ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 19, Issue 4, 2026

Online - 2455-3891
Print - 0974-2441

Research Article

RAPID ATTENUATED TOTAL REFLECTANCE–FOURIER TRANSFORM INFRARED SPECTROSCOPIC QUANTIFICATION OF ATENOLOL IN ITS MICROSPHERES AND TABLETS: A GREEN APPROACH

ANNAPOORANI ARJUNAN*, RUBY STANLYRAJ, KUMAR MOHAN

Department of Pharmaceutical Chemistry, Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation (Deemed to be University), Salem, Tamil Nadu, India.

***Corresponding author: Annapoorani Arjunan; Email: annapooraniarjun24@gmail.com**

Received: 15 January 2026, Revised and Accepted: 28 February 2026

ABSTRACT

Objective: A solvent-free direct quantification of atenolol (ATN)-loaded microspheres and its tablets by utilizing attenuated total reflectance (ATR)–Fourier transform infrared (FTIR) spectroscopy was the prime objective of the current research work.

Methods: Developing a non-destructive analytical method to quantify the polymer-based analyte is a tremendous task. Since there is a lacuna in the analysis of drugs in the presence of interfering formulation excipients, we proposed an ATR-FTIR spectroscopic method for the qualitative and quantitative estimation of ATN in its polymer-based microsphere formulations. This ATR-FTIR spectroscopic analysis is based on the measurement of the absorption bands and deriving the linearity calibration curve for the effective quantification of ATN in its formulations.

Results and Discussion: The prominent absorption was found at 1235 cm^{-1} due to the stretching of the C-O-C aromatic ether linkage moiety of ATN. The linearity of absorbance versus the concentration was found in the range 10–100%w/w with the r^2=0.9960. The high percentage of recovery of ATN in microspheres and its marketed tablets (99.76 and 99.66% w/w) demonstrates the compliance of the accuracy study limits as per the International Council for Harmonisation guidelines. Precision study results showed acceptable % relative standard deviation values. The limit of detection and limit of quantification values (0.7 % w/w and 2.0 % w/w, respectively) indicated the high sensitivity of the method. The polymer excipients of the ATN-loaded microsphere and in the commercial tablet preparation did not interfere with the active drug.

Conclusion: Thus, the developed ATR-FTIR spectroscopic method is non-destructive, solvent-free, green, inexpensive, accurate, and rapid technique for quantitative determination of ATN in their polymer microspheres and tablet formulations.

Keywords: Atenolol, Attenuated total reflectance–Fourier transform infrared spectroscopy, Quantification, Validation, Analysis.

 DOI: http://dx.doi.org/10.22159/ajpcr.2026v19i4.58212. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Atenolol (ATN) is chemically identified as 2-(4-{2-hydroxy-3-[(propan-2-yl)amino]propoxy}phenyl)acetamide. It is a second-generation, selective β1-selective adrenergic receptor antagonist, used in the treatment of hypertension, edema, and long-term management of patients with angina pectoris [1, 2].

ATN is listed in the Indian Pharmacopoeia [3], which also specifies a ultraviolet (UV) spectrophotometric technique for tablet assay. In addition, the medication is included in the US Pharmacopoeia, which details two-stage high-performance liquid chromatographic (HPLC) analysis procedures.

Due to alarming rises in the hypertensive crisis around the globe, the need for higher production of ATN formulations demands a faster analytical tool for its qualitative and quantitative analysis.

Fourier transform infrared (FTIR) spectroscopy is a widely recognized technique for the identification and verification of functional groups in drugs and impurities. In the recent times, it is widely used analytical tool as a non-destructive and rapid technique. It is a solvent-free and non-destructive technique that requires no or fewer sample preparation steps for quantification. FTIR spectroscopic quantification of amlodipine besylate [4], zidovudine [5], lorazepam [6], ciprofloxacin [7], and ibuprofen [8] has been reported in the literature by measuring the transmittance or absorbance of drugs in potassium bromide as pellets. Further, this technique was used for the determination of sucrose [9], monitoring of bioprocess and fermentation process [10].

A variety of chromatographic techniques, including HPLC technique, were reported earlier for the evaluation of ATN in bulk and its tablets [11-14]. Further simultaneous quantification of ATN in its combined dosage forms was quantified using the reversed-phase HPLC (RP-HPLC) technique [15-17].

There have been reports of ATN's spectroscopic determination [18,19] and quantitative forensic application [20]. In addition, several techniques such as continuous flow injection turbidimetric analysis [21] and visible spectroscopy [22] were reported for the determination of ATN.

Although HPLC, UV spectroscopic, and conventional methods are routinely used, these methods require toxic solvents such as methanol, acetonitrile, and n-hexane. Moreover, sophisticated sample preparation steps such as liquid–liquid or liquid–solid extraction require several tedious cleanup steps. Further, they are time-consuming and require technical expertise. An ATR-FTIR spectroscopic method [23] was reported earlier by Annapoorani *et al* using the carbonyl amide functional group as the optimized wavenumber for its analysis.

The earlier work often faces broad interference from hydrogen bonding or moisture when selecting the C=O stretching bond of carbonyl amide ($-CONH_2$) at 1650 cm^{-1}. The C-O-C ether stretching peak falls within the fingerprint region around 1000–1300 cm^{-1}, and it allows for more

precise identification of specific chemical compositions, as these sharp peaks provide a unique signature of the structural arrangement of the selected drug and enable more accurate identification of particular chemical entities [24].

ATN-loaded alginate microspheres are proposed to be utilized as a model dosage form to rigorously challenge the ATR-FTIR analytical method's ability to accurately quantify the active ingredient within a complex, multi-excipient system. By incorporating the drug within a sophisticated matrix – such as a biodegradable, hydrophilic, or stimuli-responsive polymer – the method must demonstrate its capacity to overcome matrix effects, such as signal suppression or enhancement and precisely determine drug content. This approach serves as a benchmarking tool to validate the method's specificity and accuracy in the presence of various formulation additives, ensuring robust performance in, for example, and quantifying drug release from a matrix system.

Hence, an attempt was made to develop a solvent-free, rapid, and non-destructive analytical tool using ATR FT-IR spectroscopy for the direct quantitative analysis of ATN in its bulk, polymer-based microspheres, and tablet formulations.

Experimental work

Reagents and chemicals

ATN active pharmaceutical ingredient (API), hydroxy propylmethyl cellulose, calcium chloride, and sodium alginate are of analytical grade and IR pure potassium bromide. The ATN tablets were procured from the local market in Salem.

Instrumentation

A BRUCKER ALPHA II ATR-FTIR spectrophotometer (Germany) was used to perform the FTIR spectroscopic analysis with a resolution of 4 cm^{-1}. FTIR spectra were obtained in the wave number range of 4000–500 cm^{-1}, with an average of 16 scans/sample. The data were gathered and analyzed using the IR OPUS program. The samples were placed on the sample stage, and a consistent pressure of N 300 GPa (or 3 Mbar) was applied using the instrument's built-in anvil for all measurements.

METHODS

Selection of wavenumber

ATN exhibits key IR peaks corresponding to its functional groups. The structure of ATN, annotated with the prominent functional group bonds of amide and aromatic ether linkage, is shown in Fig. 1. The absorbance ATR-FTIR spectrum of ATN given in Fig. 2 clearly depicts distinctive absorption peaks that correlate to the stretching vibrations of the various ATN functional groups. The characteristic absorption peaks corresponding to stretching vibrations of different functional groups of ATN were compiled in Table 1. A strong band in the 3300–3400 cm^{-1} ranges for N-H and O-H stretching, a 1630–1650 cm^{-1} peak for the amide carbonyl (C=O) stretching (amide I band), and another peak around 1230–1250 cm^{-1} for the C-O-C aromatic ether stretching. Other bands at ~1510 cm^{-1} are attributed to aromatic C=C stretching and ~800–820 cm^{-1} to aromatic C-H out-of-plane bending. An uncommon peak in relation to the formulation excipients from the ATN fingerprint region was found to determine the optimal wavenumber. Fig. 3 reveals that the overlay ATR-FTIR spectra of ATN were obtained for a specific concentration, and the absorbance peak between 1240 and 1250 cm^{-1} that results from the C-O-C aromatic (Ar-O-R) ether bond stretching with 1235 cm^{-1} was selected to obtain the calibration curve for calculating the linearity range (r^2).

Preparation of calibration curve

ATN was mixed with KBr to prepare homogeneous mixtures containing 0.1–100% (w/w) of ATN. The absorbance of each calibration standard of ATN was measured in six duplicates, at the optimized wavenumber of 1235 cm^{-1} matching the C-O-C stretch of the aromatic ether molecule

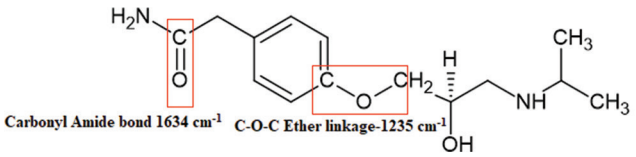

Fig. 1: Structure of atenolol

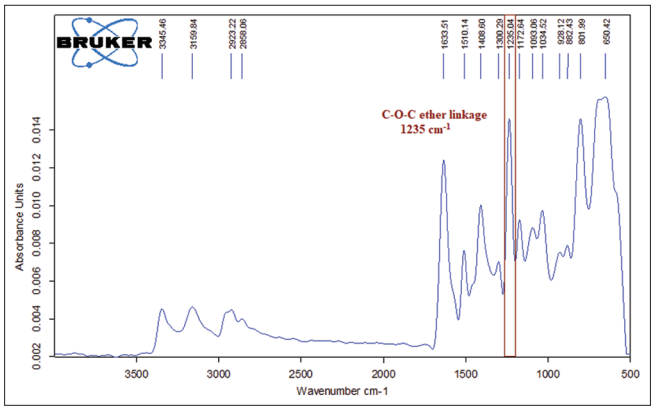

Fig. 2: ATR-FTIR absorbance spectrum of atenolol

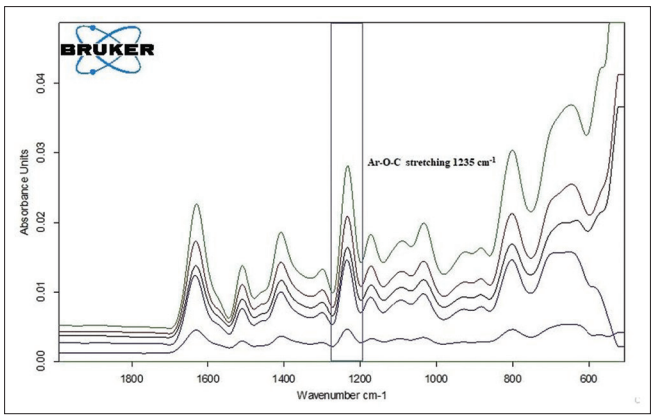

Fig. 3: Overlain attenuated total reflectance-Fourier transform infrared spectra in the fingerprint region for atenolol at different concentrations

Table 1: ATR absorption peaks of atenolol

IR frequency band (cm^{-1})	Bond	Functional group
~ 3346	-O-H	Hydroxyl group
~3160	-H-N	Amino group
~2923	-C-H	Methyl group
~2858	-C-H	Methylene group
~1634	-C=O	Carbonyl amide group
~1614	-Conjugated C=C (aromatic)	Benzenoid group
~1235	Ar- O-R	Aromatic ether group
~801	-C=CH_2	Methylene group

Note: Spectra recorded in ATR mode on pure atenolol powder. ATR: Attenuated total reflectance, IR: Infrared

to create the calibration curve; the mean of six measurements was utilized.

Formulation of ATN-loaded microspheres

Ionotropic gelation was used to create ATN-loaded mucoadhesive microspheres [25-29]. Three distinct formulations were prepared using the polymer hydroxypropyl methylcellulose: Drug concentration

in the 1:1 ratio. To ensure complete dissolution, 500 mg of precisely weighed ATN was dissolved in 50 mL of distilled water with the aid of a magnetic stirrer. The ATN solution was thoroughly mixed with a specified quantity of polymer and sodium alginate and sonicated for 10 minutes to eliminate the entrapped air bubbles.

The drug polymer mixture was dropped slowly using a 23-gauge needle from a distance of 6 cm into the beaker holding 5% w/v calcium chloride solution to enable gelation with the aid of a magnetic stirrer.

The moist microspheres are collected and washed thrice with an aliquot of 50 mL of distilled water to get rid of the unreacted calcium chloride residues, followed by drying at 40°C in an oven for 6 h. The formulated microspheres were saved for further analysis.

Validation

ATR-FTIR analytical method was validated as per the International Council for Harmonisation (ICH) guidelines for specificity, linearity, range, accuracy, precision, detection limit, quantitation limit, and ruggedness (ICH Q2A 1995, ICH Q2B 1996) [30,31].

Specificity

The wavenumber selected for analysis was checked for the specificity of ATN in combination with its formulation excipients. The ATN API with its formulation excipients was scanned for possible interactions with the formulation excipients to check the specificity of the proposed method.

Linearity

The linearity of calibration curve was assessed by linear regression. Calibration curves were plotted over the concentration range of 0.1–100% w/w for ATN. Each sample was analyzed 6 times and averages were calculated. The calibration curve was constructed by taking concentration on the X-axis and absorbance on the Y-axis. The linearity was evaluated by linear regression analysis. This was calculated by the least squares regression method. The correlation coefficient and Y-intercept of the calibration curve were calculated.

Accuracy

Recovery experiments were conducted at concentration ranges of 50, 80, and 120% 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.

Precision

Precision studies were conducted to determine the reproducibility of results. The precision of the method was checked by repeated scanning and measurement of the absorbance of the infrared band at 1235 cm^{-1} (n=6) of 50 mg of ATN in KBr without changing the parameters for the method.

Intermediate precision

The intraday, inter-day, and inter-analyst precision of the proposed methods was 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 ATN (50 mg). The results were reported in terms of relative standard deviation (RSD).

Detection limit

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value. The limit of detection (LOD) is determined by utilizing the equation below:

$$LOD = 3.3\frac{\sigma}{S}$$

Quantification limit

The lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy is termed the quantitation limit. The quantitation limit is a parameter of quantitative assays for low levels of compounds in sample matrices and is used particularly for the determination of impurities and/or degradation products. The limit of quantification (LOQ) is determined by utilizing the equation below:

$$LOQ = 10\frac{\sigma}{S}$$

Ruggedness

The ruggedness of a proposed analytical procedure was measured for its capacity to remain unaffected by small but deliberate variations in method parameters and provides an indication of its reliability during normal usage.

The validated analytical method can be carried forward for the routine analysis of ATN loaded in tablets and polymer-based dosage forms for the simultaneous qualitative and quantitative analysis.

Analysis of marketed ATN microspheres and tablet formulations

20 tablets were accurately weighed, and the triturated tablet powder equivalent to 50 mg of ATN from its commercial tablets HYPRES 50 (ATNT1) and TENOLOL 50 (ATNT2) was weighed accurately and mixed with the finely powdered IR-pure potassium bromide to get around 100mg. Powders were mixed and ground until obtaining a homogeneous powder. Dilutions with potassium bromide were made to give a final concentration of 50 mg. The process was repeated for sample preparation using drug-loaded microspheres. The analysis was carried out using six samples which were analyzed in six replicates. The sample absorbance of the ATN was compared with the standard using the calibration curve parameter and the concentration of active drug was calculated by interpolation method. The determined concentration was subjected to statistical analysis to predict the reliability of the method. The RSD is determined for each determination and it is considered to be acceptable if it falls below 2%.

Comparative evaluation of ATT-FTIR and RP-HPLC methods

A comparative evaluation of the proposed ATR-FTIR spectroscopic method was performed by comparing with the reported RP-HPLC method for the quantification of Atenolol and its formulations [32]. The recovery values obtained from ATR-FTIR spectroscopy and HPLC methods were compared by applying the t-test for paired samples.

RESULTS AND DISCUSSION

The method is based on the measurement of absorbance of infrared radiation at the absorption band C-O-C stretch of ether (Ar-O-R) centered at 1235 cm^{-1}, which is typically in the range 1275–1195 cm^{-1} because those absorption bonds did not occur in the excipients present in ATN-loaded microspheres and its tablets.

Validation

The proposed method was validated as per ICH guidelines.

Specificity

Specificity was studied for the examination of the interaction of various excipients present in the tablet dosage form with ATN. Fig. 4 shows the stacked spectrum of ATN API along with the ATN-loaded tablets and microspheres, which clearly dictates the drug polymer compatibility. There are no significant shifts in the characteristic drug peak 1235 cm^{-1}.

Linearity and range

The calibration curve was obtained for a series of concentrations in the range of 1–100 mg and it was found to be linear. The linear regression equation was y=0.00046×+0.0005 with a correlation coefficient value of 0.9960 which was within the acceptance criteria. Results obtained for linearity are shown in Fig. 5 and Table 2.

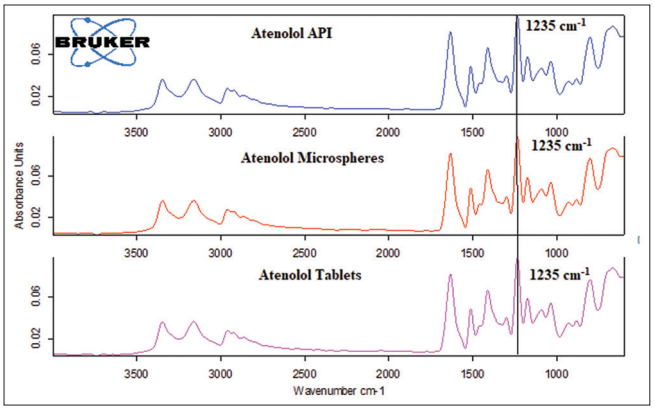

Fig. 4: Stacked spectrum of atenolol and its microsphere and tablet dosage for specificity studies

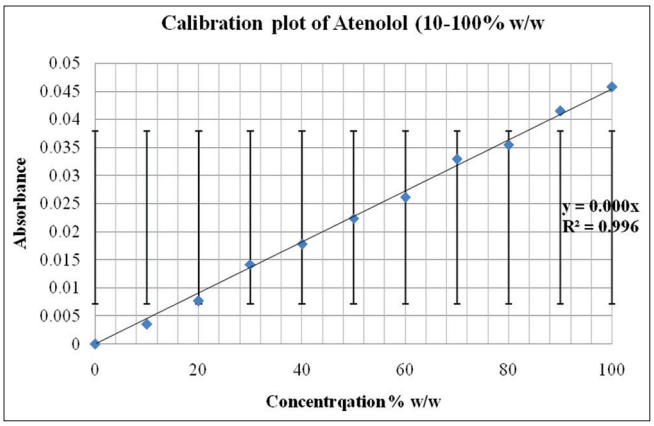

Fig. 5: Calibration curve for atenolol (n=6/point) showing absorbance at 1235 cm^{-1} versus concentration (% w/w)

Table 2: Linearity studies results

Concentration (% w/w)	Absorbance
10	0.0038
20	0.0077
30	0.0142
40	0.0178
50	0.0224
60	0.0261
70	0.0329
80	0.0354
90	0.0415
100	0.0458

Table 3: Results of linearity, LOD and LOQ

Parameter	Result
Linearity	10–100% w/w
Range	10–100% w/w
Slope	0.000462
Intercept	0.00056
R^2	0.9960
LOD	0.7% w/w
LOQ	2.0% w/w

LOD: Limit of detection, LOQ: Limit of quantification

Detection and quantification limit

The lowest limit ATN that can be detected by the proposed method was found to be 0.7% w/w. The lowest limit of quantification by the proposed method was found to be 2.0% w/w (Table 3).

Accuracy

Accuracy was found by a recovery study from prepared samples (three replicates) with a standard physical mixture. Recovery was carried out by the standard addition method at three different levels which is 50%, 100%, and 150%. The % recovery was calculated and was found to be in the range of 99.66–99.76% w/w. This was found to be well within the acceptance criteria of 98–102%. This showed that the recovery of ATN by the proposed method was satisfactory (Table 4).

Precision

The precision of the method was expressed as the percentage of the RSD (% RSD). Repeatability was checked with multiple measurements of the ATN with a replicate of 6 times (ATN, ATNMS, and ATNT1 and T2) at a concentration of 50 %w/w, with subsequent calculation of the % RSD. As shown in Table 5, the % RSD values for the precision studies for ATN, ATNMS, and ATNT1 and T2 are 0.0424, 0.0802, and 0.0793 and 0.1132. It is well inside the acceptable range of <2.0%.

Intermediate precision

Intermediate precision was used to measure repeatability, and this was achieved by collecting enough samples within a day (intraday) and the next three days for interday precision. For each case, intra-day and inter-day % RSD were calculated and were found to be 0.02830 and 0.05667. These values were well within the acceptance limit of ±2.0%. This proves that the precision of the method was sensitive, satisfactory, and good (Table 6).

Ruggedness

Ruggedness was determined by performing reproducibility using six replicate preparations of standard ATN and was analyzed by different analysts. The % RSD was calculated and it was found to be 0.05667, which was well within the acceptable criteria not more than (NMT) 2.0%. It was concluded that the analytical technique was found to be rugged and showed good repeatability (Table 7).

Analysis of ATN microspheres and its tablets

The validated method was applied for the assay of ATN in its microspheres (ATNMS) and their commercial tablets (ATNT1 and ATNT2 50 mg). The % assay was calculated from the standard calibration curve. The assay results for ATN API, ATN microspheres, its tablet formulations ATNMS, ATNT1, and ATNT2 were 99.96, 99.92, and 100.02 % w/w, respectively (Table 8). It presented good agreement within the labeled content. Thus, the method developed in the present investigation is solvent-free, simple, non-destructive, rugged, rapid, and precise. Hence, the developed method can be successfully applied for the estimation of ATN in bulk, polymer-based microspheres, and its tablet dosage forms. The ATR FTIR spectroscopic method reported earlier used C=O carbonyl amide stretching as the optimized absorbance peak and the current work has chosen a peak in the fingerprint region which is more accurate for the exact spectral imaging of a drug. The correlation of the results of the proposed method with the reported method was equally good. The HPLC and spectrophotometric methods utilized expensive, hazardous, and toxic solvents. Moreover, the reported conventional analytical methods were less accurate and non-reproducible. Hence, the rapid analysis time with less technical expertise keeps this ATR FTIR spectroscopic method at a high level when compared with the reported methods.

Table 4: Accuracy test results of ATN

Sample	Spike level %	Amount added (mg)	Amount found (mg)	Recovery %	Mean recovery ± (%).	STD	% RSD
ATNMS	50	25	24.88	99.52±0.035	99.76	0.210	0.211
	80	40	39.94	99.85±0.201			
	120	60	59.92	99.91±0.100			
ATNT1	50	25	24.98	99.92±0.832	99.66	0.3515	0.353
	80	40	39.92	99.80±0.115			
	120	60	59.86	99.26±0.128			

Spectra recorded in ATR mode on atenolol microspheres and tablets. ATN: Atenolol, ATNMS: Atenolol microsphere, ATNT: Atenolol tablet, STD: Standard deviation, % RSD: percentage of the relative standard deviation

Table 5: Results obtained from precision studies

Sample	Measured Assay (%)*	Mean %	STD	% RSD
ATN API	49.92 mg	99.82	0.0424	0.0424
ATNMS	49.96 mg	99.92	0.0802	0.0802
ATNT1	50.01 mg	100.06	0.0794	0.0793
ATNT2	49.88 mg	99.76	0.1132	0.1132

*(n=6). ATN: Atenolol, API: Active pharmaceutical ingredient, ATNMS: Atenolol microsphere, ATNT: Atenolol tablet, STD: Standard deviation, % RSD: percentage of the relative standard deviation

Table 6: Results obtained from intermediate precision studies

Tests	Assay %	Mean %	STD	% RSD
Intra-day analysis	99.88	99.91	0.02828	0.02830
Interday analysis	99.94			

STD: Standard deviation, % RSD: Percentage of the relative standard deviation

Table 7: Results obtained from ruggedness studies

Tests	Assay %	Mean %	STD	% RSD
Inter-analyst	99.84	99.80	0.05656	0.05667
Intra-analyst	99.76			

STD: Standard deviation, % RSD: percentage of the relative standard deviation

Table 8: Analysis results of ATN formulation

S. No.	Formulations	Formulation code	Label claim	Estimated amount	% Drug content
1.	ATN Microsphere	ATNMS	50 mg	49.98 mg	99.96
2.	ATN Tablet	ATNT1	50 mg	49.96 mg	99.92
3.	ATN Tablet	ATNT2	50 mg	50.01 mg	100.02

ATN: Atenolol

Comparative evaluation of ATR-FTIR spectroscopy and RP-HPLC method

The recovery values obtained from the proposed ATR-FTIR spectroscopy and RP-HPLC method for ATN were compared by applying t-test for paired samples.

t-test

The t-test was performed to prove that there is no significant difference between the recovery values of new ATR-FTIR spectroscopy and the existing RP-HPLC method. The t-value was calculated from the mean of the difference between the paired samples and standard error of the difference, and the calculated t-value was compared with the t-value at p=0.05 from t-table.

Null hypothesis

There is no significant difference in the recovery values of new ATR-FTIR spectroscopic method and existing RP-HPLC method.

Table 9: t-test data of ATR-FTIR Spectroscopy and RP-HPLC method

S. No.	FTIR recovery (%) X_1	HPLC recovery (%) X_2	Difference X_1-X_2=d	$(X_1-X_2)^2=d^2$
1	99.92	100.39	−0.38	0.76
2	99.82	100.35	−0.49	0.98
3	99.26	100.63	−1.37	2.74
Total			$\Sigma d=-2.24$	$\Sigma d^2=4.48$

ATR: Attenuated total reflectance, FTIR: Fourier transform infrared, RP-HPLC: Reversed-phase-high-performance liquid chromatographic

p-value and statistical significance

The two-tailed p=0.4226 by conventional criteria; this difference is considered to be not statistically significant.

The confidence interval

The mean of ATR-FTIR minus RP-HPLC equals −0.0133 95% confidence interval of this difference is from −0.0707 to 0.0440. The calculated t-value is lesser than the tabulated value (p=0.05). Therefore, the null hypothesis stating that there is no significant difference between the recovery values of two methods, new FTIR method and the existing HPLC method, is accepted at p=0.05. The difference between the recovery values of two methods is not a real difference because the level of significance is very low (Table 9).

CONCLUSION

ATR-FTIR spectroscopy is a widely recognized technique that has been used to identify several compounds, such as pharmaceuticals, cosmetics, foods, and bioprocess monitoring. The method is considered to be superior in comparison to the conventional methods which require expensive equipment, hazardous solvents, and deman sample pretreatments. The RP-HPLC method utilizes approximately 20 mL of toxic organic solvents per sample and around 200 mL of solvents per set of quantitative analysis. The proposed ATR-FTIR spectroscopic method eliminates the use of hazardous and expensive solvents by solvent-free evaluation.

The quantification of ATN through ATR-FTIR spectroscopy is accomplished with the requirements of specificity, precision, and accuracy to be used as a method for the quality control of polymer-based dosage forms and in pharmaceuticals.

The method has been evaluated for specificity, linearity, accuracy, precision, and ruggedness to assess the suitability of the analytical method. The method was applied to marketed samples and proved that it was selective and linear between the concentrations 10-100% w/w, and the correlation coefficient value was found to be (r^2) 0.9960. The developed method was found to be precise, as the % RSD value for repeatability and intermediate precision was less than 2.0%. Further, the percentage recovery was well within the ICH guidelines. We conclude that our work on developing a novel ATR-FTIR spectroscopic method was aimed at focusing on the implementation

of sustainable green analytical technique and it is a powerful process analytical technology tool for real-time monitoring of pharmaceutical formulations by enabling in-line qualitative and quantitative analysis of active medicaments and its formulations. It facilitates Quality by Design by providing instant, non-destructive data on process parameters. The technique allows for the monitoring of critical quality attributes to control pharmaceutical manufacturing processes, reducing process variations, and improving consistency. It supports continuous manufacturing by providing immediate feedback, replacing traditional time-consuming, offline, laboratory-based quality testing. Hence, the proposed method serves as an eco-friendly alternative tool by replacing conventional analytical methods developed with the aid of hazardous solvents with our no-solvent green technique without hindering method performance. The future scope of our work is to perform simultaneous analysis of ATN in combined dosage forms.

ACKNOWLEDGMENTS

The authors thank the management of Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation (Deemed to be University), Salem, Tamil Nadu, India, for providing all the facilities for the successful completion of this research work.

AUTHORS' CONTRIBUTIONS

Author Annapoorani Arjunan designed the research work and performed the analysis; author Ruby Stanlyraj drafted the data collection strategy and interpretation of results. Author Kumar Mohan helped in the critical revision of the research work.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

The authors hereby declare that no funding was received for this study.

REFERENCES

1. Sweetman SC. Martindale. London: Pharmaceutical Press; 2005. p. 865, 933, 47.
2. O'Neil MJ, Heckelman PE, Koch CB, Roman KJ, editos, The merck index - An encyclopedia of chemicals, drugs, and biologicals. 14ed. Whitehouse Station, NJ: The Merck Index, Merck and Co., Inc.; 2001. p. 147.
3. Ministry of Health and Family Welfare. Indian Pharmacopoeia, Controller of Publications. Vol. 4. New Delhi: Ministry of Health and Family Welfare, Government of India; 1996. p. 72-5.
4. Annapoorani A, Ruby S, Kumar M. Eco-friendly quantitative assessment of amlodipine besylate in its microspheres and commercial tablets using ATR-FTIR spectroscopy. Int J Drug Deliv Technol. 2025;15(3):1094-100.
5. Bansal R, Guleria A, Acharya PC. FT-IR method development and validation for quantitative estimation of zidovudine in bulk and tablet dosage form. Asian J Pharm Sci. 2011;4(3):306-13.
6. Konoz E, Sarrafi AH, Samadizadeh M, Boreiri S. Quantitative analysis of lorazepam in pharmaceutical formulation through FTIR spectroscopy. E-J Chem. 2012;9(2232):2238.
7. Bhoomendra B, Sirajunisa T, Sunil DA. Validated method for the quantitation of ciprofloxacin hydrochloride using diffuse reflectance infrared Fourier transform spectroscopy. Int J Spectrosc. 2014;12:1-6.
8. Patraa KC, Kumarb KJ, Sahooa SK, Suresha P. Rapid FTIR method for estimation of sucrose in a traditional Indian polyherbal formulation. Euras J Anal Chem. 2010;5:73-80.
9. Mazarevica G, Diewok J, Baena JR, Rosenberg E, Lendl B. On-line fermentation monitoring by mid-infrared spectroscopy. Appl Spectrosc. 2004;58(7):804-10.
10. Matkovic SR, Valle GV, Briand LE. Quantitative analysis of ibuprofen in pharmaceutical formulations through FTIR spectroscopy. Lat Am Appl Res. 2005;25:189-95.
11. Yilmaz B, Arslan S, Asci A. HPLC method for determination of atenolol in human plasma and application to a pharmacokinetic study in Turkey. J Chromatogr Sci. 2012;50(10):914-9. doi: 10.1093/chromsci/bms090, PMID 22718748
12. Kumar N, Verma N, Songh O, Joshi N, Singh KG. Estimation of atenolol by reverse phase high performance liquid chromatography. E J Chem. 2010;7(3):962-6.
13. El-Alfy W, Ismaiel OA, El-Mammli MY, Shalaby A. Determination of atenolol and trimetazidine in pharmaceutical tablets and human urine using a high performance liquid chromatography-photo diode array detection method. Int J Anal Chem. 2019;2019:9625849. doi: 10.1155/2019/9625849, PMID 30719043
14. Elkady EF, Fouad MA, Faquih AA. A versatile stability-indicating liquid chromatographic method for the simultaneous determination of atenolol, hydrochlorothiazide and chlorthalidone. Curr Pharm Anal. 2020;16(8):1037-51. doi: 10.2174/1573412915666190523122525
15. Madhusudhan P, Reddy KV, Singh SA. Novel isocratic RP-HPLC method development and validation for simultaneous determination of atenolol and nifedipine in tablet dosage form. Univers Rev. 2018;7(9):412-21.
16. Peleshok K, Piponski M, Kovalenko S, Ahmed H, Abdel-Megied A, Ezike OF. New liquid chromatography assays for simultaneous quantification of antihypertensives atenolol and valsartan in their dosage forms. J Sep Sci. 2021;44(2):565-75. doi: 10.1002/jssc.202000859, PMID 33226168
17. El-Gindy A, Emara S, Mostafa A. HPLC and chemometric-assisted spectrophotometric methods for simultaneous determination of atenolol, amiloride hydrochloride and chlorthalidone. Farmaco. 2005;60(3):269-78. doi: 10.1016/j.farmac.2004.11.013, PMID 15784248
18. Goebel K, Rolim CM. Validation of UV spectrophotometric and HPLC methods for quantitative determination of atenolol in pharmaceutical preparations. Lat Am J Pharm. 2007;26(5):760-5.
19. Vaikosen EN, Bioghele J, Worlu RC, Ebeshi BU. Spectroscopic determination of two beta blockers-atenolol and propanolol by oxidative derivatization using potassium permanganate in alkaline medium. Rev Anal Chem. 2020;39(1):56-64. doi: 10.1515/revac-2020-0103
20. Kori S, Goyal J, Sharma S, Pahade NK, Tandekar M. Method development and validation of atenolol drug by spectrophotometric and HPLC technique in forensic application. Int J Sci Res. 2013;4:438.
21. Al-Awadie NS, Khudhair AF. Determination of Atenolol in pharmaceutical formulations by continuous flow injection analysis via turbidimetric (T180o) and scattered light effect at two opposite position (2N90o) using Ayah 4SW-3D-T180-2N90- Solar-CFI analyser. Iraqi J Sci. 2014;55(1):12-26.
22. Madhurai P, Babu GR, Rao PS, Kiran BS, Kumari MV. Quantitative estimation of atenolol in pharmaceutical dosage forms by using visible spectroscopy. Int J Pharm Chem Biol Sci. 2015;5(3):557-60.
23. Annapoorani A, Ruby S, Kumar M, Bhuvaneswari R. Simple, rapid, and a green derivative ATR-FTIR spectroscopic method for the analysis of atenolol loaded microspheres and its tablet formulations. Biol Forum Int J. 2023;15(5):1051-7.
24. Fiveable. 18.8 Spectroscopy of Ethers. United States: Fiveable; 2024 May 7.
25. Almirall J. Quantitative analysis in drug formulations: methods, challenges, and innovations. Pharm Anal Chem. 2024;9:234.
26. Das S, Mandal S, Mandal S, Saha S. Design, development, and evaluation of vildagliptin-loaded crosslinked sodium alginate and *Moringa* gum microspheres by ionotropic gelation method and *in silico* study using pk-sim software. Asian J Pharm Clin Res. 2026;19(2):97-107.
27. Al-Tahami K. Preparation, characterization, and *in vitro* release of ketoprofen loaded alginate microspheres. Int J Appl Pharm. 2014;6(3):9-12.
28. Nayak AK, Pal D, Pradhan J, Hasnain MS. Fenugreek seed mucilage-alginate mucoadhesive beads of metformin HCl: Design, optimization and evaluation. Int J Biol Macromol. 2013;54:144-54. doi: 10.1016/j.ijbiomac.2012.12.008, PMID 23246901
29. Dey P, Sa B, Maiti S. Impact of gelation period on modified locust bean-alginate interpenetrating beads for glipizide delivery. Int J Macromol. 2015;76:176-80.
30. ICH. Q2A. Guidelines on validation of analytical procedure: Definitions and terminology. Fed Regist. 1995;60:11260.
31. ICH. Q2B. Guidelines on validation of analytical procedure: Methodology. Fed Regist. 1996;60:27464.
32. Indrani B, Ghosh SK. Development and validation of stability indicating RP-HPLC method for the determination of atenolol and hydrochlorthiazide in combined solid dosage form. Int J Pharm Pharm Sci. 2015;7(2):489-92.