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Application Of Condensation Reactions For The Estimation Of Alfuzosin Hydrochloride In Bulk Drugs And In Pharmaceutical Formulations

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ABSTRACT

Three simple spectrophotometric methods are described for the determination of alfuzosin hydrochloride (AFZ) in bulk drugs and in pharmaceutical formulations. The methods are based on the formation of coloured condensation products with aromatic aldehydes namely p-dimethyl aminobenzaldehyde (PDAB), p-dimethyl aminocinnamaldehyde (PDAC) or vanillin (3-methoxy-4-hydroxy benzaldehyde) and exhibiting maximum absorption at 565 nm, 560 nm and 580 nm respectively. The optimum experimental parameters for the color production are selected. Beer's law is valid with in a concentration range of 20 - 100 µg/ml for PDAB, 8.0 - 40.0 µg/ml for PDAC and 12-60 µg/ml for vanillin. The results obtained are reproducible and are statistically validated and found to be suitable for the assay of alfuzocin hydrochloride.

KEYWORDS

Alfuzosin hydrochloride;
Spectrophotometry;
PDAB;
PDAC;
Vanillin;
Determination.

INTRODUCTION

Alfuzosin hydrochloride (AFZ)[1] is a alpha 1-receptor blocker and is chemically known as N-[3-[(4-amino-6,7-dimethoxy-quinazolin-2-yl)-methyl-amino] propyl] oxolane-2-carboxamide hydrochloride. It is used for the treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia. Literature survey reveals that, chromatographic[2-5] method has been reported for the estimation of AFZ. To the best of our knowledge, there is no work in the literature reported about the spectrophotometric method for the analysis of AFZ in either biological fluids or pharmaceutical formulations. Hence the author has made an attempt to develop three simple and sensitive spectrophotometric methods for the estimation of AFZ in pure drug and in pharmaceutical formulations. The methods are based on the formation of coloured condensation products[6,7] of drug with aromatic aldehydes namely p-

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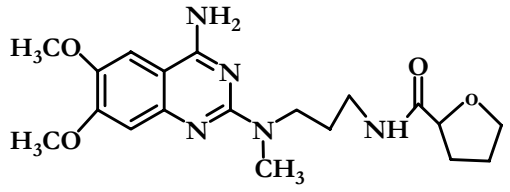
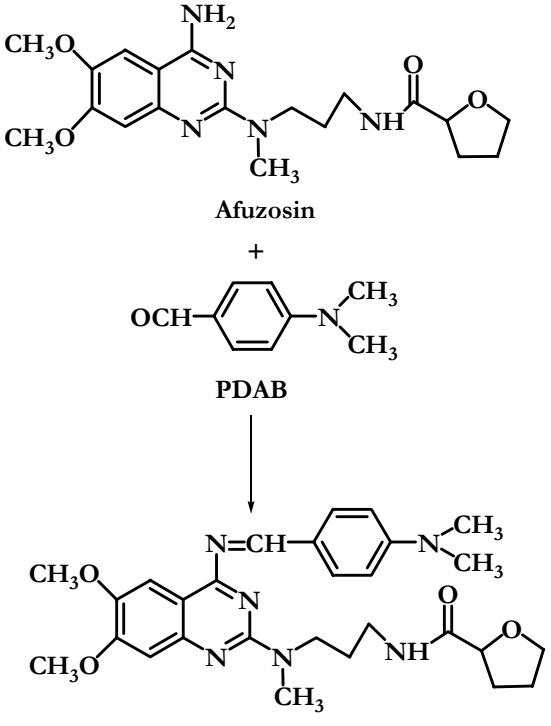


Figure 1: Structure of alfuzosin



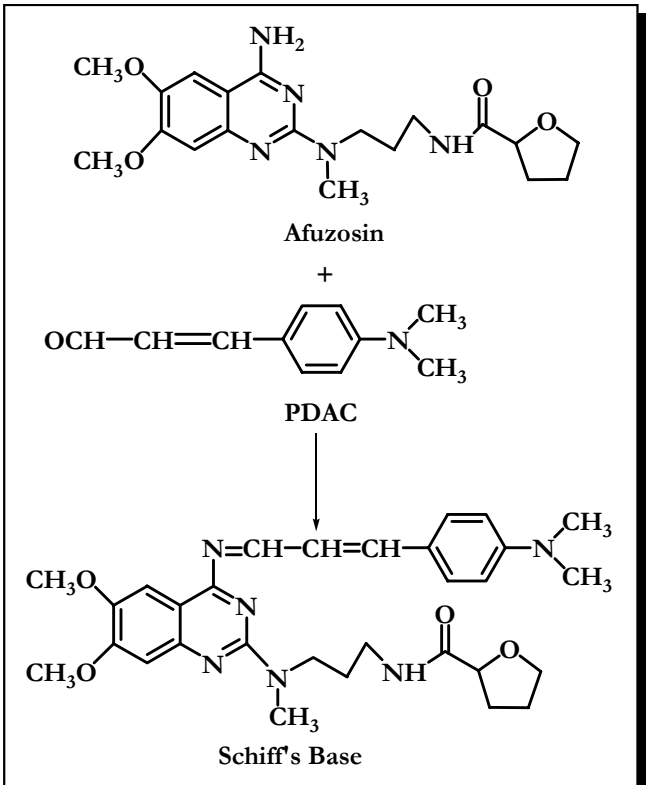
SCHEME 1: Possible reaction pathway between alfuzosin and PDAB

dimethyl aminobenzaldehyde (PDAB), p-dimethyl aminocinnamaldehyde (PDAC) or vanillin (3-methoxy-4-hydroxy benzaldehyde) and exhibiting maximum absorption at 565 nm, 560 nm and 580 nm respectively. The possible reaction pathways were shown in SCHEMES 1, 2 and 3.

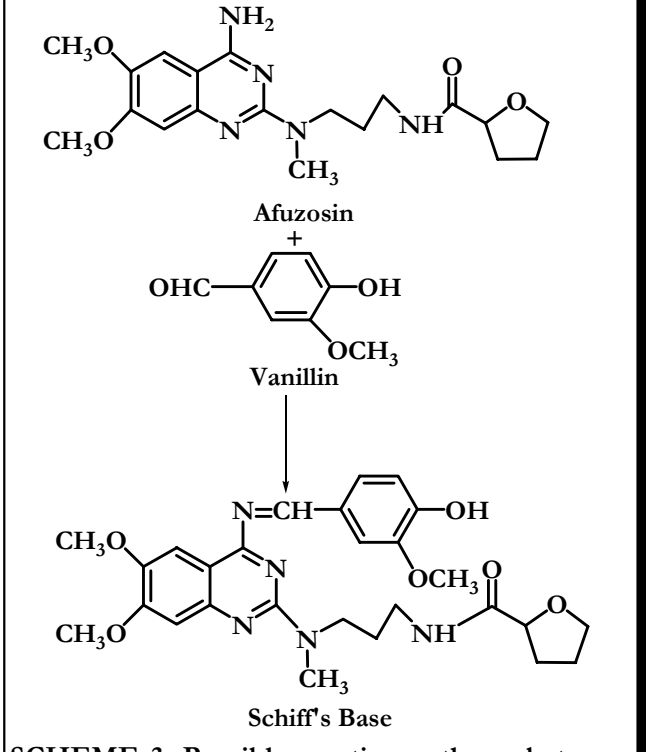
EXPERIMENTAL

Apparatus

All spectral and absorbance measurements were made on a systronic model 106 digital spectrophotometer with 10mm matched quartz cells.



SCHEME 2: Possible reaction pathway between alfuzosin and PDAC



SCHEME 3: Possible reaction pathway between alfuzosin and vanillin

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Materials and reagents

All chemicals used were of analytical reagent grade. AFZ was obtained from Dr.Reddy's labs Hyderabad. Methanolic solutions of PDAB (1%), PDAC (1%) and vanillin (0.5%) were prepared. Sulphuric acid and methanol were used in the investigation.

Standard solutions

Stock solution (1000 μg/ml) was freshly prepared by dissolving 100mg of AFZ in 100ml of distilled water and then this was further diluted with methanol so as to obtain a working standard solution of 400 μg/ml for all the methods.

General procedure and calibration

PDAB method

In to 10 ml measuring flasks, different aliquots of working standard solution (0.5-2.5 ml) were transferred to provide final concentration range 20-100 μg/ml. To each flask, appropriate volume of methanol was added to bring the total volume to 3 ml, 1 ml of PDAB and 3 ml of sulphuric acid were successively added and heated on a boiling water bath for 25 min. The solutions were cooled and made up to volume with methanol. The absorbance of each solution was measured at 565 nm against the reagent blank. The concentration of the unknown was read from the calibration graph or computed from the regression equation.

PDAC method

In to 10 ml measuring flasks, different aliquots of working standard solution (0.2- 1.0 ml) were transferred to provide final concentration range 8-40 μg/ml. To each flask, appropriate volume of methanol was added to bring the total volume to 2 ml, 1 ml of PDAC and 3 ml of sulphuric acid were successively added and heated on a boiling water bath for 25 min. The solutions were cooled and made up to volume with methanol. The absorbance of each solution was measured at 560 nm against the reagent blank. The concentration of the unknown was read from the calibration graph or computed from the regression equation.

Vanillin method

Into 10 ml measuring flasks, different aliquots of working standard solution (0.3-1.5 ml) were transferred to provide final concentration range 12-60 μg/ml. To each flask, appropriate volume of methanol was added to bring the total volume to 2 ml, 1.5 ml of vanillin and 3 ml of sulphuric acid were successively added and heated on a boiling water bath for 25 min. The solutions were cooled and made up to volume with methanol. The absorbance of each solution was measured at 580 nm against the reagent blank. The concentration of the unknown was read from the calibration graph or computed from the regression equation.

RESULTS AND DISCUSSION

The optical characteristics such as Sandell's sensitivity, molar absorptivity, precision and accuracy were found by performing eight replicate determinations containing 3/4th of the amount of the upper beer's law limits. The measured standard deviation (S.D.), Relative standard deviation (RSD), and confidence limits can be considered satisfactory for all the three methods and are summarized in TABLE 1.

Commercial formulation of AFZ was successfully analyzed by the proposed and reference methods. The values obtained by the proposed and reference methods are presented in TABLE 2. As an additional demonstration of accuracy, recovery experiments were performed at two levels by adding 5 mg and 10 mg of pure drug to the pre-analyzed formulations. The percentage recovery values (average ± S.D. of five determinations) are 99.97±0.1, 100.01±0.04 and 99.95±0.5 for the first level; 99.99±0.09, 99.98±0.2 and 99.99±0.6 for the second level for tablets-1; and 100.00±0.4, 99.99±0.08 and 99.97±0.8 for the first level; and 99.98±0.3, 99.97±0.8 and 99.97±0.6 for the second level for tablets-2 for methods PDAB, PDAC and vanillin respectively. There is no interference in the proposed analytical methods. In conclusion the proposed spectrophotometric method for the estimation of AFZ is simple, sensitive, and accurate and can be used for the routine quality control of the drug in bulk as well as in pharmaceutical formulations.

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TABLE 1: Optical, regression characteristics and precision of the proposed methods for AFZ

Parameter	PDAB	PDAC	Vanillin
λ_{max} (nm)	565	560	580
Beer's law limits (μg ml^{-1})	20 - 100	8.0 - 40	12 -60
Detection limits (μg ml^{-1})	0.455	0.214	0.420
Molar absorptivity (L $mole^{-1}$ cm^{-1})	3.50 x 10^3	9.07 x 10^3	6.13 x 10^3
Sandell's sensitivity (μg cm^{-2} / 0.001 absorbance unit)	0.120	0.046	0.069
Regression equation (Y = a + bC)			
Slope (b)	8.2 x 10^{-3}	2.1 x 10^{-2}	1.44 x 10^{-2}
Standard deviation of slope (S_b)	0.20 x 10^{-4}	0.60 x 10^{-4}	0.5 x 10^{-3}
Intercept (a)	7.00 x 10^{-4}	0.8 x 10^{-3}	-3.20 x 10^{-3}
Standard deviation of intercept (S_a)	1.26 x 10^{-3}	1.53 x 10^{-3}	1.67 x 10^{-3}
Standard error of estimation (S_e)	1.20 x 10^{-3}	1.46 x 10^{-3}	3.13 x 10^{-3}
Correlation coefficient (r)	0.9999	0.9999	0.9999
Relative standard deviation (%) [a]	0.170	0.202	0.213
% Range of error(Confidence limits)[a]			
0.05 level	0.142	0.169	0.178
0.01 level	0.210	0.251	0.264
% Error in bulk samples [b]	0.019	-0.036	0.210

[a]Average of eight determinations; [b] Average of three determinations. In Y =a + bC, Y is absorbance and C is concentration.

TABLE 2: Results of analysis of tablet formulations containing AFZ

Formulation	Labeled Amount (mg)	% Recovery*			
		PDAB	PDAC	Vanillin	Reference Method*
Tablets-1	10	99.98	100.02	99.97	100.05
Tablets-2	10	100.01	99.99	99.99	100.01

*** Recovery amount was the average of five determinations**
**** UV method developed in our laboratory**

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