversed phase HPLC analysis for finding out the intra-and inter-day variations. The recovery studies were carried out by adding known amount of Alfuzosin to the preanalysed smaples and subjecting them to the proposed HPLC method.

Assay of alfuzosin in tablets

Fifty tablets each containing 10 mg were weighed and powdered. An accurately weighed portion of the powder equivalent to 100 mg of alfuzosin was transferred to 100 mL volumetric flask containing 50 mL of acetonitrile. The contents of the flask were sonicated for 15 min. to dissolve alfuzosin and made upto volume with mobile phase and the resulting mixture was filtered through a 0.45 μm filter. 2 mL of this solution was added to 100 mL volumetric flask and made upto the volume with mobile phase. This solution (20 μL) was injected five times into the column. The mean values of peak areas of five such determinations were calculated and the drug content in the tablets was quantified using the regression equation obtained above. The same procedure was followed for the estimation of alfuzosin in other co mmercially available tablet dosage forms.

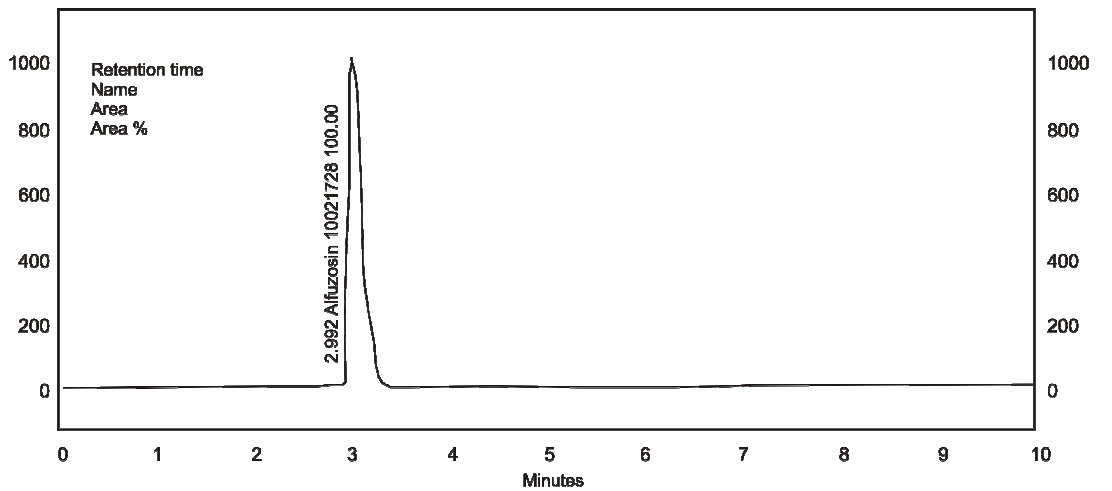

Fig. 1 : A typical chromatogram for alfuzosin

RESULTS AND DISCUSSION

The present study was carried out to develop a specific, sensitive, precise and accurate reversed phase HPLC method for the analysis of alfuzosin hydrochloride in pharmaceutical tablet dosage forms. The column pressure varied from 175-185 kg/cm^2. The retention time for alfuzosin was 2.992 min for a run period 15 min. Each of the sample was injected 5 times and the same retention times were observed in all cases. The peak areas of different concentrations set up as above were calculated and these are shown in Table 1. The peak areas for drug solution was reproducible as indicated by low coefficient of variation (1.45%). A good linear relationship (r = 0.9956) was observed

between the concentration of alfuzosin and the respective peak areas. The calibration graph was found to be y = - 812.3 + 79525.85 x, where 'y' is the peak area and 'x' is the concentrations of alfuzosin in the range of 0.02 to 20 μg/mL when alfuzosin solutions containing 8 μg/mL, 12 μg/mL and 20 μg/mL were analysed by the proposed reversed phase HPLC method for finding out intra-day and inter-day variations, a low coefficient of variation was observed (Table 2). This shows that the present HPLC method is highly precise. The amount of alufzosin from the preanalysed samples containing known amounts of the drug are shown in Table 3. About 96.50% alfuzosin could be recovered from the preanalyzed samples indicating the high accuracy of the proposed HPLC method.

Table 1. Calibration of HPLC method for the estimation of alfuzosin

S. No.	Concentration of alfuzosin (μg/mL)	Peak area*	C.V. (%)
1.	0.02	8866288	0.970
2.	0.04	17732576	1.250
3.	0.06	26598864	1.390
4.	0.08	35465152	1.070
5.	0.10	44331440	1.038
6.	0.20	88662880	0.280
7.	0.40	17732576	0.095
8.	1.00	44331438	1.054
9.	2.00	886628830	0.776
10.	4.00	177325750	0.852
11.	8.00	3546515100	0.042
12.	12.00	1359772901	1.450
13.	16.00	7093030405	0.006
14.	20.00	886628901	1.045

* mean of six determination

Table 2. Inter and intra-day precision for alfuzosin assay in pharmaceutical dosage forms by the proposed HPLC method

Alfuzosin concentration μg/mL	Concentration of alfuzosin found on			
	Intra-day		Inter-day	
	Mean n = 5	C.V. (%)	Mean n = 5	C.V. (%)
8	7.98	0.93	8.04	0.87
12	12.01	0.35	12.05	1.43
20	20.06	1.44	19.99	0.75

The drug content in the tablets was quantified using the proposed analytical method. The mean content of alfuzosin in two different brands of tablet dosage forms is shown in Table 4.

Table 3. Recovery of alfuzosin using proposed HPLC method

Amount of drug added (μg/mL)	Mean (± sd) amount found (μg) (n = 5)	Mean (±sd) % of recovery (n = 5)
4	3.991 ± 0.35	99.77 ± 1.24
8	8.014 ± 0.61	100.17 ± 1.01
12	12.107 ± 0.09	100.89 ± 0.88

Table 4. Mean (± sd) amount of alfuzosin in tablet dosage forms by proposed HPLC method

Tablets *	Labelled amount of drugs (mg)	Mean (± s.d) amount found (mg) (n=5)	Mean (± s.d.) purity
T_1	10	9.65 ± 0.02	96.50
T_2	10	9.76 ± 0.03	97.66

* T_1 = Alfoo Dr. Reddy's laboratories; *T_2 = Alfusin cipla pharmaceuticals are tablets from different manufacturer.

The absence of additional peaks indicates no interface of the excipients used in the tablet. The tablets were found to contain 96.50-97.66% of the labelled amount. The low

% CV indicates the reproducibility of the assay of alfuzosin in the tablet dosage form. The proposed reversed phase HPLC method was found to be simple, precise, highly accurate, specific and less time consuming.

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