

Review Article

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Recent applications of quantitative analytical FTIR spectroscopy in pharmaceutical, biomedical, and clinical fields: A brief review

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Abstract: Qualitative Fourier transform infrared (FTIR) spectroscopy has long been established and implemented in a wide variety of fields including pharmaceutical, biomedical, and clinical fields. While the quantitative applications are yet to reach their full potential, this technique is flourishing. It is tempting to shed light on modern engaging and the applicability of analytical quantitative FTIR spectroscopy in the aforementioned fields. More importantly, the credibility, validity, and generality of the application will be thoroughly demonstrated by reviewing the latest published work in the scientific literature. Utilizing FTIR spectroscopy in a quantitative approach in pharmaceutical, biomedical, and interdisciplinary fields has many undeniable advantages over traditional procedures. An insightful account will be undertaken in this regard. The technique will be introduced as an appealing alternative to common methods such as high performance liquid chromatography. It is anticipated that the review will offer researchers an update of the current status and prospect on the subject among the pharmacy and biomedical sciences both in academic and industrial fields.

Keywords: FTIR spectroscopy, quantitative analysis, qualitative analysis, pharmaceutical, biomedical

1 Introduction

For decades, several well-known spectroscopic techniques have been successfully employed for laboratory analytical purposes including material analyses. Until recently, the infrared (IR) spectroscopy has been mainly used in analytical chemistry applications for qualitative outcomes, that is, to obtain general and wide analytical qualities of a broad range of samples. However, recent development in chemometrics and software algorithms enabled efficient artificial intelligence techniques in association with evolution of sophisticated instrumental technologies, and hence, IR spectroscopy has been proved as a powerful quantitative analytical technique [1]. Fourier transform infrared (FTIR) spectroscopy represents a modern and popular technique that reintroduced IR spectroscopy as a powerful and reliable analytical technique. IR spectroscopy is a result of molecular absorption of energy from a passing electromagnetic radiation in the IR frequency regions. Absorption of energy leads to several excited molecular vibrational and rotational states. The resultant spectrum is unique and highly characteristic. Recent FTIR technique developments rendered the tool as applicable to both quantitative and qualitative purposes of analyses [2,3].

1.1 Regions of IR radiation

The frequency region of the spectrum between 12,500 and 10 cm⁻¹ is known as the IR region. It is subdivided into three regions as presented in Table 1 [4].

1.2 Sample preparation for IR spectroscopy

Current FTIR spectrometers enable obtaining the spectrum of almost all types of samples. Additionally, both methodologies, transmission or reflectance spectra, can

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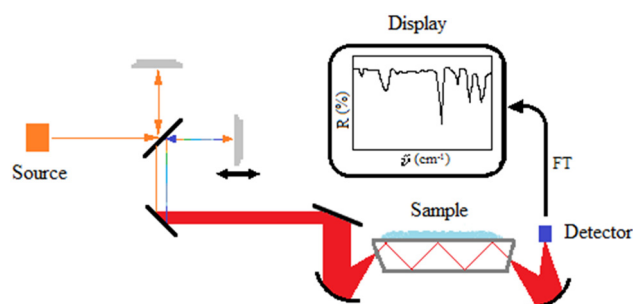
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Table 1: List of infrared regions

IR radiation range	Far-infrared	Middle-infrared	Near-infrared
Wavelength range (μm)	50–100	2.5–50	0.78–2.5
Wavelength number (cm^{-1})	200–10	4,000–200	12,500–4,000

be easily recorded for samples with little or no preliminary preparations [1]. Classically, in traditional spectrometers, the sample must be mixed with an inert and IR silent alkali halide such as KBr (or KCl) in a ratio of 1:100 by mass. The mixture is then pressed under tremendous pressure (10,000 psi) to produce a disk or glass pellet. However, the procedure might suffer from structural alterations due to the high pressure used or the hygroscopic nature of the pressed material that might also cause water or humidity absorption. Moreover, a mull is a less invasive sample preparation. In a mull, the sample is dispersed in Nujol which is a mineral oil. Nevertheless, other oily chemicals such as fluorolube and hexachlorobutadiene were found practically valuable [2,5]. In the Nujol sample preparation procedure, solid samples are finely ground and mixed with the oil. The sample is then placed between two plates of a metal halide that is IR transparent. Accordingly, the procedure eliminates the need for high pressure that might alter the sample composition in some cases. In spite of that, the oil itself has substantial interferences and strong IR absorbance bands. Diffuse reflectance IR Fourier transform spectroscopy is a sampling procedure in which the sample is diluted with KBr or KCl matrices. The optimum mixing ratio is around 1–5% w/w analyte. Unlike Nujol oil, metal halides are non-absorbing in any of the IR regions. The technique is also applicable to liquid or solute samples through dissolving the sample in a volatile solvent. The sample is then applied to a KBr disk followed by evaporating the solvent. When an IR radiation collides with the sample in this technique, it will be absorbed, reflected, and diffracted. The diffusely reflected radiation provides invaluable structural vibrational information assuming a powdered sample having consistent particle size. A modern and more versatile sampling technique relies on applying the sample on an IR-transmitting crystal made of Ge or ZnSe with high refractive index. The technique is known as attenuated total reflectance (ATR). For solid samples, an intimate contact of the sample to the crystal is maintained throughout the measurement. The spectrum is recorded from the passing and sample penetrating IR radiation directed through the crystal. As such, the technique requires little or no sample preparations [5], as shown in Figure 1. Coupled with an optical microscope, the FTIR spectrometers are capable of simultaneously

**Figure 1:** Schematic diagram of ATR-FTIR spectrometer.

recording chemical and physical properties of tiny quantity of samples [6]. Key advantages of the technique include the fact that a valuable spectrum can be recorded for an area as small as $10\ \mu\text{m} \times 10\ \mu\text{m}$, that is, the effective limit of the IR radiation. A spectrum can be recorded for samples through either reflectance, transmittance, or ATR modes. The requirement for a small amount of a sample is also an appealing advantage.

2 Merits of FTIR spectroscopy

The signal-to noise ratio (SNR) of a peak in an IR spectrum is a vital measure of spectral qualities. Modern spectrometers are equipped with powerful software algorithms that reveal this ratio on the spectrum. SNR is defined by Eq. 1:

$$\text{SNR} = \text{Signal/Noise} \quad (1)$$

FTIR spectrometers are characterized by allowing us to record spectra with higher SNRs compared to traditional spectrometers. Basically, the signal quality is determined by the amount of radiation hitting the detector. Lighter radiations bring about better spectra qualities. As such it is typical to obtain an SNR of 100 or higher by modern FTIR spectrometers. The amount of light beam reaching the detector is measured by throughput. Non-FTIR spectrometers suffer relatively low SNRs. The reason might be attributed to the fact that the beam in such instruments needs to pass through slits, prisms, gratings, and gets reflected by many mirrors. Consequently, substantial amount of beam intensity will be

lost in the process. New FTIR spectrometers devoid the passing of light beam through all these parts, which lead to keeping the IR beam received by the detector intense, hence greatly enhancing the signal resolution levels.

Multiplex or Fellgett advantage is another valuable characteristic of the FTIR spectrometers [7]. The concept can be simplified by expressing SNR as:

$$\text{SNR} \propto t^{1/2} \quad (2)$$

where t is the time spent observing the intensity of the light. Moreover, according to Eq. 2, increasing the time term (t) can be achieved by adding a number of scans together (N : number of added scans) rather than recording only a single one. Typically, an average spectrometer can record around 50 scans every minute. Since N is proportional to time, Eq. 2 can be rewritten as Eq. 3:

$$\text{SNR}N \propto t^{1/2}, \quad (3)$$

where N is the number of scans.

Equation 3 nicely explains the Multiplex or Fellgett advantage. In practice, the SNR of recording an FTIR spectrum by one scan only can be enhanced to tenfold improvement by simply recording and adding 100 scans.

The resolution of FTIR spectrometers is comparably much higher than that of traditional instruments. Resolution is a measure of wavenumber precision and reproducibility [8]. The use of a LASER as an internal standard allows recording an IR spectrum with a wavenumber resolution up to a precision of 0.01 cm^{-1} .

The prevalence and popularity of FTIR spectrometers in most laboratories worldwide might be attributed to the abovementioned advantages. A spectrometer allowing 10–100 times better SNR will be a highly appealing choice over classical instruments [2].

3 Applications of FTIR spectroscopy in pharmaceutical analysis

FTIR has been and is still an indispensable spectroscopic technique for gaining significant structural information of organic molecules. Functional group characterization and detection is mainly centered at the mid-IR region ($4,000\text{--}400 \text{ cm}^{-1}$). Consequently, organic chemists relied profoundly on the qualitative merits of the IR spectra and collected data have been used mainly for a diagnostic necessity. The same technique has been reintroduced as a powerful tool for quantitative determinations.

Table 2: List of selected drugs and pharmaceutical dosage forms analyzed using FTIR spectroscopy

Analyzed drugs/group	Citations
Antiparasitic	
Artemether and lumefantrine (antimalarial drugs)	[11]
Antiparasitics: thiabendazole, febantel, toltrazuril, and fluazuron	[12]
Artemisinin (antimalarial drug)	[13]
Antibiotics	
Kanamycin Sulfate	[10]
Amoxicillin	[14]
Aztreonam	[15]
Doxycycline	[16]
Amikacin	[17]
Erythromycin	[18]
Azithromycin	[19]
Ciprofloxacin tablets	[20]
Ampicillin sodium	[21]
Ceftazidime in powder	[22]
Analgesics/anti-inflammatory	
Diclofenac sodium	[23]
Acetaminophen and ibuprofen	[24]
Anti-inflammatory drugs: etodolac, tolfenamic acid, bumadizone, and diacerein	[25]
Tolfenamic acid	[26]
Ibuprofen and paracetamol	[27]
Antihypertensives	
Amlodipine besylate	[28]
Cilnidipine	[29]
Atenolol	[30]
Furosemide(diuretic)	[31]
Antidiabetic drugs	
Teneligliptin	[32]
Acarbose	[33]
Gliclazide	[34]
Antivirals	
Acyclovir tablet	[35]
Efavirenz	[36]
Counterfeit drug products	
Counterfeit paracetamol tablets	[37]
Counterfeit pharmaceutical and herbal preparations (Mini review)	[38]
Narcotic/psychotropic drugs	
Levosulpiride (antipsychotic)	[39]
Methamphetamine	[40]
Cocaine (narcotic and psychotropic)	[41]
Methamphetamine	[42]
Miscellaneous	
Mycophenolate mofetil (immunosuppressive agent)	[43]
Pharmaceutical products (review)	[44]
Group of pharmaceutical drugs (review)	[9]
Number of pharmaceutical products (review)	[45]
Herbal medicine review	[46]

Pharmaceutical analysis has been the major beneficiary recipient sector. The basic principle behind the

quantitative nature of the technique is attributed to the fact that the quantized absorption of energy by analytes at certain wavelengths is directly proportional to the concentration of functional groups present [9].

Due to their low cost, high accuracy, and precision, many researchers investigated the development of FTIR analytical techniques for the quantitative analysis of different pharmacological groups in pure form and certain pharmaceutical dosage forms (Table 2). The FTIR used in the simultaneous analysis of the content of tablet dosage form containing caffeine, paracetamol, and aspirin was found to be appropriate as high performance liquid chromatography (HPLC), although with lower sensitivity [10]. On the other hand, the merits of FTIR spectroscopy were noted to be simpler, faster, and economical compared to HPLC. It will be possible in the future to extend the area of pharmaceutical applications to study content uniformity of unit solid dosage forms and measure the degree of solid material dryness.

3.1 Analysis of herbal medicine by FTIR

IR spectrum contains abundant structural information and has become a classic analytical method for the structure of organic compounds. Currently, FTIR spectroscopy has been growing rapidly due to but not limited to, rapid workmanship, high repeatability, easy to operate, and less expensive. Development of FTIR techniques and combined with math or computer systems such as two-dimensional correlation analysis makes an increased the use of FTIR system in the evaluation of herbal quality analysis [46]. A review on how FTIR is used to control the quality and quantity of herbal raw materials as well as some applications has been reported [47]. Determination of flavonoid content in medicinal plant extracts using IR spectroscopy signifies a simple and steadfast economical tool. In combination with refined chemometrics, IR spectroscopy can be endowed to obtain analytical data comparable to several other time-consuming, accompanied by tedious procedures, costly spectroscopic and chromatographic techniques. Flavonoid content in several extracts of medicinal plant leaves (by means of ultrasonication and maceration) has been calibrated and classified by partial least square and linear discriminant analyses, respectively [48].

3.1.1 The utility of FTIR in the detection of counterfeit drugs

FTIR and many IR spectroscopic techniques have been used in the identification and detection of many counterfeited

pharmaceutical preparations. A study by Neves *et al.* [49] showed that the FTIR method can be used to detect many samples of anabolic steroids and their results indicated that the FTIR method is fast, reliable, and suitable to replace GC-MS methods used in the analysis of Durateston® to detect counterfeiting. In another study, counterfeit paracetamol tablets from different countries were investigated by Lawson *et al.* [50]. The authors concluded that ATR-FTIR can identify counterfeit tablets rapidly without the need for solvent extraction. Furthermore, FTIR was employed successfully in the counterfeit detection and quality control of some antidiabetic drugs [51].

4 Applications of FTIR spectroscopy in the biomedical field

4.1 Clinical applications

FTIR has evolved as a valuable technique in the fields of biology and medicine [52]. The spatial resolution attained allows for monitoring chemical composition alterations and changes in a subcellular level [53]. Accordingly, biological activities such as cell cycle, necrosis, or apoptosis can be observed in real-time tracing. It was also demonstrated that enzymatic assays can be accomplished with the appropriate experimental set up by this technique. Several bioprocesses were probed by the technique in a real-time approach [54–56]. In Section 5, some representation of recently published research will be introduced to demonstrate the applicability of quantitative FTIR in biomedical (medicinal, clinical, and biological) scenarios.

Recently, numerous articles appeared in the scientific literature that are devoted to the medical diagnostic capability of vibrational FTIR spectroscopy. Table 3 highlights most of the well-recognized literature survey outcome.

FTIR and other vibrational spectroscopic techniques are still in the experimental and research phase concerning biomedical fields. Serious drawbacks and limitations hindered its success regardless of the well-recognized features of the technique. The following are the attractive features of FTIR in biomedical setups:

- (1) Availability of sophisticated advanced instrumentation.
- (2) Powerful data processing software is handy.
- (3) The non-destructive nature of the technique.
- (4) Small samples are required for complete analysis with relatively easy sample preparations.

Table 3: Selected publications on the medical diagnostic capability of vibrational FTIR spectroscopy

Title	Citations
FTIR as a cancer screening and diagnostic tool: a review and prospects	[57]
Vibrational spectroscopy fingerprinting in medicine: from molecular to clinical practice	[58]
FTIR: applications in medicine	[52]
Applications of FTIR spectrophotometry in cancer diagnostics	[59]
Using Fourier transform IR spectroscopy to analyze biological materials	[60]
ATR-FTIR spectroscopic imaging: recent advances and applications to biological systems	[61]
Clinical application of FTIR imaging: new reasons for hope	[62]
Vibrational spectroscopic mapping and imaging of tissues and cells	[63]

- (5) Fast and adaptable to online measuring modes.
- (6) Relatively low cost and service.
- (7) High and comparable spatial resolution without fading the SNR.
- (8) No need to stain, label, or add any contrast reagents to the sample under testing.

However, since biological living samples are complex, substantial drawbacks and limitations render the technique inapt for medicinal, biological, or clinical applicability. Hence, the technique in its current status did not find its way among the arsenal of spectroscopic diagnostic techniques. Biological samples consist of plenty of molecules including water, lipids, proteins, nucleic acids, and sugars. Water in specific has an abundant IR activity, resultant interferences cannot be avoided or pose a great deal of complexity. Minimizing water effect was discussed in detail by Bonnier et al. [64]. Hence, recent *in vivo* studies brought promising results, though most suffer low reproducibility and vague statistical analysis outcomes.

Research groups around the globe have been active in overcoming biomedical applicability barriers of FTIR. Impressive development has been achieved particularly in issues related to sample preparation, selection, or pre-treatment. Notable progress has been made employing FTIR coupled with complementary analytical methods or techniques such as X-ray fluorescence microscopy.

Optimizing FTIR for disease diagnosis purposes poses a perplexing process in terms of best sample selection [65]. Several publications have appeared recently to exclusively address this crucial aspect. Table 4 gives a glimpse of those undertaking biofluid samples.

Early diagnosis of diseases by IR spectroscopy is an attractive appeal to clinicians and health care developers. Several active research groups have been exploring the practicality and applicability of testing and monitoring disease progression. FTIR spectroscopy may be used in the future by non-spectroscopist to interpret images in the diagnostic field, provided that appropriate software is developed to address this need. Table 5 lists the most prominent published literature during the past decade.

5 Applications of FTIR spectroscopy in the biological field

5.1 Protein imaging

Recent progress of chemometrics and FTIR spectroscopy enabled researchers to explore the feasibility of the technique to acquire insight information about proteins. Protein molecules are complex by nature, hence current techniques

Table 4: Selected publications on using FTIR spectroscopy for biofluid analysis

Title	Citations
Body fluids	
Vibrational spectroscopy in body fluids analysis	[66]
The detection and discrimination of human body fluids using ATR-FTIR spectroscopy	[67]
Improved protocols for vibrational spectroscopic analysis of body fluids	[64]
Vibrational spectroscopy of biofluids for disease screening or diagnosis: translation from the laboratory to a clinical setting	[68]
FTIR spectroscopy of biofluids revisited: an automated approach to spectral biomarker identification	[69]
Human and animal cell	
Vibrational spectroscopic methods for cytology and cellular research	[70]

Table 5: Selected publications on using FTIR spectroscopy for early diagnosis of diseases

Disease	Title	Citations
COVID-19	Spectroscopy as a tool for detection and monitoring of coronavirus (COVID-19)	[71]
Brain cancer	Development of high-throughput ATR-FTIR technology for rapid triage of brain cancer	[72]
Fatal hypothermia and hyperthermia	Biochemical detection of fatal hypothermia and hyperthermia in affected rat hypothalamus tissues by FTIR	[73]
Oral cancers	A comparative profiling of oral cancer patients and high risk Nisar users using FTIR and chemometric analysis	[74]
Multiple sclerosis	Relapsing–remitting multiple sclerosis diagnosis from cerebrospinal fluids via FTIR coupled with multivariate analysis	[75]
Leukemia	Probing the action of a novel anti-leukemic drug therapy at the single cell level using modern vibrational spectroscopy techniques	[76]
Breast cancer	Application of FTIR spectroscopy on breast cancer serum analysis	[77]
Skin cancer	FTIR spectroscopy study in early diagnosis of skin cancer	[78]
Ewing sarcoma of bones	FTIR spectroscopy of paraffin and deparaffinized bone tissue samples as a diagnostic tool for Ewing sarcoma of bones	[79]
Cervical cancer	ATR-FTIR and multivariate analysis as a screening tool for cervical cancer in women from northeast Brazil: A bio spectroscopic approach	[80]
Breast cancer	FPA-FTIR microspectroscopy for monitoring chemotherapy efficacy in triple-negative breast cancer	[81]
Bipolar and schizophrenia	FTIR spectroscopy and multivariate analysis as an auxiliary tool for diagnosis of mental disorders: Bipolar and schizophrenia cases	[82]
Breast cancer	Chemotherapeutic response to cisplatin-like drugs in human breast cancer cells probed by vibrational microspectroscopy	[83]
Oral cancers	Recurrence prediction in oral cancers: a serum Raman spectroscopy study	[84]
Ovarian cancer	Segregation of ovarian cancer stage exploiting spectral biomarkers derived from blood plasma or serum analysis: ATR-FTIR spectroscopy coupled with variable selection methods	[85]
Galactosemia	Rapid screening of classic galactosemia patients: a proof-of-concept study using high-throughput FTIR analysis of plasma	[86]
Lidocaine in urine	Determination of lidocaine in urine at low ppm levels using dispersive microextraction and ATR-FTIR measurements of dry films	[87]
Cervical cancer	Cervical cancer detection based on serum sample Raman spectroscopy	[88]
Lung cancer	FTIR spectroscopic comparison of serum from lung cancer patients and healthy persons	[89]
HIV/AIDS	Mid-ATR-FTIR spectroscopic profiling of HIV/AIDS sera for novel systems diagnostics in global health	[90]
Venereal cancer	Progress in FTIR spectroscopic imaging applied to venereal cancer diagnosis	[91]
Colorectal cancer	Evaluation of FTIR spectroscopy as diagnostic tool for colorectal cancer using spectral analysis	[92]
Aging	Variability of protein and lipid composition of human substantia nigra in aging: FTIR microspectroscopy study	[93]
Urinary calculi	Analysis of the chemical composition of urinary calculi using FTIR: A preliminary study	[94]
Gliomas	Investigating the rapid diagnosis of gliomas from serum samples using infrared spectroscopy and cytokine and angiogenesis factors	[95]
Lung cancer	Detection of lung cancer tissue by attenuated total reflection-FTIR- a pilot study of 60 samples	[96]
Leukemia	Distinction of leukemia patients' and healthy persons' serum using FTIR spectroscopy	[97]
Ovarian cancer	FTIR spectroscopy coupled with a classification machine for the analysis of blood plasma or serum: a novel diagnostic approach for ovarian cancer	[98]
Renal failure	Diagnosis of renal failure by infrared spectrometric analysis of human serum samples and soft independent modeling of class analogy	[99]
Breast cancer	ATR-FTIR spectroscopic imaging for breast histopathology	[100]
Atherosclerosis	Protein profile in the vascular wall of atherosclerotic mice analyzed <i>ex vivo</i> using FTIR spectroscopy	[101]

(continued)

Table 5: (continued)

Disease	Title	Citations
Kidney stone	The establishment of a standard and real patient kidney stone library utilizing FTIR spectroscopy with a diamond ATR accessory	[102]
Chronic hepatitis C	Noninvasive assessment of hepatic fibrosis in patients with chronic hepatitis C using serum FTIR	[103]
Lesions in aorta	Imaging of lipids in atherosclerotic lesions in aorta from ApoE/LDLR/mice by FTIR spectroscopy and hierarchical cluster analysis	[104]
Autoimmune-mediated demyelination	Early detection of the chemical changes occurring during the induction and prevention of autoimmune-mediated demyelination detected by FTIR imaging	[105]
Lung cancer	Evaluation of FTIR spectroscopy as a diagnostic tool for lung cancer using sputum	[106]
Diabetes	FTIR spectroscopy in diagnosis of diabetes in rat animal model	[107]
Prostate cancer	Investigating FTIR based histopathology for the diagnosis of prostate cancer	[108]
Lymph node	Spectral detection of micrometastases in lymph node histopathology	[109]
Lung cancer	Infrared spectroscopy characterization of normal and lung cancer cells originated from epithelium	[110]
Quantification of plasma creatinine	Toward point-of-care diagnostic metabolic fingerprinting: quantification of plasma creatinine by infrared spectroscopy of microfluidic-processed samples	[111]
Barrett esophagus and esophageal adenocarcinoma	Characterization of Barrett esophagus and esophageal adenocarcinoma by FTIR microscopy	[112]
Fetal lung maturity	Comparison of IR spectroscopic and fluorescence depolarization assays for fetal lung maturity	[113]

are used to study these molecules from every corner. It is essential to have a highly resolved 3D protein structure to recognize these molecules' mechanisms of action. Additionally, several drugs are protein active site-based designs, hence, fully resolved structures became immensely important for rational drug design approaches. FTIR spectroscopy has also been applied to investigate several therapeutic proteins [114].

Currently, X-ray diffraction is the technique of choice to study crystallizable proteins. Obtaining a highly resolved 3D structure of proteins by this powerful method has inherently few drawbacks. Preparing a well-diffracting crystal of proteins can be time-consuming and challenging [115]. Furthermore, the technique will be inadequate for solutions of proteins. Their preparation will surely be concomitant with severe denaturing. Furthermore, the protein will tend to aggregate at higher concentrations. This will ultimately be reflected in the resolution of structures obtained [116]. Several cases and techniques demonstrated that the surfaces encountered throughout the protein isolation process have a great effect on protein performance, an effect that is still requires more investigated research studies [117].

One more limitation of the current analytical protein imaging techniques considering X-ray is that the images obtained are in a static mode. It is well-established that proteins are dynamic catalysts that change their conformations constantly. These techniques will be blind-sided to such dynamics, while protein conformations are essential for its function.

FTIR spectroscopic techniques have gained attention due to its non-invasive and fast nature to explore proteins and several other biological materials [118] including DNA [119], carbohydrates, and lipids [120]. It is also applied to explore biological tissues [121–123], cells [124], or whole organisms [125,126]. Additionally, the technique accompanied by chemometric data analysis was employed to monitor drug target binding processes [127].

Due to the inherent limitations of current analytical techniques to obtain highly resolved quaternary structures of proteins as mentioned above, the FTIR spectroscopy provided an appealing alternative. A successful story that might demonstrate the attractiveness of FTIR spectroscopy when it provides an economic, affordable alternative has been published recently [128]. In this work, Devlin et al. have provided manufacturers and regulators with a high-quality analysis approach of crude heparin. In early 2008, the world witnessed a heparin crisis. Baxter produces half of the world supply of heparin. A contaminated lot initiated a cascade of unexplained side effects associated with heparin therapy that resulted in about 350 adverse events and more than 150 deaths in the US alone. Several other countries suffered similar occurrences that generated international attention. The FDA in collaboration with pharmaceutical industry laboratories and an international consortium immediately launched a mission to identify the responsible contaminants. The analytical tests used to identify the toxin and detect any differences

between the suspected and reference heparin samples included optical rotation, capillary electrophoresis, and 1D $^1\text{H-NMR}$ [129]. Only then, over sulfated chondroitin sulfate was recognized as the contaminant responsible for the crisis [130].

In a recently published article [71], the authors, Khan and Rehman, argued that viral and bacterial proteins or even antibody proteins created as a response of the immune system can be efficiently detected by various vibrational spectroscopic techniques. The global fight against the SARS-CoV-2 (COVID-19) pandemic has been greatly hindered by the lack of reliable, rapid, and economic detection and monitoring testing protocols. The current standard testing of the virus is based on polymerase chain reaction principles. The test relies on the viral DNA amplification followed by detection. However, although the test is highly sensitive, it is time-consuming, and requires tedious sample preparation and lengthy procedures. The bacterial and viral infection detection based on various spectroscopic techniques and in particular IR has never been so crucial. The development of rapid and cost-effective, real-time monitoring capabilities, rigorous, and sensitive diagnostic techniques will tremendously strengthen the global fight against highly contagious merciless COVID-19. The authors emphasized that an IR or Raman spectroscopy-based methodology will not only have the potential of rapid diagnostic capabilities but also viral monitoring and drug designing. The monitoring process will reveal viral infection pathways. Consequently, a collective understanding of viral invasion can be determined and understood.

5.2 Drug efficiency monitoring

FTIR spectroscopy approach of enabling biomedical scientists to track biological processes and drug efficiency within samples has never been so accessible. Additionally, the technique can detect such processes on a molecular level [131].

It might be insightful to demonstrate this perspective by the work of Sundaramoorthi et al. [132]. The authors provided an interesting methodology to monitor the efficacy of metformin hydrochloride while treating type-2 diabetic patients. They were able to use a single human hair fiber to compare results obtained for pre- and post-treatment with healthy population. Results showed that significant and statistically validated differences of associated diagnostic biomarkers were obtained based on FTIR measurements.

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