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Development and Validation of First Order Derivative Spectrophotometric Method for Estimation of Alfuzosin Hydrochloride and Solifenacin Succinate in Combined Dosage Form

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ABSTRACT

A rapid, precise, accurate and specific first-order derivative spectrophotometric method was developed for the determination of alfuzosin hydrochloride and solifenacin succinate in combined dosage form. The technique was applied using methanol as solvent. The first-order derivative spectra were obtained and determination was made at 257 nm for alfuzosin hydrochloride and at 223 nm for Solifenacin succinate. The linearity was established over the concentration range of 6-36 µg/ml and 3-18 µg/ml for alfuzosin hydrochloride and solifenacin succinate, with correlation coefficient (r2) of 0.9985 and 0.9992, respectively. Interday and intraday studies showed repeatability of the method. The method was found to be specific and robust. The method was successfully applied to pharmaceutical formulation, with no interference from excipients as indicated by the recovery study. Results of analysis were validated statistically and by recovery studies. The proposed method is easy to apply, low cost, does not use polluting reagents and require relatively inexpensive instruments.

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1. INTRODUCTION

Alfuzosin HCl (ALF), (R, S)-N-{3-[(4-amino-6,7-dimethoxy2quinazolinyl)methylamino]propyl} tetrahydro-2-furancarboxamide hydrochloride (Fig.1), is used in the treatment of benign prostatic hyperplasia (BPH). ALF is an α1-adrenoreceptor blocker, can cause smooth muscles in the bladder neck and prostate to relax, resulting in an improvement in urine flow and a reduction in symptoms of BPH. The molecular weight of alfuzosin hydrochloride is 425.9. Alfuzosin hydrochloride is a white to off-white crystalline powder that melts at approximately 240°C. It is freely soluble in water, sparingly soluble in alcohol, and practically insoluble in dichloromethane[1].

Solifenacin succinate (SFS) is butanedioic acid, compounded with (1S)- (3R)- 1- azabicyclo [2, 2, 2] oct- 3- yl 3, 4- dihydro- 1- phenyl- 2(1H)- isoqinoline carboxylte (Fig. 2), and used for the treatment of overactive bladder in adults with symptoms of urinary incontinence, urinary urgency and urinary frequency. Solifenacin succinate is a novel muscarinic receptor antagonist, approved for the treatment of overactive bladder with affinity for muscarinic M3 receptor subtype, high degree of selectivity and to the fact that most tissues or organs express multiple muscarinic receptors[2,3].

RP-HPLC, UPLC, HPTLC, and spectrophotometric methods for estimation of ALF in combination with other drugs are reported [4-7]. The literature survey also revealed the report of RP-HPLC, Ultra fast liquid chromatography, LCMS, and spectrophotometric methods for estimation of SFS [8-12]. Literature survey reveals that only one HPTLC[13] method available for simultaneous estimation of ALF and SFS in combined dosage form. As, no UV spectrophotometric method was developed for the simultaneous estimation of ALF and SFS, so the aim of the study was to develop and validate first-order derivative UV spectrophotometric method for simultaneous estimation of ALF and SFS in bulk and combined dosage form.

2. MATERIALS AND METHODS

A Shimadzu UV/VIS double beam spectrophotometer (model 1800) with 1 cm matched quartz cells, were used for all spectral measurements. All the chemicals used were of A.R. grade and pure drug sample of alfuzosin hydrochloride was obtained from Sun pharmaceutical Ltd. Vadodara, Gujarat and pure solifenacin succinate was gifted by Alembic pharmacuetical Ltd.

Karkhadi, Gujarat. Capsules of ALF and SFS in combine dosage form with 10 mg ALF and 5 mg SFS label claim were procured.

2.1 Preparation of standard stock solution

Accurately weighed portion of ALF and SLF 10 mg were transferred to a separate 100 ml volumetric flask and dissolved and diluted to the mark with methanol to obtain standard solution having concentration of ALF (100 µg/ml) and SLF (100 µg/ml).

2.2 Preparation of sample solution

The content of twenty capsules was transferred and mixed. From this, powder which is equivalent to 100 mg Alfuzosin hydrochloride and 50 mg Solifenacin succinate was taken and the drugs were extracted into a 100 ml volumetric flask containing 50 ml methanol, sonicated for 30 min and diluted to100 ml with methanol. The resulting solution was filtered through a 0.45 µm membrane filter. This solution was further suitably diluted to get concentration, which is equivalent to 100 µg/ml of ALF 50 µg/ml of SFS. From this stock, 1 ml of solution was taken and diluted upto 10 ml with methanol which contains 10 µg/ml ALF and 5 µg/ml SFS.

2.3 Spectrophotometric measurements

In this method solutions of ALF and SFS were prepared separately by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. The absorption spectra thus obtained were derivatized to first order. From the spectra of both drugs ALF and SFS, wavelengths were selected for quantitation, 257 nm for ALF (zero cross for SFS) and 223 nm for SFS (zero cross for ALF).

3. Validation of proposed method

3.1 Linearity

Linearity was observed over a concentration range 6-36 µg/ml for ALF and 3-18 µg/ml for SFS, when measured at the wavelengths 257 nm (zero cross for SFS) and 223 nm for (zero cross for ALF). Calibration curves were constructed for ALF and SFS by plotting absorbance versus concentrations at both wavelengths. Each reading was average of three determinations.

3.2 Precision:

3.2.1 Repeatability

The precision of the instrument was checked by repeated scanning and measurement of absorbance of solutions (n = 6), for ALF (18 µg/ml) and SLF (9 µg/ml) without changing the parameter of the proposed spectrophotometric method.

3.2.2 Intermediate precision

The intraday and interday precision of the proposed method was determined by analyzing the corresponding responses 3 times on the same day and on 3 different days over a period of 1 week for 3 different concentrations of standard solutions of ALF (12, 18 and 24 µg/ml) and SLF (6, 9 and 12 µg/ml). The result was reported in terms of relative standard deviation (% RSD).

3.3 Accuracy (recovery study)

Accuracy of the developed method was confirmed by recovery study as per ICH guidelines at three different concentration levels of 50 %, 100 %, and 150 % by replicate analysis (n=3). Here to a preanalysed sample solution, standard drug solutions were added and then percentage drug content was calculated. The recovery study indicates that the method is accurate for quantitative estimation of ALF and SFS in capsule dosage form as the statistical results are within the acceptance range (S.D. < 2.0).

3.4 Specificity

The specificity of an analytical method is ability to measure accurately an analyte in presence of interferences like synthetic precursor, excipients, degradants, or matrix component. Comparison of UV spectrum of standard mixture and formulation shows specificity of method. The derivative spectrophotometric method is able to access the analyte in presence of excipients, and, hence, it can be considered specific.

3.5 Limit of Detection and Limit of Quantification

The limit of detection (LOD) and the limit of quantification (LOQ) of the drug were derived from the calibration curves by using the following equations as per International Conference on Harmonization (ICH) guidelines.

Limit of Detection and Limit of Quantitation were calculated using following formula

$$LOD = 3.3 (SD)/S \text{ and } LOQ= 10 (SD) / S,$$

Where SD=standard deviation of response (absorbance) and S= slope of the calibration.

4. RESULTS AND DISCUSSION

Absorption of ALF at ZCP of SFS and absorption of SFS at ZCP of ALF was taken (Figures 3, 4 and 5). The % assay ± S.D were found to be for ALF 99.16 ± 0.05131 & for SFS 99.09 ± 0.1929, respectively (Table 1). No interference was observed from the pharmaceutical excipients. The method was successfully applied to pharmaceutical formulation, with no interference from excipients as indicated by the results of recovery study (Table 2). The repeatability, intraday precision and interday precision were expressed in terms of relative standard deviation (RSD). For intraday and interday precision % RSD for ALF and SFS was found to be satisfactory (Table 3,4,5). Results of all validation parameters are shown in (Table 6). Hence, the proposed method was evaluated statistically and was validated in terms of linearity, accuracy and precision. The present work provides an accurate and sensitive method for the analysis of ALF and SFS in bulk and capsule formulation.

5. CONCLUSION

Based on the results obtained, it was found that the proposed method is accurate, reproducible, and economical and can be employed for routine quality control of ALF and SFS in bulk and its dosage form.

ACKNOWLEDGMENT

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FIGURES

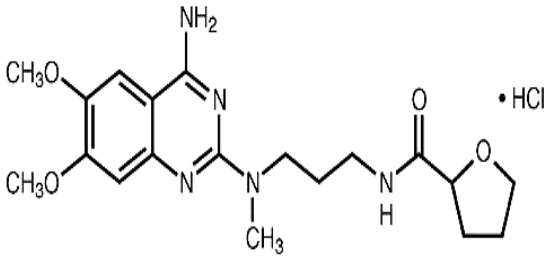

Figure 1: Structure of ALF

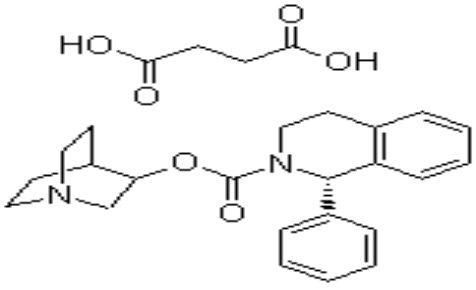

Figure 2: Structure of SFS

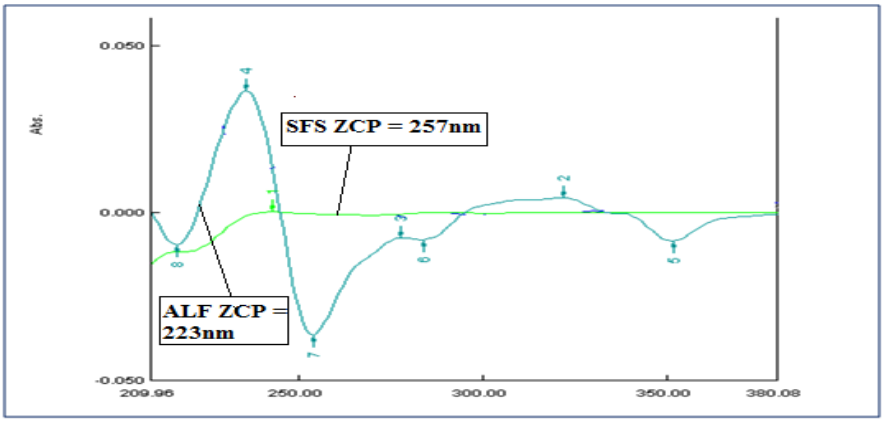

Figure 3: Overlain first order derivative spectrum of ALF and SFS

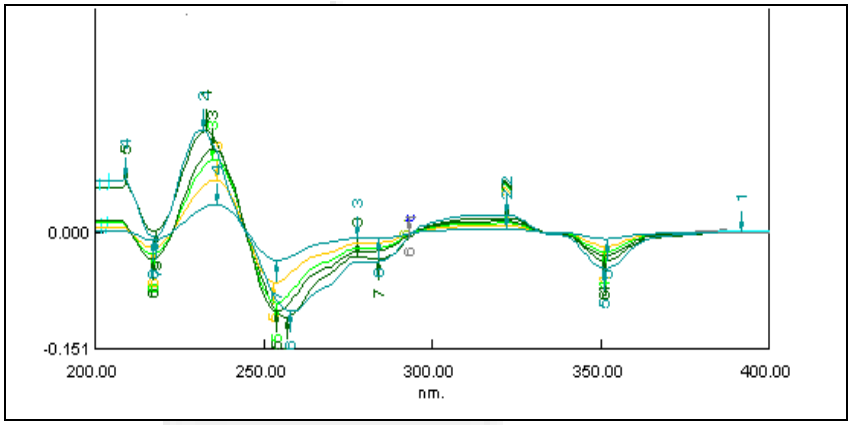

Figure 4: Overlain first order derivative spectra of ALF

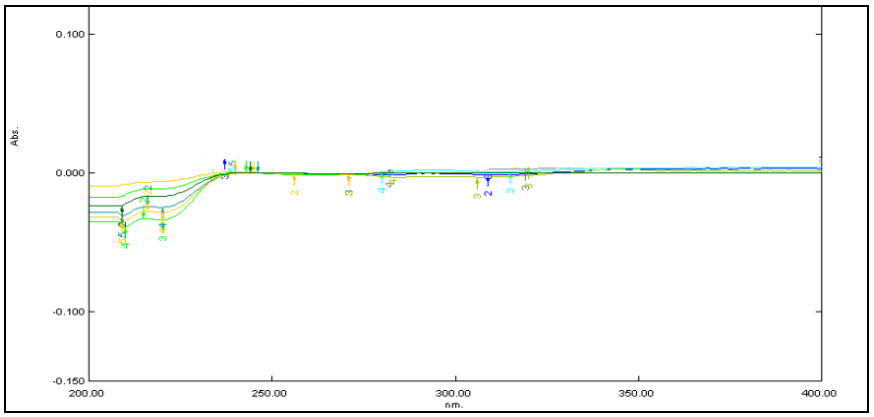

Figure 5: Overlain first order derivative spectra of SFS

Table 1: Assay results for the combined dosage form

Formulation (capsule)	Label claim (mg)		Amount found (mg)		% Label claim Assay ± SD	
	ALF	SFS	ALF	SFS	ALF	SFS
	10 mg	5 mg	9.98	4.90	99.16 ± 0.05131	99.09 ± 0.1929

Table 2: Statistical analysis for accuracy of proposed method (n=3)

Drugs	Level	Amount present (µg/ml)	Amount spiked (µg/ml)	Total amount of drug (µg/ml)	%Recovery	%RSD
ALF	50%	12	6	18	99.38	0.94
	100%		12	24	99.87	0.46
	150%		18	30	98.97	0.87
SFS	50%	6	3	9	102.12	1.15
	100%		6	12	95.08	1.4
	150%		9	15	100.66	1.3

Table 3: Repeatability of ALF and SLF (n=6)

Concentration(µg/ml)		Absorbance		S.D		% RSD	
ALF	SFS	ALF	SFS	ALF	SFS	ALF	SFS
18	9	0.0652	0.0090	0.000196	0.000132	0.30	1.4
18	9	0.0650	0.0092				
18	9	0.0655	0.0090				
18	9	0.0650	0.0093				
18	9	0.0651	0.0090				
18	9	0.0650	0.0092				

Table 4: Intraday precision of ALF and SFS (n=3)

Concentration (µg/ml)		Absorbance ± %RSD	
ALF	SFS	ALF	SFS
12	6	0.0539 ± 1.7	0.0062 ± 0.82
18	9	0.0667 ± 0.96	0.0092 ± 1.2
24	12	0.077 9± 0.46	0.0123 ± 1.7

Table 5: Interday precision of ALF and SFS (n=3)

Concentration (µg/ml)		Absorbance ± %RSD	
ALF	**SFS**	**ALF**	**SFS**
12	6	0.0553 ± 1.2	0.0064 ± 1.7
18	9	0.0665 ± 1.8	0.0092 ± 1.8
24	12	0.0772 ± 1.1	0.0119 ± 1.2

Table 6: Optical and Regression Analysis Data and Validation Parameter of first derivative results of ALF and SFS

Parameters		First-derivative UV Spectrophotometry	
		ALF at 257 nm	**SFS at 223 nm**
Concentration range (µg/mL)		6-36	3-18
Molar absorptivity ($L\ mol^{-1}\ cm^{-1}$)		0.400183×10^6	0.10219×10^6
Sandell's sensitivity ($\mu g/cm^2$/0.001A.U)		0.00106	0.00470
Slope		0.002	0.0011
Intercept		0.030	0.0007
Correlation coefficient (r^2)		0.9982	0.9992
LOD (µg/mL)		0.95	0.45
LOQ (µg/mL)		2.88	1.53
Accuracy (recovery, n = 3), %	50%	99.38 ±0.0404	102.12 ±0.0519
	100%	99.87 ±0.0577	98.08 ±0.1096
	150%	98.97 ±0.0513	100.66 ±0.1039
Repeatability (RSD, n = 6), %		0.30	1.4
Interday (n = 3)		0.46-1.7	0.82-1.7
Intraday (n = 3)		1.1-1.8	1.2-1.84