

Quantitative Analytical applications of FTIR Spectroscopy in Pharmaceutical and Allied Areas

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ABSTRACT

Glancing at the recent advances, Fourier Transform Infrared Spectroscopy (FTIR) has emerged as a powerful analytical technique used in pharmaceutical sciences. This paper delineates FTIR as a quantitative tool used now-a-days and other analytical applications in pharmaceutical and allied areas. The use of FTIR is not only limited to pharmacy field, but had also widened its horizon to agriculture, polymer, petroleum and environmental analysis. This paper summarizes how FTIR is used to quantify different pharmaceutical dosage forms. Hence FTIR spectroscopy can turn out to be a potent alternative over other analytical methods which are time consuming and laborious.

Keyword: Applications, Baseline Method, Chemometrics, Fourier Transform Infrared Spectroscopy (FTIR), IR Spectroscopic Techniques, Quantitative Analysis, Vibrational Spectroscopy.

INTRODUCTION

Infrared spectroscopy, also referred as vibrational spectroscopy, is a standard method of analytical pharmacy and chemistry, providing the images of vibration of atoms of compound. It is one of the most common spectroscopic techniques used by organic and inorganic chemists. [1-4] It is based on the nature of interaction of the IR radiation with the vibrational modes of molecules. IR spectra are due to the changes in vibrational energy, accompanied by changes in rotational energy. [5] The absorption of IR radiation corresponds to energy changes on the order of 8-40 KJ/mole. [6] The pre-requisite for the molecule to interact with IR radiation is the presence of a permanent dipole which varies continuously in its magnitude. IR spectroscopy is fast, relatively inexpensive technique used to determine the chemical functional groups in the sample as different functional groups absorb characteristics frequencies of IR radiation and hence helps in structure elucidation. [7,8]

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The name of the region is derived from the fact that IR radiation is electromagnetic radiation in the wavelength region that is adjacent to and of less energy than visible radiation. [9] Due to unique fingerprinting capability of IR spectroscopy, the coupling with chromatographic method improves the analysis of complex mixtures. HPLC-FTIR is a high-throughput automatable hyphenated technique in burgeoning field of combinatorial chemistry. [10] Wide range of sample types such as solid, liquid and gas can be scanned from about 4000-400 cm^{-1} . This energy range is higher than necessary to promote molecules only to their lowest excited vibrational states and lower than typical values necessary for electron excitation in molecules. By use of modern instruments, infrared spectra of materials at low picogram level can be obtained. This ability of identifying materials under such a wide variety of conditions have entitled this technique as "work-house" of analytical sciences. [11,12]

INFRARED REGION

The frequency region of the electromagnetic spectrum between 12800 cm^{-1} and 10 cm^{-1} is known as IR region. The IR region is usually sub-divided into 3 regions based on the nature of interaction of radiation with molecules as well as the requirements of

instrumentation. The regions are given in Table 1 as follows: [2,3,5,13]

Table 1: IR Spectral Region

REGION	WAVELENGTH (μm)	WAVENUMBER (cm^{-1})	FREQUENCY (ν) Hz	APPLICATION
Near	0.78 – 2.5	12800 – 4000	3.8×10^{14} – 1.2×10^{14}	Quantitative analysis
Middle	2.5 – 50	4000 – 200	1.2×10^{14} – 6×10^{12}	Identification of functional group, Quantitative analysis, Detecting impurities
Far	50 – 100	200 – 10	6×10^{12} – 3×10^{11}	Analyze structure of molecule
Most used	2.5 – 15	4000 – 670	1.2×10^{14} – 2×10^{13}	Mostly Quantitative analysis

PRINCIPLE

At temperatures above absolute zero, all the atoms in molecules are in continuous vibration with respect to each other. When the frequency of a specific vibration is equal to the frequency of the IR radiation directed on the molecule, the molecule absorbs the radiation. The absorptions of infrared radiations causes an excitation of molecule from a lower to higher vibrational level. Each vibrational level is associated with a number of closely spaced rotational levels. The infrared spectra are considered as vibrational – rotational spectra. All the bonds in the molecule are not capable of absorbing infrared energy but only those bonds which are accompanied by a change in dipole moment will absorb in IR region. Such vibrational transitions are called as infrared active transitions. The vibrational transitions which are not accompanied by a change in dipole moment of the molecule are not directly observed and these are infrared inactive. IR spectra are obtained by detecting changes in transmittance (or absorption) intensity as a function of frequency. Most commercial instruments separate and measure IR radiation using dispersive spectrometers or Fourier transform spectrometers. Fourier transform spectrometers have replaced dispersive instruments for most applications due to their superior speed and sensitivity. They have greatly extended the capabilities of infrared spectroscopy and have been applied to many areas that were very difficult or nearly impossible to be analyzed by dispersive instruments. Instead of viewing each component frequency sequentially, as in a dispersive IR spectrometer, all frequencies are examined

simultaneously in Fourier transform infrared (FTIR) spectroscopy. [4, 14]

DIFFERENT IR SPECTROSCOPIC TECHNIQUES

Different techniques used to acquire IR spectra are described here. [15]

1. KBr Disc Technique:

Pellets are used for solid samples that are difficult to melt or dissolve in any suitable IR-transmitting solvents. The sample (0.5 to 1.0 mg) is finely ground and intimately mixed with approximately 100 mg of dry potassium bromide (or other alkali halide) powder. By applying sufficient pressure, the mixture is pressed into a transparent disc. Grounding the sample particles to 2 μm or less in size will minimize the band distortion due to scattering of radiation. The IR spectra produced by the pellet technique often exhibit bands at 3450 cm^{-1} and 1640 cm^{-1} due to absorbed moisture.

2. Attenuated Total Reflectance (ATR technique):

IR spectra of those samples that cannot be readily examined by the normal transmission method can be obtained by ATR spectroscopy. Mostly suitable for studying thick or highly absorbing solid and liquid materials, including films, coatings, powders, threads, adhesives, polymers, and aqueous samples. The sample is normally placed in close contact with a more-dense, high-refractive-index crystal such as zinc selenide, thallium bromide–thallium iodide (KRS-5), or germanium. ATR requires little or no sample preparation for most samples and is one of the most versatile sampling techniques.

3. Specular Reflectance:

This is a nondestructive method for measuring thin coatings on selective, smooth substrates without sample preparation. It basically involves a mirror like reflection and produces reflection measurements for a reflective material. Thin surface coatings in the range from nanometers to micrometers can be routinely examined with a grazing angle (typically 70 to 85°) or 30° angle of incidence, respectively.

4. Diffuse Reflectance (DRIFT spectra):

An alternative to pressed-pellet or mull techniques which is mainly used for acquiring IR spectra of powders and rough surface solids such as coal, paper, and cloth. Special reflection accessories are designed to collect and refocus the resulting diffusely scattered light by large ellipsoidal mirrors, while minimizing or eliminating the specular reflectance, which complicates and distorts the IR spectra. This energy-limited technique was not popular until the advent of FTIR instruments. This technique is often called diffuse reflectance infrared Fourier transform spectroscopy (DRIFTS).

5. Photoacoustic Spectroscopy (PAS):

An useful extension of IR spectroscopy, suitable for examining highly absorbing samples that are difficult to analyze by conventional IR techniques. The size and shape of the sample are not critical. PAS spectra can be obtained with minimal sample preparation and without physical alteration from a wide variety of samples such as powders, polymer pellets, viscous glues, single crystals, and single fibers.

General Applications of FTIR Spectroscopy

The areas where FTIR is applicable are listed below:

1. Agricultural / Food
2. Polymer
3. Petroleum and fuel industry
4. Environmental
5. Textiles
6. Biomedical / Clinical

7. Pharmaceutical and cosmetics

Agriculture / Food:

a) Prediction of soil macronutrients:

Yong he *et al.*, investigated the potential of near-infrared spectroscopy to estimate Nitrogen (N), Phosphorous (P), Potassium (P), Organic Matter (OM) and pH content in a loamy mixed soil. The spectral features of soil materials in the NIR spectral region are associated with vibration modes of functional groups that are overtones or the combination of vibration bands of light atoms that have strong molecular bonds. Hence it is possible to measure soil contents such as moisture, organic C and N using NIR technique. To correlate wavelength information with each constituent concentration, principal component analysis / partial least square (PCA / PLS) was used as multivariate analysis technique. Observing the regression coefficient results obtained we can say that, NIR spectroscopy is emerging technique that could be considered to have good potential for assessing soil N, OM and pH. NIRS could be useful in site as a rapid technique that could be combined with geographic information system (GIS) and precision farming principles application.^[16] Also Madari B. E *et al.*, analyzed soil samples for total C, N, sand, silt and clay composition.^[17]

b) Characterizing edible oils & fats:

N. Vlachos *et al.*, have extended the use of FTIR to the field of food research especially to study edible oils and fats. They have used FTIR for mainly 2 purpose: i) to determine adulteration of extra virgin olive oil and ii) to monitor oxidation process of corn oil samples. Here as mid-IR spectra are able to differentiate the intensity and exact frequency at which the maximum absorption of the bands appear according to nature and composition of sample, they are used to characterize edible oils and fats. A band shift observed due to C-H stretching vibration of the cis-double bond allows the determination of extra virgin oil adulteration and FTIR combined with discriminant analysis (DA) and PLS used to quantify this

adulteration. The oxidation of oil occurs when it is exposed to air, heating, light or catalyzers and this will facilitate the degradation process. Hence FTIR is used to measure the carbonyl compounds produced due to oxidation. [18]

Polymer:

a) Polymer Characterization:

Polymer products are not singular species, but rather, they are population of polymer molecules varying in composition and configuration. James L. Dwyer *et al.*, carried out polymer characterization by combined chromatography-infrared spectroscopy that provides benefits of resolving polymer population into discrete entities that can be identified. No other technique has the potential to provide as much information about polymer characterization as FTIR can provide. Characterization of distributed composition and structural properties is essential to optimize physical properties of polymer. The combination of LC-FTIR instrumentation coupled with the interpretative capabilities of infrared software greatly assists in interpretation of IR spectra and renders hyphenated LC-FTIR a practical working technique for polymer scientists and synthesis chemists. [19]

b) Degree of conversion in dental composites:

Moreas L.P.G *et al.* used FTIR as a tool for determining the degree of conversion (DC) in dental composites composed of at least two dimethacrylate monomers. The DC is determined by the proportion of the remaining concentration of the aliphatic C=C double bonds in a cured sample relative to the total number of C=C bonds in the uncured material. To determine DC two spectral infrared regions can be used; NIR or MIR. In the MIR region, DC is determined by measuring the intensity (or area) decrease of the methacrylate (C=C) stretch absorption band at $1,638\text{ cm}^{-1}$ as the methacrylate monomer is converted to polymer. In the NIR region, there are two aliphatic bands that can be used, one

at $6,165\text{ cm}^{-1}$ (overtone= CH_2) and the other at $4,743\text{ cm}^{-1}$. Hence, the study of conversion degree in dental composites by FTIR technique provides a better understanding of these materials, which is expected to optimize the polymerization process. This will result in improved dental restorations with aggregated higher quality and durability. [20]

Petroleum & fuel industry:

Michael D. Judge, investigated the viability of NIR spectroscopy technique for the quality control analysis of ingredient concentrations in rocket propellant fuel liquid pre-mix. The propellant pre-mix comprised of polybutadiene pre-polymer, a plasticizer and 2 antioxidants. Formerly, the pre-mix was tested for viscosity as a quality control test. So ameliorated method for monitoring correct ingredient ratios in the slurry was needed. Watching at the results of this study, it was ascertained that NIR spectroscopy offered a fast and convenient method of validating the % level of all 4 constituents while requiring no sample preparation. The NIR technique demoed a high level of accuracy and precision with an added advantage of allowing monitoring of antioxidants depletion in the pre-mix on ageing. [21]

Environmental:

Andreas Beil *et al.* used passive FTIR spectrometry for remote sensing of atmospheric pollution. It permits detection and identification of pollutant clouds in the atmosphere. In this study, the measurement technique and a data analysis method does not require a previously measured background spectrum are described. Here the ambient infrared radiation is detected. Passive remote sensing is the only detection method, which allows mobile, fast, man-held and stand-off detection of hazardous chemical agents. [22]

Textile:

Angela Allen *et al.* conducted analysis of cotton trash using FTIR. Botanical cotton trash including leaf, stem, hull, bark etc. poses a problem in processing efficiency

and quality of cotton throughout ginning and textile processing. Here FTIR spectroscopy is utilized to develop a database for classifying different trash found in cotton. The evaluation of cotton trash in mid-IR region of 4000 to 650 cm^{-1} has provided the means for development of a spectral database that distinguishes the type of cotton trash based on chemical composition. During ginning and textile processing, cotton trash undergoes different physical modifications that affect the FTIR spectroscopic properties. The application of reduction in particle size of trash and heat treatment led to changes in FTIR spectra revealing the complex arrangements within each trash and the irreversible loss of volatile components associated with water respectively. Hence results indicate that both thermal treatment and variations in trash particle size significantly affect the resultant FTIR spectra, which necessitates an expansion of the database to include these effects. [23]

Biomedical / Clinical:

FTIR spectroscopic imaging in ATR mode is a powerful tool for studying biomedical samples. Kazarian S. G. *et al.*, described recent advances in the application of ATR-FTIR imaging to dissolution of pharmaceutical formulation and drug release. Here two different ATR accessories to obtain chemical images of formulations in contact with water as a function of time are presented. The innovative use of diamond ATR accessory permitted in situ imaging of tablet compaction and dissolution. This was applied to obtain images of skin surface and spatial distribution of protein and lipid rich domains. The preliminary result of this study demoed the possibility of studying the skin surface in contact with topical formulations to probe the mechanism of transdermal delivery. This is for the first time that it has been possible to acquire FTIR images of arterial tissue in contact with solutions containing drug molecule. This approach may help in understanding the mechanism of treatment of atherosclerosis. [24]

Pharmaceutical & cosmetics:

a) Blend homogeneity:

Lyon R. C *et al.*, conducted a study to evaluate NIR spectroscopic imaging as a tool to access a pharmaceutical quality assurance problem – blend uniformity in the final dosage product. NIR spectroscopic imaging is a unification of digital imaging and molecular spectroscopy which helps providing a visual distribution of components within formulation. Contrastingly, traditional spectroscopy cannot directly determine the spatial distribution of components in final product. This study was carried out on the blend uniformity of furosemide and microcrystalline cellulose tablets prepared by deliberately varying the homogeneity of the components by NIR imaging and by traditional NIR spectroscopy. As a result, each grades of tablets were clearly distinguished quantitatively by NIR spectral imaging and traditional NIR spectroscopy demonstrating the power of this new imaging tool for assessing pharmaceutical quality assurance. [25]

b) Analysis of lard in cream cosmetics:

Abdul Rohman *et al.*, carried out analysis of lard in cream cosmetic formulations using FTIR spectroscopy and chemometrics. Lard rendered from fatty porcine tissue is the most powerful choice as viscosity enhancing agent in several cosmetic products which is prohibited for use by followers of some religions. So the authors developed FTIR spectroscopy combined with PLS and discriminant analysis (DA) for the quantification and classification of lard in creams. Hence FTIR emerged as a potential analytical technique for quantitation and classification of lard in cream cosmetics with total analysis time of about 3 min/one sample measurement. [26]

Quantitative Applications Of IR Spectroscopy In Pharmacy

Historically, the practice of finding the drug content in pharmaceutical formulations comprises of analytical

methods with the disadvantage of time consuming and laborious processes for straining the drug from complex matrix and sample preparation. To overcome this hurdle, diverse spectroscopic methods have been applied to evaluate the drug content in formulations.

[27] Quantitative analysis of the components in pharmaceutical preparations is based on the Beer-Lambert's law. [28]

Here are mentioned some quantitative applications of FTIR spectroscopy in different pharmaceutical formulations.

1. Juanita Hughes *et al.*, developed a rapid quantification technique of methamphetamine (MA) using ATR-FTIR and chemometrics to help detect the drug by vigilance agencies. As GC/MS methods used for this work earlier was lengthy and expensive, a new analytical method was developed. 96 illicit drug seizures containing MA were analyzed using FTIR-ATR combined with PLS model. It was seen that principal peak PLS model gave an excellent RMSEP and r^2 which shows best correlation between the currently used UPLC-UV method and this new proposed FTIR-ATR method was even more impressive. [29]

2. Okan Atay *et al.*, described quantitative determination of disulfiram containing pharmaceuticals by IR spectroscopy and HPLC methods. In this study, KBr disc technique was used and dehydrocholic acid (DHCA) was employed as internal standard. The specific absorption bands at 914 and 1705 cm^{-1} were chosen for DSF and DHCA respectively. For HPLC method mefrusid was chosen as internal standard and it was separated from DSF by isocratic system from the mobile phase mixture of methanol-phosphate buffer. The suggested methods of IR and HPLC were compared with each other and also with official method in BP 1999 for DSF. The results acquired were compared with student's t test and Fisher F test statistically and indicated that they were statistically insignificant. Hence the suggested

method could be used as an alternative method in solid dosage form containing DSF as the active compound. [30]

3. Pandey S. *et al.*, proposed a simple, accurate and sensitive spectroscopic method for the assay of ciprofloxacin in tablet by least square treatment of FTIR data obtained at the wavenumber corresponding to the -CO group centered at 1707 cm^{-1} . The method comprises of extraction of the active ingredient with methanol followed by phosphate buffer pH 6. The method was validated and the parameters were found to be highly satisfactory, indicating linearity, selectivity, precision, accuracy, robustness and adequate detection and quantification limit. However, the statistical results were also compared with the other techniques reported in literature and were found to be similar to all methods. Thus, present method opens possibility of applying IR spectroscopy to quantify other ingredients than ciprofloxacin. [31]

4. O. Atay *et al.*, discussed the method for the quantitative determination of amlodipine (AMP) in solid dosage form by IR spectroscopy. KBr disc was used and disulfiram was used as internal standard. The specific absorption bands at 693 and 913 cm^{-1} were selected for AMP & DSF respectively. Baseline technique is used for quantitative determination which is based on Beer's law where in P_B and P_0 points of absorption peaks are assigned. The regression equation was constructed using AMP/DSF concentration ratio as (X) values and the ratio of $\log P_B - \log P_0$ of AMP and $\log P_B - \log P_0$ of DSF as (Y) values. In HPLC method, mefrusid used as internal standard and separation was achieved using mobile phase mixture of water-methanol-phosphate buffer. Recovery experiments were conducted to determine the accuracy of proposed methods. The results obtained were compared using student's t test and Fisher F test statistically and were found insignificant. [32]

5. Mehtap Gokceet *al.*, described IR, UV spectroscopy and HPLC method for quantitative determination of amisulpride (AMS) in dosage form. For IR method, dehydrocholic acid was used as internal standard. The specific absorption bands at 1057 and 1705 cm^{-1} were chosen for AMS and DHCA respectively. Baseline technique was employed for quantitation based on Beer's law where in P_B and P_0 points of absorption peaks are assigned. In HPLC method, AMS is determined by gradient system in the mobile phase consisting of methanol and phosphate buffer using atenolol (ATN) as an internal standard. For U.V method, 280 nm was chosen as λ_{max} for determination. The results obtained from all 3 methods were compared by student's t-test and Fisher F test statistically and found to be almost equivalent. So IR spectroscopy can be used as an alternative technique for quantitation.^[33]
6. Ashok Peepliwal & Bansal R *et al.*, studied IR and UV spectroscopic methods for the quantitation of Zidovudine (AZT) from solid dosage form. In IR method, KBr disc technique was used and ursodeoxycholic acid (UDCA) was used as internal standard. The absorption bands at 2105 and 2931 cm^{-1} were chosen for AZT and UDCA respectively. The baseline technique as described earlier was used here for quantitation. The values of P_B and P_0 were calculated using infrared spectrum of samples and equation of regression was constructed. For U.V method 266 nm was chosen as λ_{max} . Also the validations of both methods were carried out and the results were compared with each other. The results of both methods were insignificant and demonstrate that IR spectroscopy is superior to other methods in terms of cost, solvents, columns and time needed.^[34,35]
7. Aline L. H. M. *et al.*, developed a method for simultaneous determination of clavulanic acid (CA) and amoxicillin (AMO) using FTIR-ATR. 27 samples were used as calibration set and 8 samples were used for prediction set. Calibration models were developed using PLS, interval PLS (iPLS), synergy PLS (siPLS) and backward PLS (biPLS). Relative standard error of prediction (RSEP) were obtained using biPLS algorithm for ATR/FTIR data. Results obtained by the proposed methodology were compared with those using HPLC and no significant differences were obtained. These results were in agreement with range allowed to the content of CA and AMO in power mixtures according to USP requirements for solid preparations. Thus, the proposed method was characterized to be less onerous, simple, solvent free, fast and reliable, allowing potential applications to simultaneous determinations of CA and AMO in solid pharmaceutical formulations for routine analyses.^[36]
8. Mazurek S. *et al.*, carried out quantification of diclofenac sodium (DS) in tablets using PLS models based on FTIR-ATR and FT-Raman spectra. Separate calibration models were built for 2 groups of tablets, standard and sustained release, containing different excipients and the RSEP were calculated and compared. It is apparent from the presented results that the quality of the constructed models noticeably depended on the homogeneity of the API distribution in the preparations. Although both methods used effectively modelled the concentration-dependent changes in the spectral data, in the case of ATR technique, it was necessary to repeat measurements at least a few times to obtain acceptable quantification errors.^[37]
9. Mohsen zeeb *et al.*, developed an on-line system with vapor-phase generation (VPG) and FTIR spectrometric detection as a direct and highly selective analytical technique for the assay of Penicillamine (PA). The CO generated under these conditions was transported by means of N_2

gas carries stream to an infrared gas cell and corresponding FTIR spectra were acquired in a continuous mode. Initially, the effect of different chemical, physical and spectroscopic parameters, such as concentration and volume of oxidant, pH, equilibrium time, reactor temperature, reactor volume, N₂ carrier flow rate and number of scans on the analytical signals were evaluated by using a short path length (10 cm) IR gas cell. At optimum experimental conditions, a relatively broad linear dynamic range, a limit of detection, a sampling frequency and a relative standard deviation (R.S.D.) was calculated. Further, the method was successfully applied to the determination of PA in pharmaceutical formulations and results compared well with those obtained by a reference colorimetric method.^[38]

10. Mahdi Sadeghi *et al.*, performed on-line VPG followed by FTIR for the quantitative analysis of water-soluble penicillin G in pharmaceutical formulations. Analytical measurements were made using the maximum absorbance of the -CO band at 2170 cm⁻¹. Various factors influencing the analytical signals were evaluated and selected. The proposed method involves calculation of linear calibration curve, LOD and a precision. The on-line system, which includes a relatively speedy oxidation of PENG to carbon monoxide with potassium iodate, reduces sample handling and omits the use of toxic reagents. In addition, the proposed method allows for an efficient matrix removal, thus reducing potential interferences. This fact is very important, and contrasts with serious interfering effects reported in the traditionally colorimetric, spectrophotometric and electrochemical methods.^[39]

11. Mazurek S. *et al.*, applied FTIR-ATR, DRIFT and FT-Raman spectroscopy for the quantification of thiamine HCl, or vitamin B₁ in tablet and was compared. PLS models were built & calibrated

and RSEP was calculated and demoed that the methods used were promising. Although all three proposed procedures can be efficient and reliable alternatives to the standard pharmacopoeial methods of vitamin B₁ quantification in solid dosage forms due to high sensitivity, low quantification errors and economic factors, it is our opinion that DRIFT spectroscopy has the highest potential to become a routine technique for the quantification of solid multi-component systems within the pharmaceutical industry.^[40]

12. A. Van Overbeke *et al.*, used FTIR-ATR to quantify ketoprofen in some pharmaceutical formulations. The ampoules were analyzed as such and a simultaneous estimation of ketoprofen and arginine base was performed. A PLS software package was applied to the calibration and prediction for a limited no. of standard solution. FTIR-ATR together with PLS quantification show promise for verifying the label-claimed content of the ingredients in simple pharmaceutical formulations within the stipulated analytical limits.^[41]

13. Moreno A. H. *et al.*, described ceftazidime quantification by IR spectroscopy for pharmaceutical preparations in powder for injection. Here the measurements of absorbance bands corresponding to aromatic ring centered by 1475-1600 cm⁻¹ were made. Validation was carried out and parameters like selectivity, linearity, precision and accuracy were determined. The linear relationship between ceftazidime concentration and absorbance measurements were made when different amounts of the drugs were used to prepare translucent pellets. This study demonstrated good linearity, precision and accuracy which proved that IR could be employed for quantitation determination.^[42]

14. Nicolle F. R. *et al.*, mentioned a novel approach for the determination of azithromycin in pharmaceutical formulation by FTIR

spectroscopy in film-through transmission mode. This study involved the evaluation of several variables such as solvent, nominal resolution, no. of scans, mode of measurement and spectral region. The method was applied to the determination of azithromycin in 6 commercial pharmaceutical formulations & recovery test employed to evaluate the accuracy and LOD in acetonitrile was calculated. The results obtained evidenced that a rapid and efficient determination of azithromycin in formulations can be performed by FTIR in transmission mode. The dial path accessory used here allowed that the procedure be executed with a very low volume of solvent (1ml) and reduced amount of sample, making the methodology greener than other available methods.^[43]

15. Ravi Prasad P. *et al.*, developed a simple and rapid method for the quantification of domperidone (DMP) and paracetamol (PAR) through FTIR in combined dosage form. The proposed method involves the measurements of peaks of -CO group at 1656 (PAR) & 1717 (DMP) cm^{-1} . The U.V spectrometric method is also described for the same and the analytical results obtained with FTIR showed good correlation with U.V method. Hence the present investigation showed that the proposed FTIR method was found to be simple, rapid & reproducible and less time consuming compared to other methods.^[44]

16. M. Ali *et al.*, performed a simple, cost-effective and environmental friendly analytical method for quantification of erythromycin in tablet formulation using transmission FTIR spectroscopy for routine quality control analysis. The calibration was carried out by using beer's law in FTIR region. The regression equation was obtained from calibration of standard followed by calculation of concentration of active drug in samples and was found within permissible limits. RMSEP and RMSECV were calculated for verification of quantitation model. The statistics

of erythromycin recovery tests revealed high recovery performance and high precision which clearly proves the validity of proposed method.^[45]

17. Aftab A. K. *et al.*, developed a quick & reliable analytical method for the quantitative assessment of cefixime in oral pharmaceutical formulations by using diamond cell ATR-FTIR spectroscopy. The calibration model was based on PLS using fingerprint region of FTIR spectrum. Excellent r^2 values were achieved with RMSE for calibration. Good agreement of press values & RMSECV values was observed, which shows the suitability of developed method. The result of present work brings about substantial support in terms of efficiency, accuracy, straightforwardness and feasibility of FTIR spectroscopy for quantification of cefixime in formulations.^[46]

18. N. Oval *et al.*, discussed a simple & precise infrared spectroscopic method for the estimation of Alverine citrate in capsule dosage form. The study involved the preparation of KBr pellet & determination of the drug by absorbance & peak area method. This method was analyzed for specificity, LOD, LOQ, Linearity, precision and accuracy. Alverine citrate showed good linearity as indicated by excellent correlation coefficient value. The sample absorbance was interpolated on the respective linearity chart and the concentration was determined. The recovery studies indicated that there is no interference of other ingredients present in formulation and demod that the FTIR technique is facile for routine analysis.^[47]

19. Sherazi S. T. H. *et al.*, applied FTIR transmission spectroscopy for the estimation of roxithromycin in pharmaceutical formulations. Conventional KBr was used for forming pellets to acquire FTIR spectra in this work. The FTIR spectra opened to TQ analyst to generate the calibration model. A simple beer's law model based upon

measurement of ν -CO band area was applied for the quantitative determination. A fine calibration curve with excellent linear regression was gained and the errors were evaluated by calculating RMSEC. The % difference in concentration of roxithromycin determined by FTIR and labeled on the tablets/capsules was within acceptable limits which demonstrates feasibility of FTIR as quantitative tool for analysis.^[48]

20. S. R Matkovic *et al.*, developed and validated the method quantification of ibuprofen in tablet dosage form. This study involves the extraction of the active ingredient with chloroform & the measurement of the area of the infrared band. The specificity, linearity, detection limits, precision and accuracy of the calibration curve, ibuprofen extraction, infrared analysis and data manipulation were determined in order to validate the method. The results were also compared with the quantification of ibuprofen by UV spectroscopic method. The values of recovery obtained were within the range. This technique extends the use of standard IR spectrophotometric method, typically used for identification purpose, to the reliable quantification purpose.^[49]

21. Ahmed S. *et al.*, described the quantitative analysis of Tolfenamic acid (TA) both as a pure compound and in tablet dosage form by FTIR and UV spectroscopy. In FTIR, a number of characteristic absorption peaks were examined and analyzed by preparing calibration curves of peak height/area versus TA content using 2 points baseline correction with fixed location and PLS regression model. In UV method, ethanolic solutions of the drug were analyzed at 288 nm. Then, the results were compared statistically for recovery, precision, accuracy & linearity with the B.P titration method & showed good recovery of TA. Hence statistical evaluation suggested that the 2 methods can be employed in Q.C of TA in

pharmaceuticals as an alternative to the titration method.^[50]

22. Konoz E. *et al.*, investigated the potential of FTIR spectrometry to quantify lorazepam in pharmaceutical preparations. The procedure was developed for fast and accurate determination of lorazepam in formulation by using beer-lambert law while reducing sample pre-treatment & providing direct measurement. Off-line extraction of lorazepam with sonication was carried out followed by direct determination in the extract through peak height measurement using baseline correction. Results obtained by FTIR were in full agreement with those obtained by a reference methodology based on UV spectrometry and thus developed procedure that offers good alternative for the determination of lorazepam in commercial products.^[51]

23. Rohman A. *et al.*, employed FTIR spectroscopy for the quantitative analysis of simethicone (SMT) in chewable tablet and suspension by determination of polydimethylsiloxane (PDMS). SMT analysis is carried out by FTIR spectroscopy due to the lack of chromophore. It quantifies PDMS component of SMT by comparing the typical spectral band for PDMS with the external standard of known concentration. As the extraction procedure used for sample preparation causes sample loss, therefore FTIR spectroscopy method have been developed and validated for linearity, sensitivity, accuracy and precision. The results obtained for precision and recoveries for SMT were within the acceptable range as stated in compendium.^[52]

CONCLUSION

Looking at the work described above we can conclude the straight forwardness and feasibility of FTIR spectroscopy in quantitation of pharmaceutical dosage forms. FTIR serve as a non-destructive, highly sensitive, highly specific and robust analytical technique by which almost any solid, liquid or gas

sample can be analyzed with little or no sample preparation procedure without using any expensive, toxic solvents and reagents, so it is economical as well as an environmentally friendly technique. FTIR is a rapid technique compared to HPLC, it consumes much lesser time, bypasses the mobile phase preparation, running and column washing time. For many drugs not containing the chromophoric group, it is very difficult to develop a method by UV or HPLC due to its molecular structure, but a method can be easily developed by using IR for such drugs.

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