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NOVEL FT-IR SPECTROSCOPIC METHOD FOR THE QUANTITATION OF ATENOLOL IN BULK AND TABLET FORMULATIONS

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ABSTRACT

A simple, specific, sensitive, accurate, precise and economical Fourier transform infrared spectroscopic method was developed for the quantitation of Atenolol in bulk and tablet dosage form. The method is based on the determination of Atenolol by the measurement of absorption of radiation at absorption band corresponding to C–O stretch of ether (Ar-O-R) centred at 1242 cm^{-1}, which is typically in the range 1274.95 – 1195.87 cm^{-1} because those absorption bands did not occur in excipients present in pharmaceutical preparation. The proposed method was validated as per ICH guidelines. The linearity of ATE was obtained in the concentration range of 10 – 70µg with correlation coefficient value (r^2) 0.9989. The mean percentage recovery was 99.76 ± 0.185. The recovery studies confirmed the accuracy of the proposed method and low values of standard deviation confirmed precision of the method.

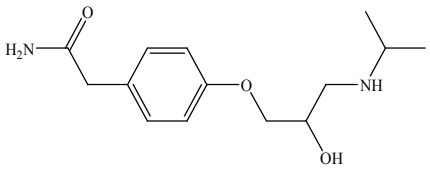
Keywords: Atenolol, FTIR, quantiation, tablet dosage form

1. INTRODUCTION

Fourier Transform Infrared Spectroscopy is a widely recognized technique for identification and verification of functional groups in compounds, impurities. It is non-contact, non-destructive and no sample preparation is required. This technique has been used to identify several compounds, such as pharmaceuticals, cosmetics and foods, but requires expensive equipments and mathematical pretreatments. Quantification of some pharmaceutical agents has been reported in the literature using FTIR spectroscopy either by measuring the transmission of analyte in potassium bromide or in chloroform [1–5].

Atenolol (ATE), chemically 2-(4-{2-hydroxy-3-[(propan-2-yl)amino]propoxy} phenyl) acetamide, (Fig. 1)[6] an Adrenergic beta-1 Receptor Antagonist, is used alone or with chlorthalidone in the management of hypertension, edema and long-term management of patients with angina pectoris[7].

Fig. 1. Structure of Atenolol



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The drug is official in the Indian Pharmacopoeia[6] which describes a UV spectrophotometric method for its assay in tablets. The drug is also official in the United States Pharmacopoeia, which describes high performance liquid chromatographic (HPLC) methods of assay, which are two-stage processes[8]. A wide range of chromatographic techniques, such as HPLC[9-13], Thin layer Chromatography[14], gas–liquid chromatography[15,16] and non-suppressed ion chromatography[17], have been used to determine ATE. Sensitive methods based on the measurement of the self-fluorescence exhibited by ATE in 0.1 M hydrochloric acid and phosphate–borate buffer have been described[18-19], Other techniques include kinetic spectrophotometry[20], differential scanning calorimetry and thermogravimetry[21], electrophoresis[22-23] and nuclear magnetic resonance spectroscopy[24]. Although HPLC methods with UV and fluorescence detection are routinely used, these methods require complicated liquid–liquid or liquid–solid extraction steps and/or several complicated clean-up steps[9-13]. They are time consuming. The kinetic method[20] is less sensitive and involves a heating step, whereas the thermal methods[21] require expensive experimental setup, in addition to being poorly sensitive. Recently, chemometric[22] and chemometric-assited spectrophotometric[23] methods have been proposed for the assay of ATE in combined dosage forms. But methods for its determination using Infrared Spectroscopic technique were not available. Hence an attempt was made to develop a simple, rapid and nondestructive method using FT-IR for the assay of Atenolol in pure and tablet forms.

2. MATERIALS AND METHODS

Chemicals and Reagents

Standard sample of Atenolol was obtained as gift sample from Hetero Drugs Limited, Hyderabad. Potassium bromide (analytical grade) was obtained from the HiMedia, Mumbai, India.

FTIR Instrumentation

The FTIR analysis was carried out on Shimadzu IRAffinity-1 FTIR spectrophotometer. FTIR spectra were recorded in the wave number range between 4000 and 650 cm^{-1}, averaging 32 scans per sample using a nominal resolution of 4 cm^{-1}. The IR solution software was used for data collection and to analyze the data.

Calibration Curve

Translucent pellets were prepared by dilution of Atenolol reference substance in potassium bromide to obtain 250mg of total weight. Calibration curves were prepared for five different Atenolol concentrations in the range of 10-70µg by diluting appropriate quantity of Atenolol (2.5, 5, 7.5, 10, 12.5, 15, and 17.5mg) with potassium bromide to get around 250 mg and triturated to ensure sample homogeneity. Each calibration standard was analyzed in the replicates of six. Absorbance corresponding to the C–O stretch of ether centred at 1242 cm^{-1} (Ar–O–R), which is typically in the range 1274.95 – 1195.87 cm^{-1} was used for the quantification and the average of six measurements was used to obtain the calibration curve. The calibration curve plotting was carried out using IR Solution software. The characteristic absorption peaks corresponding to stretching vibrations of different functional groups of Atenolol as shown in Figure 2 and compiled in table 1.

Method Validation

The proposed method was validated as per ICH guidelines for specificity, precision, accuracy, and linearity, intermediate precision[25-26].

Specificity

The wavelength selected for analysis was specific for ATE and there was no blank and excipient interference. Results obtained were shown in Figure 3-4

Linearity

The linearity of calibration curve was assessed by linear regression. Calibration curves were plotted over the concentration range of 10-70µg/mg for ATE. Each sample was analysed six times and averages were calculated. The calibration curve was constructed by taking concentration on the X- axis and absorbance / area on the Y – axis. The linearity was evaluated by linear regression analysis. This was calculated by the least square regression method. The correlation coefficient and Y- intercept of the calibration curve were calculated. Results obtained for linearity were shown in Figure 5-6 and table No. 2.

Accuracy

Recovery experiments were conducted at concentration range of 50, 100 and 150% to validate the accuracy of the test method. Each test preparation was prepared in triplicate and the analysis was performed in triplicate. The assay value at the beginning of validation was considered as the true value (100%) for recovery calculations. From the analyzed data, % assay and % recovery were calculated and reported in table No. 3.

Precision

The precision of the method was checked by repeated scanning and measurement of the absorbance of the infrared band at 1242 cm^{-1} (n = 6) of 40µg of ATE per mg of KBr without changing the parameters for the method. The repeatability was expressed in terms of relative standard deviation (RSD) and reported in table No. 4.

Intermediate Precision

The intraday, inter-day and inter-analyst precision of the proposed methods were performed by analyzing the corresponding responses 6 times on the same day and on 2 different days over a period of 1 week for assay level concentrations of standard solutions of ATE (40 µg). The results were reported in terms of relative standard deviation (RSD) in table no. 5.

Analysis of Marketed Tablet Formulations

20 tablets were accurately weighed and triturated and a powder weight equivalent to 10mg of Atenolol was weighed accurately and diluted with potassium bromide to get around 250mg. Powders were mixed and ground until obtaining a homogeneous powder. This powder mixture was crushed in a mechanical die pres to form translucent pellet. Dilutions with potassium bromide were made to give final concentration 40 µg. The analysis was carried out using six samples which were analyzed in six replicates.

3. RESULTS & DISCUSSION

The method is based in the measurement of absorption of radiation at absorption band C–O stretch of ether (Ar-O-R) centred at 1242 cm^{-1}, which is typically in the range 1274.95 – 1195.87 cm^{-1} because those absorption bonds did not occur in excipients present in pharmaceutical preparation. The proposed method was validated as per ICH guidelines.

The calibration curve was obtained for a series of concentration in the range of 10 – 70µg and it was found to be linear. The linear regression equation was y = 0.0286x + 0.7633 with correlation coefficient value 0.9989 which were within the acceptance criteria.

Specificity was studied for the examination of various excipients present in the tablet dosage form of atenolol. The results indicated that they did not interfere in the assay.

The precision was measured in terms of repeatability, which was determined by sufficient number of sample within the day (intraday) and next consequent three days for inter day precision. For each cases %RSD was calculated and was found to be 0.1783 for intraday and 0.1688 for inter day precision. These values were well within the acceptance limit ± 2.0%. This showed that the precision of the method was satisfactory, good.

Accuracy found out by recovery study from prepared samples (three replicates) with standard solution. Recovery was carried out standard addition method at three different levels which is 50%, 100% and 150%. The % recovery was calculated and was found to

be 99.76 and ±0.185. This was found to be well within the acceptance criteria of 98 – 102%. This showed that the recovery of atenolol by proposed method was satisfactory.

Ruggedness, intermediate precision performed by using six replicate preparations of standard atenolol which were prepared and analyzed by different analysts or two different days over a period of one week, the % RSD was calculated and it was found to be 0.1785, which was well within the acceptable criteria NMT 2.0%. It was concluded that the analytical technique showed to be rugged and showed good repeatability.

The validated method was applied for the assay of commercial tablets of Atenolol (Itel 50, 50mg). The % assay was calculated from standard calibration curve. The results 99.92 ± 0.10 presented good agreement within the labeled content. Thus the method developed in the present investigation is simple, sensitive, accurate, rugged, rapid and precise.

Hence, the developed method can be successfully applied for the estimation of atenolol in bulk and tablet dosage form.

Figure 2: IR Spectrum of Atenolol

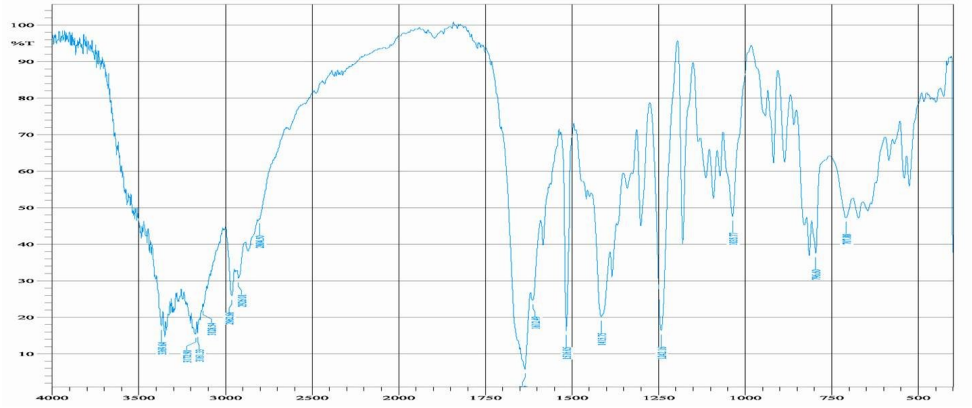

Figure 3: Specificity - FTIR spectrum of Atenolol (10 µg/mg of ATE)

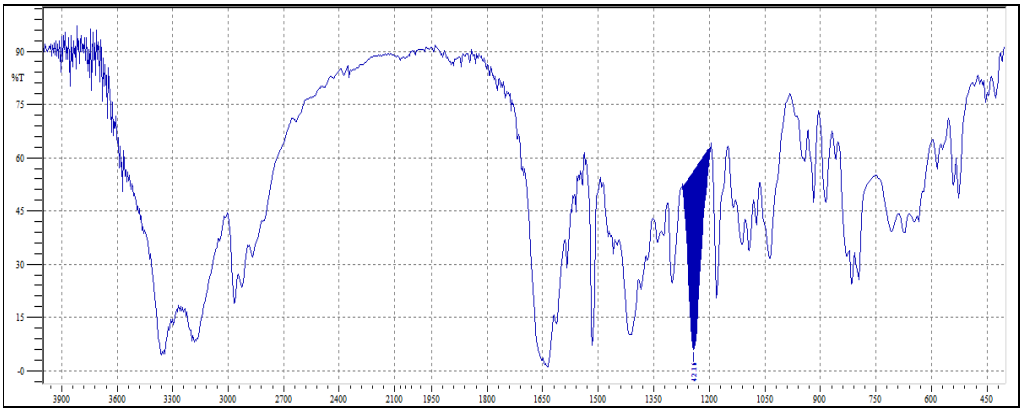

Figure 4: Specificity - FTIR spectrum of Atenolol Tablet Dosage form

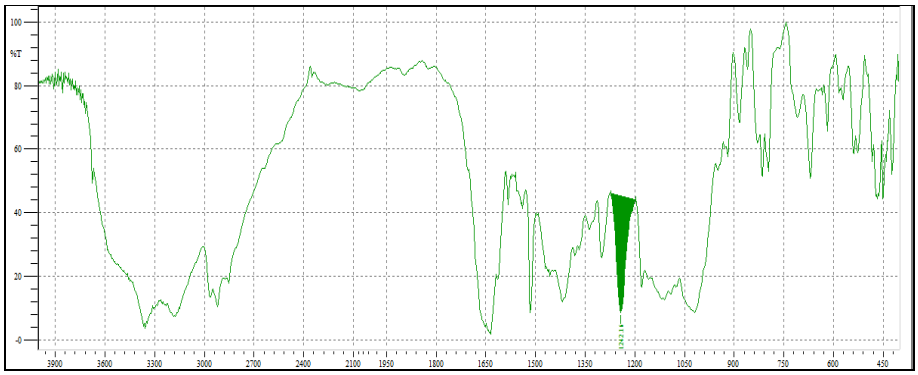

Figure 5: Overlay spectra of ATE (10 - 70 µg)

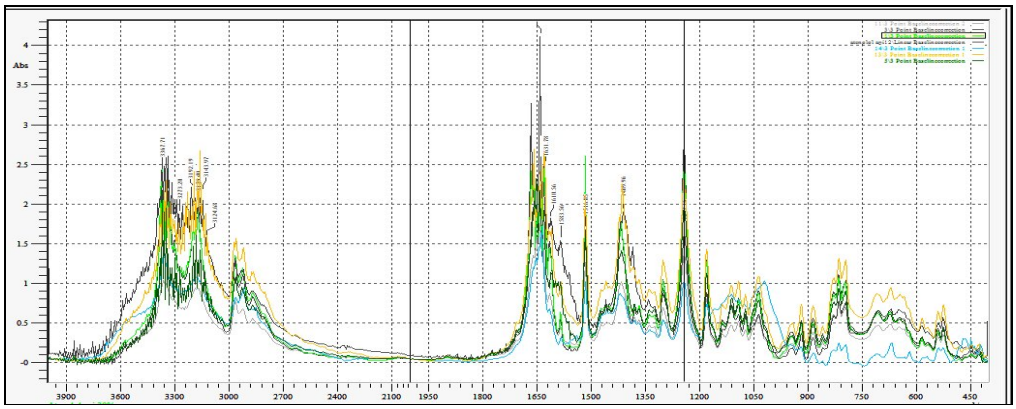

Figure 6: Linearity plot of ATE (10-70 µg)

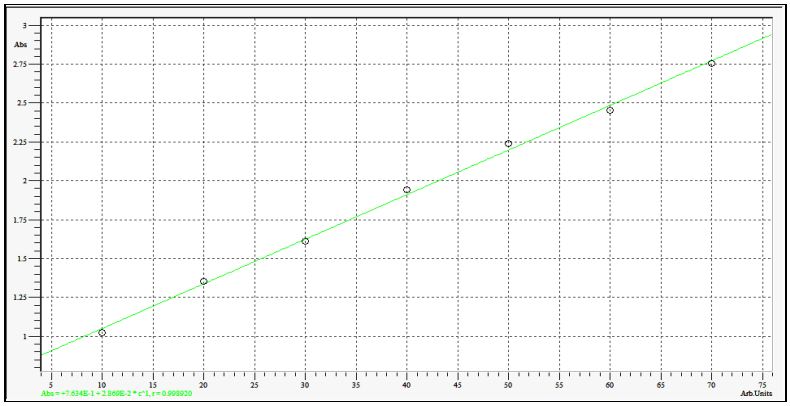

Table 1: Absorption peaks of Atenolol

IR Frequency Band (cm^{-1})	Group Responsible
3368	-OH
3198-3071	H-N
2966	C-CH_3
2924	CH2
2870	C-H
1666	C=O
1649	O=C-NH_2
1614	Conjugated C=C (aromatic)
886	C=CH_2

Table 2: Linearity studies results

S. No	Concentration, µg	Absorbance
1	10	1.020981
2	20	1.35496
3	30	1.610332
4	40	1.941522
5	50	2.237735
6	60	2.455538
7	70	2.755921
Correlation coefficient		0.99892
Slope		0.0286
y-intercept		0.7633

Table 3: Accuracy test results

S. No	Spiked level %	Amount Spiked, µg	Amount recovered, µg	% Recovery	Mean	STD	% RSD
1.	50	20	19. 89	99.45	99.47	0.176	0.177
2.	50	20	19.86	99.30			
3.	50	20	19.93	99.65			
4.	100	40	40.03	100.08	99.89	0.218	0.219
5.	100	40	39.98	99.95			
6.	100	40	39.86	99.65			
7.	150	60	59.86	99.77	99.92	0.159	0.159
8.	150	60	60.05	100.08			
9.	150	60	59.94	99.90			

Table 4: Results obtained from Precision test

Sample	Assay	Mean	STD	% RSD
Sample 1	101.34	100.694	0.625564	0.621252
Sample 2	99.79			
Sample 3	101.12			
Sample 4	100.87			
Sample 5	100.35			

Table 5: Intermediate Precision test

Tests	Mean	STD	% RSD
Intraday Analysis	99.65	0.4225	0.1785
Inter-day Analysis	99.88	0.4109	0.1688
Inter-analyst Analysis	99.60	0.7644	0.5843

4. CONCLUSION

Fourier Transform Infrared Spectroscopy is a widely recognized technique has been used to identify several compounds, such as pharmaceuticals, cosmetics and foods, but requires expensive equipments and mathematical pretreatments. The quantitation of Atenolol through infrared spectroscopy accomplishes with the requirements of specificity, precision, and accuracy in order to be used as a method for the quality control of pharmaceuticals. The method has been evaluated for linearity, accuracy, precision and ruggedness in order to ascertain the suitability of the analytical method. The method was applied to marketed samples. It has been proved that the method was selective and linear between the concentrations 10 - 70 µg and correlation coefficient value was found to be 0.9989. The developed method was found to be precise as the % RSD value for repeatability and intermediate precision were 0.1783 and 0.1688, which were less than 2.0%. The percentage recovery was found to be 99.76 ± 0.185. The method is very simple, rapid and economic nature, which makes it especially suitable for routine quality control work.

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