Applications of FTIR Spectroscopy: Review

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ABSTRACT: FTIR spectroscopy is powerful optical spectroscopy based on vibration measurement of an excited molecule by IR radiation at a specific wavelength range, which identifies the vibration characteristics of chemical functional groups in a sample. It is a fast and non-destructive analytical method.However it is suitable for analysis of solid, liquid and biotechnological pharmaceutical forms. Fourier-transform infrared (FTIR) spectroscopy has become a valuable analytical technique for structural or functional studies related to foods as a rapid, cost-efficient, and sensitive physicochemical fingerprinting method. FTIR is used to determine among structural and geometric isomers, identify all types of organic and many types of inorganic materials, quantify species in difficult mixtures, determine the molecular composition of surface species, and identify molecular orientation in polymers and solutions. This review focuses on pharmaceutical FTIR applications used for qualitative and quantitative analysis. The FTIR is helpful to identify and quantify the active constituents. It is also advanced in analysis of biomedical, food, drug and counterfeit drugs.

KEYWORDS: FTIR Spectroscopy, Counterfeit drug analysis, Biomedicals

INTRODUCTION

The measurement of infrared light absorption (or transmission) by a material as a function of wavelength is known as infrared (IR) spectroscopy (or frequency). The IR spectrum is produced as a plot of absorption (or transmission) versus wavelength (or frequency). The fundamental heat spectrum of materials, which is principally caused by molecular vibrations and their corresponding rotating absorption bands, is examined using infrared spectroscopy. [1]The IR spectroscopy was the first structural spectroscopic technique and is an analytical method which is used to characterize the bonding structure of atoms based on the interaction of the IR radiation at which the substance absorbs and lead to the production of vibration in molecules. It gives the techniques for identification and characterization of chemical structures to obtain information from biological to composite materials, from liquids to gases. [3]The basic principle of IR is measurement of amount of IR radiation by absorption, emission or reflection. It is also called as vibrational spectroscopy. It is widely used for structural elucidation of molecules. The spectral regions can be divided into further 3 regions; the FAR Infrared (400-10 cm^{-1}), MIDInfrared (4000-400 cm^{-1}), NIR (13000-4000 cm^{-1}). It is based on the absorption pattern of other compounds including isomers. When reference spectra available, most compound can be obvious identified on the basis of spectra of IR. [2]

Most widely used IR is MIR, but remaining both can also provide important information. FTIR is real time measurement analytical method and non-destructive technique, which is unable to identify the unknown compounds (quantitative determination) and their corresponding concentration (qualitative determination) from liquid, gas or solid samples. During vibrations, there is change in the dipole moment. In this case we can called as IR active substances and a radiation corresponds to a change in dipole moment. For IR inactive substances, the dipole moment is zero, there is no matter how long the bond is in the molecule (IR -active; polar bonds, asymmetric molecules. IR inactive; non-polar bond, symmetrical molecule).In IR each chemical bond has a very specific vibrational frequency which is corresponding to an energy level.

$E=h\nu=hc/\lambda$

Where,

h=planks constant

ν =frequency,

c=speed of light,

λ= wavelength. [3]

The IR spectra of an organic compound provide a unique fingerprint, which can be readily distinguished from the IR absorption pattern of other compounds including isomers.

PRINCIPLE AND WORKING:

Michelson Interferometer:

In FTIR spectrometer, there are two beams Michelson interferometer is present, which is shown in the following figure1. It consists of two mirrors which is mutually perpendicular to each other,in which one is fixed and another is movable. There is source and detector also present. A beam is emitted by a source and splits ittwo by beam splitter .The reflected part of the beam travels to the fixed mirror, is reflected there and heat the beam splitter again. The sample will get transmitted. Because the two splitted beams are spatially coherent, they interfere on recombination. The beam, modulated by the movement of the mirror, leaves the interferometer

and finally focused on the detector. The signal is then detected by detector, the interferogram, is thus radiation of intensity of the combined beams as a function of the movable mirror. The conversion of interferogram into a spectrum is done by using Fourier transformation. One of the most essential steps for obtaining an FTIR spectrum are First; to produce an interferogram with and without a sample in the beam, second; to transforms these interferograms into spectra of the source with and without sample absorption. Then the ratio of first and second is the IR transmission spectrum of the sample. The values produced by the interferogram, which is a function of time, are referred to as the time domain. To create a frequency domain, which is then Fourier analyzed to produce a spectrum, the time domain must first undergo Fourier transformation.

A typical FTIR spectrometer is made up of a source, an interferometer, a sample compartment, a detector, an amplifier, an A/D converter, and a computer. The sample passes through the interferometer and arrives at the detector as a result of radiation from the source. The signal is subsequently boosted and transformed into a digital signal by an amplifier and an analog-to-digital converter, respectively. Finally, a computer receives the signal and executes the Fourier transform on it. Figure 1 illustrates the block diagram of an FTIR spectrometer. [4]

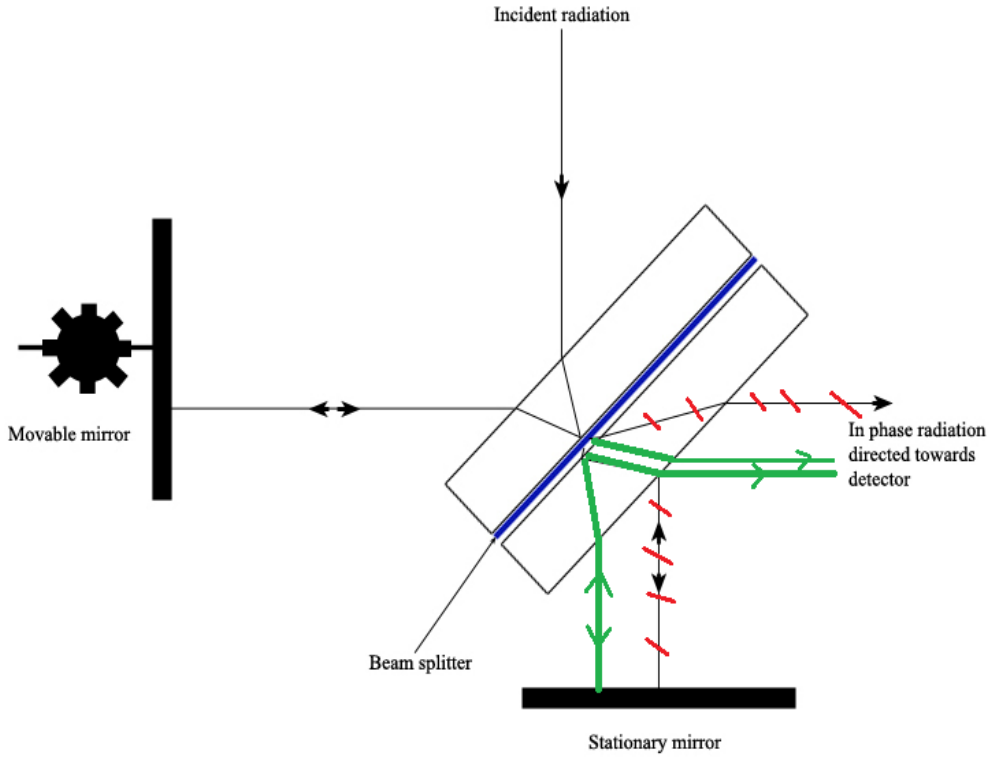

Figure No-1: Schematic diagram of Interferometer

APPLICATIONS OF FTIR SPECTROSCOPY IN PHARMACEUTICAL ANALYSIS:

FTIR has always been and continues to be a crucial spectroscopic method to learn important structural information about organic molecules. Characterization of functional groups and the mid-IR area is where detection is primarily focused. (4,000-400 cm−1). Consequently, organic chemists relied on deeply on the virtues of the IR spectra's quality and mostly a diagnostic has been done using the data collected necessary. The identical method has been distributed once more as a strong tool for quantitative measurement

List of selected drugs and pharmaceutical dosage forms analysed using FTIR spectroscopy

(Khairi Mustafa fahelelbom, abullah saleh ,moawia M.A Al Tabakha and akram A Ashames ;recent applications of quantitative analytical FTIR spectroscopy in pharmaceutical,biomedical,and clinical fields: A brief view)

Table No 1: List of selected drugs and pharmaceutical dosage forms analysed using FTIR spectroscopy

Sr No.	Analysed drug	Sr.No	Analysed drug
A]	Antiparasitic	**E]**	Antihypertensive
1.	Artemether and lumefantrine	**1**	Amlodipine besylate
2.	Thiabendazole	**2**	Cilnidipine
3.	Toltrazuril	**3**	Atenolol
4.	Artemisinin (antimalarial)	**4**	Furosemide

B]	Antibiotics	**F]**	Antidiabetic
1	Kanamycin sulphate	**1**	Teneligliptin
2	Amoxicillin	**2**	Acarbose
3	Aztreonam	**3**	Gliclazide
4	Doxycycline	**G]**	Counterfeit drug product
5	Amikacin	**1**	Counterfeit paracetamol tablet
6	Erythromycin	**2**	Counterfeit pharmaceutical and herbal preparation
7	Ciprofloxacin	**H]**	Narcotics and psychotropics drug
8	Ampicillin sodium	**1**	Levosulpiride
C]	Analgesic/anti-inflammatory	**2**	Methamphetamine
1	Diclofenac sodium	**3**	Cocaine
2	Acetaminophenand ibuprofen	**I]**	Miscellaneous
3	Etodolac, tolfenamic acid	**1**	Mycophenolate mofetil (immunosuppressive agent)
4	Ibuprofen and paracetamol	**2**	Pharmaceutical products
D]	Antivirals	3	Herbal medicine
1	Acyclovir tablet		
2	Efavirenz		

Characterization of functional groups and the primary focus of detection is the Numerous studies investigated into the invention of FTIR analytical techniques for the quantitative analysis of various pharmacological groups in pure form and some pharmaceutical dosage forms due to their low cost, high accuracy, and precision (above table). Although less precise, the FTIR employed in the simultaneous analysis of the caffeine, paracetamol, and aspirin content in tablet dosage form was shown to be suitable as liquid chromatography (HPLC) [5] Furthermore, FTIR spectroscopy was found to have advantages over HPLC that were simpler, faster, and more premium. Future generations will have the capacity.

1. Analysis of herbal medicine by FTIR:

The IR spectrum is a conventional research technique for determining the structure of organic compounds since it contains a wealth of structural data. FTIR spectroscopy has been expanding quickly recently, in part because it is less expensive, easy to use, and produces results quickly. The use of FTIR systems in the assessment of herbal quality analysis has expanded as a result of the development of FTIR techniques and their combination with quantitative or computer systems such two-dimensional correlation analysis [6]. The quality and amount of raw herbal materials can be controlled using FTIR, and various applications have been evaluated [7]. Using IR spectroscopy to measure the flavonoid content of medicinal plant extracts indicates an easy and reliable economical tool. When used in combination with advanced chemometrics, IR spectroscopy is capable of producing analytical data that is comparable to that produced by a number of other time-consuming, labor-intensive, and costly spectroscopic and chromatographic techniques.

Partial least square and linear discriminant analyses have been used to calibrate and identify the flavonoid content of various extracts of medicinal plant leaves (by means of ultrasonication and maceration) [8].

2. The utility of FTIR in the detection of counterfeit drugs:

Many counterfeit pharmaceutical preparations have been identified and found using FTIR and other IR spectroscopy techniques. Neves et alstudy's [9] shown that the FTIR approach may be used to identify a diversity of anabolic steroid samples, and their findings suggested that the FTIR method is rapid, reliable, and suitable to substitute GC-MS methods in the analysis of Durateston® to identify fake products. In a different study, Lawson et al. [10] looked into counterfeit paracetamol tablets from several countries. The authors came to the conclusion that ATR-FTIR can carry out the following fake tablets without the use of solvent extraction. Furthermore, FTIR was successfully used in the quality control and counterfeit detection of various anti-diabetic medications [11].

3. Characterization of Diamond by using FTIR:

A natural diamond and a fake diamond can be distinguished from one another using FTIR spectroscopy. The three-phonon region (4000-2600 cm^{-1}) for intrinsic diamond and B or H in diamond, the two-phonon region (2600-1500 cm^{-1}) for diamond and B in diamond, and the one-phonon region (1500-400 cm^{-1}) for N or B impurity in diamond are possible divisions of the diamond FTIR spectrum. There are certain peaks in the 4000-1500 cm^{-1} region that may be the result of the diamond lattice's C-C bonds vibrating. The absorption bands in the spectral range 2700 - 1600 cm^{-1} (centered at about 2500, 2380, 2030, and 1970 cm^{-1}), which are caused by carbon itself, describe the spectrum for pure natural diamond. Diamond type I nitrogen can be given to the bands between 1500 and 1000 cm^{-1}. The FTIR spectrum shows peaks at about 1280 cm^{-1} (IaA) and 1175 cm^{-1}(IaB) for aggregated N impurities (type Ian), and at 1345 cm^{-1} and 1135 cm^{-1} for isolated N (type Ib). The diamond type II may contain a variety of impurities or adsorbed gases with unaggregated nitrogen or with hardly discernible nitrogen (hydrogen, boron). (6) Diamond-absorbed hydrogen's C-H

stretch vibrational mode is responsible for peak values between 3500 and 2600 cm^{-1}. In the spectrum of boron absorbed on diamond, it is distinguished by peaks about 2800–2460 cm^{-1} that are attributed to boron. [12]
A fake diamond is Zirconia (ZrO2), synthetic Moissanite (SiC), Yttrium aluminium garnet (YAG), etc. from a chemical perspective. The garnet spectrum contains peaks at 800-400 cm1 that can be attributed to the Y-O and Al-O vibration mode, while the zirconia spectrum lacks an absorption band in the range 4000-1200 $cm^{-1,}$ synthetic Moissanite is characterized by peaks in the range 2400-1200 cm^{-1}, with intensity lower than in the case of a natural diamond, a garnet spectra present. [13]

4. Application of FTIR in Food:

4.1 Meat analysis

It is being developed a methodology for FTIR spectroscopy to quickly analyze the fat and protein content in sausage emulsions. Basic regulatory standards must be met by sausage formulations, and if performed incorrectly, they may need to be costly revised. By adding a warm, diluted base to ground meat and mixing it for one minute (using a device like a Polytron), it is able to transform the mixture into an emulsion that resembles milk. After blending the resultant solution and passing it through a 40 pm CaF transmission cell or onto an ATR plate, the spectrum can be recorded and the absorbance of the solution's primary constituents (fat and protein) can be quantified analysis.According to preliminary results [14] it is possible to quantify the amount of fat, protein, and total solids in ground beef with an accuracy of ±0.2% in comparison to values obtained by standard rules and an analysis time of -5 min/sample. It would be easier for the industry to use an FTIR method if reconstitute, shelf-stable, calibration meat standards were developed. These can be made using pre-analyzed, freeze-dried meat combinations that are then reconstituted and used to calibrate the instrument or perform calibration checks, as has been done for meat analysis**.[**15**]**

4.2. Fats and Oils

An AOCS Official Method uses dispersive infrared spectroscopy to identify solitary tram linkages in fats and oils (AOCS, 1989). Because samples can be evaluated neatly, using FTIR spectroscopy significantly simplifies this procedure from a sample handling perspective. Moreover, it has been demonstrated that the FTIR approach offers greater accuracy, a considerable reduction in overall analysis time (2.5 min/sample), and is implementable[16] The determination of the iodine value (IV) and saponification number (SN), two crucial parameters in the fats and oils processing business, can be time-consuming using the conventional procedures. Although the results from this early work with dispersive instruments and transmission sampling methods demonstrated the potential utility of this approach, its application has been restricted **[**17**]**. The idea of using IR spectroscopy as a method of quickly determining IV has been around for some time. Samples provided by a vegetable oil processor or purchased locally were evaluated in duplicate for IV and SN by the FTIR method as well as by a more adaptable FTIR/ATR method based on peak height measurements [18**].**On a heated (65°C) ATR crystal, the samples were analyzed neatly, with the analysis and prediction times for both IV and SN being in the range of 2 mm/sample. With a significant reduction in analytical time and effort, the IV and SN readings obtained by FTIR were within k3.0 and 2.5 units, respectively, of the chemical values, sufficient for regular quality control tests.
It will probably eventually be further uses for FTIR spectroscopy in the analysis of fats and oils. A clear candidate is the analysis of oil degradation using the peroxide value. When oil is heated over an ATR crystal, the peroxide peak in the FTIR spectrum grows over time, which indicates that the initial peroxide load can be measured and the oil's future sensitivity to oxidation tracked. In a manner similar to the active oxygen method, oxidation of oil can therefore be simulatively performed under controlled conditions on an ATR crystal. It is possible that FTIR may be used to carry out a number of typical fat and oil analyses simultaneously. [19]

5. Application of Fourier Transform Infrared Spectrophotometry in Pharmaceutical Drugs Analysis:

For the quick and accurate analysis of acetylsalicylic acid (**ASA**) in various pharmaceutical goods, a Fourier transform infrared spectrometric method was created [20]. The best way to identify the active ingredient in medication mixtures was determined by comparing conventional KBr spectra. Data processing included the use of Beer-law Lambert's and the main components regression (PCR+) and partial least squares (PLS) chemometric procedures. The authors investigated whether it would be possible to quantify ASA in pharmaceutical products at 1,605.49 cm1 using the Beer-Lambert law. The authors recommend using the PCR+ approach due to the extremely similar results and the lower relative standard deviation (RSD; 3.0 percent).
Ascorbic acid (vitamin C) and biotin (vitamin H) were quickly and accurately measured using FTIR spectrometry in various pharmaceutical goods. To identify the active ingredients in medication formulations, conventional KBr spectra were examined. In the data processing, the Beer-Lambert law and chemometric techniques were used [21]. For a large number of higher primate species [22], which make about 20% of all mammalian species, as well as a small number of other species like the guinea pig and a few species of birds and fish, vitamin C is an essential nutrient. An ureido (tetrahydroimidizalone) ring united with a tetrahydrothiophene ring makes up the water-soluble vitamin H or B7.

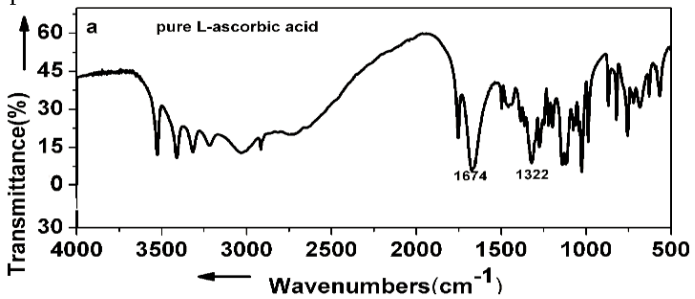

Figure No 2: Vitamin- C FTIR SPECTRUM

Because carbamazepine is poorly soluble and has known bioavailability issues related to its polymorphism, during medication formulation, a form (C-monoclinic or form IV) that is less soluble than the pharmaceutically acceptable (P-monoclinic or form III) can arise. The drug formulators therefore value the quantitative study of form IV in form III. By using DRIFTS spectral data

modified using the standard normal variate transformation (row centering and scaling) and the lazy learning algorithm, a quick and easy nondestructive approach for measuring form IV in form III was created [26]. Diffuse reflectance FTIR spectroscopy in combination with contemporary multivariate calibration techniques, such as support vector machines (SVMs), lazy learning (LL), and partial least squares prediction. In this investigation, the quantification of carbamazepine crystal forms in ternary powder combinations (I, III, and IV) was done using partial least squares (PLS) regression [23]. Using the Kennard-Stone methodology, the data were divided into training and test subsets for two spectral regions (675-1,180 and 3,400-3,600 cm1). It was discovered that all of the chosen algorithms outperform PLS regression (RMSEP, or root mean square error of prediction) by values ranging from 3.0 to 8.2 percent.

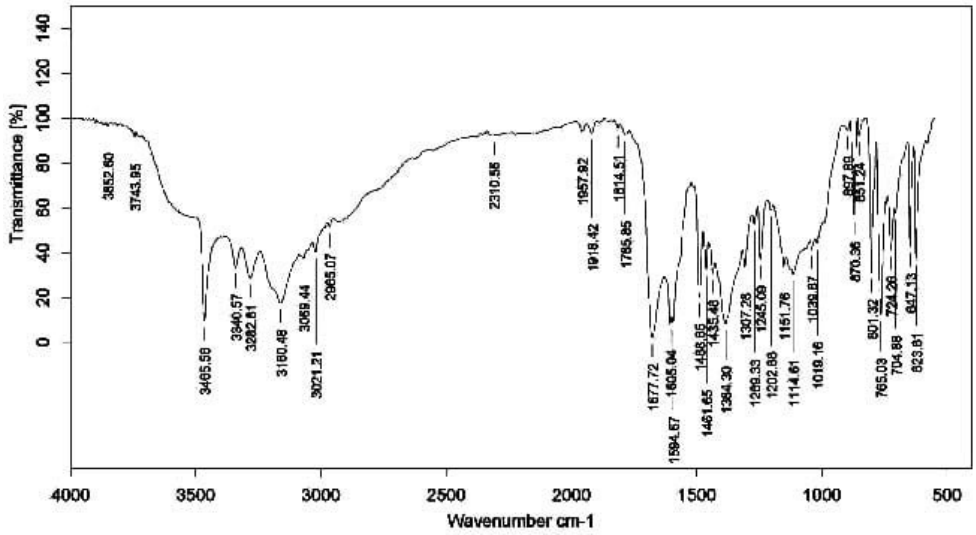

Figure No 3: FTIR SPECTYRUM OF CARBAMAZEPINE

6. FTIR Appliance in the Legitimacy and Detection of Food Adulterants:

The certification, verification, and authenticity of produce should be clearly defined by its variety, commodity, or geographical origin as expensive ingredients are more susceptible to fraud, adulteration, or unintentional mislabeling. This has been an extremely important point for regulatory agencies, retailers, food processors, and especially for consumers. A unique, quick method that legalizes these claims is therefore in need in this day and age. In this crucial scenario, FTIR has emerged as a promising technique that can be used to analyze herbal goods, fruit juices, dairy, agricultural products, edible oils, and other items. It can be used as FT-Near-Infrared and FT-Mid-Infrared using a variety of statistical approaches. FTIR has that is seen as being its finest benefit from a regulatory standpoint. FTIR has a wide range of advantages, including a short processing time (only 1 to 2 minutes), the capable of recognizing a large number of adulterants with a single spectrum, and the lack of sample preparation needed due to its rapid speed. As a result, it produces the least amount of waste. Additionally, it preserves the sample, which is deemed to be one of its major regulatory advantages. [24].

6.1. Adulteration in natural oils:

Dietary supplement oils (DSOs), such as grape seed oil, evening primrose oil, burageseed oil, and flax oil, are contaminated with cheaper and less beneficial oils, which is a tragic situation that has led to both a food safety and a food quality issue. Since different brands of the same oil can have different variants due to selection, processing methods, and plant origin, including oil types with fundamentally comparable compositions or identical creations, misclassifications of genuine oils can occur. DSOs are allegedly being 2 to 20 percent v/v contaminated with less expensive cooking oils [25].

6.2 Adulteration in juices :

Juices, syrups, and purees have been identified as outstanding candidates for the detection of adulteration using FT-NIR spectroscopy. For further financial advantage, these products are occasionally contaminated with syrups, corn, cane, beet sugars, and less expensive juice concentrates. Researchers used FT-NIR and factorial discriminant analysis to establish that grapefruit juice, orange pulp-wash, and an artificial sugar/acid blend have been used to adulterate orange juice [26].

6.3 Adulteration in honey:

The adulteration of sugars refutes the claim that honey is a distinctive material made by honeybees, and it is frequently seen that adulteration in common markets occurs when honey is diluted with either simple or complex sugars [27]. Due to adulterants' imitation of honey's natural sugar profile, which consists of 31.2 percent glucose and 38.2 percent fructose, it is difficult to distinguish between adulterants and pure honey. Because honey can vary greatly depending on the climate, flower, kind of bees using it, development, storage, and processing conditions, adulteration can also be difficult to spot. The time-consuming and expensive carbon isotope ratio test is now used to determine how transparent honey is. Thus, the FT-MIR approach is used to verify the authenticity of honey, but the spectra must be corrected against a water background in order to accurately make water signals overlap the signals of the solute. The analysis was focused on the area (800-1500 cm1) where the sugars communicate. Typically, 7 to 25 percent of invert sugar, glucose, sucrose, and fructose are added to honey to make it sweeter. PLS and LDA data compression, respectively, were entirely successful in classifying complicated and simple sugars. The achievement rate dropped to 95.5 percent as a result of combining the honey from several assortments, which require more components. To combine honey from various origins and with numerous adulterants, more effort must be done [28].

7. Applications of FTIR spectroscopy in the biomedical field:

The study of biology and medicine has found great use using FTIR [29]. Monitoring based on chemical composition and changes at the micro level are made possible by the spatial resolution reached [30]. Thus, real-time tracing allows for the observation of biological processes like the cell cycle, necrosis, or apoptosis. It was also shown that using this technique, enzymatic tests can be carried out with the right experimental setup. The method was used to conduct real-time investigations into a number of bioprocesses.

The following are some appealing FTIR characteristics in biomedical configurations:

- ✓ The availability of highly developed instrumentation.
- ✓ It is useful to have strong data processing software.
- ✓ The technique's lack of destructiveness.
- ✓ For thorough analysis using relatively simple sample preparations, few samples are needed.
- ✓ Quick and flexible for online measurement modalities.
- ✓ Fairly inexpensive price and service.
- ✓ High spatial resolution with equivalent pixel density without SNR degradation.
- ✓ The substance being tested does not require staining, labeling, or the addition of any contrast agents.
- ✓ FTIR as a cancer screening and diagnostic tool: a review and prospects [32]
- ✓ Vibration spectroscopy fingerprinting in medicine: from molecular to clinical practice [33]
- ✓ FTIR: applications in medicine [29]
- ✓ Applications of FTIR spectrophotometry in cancer diagnostics [34]
- ✓ Using Fourier transform IR spectroscopy to analyze biological materials [35]
- ✓ ATR-FTIR spectroscopic imaging: recent advances and applications to biological systems [36]

CONCLUSIONS:

The present review expresses that FTIR technique analyses different biomedicals, food, and counterfeit drug with high output, zero impurity, rapid cost analysis. It also applicable for API quality control. This review on FTIR technique will be useful for herbal analysis which helps in understanding in available application.

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