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# First and Second Derivative Spectrophotometric Methods for Determination of Alfuzosin in Pharmaceutical Dosage Form

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## ABSTRACT

Two simple, accurate and reproducible first and second derivative spectrophotometric methods have been developed for the determination of alfuzosin in pharmaceutical formulation. The solutions of standard and sample were prepared in methanol. For the first method, UV spectrophotometry, the quantitative determination of the drug was carried at 245 nm and the linearity range was found to be 1-5 µg/ml. For the first and second derivative spectrophotometric methods the drug was determined at 237 nm and 245 nm. The calibration graphs constructed at their wavelength of determination were found to be linear for UV and derivative spectrophotometric methods. The proposed methods have been extensively validated as per ICH guidelines. The described methods can be readily utilized for the analysis of pharmaceutical formulation. There was no significant difference between the performance of the proposed methods regarding the mean values and standard deviations. Developed spectrophotometric methods in this study are simple, accurate, and precise.

**Keywords:** Alfuzosin, First derivative spectrum, Second derivative spectrum, ultraviolet spectrophotometry.

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## INTRODUCTION

ALF is (R,S)-N-[3-[(4-amino-6,7-dimethoxy-2quinazolinyl)methylamino]propyl]tetrahydro -2-Furan carboxamide hydrochloride. ALF is a selective α-1 adrenoreceptor blocking agent. It works by relaxing the muscles in the prostate and bladder neck, making it easier to urinate. The symptoms associated with benign prostatic hyperplasia (BPH) such as urinary frequency, nocturia, weak stream, hesitancy and incomplete emptying are related to two components, anatomical (static) and functional (dynamic) It is used to treat the signs and symptoms of benign enlargement of the prostate, by increasing the flow in urine which is reduced by benign prostatic hypertrophy[3-5].Literature survey revealed rapid tandem mass spectrometry method for alfuzosin in plasma[8], HPLC[9,10] methods reported for analysis of alfuzosin alone in pharmaceutical dosage form and in biological samples. HPLC determination of alfuzosin in biological fluids with fluorimetric detection. Analysis of alfuzosin hydrochloride in Human serum and simulated gastric juice by voltammetry. Derivative spectrophotometry is an analytical technique of great utility for extracting both qualitative and quantitative information from spectra composed of unresolved bands, and for eliminating the effect of baseline shifts and baseline tilts. Derivative spectrophotometry is now a reasonably prized standard feature of modern micro-computerized UV spectrophotometry[7] .There is lack of HPLC equipment in many resource limited countries. In poor countries, where such equipment is available, the high cost of HPLC grade solvents and columns, and the lack of possibility to analyze many samples simultaneously significantly affect timely release of laboratory results for action. Hence an attempt has been made to develop simple, sensitive, rapid, accurate, precise and economical UV spectrophotometric methods for the estimation alfuzosin by UV, first and second derivative spectrophotometric methods in tablet formulation.

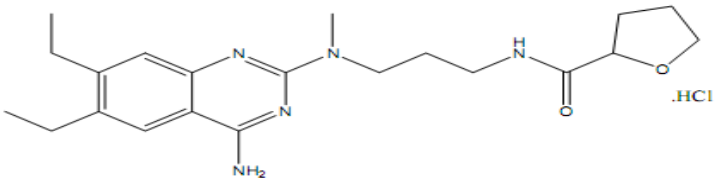


**Figure 1.Chemical structure of alfuzosin**

## MATERIALS AND METHOD

### Chemicals

Pure drugs Alfuzosin is obtained as gift sample Wockhardt Pharma Pvt. Ltd., Aurangabad (Maharashtra).Methanol used was of analytical grade and was purchased from Merck Chemicals, India.

**Instrumentation**

UV and derivative spectra of the solutions were recorded on double beam UV–Vis spectrophotometer Jasco V-630 using 10mm path length quartz cells with fixed slit width of 2 nm at a scanning speed of 1000nm/min, scan range of 200–400 nm, data pitch 0.5nm.

**Methods**

**Selection of Solvent:**

The derivative spectra's of ALF in different solvents like water and ACN did not show any favorable zero crossing points, but when dissolved in methanol the derivative spectra's of both drugs showed zero crossing points. Hence methanol was selected as the solvent for the method.

**Selection of derivative method:**

Both first and second derivative spectra's showed zero crossing points in methanol solvent and their absorbance's were good. Thus first and the second derivative method was selected because the spectral characteristics and resolution were good in these derivative spectra.

**Selection of wavelengths**

For the first and second derivative spectrophotometric methods the drug was determined at 237 nm and 245 nm which shows considerable absorbance.

**Preparation of standard solution**

ALF 10 mg was accurately weighed, transferred to separate 10 ml volumetric flasks, and make up the volume upto10 ml methanol.(Stock solution of 1000µg/ml).

**Preparation of working standard solution**

100 µg/ml of ALF was prepared by diluting 1 ml of stock solution upto 10 ml with methanol. The working standard solutions were prepared by dilution of the stock solution with methanol to get a concentration range of 1,2, 3, 4, 5 µg/ml for first and second derivative spectrophotometric methods. Methanol was used as a blank.

**Validation Parameters**

**Linearity**:

Different aliquots of ALF (1-5 ml) with different concentrations (1-5 µg/ml)) were prepared by serial dilutions with methanol from individual standard stock solutions to construct Beer's law plot for ALF and then Absorbances of these solutions were measured at 237 nm for first order derivative spectroscopy and at 245 nm for second order spectroscopy.

**Precision:**

The Precision of the method was determined by the analysis of the analyte using the proposed

developed method. The low value of %RSD showed that the methods were precise for both first and second derivative spectroscopy.

**Limit of Detection (LOD) and Limit of Quantification (LOQ)**:

The limit of detection (LOD) and limit of quantification (LOQ) of the drugs were derived by calculating the signal-to-noise ratio.

LOD = 3.3 X σ/S LOQ = 10 X σ/S Where, σ = the standard deviation of the response S = slope of the calibration curve.

**Accuracy**

The recovery studies were carried out at three different levels i.e. 80 %, 100% and 120 % levels. To assure the reliability of the above method recovery studies were carried out by mixing a known quantity of the standard drug with the sample formulation and the contents were analyzed by the proposed method for both first and second derivative spectroscopy.

**Assay procedure:**

Twenty tablets were weighed and the average weight was calculated. The tablets were powdered and a quantity equivalent to 10 mg of ALF was dissolved in 10 ml methanol in a 10 ml volumetric flask, by shaking and sonication, then diluting to volume with methanol. The solutions were filtered through a 0.45 µm nylon filter and sonicated for about 45 min and then volume made up with methanol. This solution was filtered to remove any insoluble matter. The filtrate was collected in a clean flask. Appropriate dilutions were made to obtain10 µg/ml with methanol from stock solution for both UV and derivative spectrophotometric methods. The amount of drug present in the formulation was calculated and results were shown in Table 4 along with % RSD values.

**Robustness and ruggedness:**

For robustness and ruggedness of analytical methods the tests mentioned below were carried out. The robustness of developed methods was tested by changing parameters such as degree of derivation, wavelength range applications of assay over different time, day and among multiple analysts. The results showed no statistical differences suggesting that the developed methods were robust and rugged.

## RESULTS AND DISCUSSION

The UV, first and second derivative spectra for alfuzosin was recorded at the wavelength of 245 nm, 237 nm, 245 nm respectively (Figure. 2-4).

**Linearity:**

The proposed method was found that the drug obeys linearity with in concentration range of 1-5 µg/ml for ALF. Regression analysis was made for the slope, intercept and correlation coefficient values. The regression equations of calibration curves were y = 0.1495x + 0.013 (r2 =0.9967) at 237 nm for first derivative spectrophotometry and y = 1.35x + 19 (r2 = 0.9992) at 245 for second derivative spectrophotometry. (Table 1).

**Table 1 Statistical data of the calibration graphs for determination of alfuzosin by proposed methods**

| Parameters | First derivative | Second derivative |
|---|---|---|
| Linearity range (1-5 µg/ml) | 1-5 | 1-5 |
| r2 ± S.D. | 0.9967 | 0.9992 |

n=6.

**Precision:**

From the precision studies it was found that the % RSD was less than 2% which indicates that the method has good reproducibility. To determine the precision of the method, alfuzosin solutions at a concentration of 2, 4, 6 µg/ml were analyzed each six times for both first and second derivative spectrophotometric methods. Solutions for the standard curves were prepared fresh everyday (Table 2).

**Table 2 Intra and Inter Day Precision**

| Parameters | Intra Day Precision | | Inter Day Precision | |
|---|---|---|---|---|
| | S. D | %RSD | S. D | %RSD |
| First derivative | 0.039 | 0.49 | 0.2 | 0.56 |
| Second derivative | 0.056 | 0.97 | 0.5 | 0.87 |

n = 6, Average of three concentrations 2, 4, 6 µg/ml

**LOD and LOQ:**

The LOD values of ALF were 0.8 and 0.7 for first and second derivative respectively. The LOQ values were found to be 2.5 µg/ml and 2.0 µg/ml respectively.

**Recovery:**

**Table 3 Recovery studies**

| concentration | Mean % Recovery | SD | %RSD |
|---|---|---|---|
| **First derivative spectrophotometric method** | | | |
| 80% | 99.98 | 0.110 | 0.121 |
| 100% | 99.85 | 0.121 | 0.133 |
| 120% | 99.67 | 0.152 | 0.164 |
| **Second derivative spectrophotometric method** | | | |
| 80% | 99.71 | 0.132 | 0.14 |
| 100% | 99.69 | 0.523 | 0.69 |
| 120% | 99.87 | 0.145 | 0.28 |

To study the accuracy of the proposed methods, and to check the interference from excipients used in the dosage forms, recovery experiments were carried out by the standard addition method The % recovery values of the pure drug were in between 99.67- 99.98 %, which indicates that the method is accurate and reveals that commonly used excipients and additives present in the pharmaceutical formulations did not interfere in the proposed method. (Table 3)

**Robustness:**

For robustness %RSD of two observations by two different analysts at two different times and two different days were calculated.

**Analysis of the marketed formulation:**

**Table 4 Assay results for the determination of alfuzosin in pharmaceutical formulation**

| Parameters | Drug Content (%) | %RSD |
|---|---|---|
| First derivative method | 99.69 | 0.65 |
| Second derivative method | 99.21 | 0.69 |

**Table 5 Summary of validation parameters**

| Parameter | First derivative method | Second derivative method |
|---|---|---|
| Wavelength (nm) | 237 | 245 |
| Linearity range (µg/ml) | 1-5 | 1-5 |
| Correlation coefficient | 0.9967 | 0.9992 |
| Limit of detection (µg/ml) | 0.8 | 0.7 |
| Limit of quantitation (µg/ml) | 2.5 | 2.0 |
| Mean recovery % | 99.833 | 99.75 |
| Precision (% ±S.D.) repeatability | 0.49 | 0.56 |
| | 0.97 | 0.87 |
| Robustness %RSD | 0.3459 | 0.4651 |

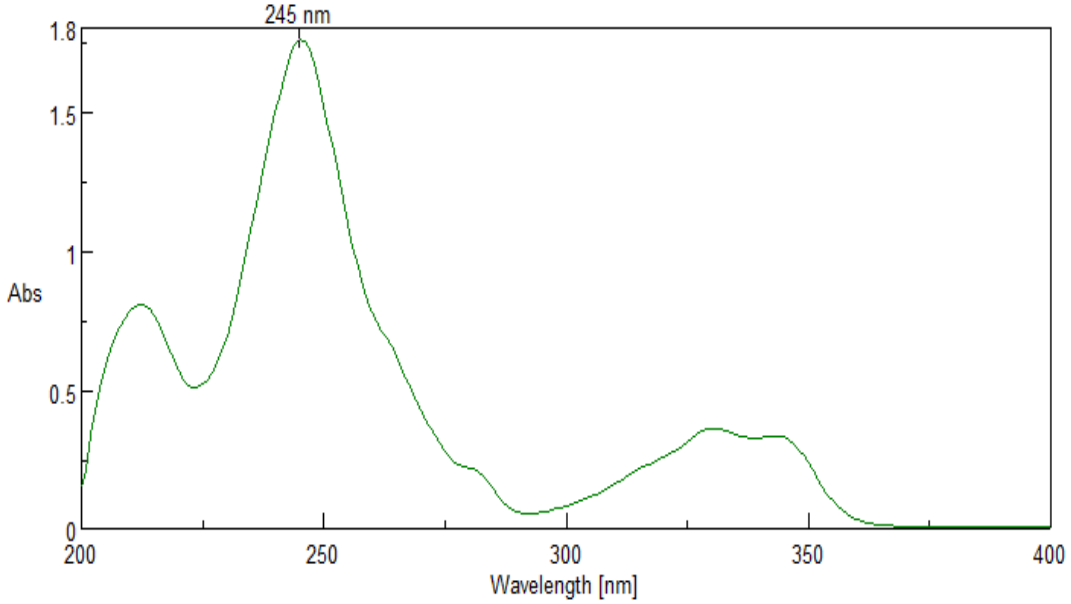


**Figure 2. UV spectrum of 10 µg/ml alfuzosin in methanol.**

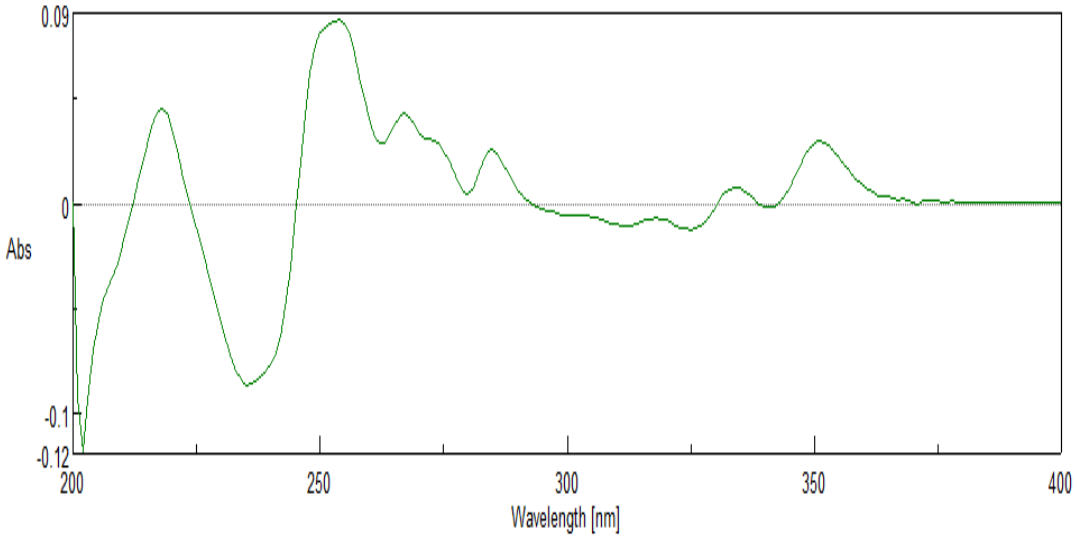


**Figure 3. First derivative spectrum of 10 µg/ml alfuzosin in methanol**

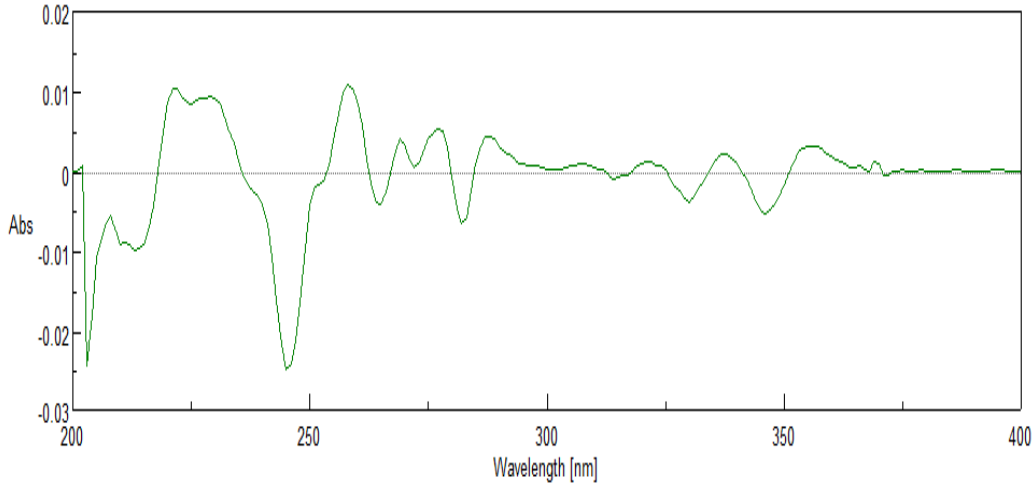


**Figure 4. Second derivative spectrum of 10 µg/ml alfuzosin in methanol**

There was no interference from the excipients commonly present in the capsules. The drug content was found to be 99.69± 0.82% with a % R.S.D. of 0.65and 99.21± 1.92% with a % R.S.D. of 0.69 for first and second derivative spectrophotometric methods respectively. It may therefore be inferred that degradation of alfuzosin had not occurred in the marketed formulations that were analyzed by this method. The low % R.S.D. value indicated the suitability of this method for routine analysis of alfuzosin in pharmaceutical dosage form (Table 4). The summary of the validation parameters is depicted in (Table 5).

## CONCLUSION

Due to high sensitivity and simple sample preparation, the methods described can be used for undergraduate studies. Moreover simple spectrophotometric methods have obvious advantages

over sophisticated instrumental analysis such as HPLC. Hence, simple and economical instrumental methods always have a role in pharmaceutical analysis. This method was validated for precision, reproducibility, linearity and accuracy as per ICH guidelines. All the above parameters lead to the conclusion that the proposed method is accurate, precise, simple, sensitive, robust and cost effective and can be applied successfully for the routine estimation of alfuzosin in bulk and pharmaceutical formulation.

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