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IR-Eco Spectra: Exploring Sustainable Exsitu & In Sity FTIR Application For Green Chemical & Pharmaceutical Analysis.

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ABSTRACT

Fourier transform infrared spectroscopy (FTIR) spectroscopy provides a unique ability to detect and characte rize complex chemicals in many industries, especially in medicine and pharmaceuticals, while reducing wast e and reducing the need for extensive modeling or use of hazardous chemicals to minimize environmental da mage. This review demonstrates the wide range of ex situ and in situ FTIR applications for species identificat ion, characterization, and quality monitoring. The accuracy of ex situ FTIR spectroscopy in identifying impur ities, monitoring crystallization processes, and modifying dosage forms can improve product quality, safety, and performance. In addition, its many capabilities, all based on green screening standards, have contributed to drug development, drug use processes, and quality control. On the other hand, in situ FTIR spectroscopy a ppears to be a new tool for real-

time investigation of drug reactions and processes, monitoring drug release kinetics, crystallization kinetics, and surface contact, and provides valuable information. The combination of ex situ FTIR accuracy and in situ FTIR dynamic capability provides a comprehensive guide to green practices, quality control, and innovation in the pharmaceutical and medical industry. This review describes the widespread use of ex situ and in situ F TIR spectroscopy as a green medicinal chemistry tool in the chemical, pharmaceutical, and pharmaceutical in dustries. However, more research is needed to unlock the full potential of FTIR and develop new application s that will enhance sustainability in these areas.

KEYWORD : Finished Product; Purity; Pharmacopeias; Raw Material; Quality Control

1. INTDRODUCTION

Fourier transform infrared spectroscopy (FTIR) is a powerful analytical technique used to identify and measu re the chemical composition of materials. Infrared spectroscopy (IR) is based primarily on the detection of m olecular vibrations excited by infrared radiation. It is based on the Fourier transform, a mathematical method that separates a signal into its frequency components. FTIR works by measuring the absorption of infrared ra diation by a sample and provides information about the molecular vibrations and functional groups present in the substance, represented by a specific spectrum. This information can be used to analyze the chemical com position of the sample, determine the purity of the product, and even detect impurities. The transmitted light can be controlled to ensure that energy is absorbed at each wavelength. By analyzing the powder absorption a nd comparing it with the chemical spectrum, information can be obtained that will allow the identification of the compound. The FTIR measurement principle is shown in Figure 1. This IRE acts as a waveguide for infra red light and as the light propagates through the sample, it interacts with the chemical functional group of the sample, creating an absorption band that can be used to control sample elements. Samples can be measured i n wet or dry conditions. It is best to dry the sample before testing to reduce moisture and therefore OH interfe rence in the IR spectrum. However, ATR allows the measurement of samples in liquid, solid and gaseous ma terials [1,2]. Infrared spectroscopy is a fast technology recognized for its analysis due to its many advantages such as green technology, low environmental impact since no organic solvent is used and leading the industr y by reducing pollution. This even eliminates waste materials from the routine process. Spectroscopy in the i nfrared range is considered a simple test that can distinguish compounds with small changes and is one of the most widely used methods for cation identification [3, 4]. To maintain accuracy and efficiency, FTIR spectr oscopy should be performed with appropriate spectral parameters. This is done immediately after data collect ion to eliminate or reduce unwanted signals in the spectrum. Misuse of these methods can compromise data r eliability [5]. Techniques such as Raman spectroscopy and highperformance liquid chromatography (HPLC) can achieve this, but when combined with FTIR, they offer a unique comparison of applied and green chemis try contents. Raman spectroscopy is frequently used in medicine and chemical analysis and has significant di sadvantages compared to infrared spectroscopy. Although Raman provides useful information, it requires hig h standards and a homogeneous reaction mixture. Fluorescence can easily interfere with Raman instruments, so it is necessary to know the initial features and characteristics in the Raman spectra. HPLC analysis provid es the highest level of sensitivity for the separation and quantification of compounds. However, disadvantage s such as greater solvent usage, longer processing times, higher costs, more production waste and again more labor prevent this benefit. Therefore, considering the general benefits of FTIR spectroscopy with green chem ical elements and its benefits in rapid research, less preparation is required for the identification of drugs; we focus on these specific procedures in our review.[1]

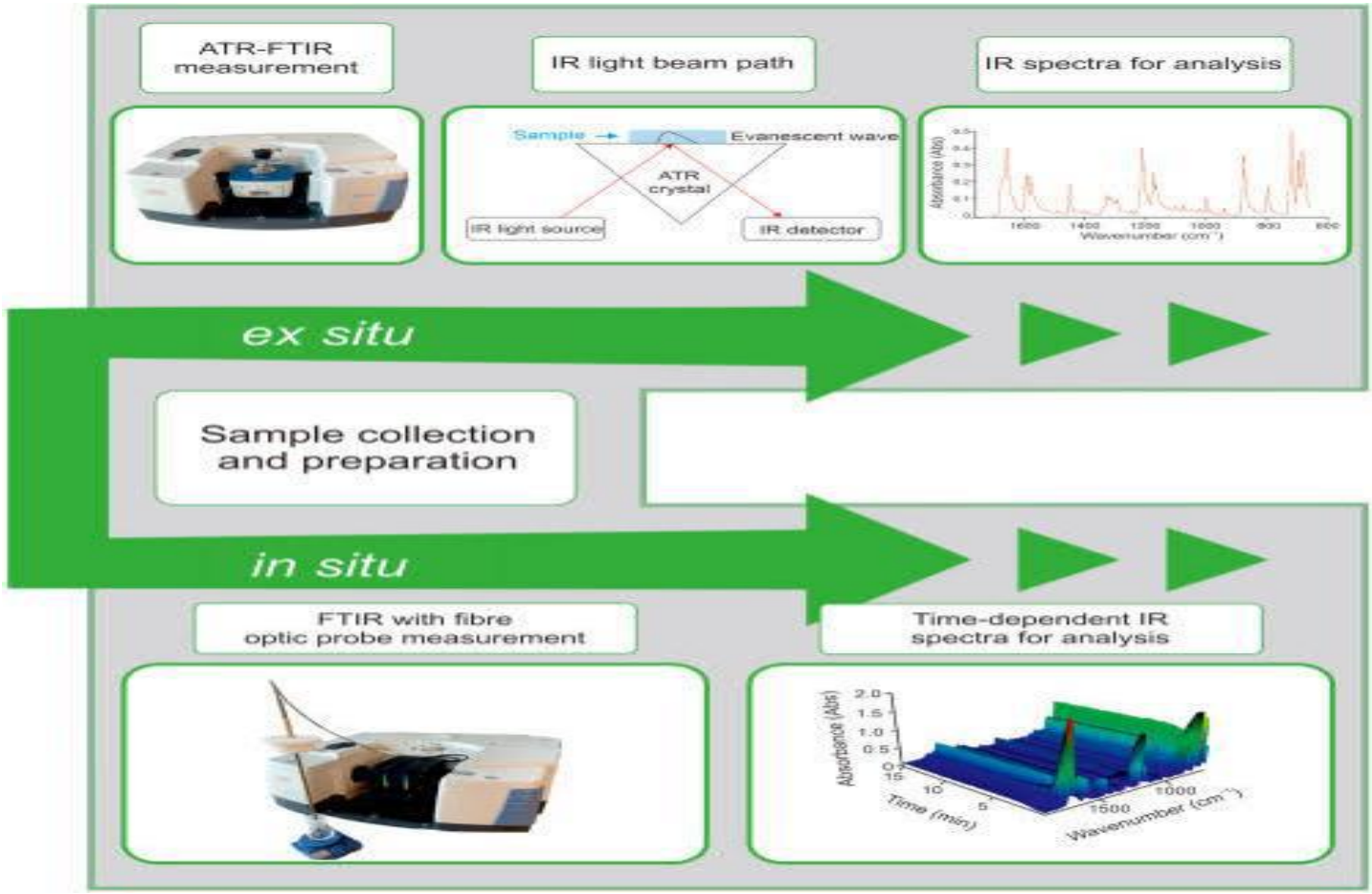

Fig. 1. The mechanism of ex situ and in situ attenuated total reflection-Fourier transform infrared spectroscopy (ATR-FTIR) use for analysis of various samples. IR: infrared.

2. Brief history of FTIR

The history of FTIR spectroscopy dates back to the 1800s when William Herschel discovered infrared ra diation and later developed infrared spectroscopy [2]. Dispersive infrared spectrometers, developed in the 1940s, use prisms or gratings to disperse infrared light and measure its absorbance [3]. In the 1950s, FTI R spectroscopy technology was developed using interferometers to detect infrared light interference and provide spectral information [4]. Arthur Schawlow and Charles Townes pioneered the FTIR spectrometer in 1960 and received the Nobel Prize in Physics in 1981 for their work on laser spectroscopy. The first c ommercial FTIR spectrometers were introduced in the 1970s and became popular in the petrochemical an d polymer fields for the analysis of organic molecules [8,9]. FTIR became a method for identifying unkn own substances in drug discovery and analysis in the 1980s [10]. The invention of micro-FTIR also allows infrared spectroscopic analysis of small samples such as single cells and bacteria [5]. T he introduction of portable and handheld FTIR equipment in the 1990s led onsite inspections in areas suc h as environmental monitoring and plant management. In the 000s, advances in FTIR imaging technolog y made it possible to visualize the molecular and structural distribution of samples, and samples began to be used in disciplines such as biological sciences and information science [6]. It has been used to study e verything from the molecular structure of proteins and DNA to the composition of complex polymers and drugs. Therefore, FTIR has become an important tool for scientists and researchers in many fields, inclu ding chemistry, biology and information science, in recent years.FTIR as a green and sustainable chemistry tool

The terms "green chemistry" and "sustainable chemistry" are often used interchangeably, which can lead to misunderstandings about the different meanings of the two fields. Green chemistry focuses on designing and optimizing chemical processes to minimize harmful products. In contrast, sustainable chemistry encompasses a broad framework that integrates economic and social considerations in relation to a holistic approach to ser vice efficiency and environmental stewardship. Although green and sustainable chemistry both aim to reduce environmental impacts and promote good chemical practices, they operate in different ways [7]. The potenti al for confusion highlights the importance of clearly interpreting and clarifying these terms to clarify the disc ussion on health. It involves the design, development, and use of chemical processes and products to reduce or eliminate the use and production of hazardous substances, as well as to reduce or eliminate waste and cons erve electricity and resources. Green chemistry aims to promote long-
term expansion by reducing the environmental impact of chemical products and processes while maintaining their economic and operational efficiency [8]. Green chemistry is important because it reduces the adverse ef fects of molecular diseases and hazards from products and reagents to humans and the environment by increa sing safety and chemical activity activity. Anastas and Warner proposed 12 principles of green chemistry in 1998. Green analytical chemistry emerged around 1995 as a branch of green chemistry that focuses on how a nalytical chemists can make their experiments more environmentally friendly. It caught the attention of phar macists: in addition to the development of tools and methods to improve the quality of drug testing, there is a n increasing effort to reduce the negative impact of drug testing on the environment and to use sustainable de velopment standards in laboratories. Green analytical chemistry should be seen as a driver of progress in anal ytical chemistry. The biggest challenge for the future in this field is to find the balance between improving th e quality of results and making the screening process more environmentally friendly. . SustainableChemistry aims to increase the efficiency of the production of natural products to meet human needs for pharmaceutical products and services, while maintaining and developing environmental quality and call [9]-3 3 3

3 FTIR processing green technology and sustainable chemistry

The terms "Green Chemistry" "Sustainable Chemistry" "" and "sustainable chemistry" are often used intercha ngeably, which can lead to a misunderstanding of the difference in meaning between the two businesses. Gre en chemistry focuses on designing and optimizing chemical processes to minimize harmful products. In contr ast, sustainable chemistry encompasses a broad framework that integrates economic and social consideration s in a holistic approach to service efficiency and environmental responsibility. Although both seek to reduce environmental impact (FTIR), the terms “green chemistry” and “sustainable chemistry” are often used interc hangeably as a form of green and sustainable chemistry, which can lead to the two misunderstandings and dif ferent meanings. Green chemistry focuses on designing and optimizing chemical processes to minimize harm ful products. In contrast, sustainable chemistry encompasses a broad framework that integrates economic and social considerations in a holistic approach to service efficiency and environmental responsibility. Although both aim to reduce environmental impact and promote chemical, green and sustainable chemistry serve different purposes [10]. The like-lihood of confusion highlights the importance of precise definitions and clarification of these concepts to ensure accurate discourse within the field of science. Green chemistry is an approach to designing and developing chemical products and processes that are ecologically sustainable, cost-effective, and safe for human health. It entails the design,development, and implementation of chemical processes andproducts that reduce or eliminate the use and creation of hazardous compounds, as well as the reduction or elimination of waste and the conservation of energy and resources. Green chemistry seeks to support long-term expansion by decreasing the environmental effects of chemical products and processes while preserving their economic feasibility and performance [18]. Green chemistry is crucial because it reduces molecular pollution and the negative effects of hazardous by-products and reagents on people and the environment by improving the safety and efficiency of chemicaloperations [11]. Anastas and Warner

introduced the 12 principles of green chemistry in 1998. However, these were primarilyintended for synthetic chemistry. Green analytical chemistryemerged as a branch of green chemistry around 1995, focusing onhow analytical chemists can make their laboratory practices more environmentally sustainable [It has gained considerable attention from chemists: besides improving instrumentation and methodologies to enhance the quality of chemical analyses, there is a growing effort to reduce the negative impact of chemical analyses on the environment and implement sustainable development principles in analytical laboratories. Green analytical chemistry should be acknowledged as a driving force for progress in analytical chemistry. The biggest challenge for the future of this field ifinding a balance between improving the quality of results and making analytical methods more environmentally friendly On the other hand, sustainable chemistry is a more comprehensive approach, considering sociological and economic factors inaddition to the fundamentals of green chemistry. Sustainable chemistry aims to increase the effectiveness of exploiting natural resources to satisfy human demand for chemical goods and services while safeguarding and improving environmental quality and human health. Although it adheres to the principles of green chemistry, it also emphasises societal welfare and economic development. In order to break the link between economic growth and environmental destruction, sustainable chemistry encourages ethical consumption and production. It adheres to the circular economic model, which aims to extend the lifespan of materials FTIR is recognised as a green and sustainable chemistry instrument in chemical and pharmaceutical analysis for several essential reasons. Firstly, FTIR analysis aligns with the principles of green chemistry by minimising the production of hazardous waste and decreasing the use of toxic chemicals. Reduced waste and chemical use make the analytical process safer and more ecologically friendly. Secondly, FTIR makes it possible to analyse materials inreal-time, obviating the need for time-consuming sample preparation and conserving energy. By encouraging energy savings and expediting the analytical process, this function is in line with sustainable and green chemistry concepts. The expedited analytical procedure advances sustainability by reducing resource consumption and encouraging energy efficiency, which aligns with broader sustainability objectives. Additionally, the molecular structure of chemicals is effectively revealed by FTIR, which helps to create chemical and pharmaceutical procedures that are more ecologically friendly. This capability promotes green and sustainable chemistry ideals by encouraging the development of safer and more effective chemical processes that eventually contribute to a sustainable future. The alignment of FTIR with the 12 principles of green chemistry is shown in Table 1. In conclusion, FTIR is a valuable tool that embodies the principles of both green and sustainable chemistry in chemical and pharmaceutical analysis, because it can analyse samples without potentially dangerous chemicals, performin situ analysis, and provide information for more environmentally friendly chemical processes.[13]

4. Use of ex situ FTIR spectroscopy as a green analytical tool in

Ex situ FTIR spectroscopy in the pharmaceutical and chemical industries, where samples are analyzed that ar e not part of the reaction or process being studied. Unlike traditional methods, samples are prepared individu ally and then analyzed using FTIR. Ex situ FTIR spectroscopy is used in the pharmaceutical industry for mat erial, quality control and contamination monitoring purposes. It identifies impurities, by-
products and contaminants in raw materials and finished products. In addition, it can examine properties such as crystallinity, polymer composition and surface activity, all of which are important for the creation of new materials and the use of nanotechnology. This analytical technique is also widely used in the pharmaceutical industry for drug development, safety assessment, and pharmacokinetic studies. It helps ensure product qualit y, safety, and efficacy by analyzing drug-
excipient interactions and quantifying drug content in dosage forms. Additionally, ex situ FTIR spectroscopy can be used to identify polymorphs, degradation products, and drug release patterns, providing valuable info rmation for drug development.[14]

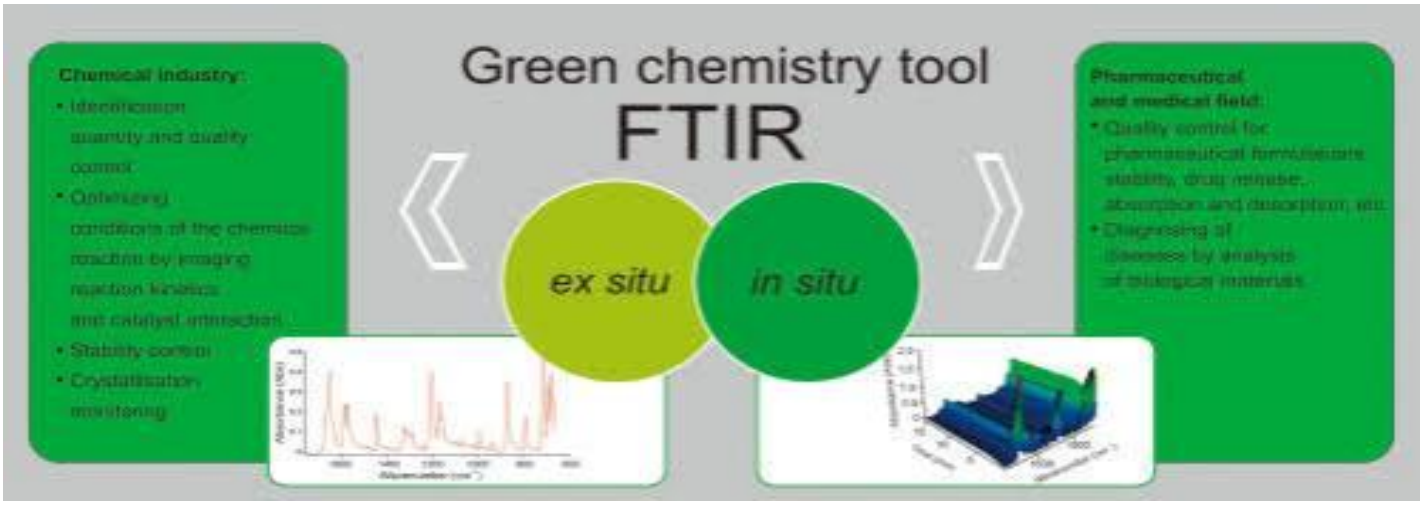

FIG 2. Green chemistry tool FTIR

Table 1 Alignment of Fourier transform infrared spectroscopy (FTIR) with the 12 principles of green chemistry.

No	Green chemistry principle	Description of FTIR usage aligning with green chemistry principle
1	Prevent waste	FTIR prevents the formation of unwanted by-products by real-time monitoring and immediate adjustments to reaction conditions and controlling the purity of substrates
2	Maximise atom economy	FTIR aids in achieving high atom economy by optimising reactions to minimise waste and maximise the conversion of starting materials into desired products.
3	Design less hazardous chemical syntheses	FTIR enables the identification and mitigation of the formation of hazardous intermediates or by-products.
4	Design safer chemicals and products	FTIR helps select reaction conditions that minimise the generation of toxic substances, as well as access the benefit-harm qualities of chemicals.
5	Use safer solvents and reaction conditions	FTIR helps choose greener solvents and auxiliaries by evaluating their interactions with reactants and products.

6	Increase energy efficiency	FTIR guides the selection of optimal reaction conditions, reducing energy consumption.
7	Use renewable feedstocks	FTIR monitors reactions involving renewable feedstocks and assesses their conversion into valuable products.
8	Avoid chemical derivatives	FTIR helps reduce the undesired derivatives by ensuring reactions proceed efficiently and by monitoring the purity of products.
9	Use catalysts, not stoichiometric reagents	FTIR assists in optimising catalyst usage by studying catalyst-reactant interactions.
10	Design chemicals and products to degrade after use	FTIR assesses the stability of products and materials, aiding in the design of substances that degrade more readily.
11	Analyse in real time to prevent pollution	FTIR's real-time monitoring helps prevent pollution by detecting and addressing issues during chemical processes.
12	Minimise the potential for accidents	FTIR provides early detection of potential hazards and enables timely interventions to prevent accidents.

The next section of the study will discuss the uses and improvements of ex situ FTIR spectroscopy in the chemical and pharmaceutical sectors, focusing on its contributions to environmentally friendly and efficient analytical practices. We aim to highlight the importance of ex situ FTIR spectroscopy as a beneficial tool in these critical areas by diving into individual case studies and significant research activitie

4.1 Identification, quality and quantity control

FTIR is widely used to determine and monitor the purity of raw materials and finished products to ensure tha t they meet appropriate standards. For example, FTIR technology can identify the composition of b-cyclodextrin and curcumin, since curcumin itself is a medicinal substance that requires the use of precipitatio n and other methods to improve stability and solubility due to its low water solubility. Another good example is the recognition obtained by Pedroso and Salgado [14], which showed that the FTIR method is suitable for the measurement of ertapenem sodium, aarenteral b-methylcarbapenem antibiotic. This method allows the characterization and quantification of ertapenem sodiu m without the need for organic solvents, since this sample is made in potassium bromide as a specific reagent . Therefore, this method can help reduce organic waste during mass production. Farooq et al. [27] conducted

quality control of diabetes drugs such as repaglinide, rosiglitazone maleate, pioglitazone hydrochloride and metformin hydrochloride using FTIR method and misjudged their application in quality control procedures a nd drug identification. Quality control is important to ensure safety and efficacy of drugs. FTIR method is a u seful method for monitoring quality control of drugs and is used in identification of many drugs. The first ste p of quantitative investigation using FTIR is to prepare information about the known structure of the target dr ug to compare its chemical composition with the sample. The resulting spectrum is compared with a referenc e spectrum to determine the drug concentration in the sample. This can be done by direct comparison to esti mate the distribution of the data or by using mathematics such as partial least squares (PLS) regression or pri ncipal component analysis (PCA). Once the relationship between the spectral data and the chemical concentr ation is established, the FTIR spectrum of the unknown sample can be used to determine its concentration. It is worth noting that the accuracy of FTIR quantitative analysis is affected by many factors, including the qual ity of the spectrum data, the stability of the sample and the application, and the resolution problem of the FTI R spectrometer. These details need to be carefully considered to ensure that the analysis results are accurate a nd reliable. Although somewhat selective, infrared spectroscopy provides evidence of specific functional gro ups, providing simplicity and cost-
effectiveness compared to other methods while maintaining high accuracy [15]The FTIR method has been us ed to measure ampicillin sodium in powder for injection in the range of 1.0–
3.0 mg/pellet [16]. It has good linearity, precision, accuracy and robustness and is suitable for routine monito ring testing. Operation. This makes it compatible with other methods used for the same purpose such as HPL C, fluorimetry and chemiluminescence spectroscopy. Infrared has also been used to develop and evaluate met hods for the measurement of ceftazidime in injectable drugs [17]. The method is based on the measurement o f the absorption loop at an average of 1,475 to 1,600 cm1 and exhibits good linearity, precision and accuracy over the dose range of 0.5 to 7.0 mg. Excipients do not affect the assay and the mean recovery is 98.98% ± 0. 70%. Other tests using the same method include cefuroxime injection [30] (linear range 5.0-
20.0 g/mL, good accuracy, standard deviation of the value is close to 2% and less than 5%), doxycycline raw material [18] (linearly in the concentration range 0.5 to 2.5 mg, correlation value 0.9991, limited test and qua ntification 0.125 and 0.378 mg, respectively), darunavir in tablets [19] (linearly in the concentration range 1. 5e3.5 mg, correlation coefficient greater than 0.9991, detection and limit feed contain 0.12 mg and 0.36 mg, r espectively) and therefore Open. Fakhlebom et al. [19] found that ATR-
FTIR spectroscopy is an effective method for the measurement of diclofenac sodium in tablet formulations. Tablet excipients do not affect the linearity of the test and method with a correlation value of 0.9994 over dru g amounts ranging from 0.2% to 1.5% (m/m). High recoveries (99.81%, 101.54% and 99.41%) and low detec tion and limiting effects reflect the high and accurate method. HPLC measurement of ketoprofen/scopolamin e and benzocaine/dextromethorphan hydrobromide in binary drug mixtures and drug formulationsm[20]. Stat istical comparisons were found to be almost the same, demonstrating its suitability for many businesses. FTI R analysis is a greener and more economical option than HPLC due to less solvent usage, mobility, reduced waste, faster processing, energy consumption. Less electricity and greater operator safety. However, HPLC a nalysis is quite useful in the separation and measurement of compounds, but this advantage also brings disad vantages such as additional solvent usage, longer working hours, more money spent, more waste and more ef fort. The specific needs of the analysis, the characteristics of the model, control limits and safety objectives s hould determine the choice of analytical equipment..

4.2. Crystallisation monitoring

Crystallization analysis is important in the pharmaceutical and pharmaceutical industry because it has a direct impact on product quality, purity, and efficiency. Researchers can use ex situ FTIR as an important analytica l tool to analyze the crystallization process, improve efficiency, and control the industry while adhering to saf ety standards. Ex situ FTIR was used to study the crystallization process, which was demonstrated by analyzi ng the transformation of amorphous acetaminophen before and after the addition of trehalose and melibiose. Spectral analysis revealed changes in the molecular shape and interactions of the nonreactive material, includ ing the product quenched before milling and the crystalline powder product. Amorphous materials exhibit lar ger and less well-
defined peaks in the spectrum compared to crystalline materials [In addition to pharmaceutical applications, FTIR spectroscopy also shows potential as an analytical tool to advance protein crystallization research. This

continues to explore the influence of surface properties on protein behavior and address important questions regarding protein structure and function [36]. Additionally, FTIR technology can measure and monitor the cr ystallization and melting properties of various vegetable oils, as exemplified by the study of Physalis peruvic a [21]

4.3. Oxidation and stability control

Oxidation processes are important in chemistry, medicine and biology, especially in the development of livin g organisms. Oxidation is defined as the loss of electrons from a molecule or atom, usually by the addition of oxygen or the removal of hydrogen. Oxidation is the second most common pharmacological degradation me chanism after hydrolysis and is very important for the development of new materials and synthetic drugs bec ause it can add functional groups, change chemical structure and form valuable products. Controlling and cha racterizing oxidative processes involved in drug metabolism is important for drug development, drug use and prediction of drug interactions, as well as for understanding the chemical process and improving synthesis S urapaneni et al. [22] studied the oxidation of ()-menthol to ()-
menthone in different solvents using FTIR spectroscopy. The solvents used in this reaction (acetic acid, aceto ne, ethyl acetate and methylene chloride) have a significant effect on the reaction kinetics and yield. Due to t he increase in hypochlorite, which is the limit of the oxidation reaction, the authors consider that the most pol ar solvent system will make the reaction fastest and best. The results showed that the reaction using the least amount of solvent, ethyl acetate, gave the best yield of ()-
menthone. Surprisingly, the reaction time was shortest in the solvent systems ethyl acetate and acetic acid, bo th of which are less polar than the primary solvent used for this reaction, acetonitrile. The authors used FTIR spectroscopy to characterize all reaction products based on ()-
menthone, which provided insights into the effects of solvent selection. This finding highlights the importanc e of using green chemistry techniques when selecting solvents for chemical reactions. Pharmaceutical formul ations often contain a lipid phase dispersed in an aqueous medium, forming an oil-in-
water (o/w) emulsion. These emulsions are important for monitoring lipid oxidation. The mechanism of O/W oxidation is more complex than that of bulk oil oxidation. Water-soluble and oil-soluble pro-
oxidants and antioxidants can interact at the oil-
water interface. Therefore, there is an urgent need for accurate and rapid analytical methods to directly measu re the oxidation of drugs and chemicals, and FTIR has been shown to be an effective method to analyze ome ga-
3 fatty acid oxidation, as demonstrated by the method of Daoud et al. [23]. FTIR spectroscopy, combined wit h recent advances in data processing and chemometrics, becomes suitable for investigating the stability and s uitability of biopharmaceuticals, such as functional properties of biomaterials, monitoring of monoclonal anti body purification, and bioactivity of biopharmaceuticals under stress.

4.4. Drug dissolution and release control

The study of drug release and solubility is important in finding new drug candidates. For preclinical testing, i t is recommended that the solubility of the drug be greater than 10 mM. Analysis of early preclinical data to d etermine solubility can help determine the need for a resource-
intensive formulation On the other hand, changes in chemical structure due to degradation and dissolution of chemical components will reduce the potency of the drug, increase performance issues, and no longer have s ufficient safety. Fear that product degradation can be dangerous. The study of forced degradation is one of th e first steps in the development of a new drug and provides the first insight into its medicinal properties. Rese archers can use FTIR data obtained from forced degradation to evaluate drug stability at different sites based on the amount of degradation impurities produced, such as the darunavir study by Modini et al. and the doxo fylline and deflazacort study by Raju et al. [24]. Abdul Halim et al. [4] attempted to use the synergistic effect of lavender essential oil to create a self-

nanoemulsified drug delivery system to improve the poor permeability and side effects of zolmitriptan (ZMT) and increase its efficacy in the treatment of migraine pain. A continuous system coupled with ATR-FTIR, water sorption, separation and computer techniques were used to estimate the percentage of dissolved ZMT over time and the permeation test. While standard analytical methods such as HPLC require continuous monitoring and re-
examination of suspended solids, FTIR analysis provides an indication of the continuous monitoring of the se questration structure of the active substances. The modified ZMT self-
nanoemulsification system produces nanoscale spheres with higher permeation power than conventional ZM T during initial dissolution. FTIR imaging has also been used to characterize the distribution of poorly water-soluble drugs in polyethylene glycol (PEG) and their separation in water [25]. It was found that amorphous n ifedipine began to crystallize in PEG-8000 for formulations with at least 10% drug content (m/m). ATR-FTIR spectroscopic imaging provides new insights into the dissolution process of nifedipine from water-soluble polymer product dispersions, which is useful for optimizing formulation manufacturing. FTIR can be used to analyze the adsorption and desorption of drugs in various delivery systems. By measuring changes in the infrared spectrum, researchers can monitor the release of drugs from the formulation and understand thei r interactions with excipients, which is important for tuning drug delivery.

Zid et al. tested mesoporous silica as a drug delivery system for naproxen [46]. It was found that the adsorpti on and desorption properties of naproxen were affected by solution pH and silica surface functionality. By co mparing the spectra of mesoporous silica, modified samples and naproxen-
loaded materials, the grafting of organic groups onto silica and the adsorption quality of naproxen can be clea rly seen. 4.5. Control of Nanoparticle Formation

Nanoparticles have made significant progress in the pharmaceutical and pharmaceutical industries. By encap sulating nanoparticles in drug-
based development, researchers can improve drug stability and bioavailability and target specific cells or tiss ues
. This prevents drug degradation, controls their release rate and helps them pass through cellular barriers. Eff ectiveness[26]. Nanoparticles can also act as catalysts in many chemical processes. Due to their large area an d specific nature of the area, they can realize efficient processes by reducing the need for expensive and ecol ogically harmful energy sources Bashir et al. Use the green method to produce ZnO nanoparticles with large pores [27]. FTIR analysis revealed the formation of ZnO nanoparticles and the presence of phytochemicals th at aid in formulation. Many studies have shown that FTIR is an important technique for the analysis of nanop article formation [28] and crystallinity characterization Replication It is still an important tool due to its ease of use, flexibility and the ability to analyze many devices with similar ones. The advantage of ex situ FTIR s pectroscopy as a green analysis is due to its non-
destructiveness, minimal preparation and minimal waste. This approach supports sustainable practices by sav ing resources and providing valuable information without compromising the integrity of the analysis model.

5. Use of in situ FTIR spectroscopy as a green analytical tool in the chemical and pharmaceutical industry

In situ FTIR spectroscopy works on the same principle as traditional FTIR, where an infrared beam is transm itted through a sample and the absorbed energy produces a specific spectrum corresponding to the molecular vibrations in the structure. In traditional ex situ FTIR spectroscopy, samples are prepared separately and then analyzed in a spectrometer. This method provides important information about the importance of the structur e, but cannot capture the dynamics of the entire reaction or process. In situ FTIR spectroscopy, on the other h and, requires the sample to be immediately placed in the FTIR spectrometer or the spectrometer to be connec ted to the reaction vessel. This allows the pattern to be continuously monitored as it changes, allowing for ti mely resolution of the progress of drug systems and time-
sensitive processes . The main work of the research is to show the impact of changes in the field of FTIR spe ctroscopy based on the use of green plants. Identification, Quality Control and More Similar to ex situ FTIR, in situ FTIR is frequently used for sample analysis, especially in commercial medical fields. It plays an impo rtant role in defining product purity, detecting impurities and identifying products resulting from the degradat ion process as suggested in various studies [61 and 65]. Powerful tools to ensure consistency and compliance with manufacturing standards in the pharmaceutical and pharmaceutical industries. An exemplary study by

Chan et al. involved the creation of ibuprofen formulations in PEG covering a range of ibuprofen concentrati on from 0% to 100%. This is done using the droplet deposition method. The ibuprofen concentration in the P EG matrix is
determined by measuring all samples simultaneously using in situ FTIR spectroscopic imaging. The analysis of FTIR spectra of these samples provides information on the molecular state of the drug and the length of po lymer swelling, which is affected by various chemical factors. Another good example is given by Ho et al. [2 9]used in situ FTIR spectroscopy to investigate the formation of fucoidan/chitosan based polyelectrolyte mult ilayers (PEM) and used ATR-
FTIR to monitor the continuous growth. The intensity of the different peaks associated with each polymer inc reases during each adsorption step and spectral analysis allows the extraction of layerspecific spectra, facilita ting the Value of the adsorbed mass at each stage. Proton modifies membrane synthesis.

5.2. Reaction kinetics and catalyst interaction control

Small differences in reaction kinetics are important for developing effective processes and good products in d rug and pharmaceutical research. A good understanding of reactions, mechanisms, catalyst effects and reactio n parameters is important. In this context, in situ FTIR seems to be an important tool that allows researchers t o grasp the complexity of reaction kinetics and make informed decisions about catalysts and reaction decisio ns to achieve the best. In situ FTIR
provides dynamic information about the dynamics by observing the stable molecular vibrations. To calculate the reaction kinetics, data on concentration versus time should be collected. Beer's law states that the absorpt ion of a substance in a mixture varies with the concentration of that substance. As reactants are converted to products, their characteristic infrared absorption bands change, getting stronger or weaker. These spectral cha nges can be recorded in situ by FTIR, providing detailed information about the outcome of the event. By calc ulating the rate of spectral changes, scientists can identify reactions, find rate-
limiting processes, and even find intermediates that escape scientific formulas. The ability to follow reaction kinetics at the molecular level allows researchers to accurately target negative reactions [30]. Selectivity, yiel d and reaction method are all strongly affected by the catalyst used. In situ FTIR provides a unique advantage in measuring the interactions between reactants and catalyst surfaces. Changes in the infrared spectrum indic ate the adsorption process, the type of association and the active sites where reactant molecules adsorb onto t he catalyst. This information is important for understanding how various catalysts affect the reaction process and has been used in many studies over the past few years Deactivation, regeneration and ideal operating en vironment.
According to research by Marinkovic et al. [79] used the electrochemical in situ FTIR technique to demonstr ate the role of Rh in promoting CeC bond cleavage in ternary PtRh/SnO2 catalysts. In addition, in situ FTIR provides quantitative confirmation of the increase in the overall oxidation process leading to CO2 production . This can be done by in situ FTIR acting as a reporter. Using these tools, scientists can quickly assess how th ese changes affect reactions, equilibria, and explosions. This rapid feedback facilitates finding the best sites f or reactions that produce better products.

5.3. Drug release control

Appropriate control of drug release from drug formulations is an important aspect of current drug delivery ai ming to increase efficacy while minimizing side effects, and in situ FTIR has proven itself as a powerful tool. Furthermore, FTIR imaging helps in visualizing changes in drug release over time. Unlike traditional degrad ation studies, this spectral imaging technique provides new insights into the changes that occur during drug d egradation. In situ FTIR imaging shows great potential in various applications including studies on multilaye red tablets, simplified high-
throughput studies, use of microfluidic devices and in situ surface treatment ATR - FTIR spectroscopy devel oped a combined ATR-
FTIR spectral imaging method and designed a polydimethylsiloxane microfluidic device specifically to study drug release from drug formulations. The separation of microformulations such as ibuprofen and PEG in flo wing water was investigated and the behavior and release of the drug in different pH environments were obse rved. It can be seen from the spectral image and ATR-
FTIR spectrum that the drug transforms from the molecular state to the crystalline form in acidic solution. Mi

crofluidic devices allow multiple microformulations to be exposed to different liquids simultaneously and pr ovide an efficient way to study multiple microformulations in a single experiment. This study also highlights the importance of analyzing the behavior of the drug after release (such as recrystallization from solution). A TR-
FTIR spectral imaging data show the phase change of ibuprofen sodium dissolved in a neutral solution int o an acidic environment.
Change. The combination of ATRFTIR spectral replication and microfluidic devices provides a method with potential for further development, from pressure measurement to the study of drug release and product behav ior in water, as a tool for learning various design and problem-
solving and dynamic methods . In situ FTIR spectroscopic imaging was used with a flow cell device to study the effect of different excipients on drug release formulations.
It was found that the difference in drug release was mainly due to drug-
polymer interactions, and the addition of sodium carbonate improved the release by reducing these interactio ns and promoting the production of more water-soluble ibuprofen.
Other successful examples of the use of in situ FTIR in drug dissolution imaging include the study of antivira l drug release by Ewing et al. [31]

5.4. Crystallisation control

The ability of a molecule to take on different crystalline forms in its components is called polymorphism. Pol ymorphs differ in physical and chemical properties such as lattice strength, melting point, heat of fusion, solu bility, dissolution rate, speed, and processing properties. These differences can affect the stability, formulatio n, potency, bioavailability, storage, and efficacy of the drug. In terms of intellectual property, a particular pol ymorph can be patented if it exhibits better properties than a previously patented polymorph, allowing compe titors to legally offer products with different crystal structures. Modification of the crystallization medium, su ch as changing the temperature, type of solvent, and chemical pH, can produce a variety of polymorphic form s [The polymorphic process can be closely monitored using in situ FTIR, allowing for instantaneous observa tion of molecular changes during crystallization. The importance of the major transition stages. Understandin g the detailed metamorphism of amorphous calcium carbonate into concrete at the molecular level is critical f or the removal of many biologically active compounds. In their study, the researchers used in situ FTIR spect roscopy to study the moisture-
induced crystallization process of amorphous calcium carbonate. This technique is useful for changes in the v ibrational properties of carbonate and water molecules, making it a useful analytical tool. Another good exam ple is provided by Chan et al. [66] described the use of in situ FTIR imaging in combination with a controlled humidity unit to monitor the crystallization of a binary mixture of two substances at the same site. Using an i nfrared focal plane array detector, the researchers studied the effect of humidity on a binary mixture of nifedi pine and nitrendipine as well as amorphous nitrendipine arranged in different molar ratios on the surface of a BaF2 window. This study also investigated the effect of sample thickness on the analysis of the results of the images using a special method for creating thickness
simple images. The FTIR spectral imaging method proposed in this paper can be used for future high-
throughput studies of large numbers of samples in controlled areas. The method also demonstrates the ability to simultaneously study changes in the crystallization behavior and polymorphism of different chemicals and their compounds. The advantage of this research proposal is that each sample can be measured according to t he chemical image, which allows the spectra of different polymorphs to be acquired and measured separately without requiring spectral subtraction. There are other important research examples where in situ FTIR is us ed to control crystallization in the pharmaceutical industry, notably the polymorphic changes of carbamazepi ne [87], rifampicin [88] and celery coxib [32] and clinical trials

5.5. Absorption and desorption control

In situ FTIR spectroscopy has proven to be an effective method for studying interactions between particles. T his technique is used in many scientific studies to help scientists unravel the complex dynamics of molecular adsorption and desorption processes. In situ FTIR can provide insight into the small-
scale interactions between adsorbate molecules and the substrate, and in many cases can lead to a better unde rstanding of material behavior. This technology is used in many fields, including catalysis, materials science, and environmental protection. . The special technique in this process requires carefully placing a high-
refractive index crystal at a specific angle to the surface pattern, thereby creating a transient wave that penetr ates the material. This method allows for instant, non-
destructive examination of surface layers without the need for sample preparation. Many studies have used H ATR-
FTIR to study adsorption and desorption phenomena in depth. For example, a recent study investigated the d esorption of glyphosate from goethite due to phosphate adsorption. Combining HATR-
FTIR spectroscopy and adsorption isotherm analysis, the researchers determined that glyphosate desorption o n the upper surface of the phosphate was significant. This effect occurs because the ratio of desorbed glyphos ate to adsorbed phosphate is 0.60 Similarly, studies have investigated the effect of humic acid on the adsorpti on/desorption behavior of glyphosate on goethite and the adsorption of dimethyl sulfide on silver-
modified bentonite [
Iron-
(hydroxy)dimethylarsinic acid is the main intermediate in the electrochemical reduction of CuO nanoparticle s [32] and CO2Local patterns of chemical and different processes of water are investigated. In situ infrared s pectroscopy is also an excellent tool for the quality and quantity of adsorbed water due to its sensitivity to wa ter and hydrogen bonding states . Redistribution Fourier Transform Spectroscopy (DRIFTS) is another useful tool for studying the environment. In contrast to HATR-
FTIR, which uses a high refractive index crystal in direct contact with the sample surface, in situ DRIFTS us es a different concept. Infrared radiation should be used to illuminate the dispersion or powder sample and ca pture the scattered reflected light for analysis. Surface chemistry, studies have shown that Cu/
Ti(H2) exhibits more than 50% higher CO2 photoreduction activity compared to Cu/Ti (air), which is attribut ed to Cu2à, OH. The effect of the group and oxygen-free sites thus improves energy transfer,
provides CO2 adsorption sites and promotes CO2 activation [100]. It seems to be a powerful technique to ins tantly probe surface intermediates. These studies exemplify the widespread use of in situ FTIR, particularly HATR-
FTIR and DRIFTS, to investigate the interactions between surfaces and molecular dynamics. In situ FTIR ha s provided precise characteristics of changes in material properties, increasing our understanding of the mater ials used and enabling new developments in various fields such as environmental science and materials engin eering. Compared to ex situ methods that require samples to be removed from their original locations, in situ FTIR can monitor molecular species adsorbed onto the material during chemical reactions. This feature is ver y useful because it allows the study of countermeasures, the identification of transient intermediates, and the monitoring of animal dynamics under real reaction conditions. In situ FTIR has the advantage of capturing pr ecise details of molecular interactions and changes without affecting physical properties. This real-
time analysis of surface[40]-
environment behavior allows for better insight into the catalytic process, the reaction process, and the role of many types of surfaces, ultimately paving the way for catalyst material design and optimization. This allows us to understand complex reaction mechanisms and intermediates, but the process requires special equipment and experiments can be complex, causing problems in applying models and settings.

6. Combination of FTIR technique with other analytical

Methods for optimizing chemical and pharmaceutical processes
Methodological synergy in chemical analysis involves integrating and combining different analytical method s or methods to obtain complete and reliable datasets on analysis models. Researchers can benefit from it by considering the limitations of each
strategy using different methods. This method allows users to better understand the composition, structure, pr operties and behavior of the model. FTIR can also be used in conjunction with other analytical methods to op timize laboratory and industrial processes. It can be combined with FTIR to observe the composition of gase ous and liquid phases during a reaction [33]. For example, Ke et al. The efficiency and reliability of the self-optimizing system were validated by two interventions, including oil-
liquid separation. a. It can be used together with FTIR to provide additional information on drug mixtures an d drug formulations As a practical example, Raman and FTIR spectroscopy were well combined with gas ch romatography when optimizing the ultrasound-
assisted extraction of bioactive compounds from acacia gum using field methodology Polysaccharides such a s galactose and glucose and proteins such as lysine and proline were detected, while the FTIR spectrum show ed the presence of functional groups such as alkanes, aldehydes, fatty amines and phenols. The presence of a ntioxidant compounds D-galactopyranose, carotenoids and lycopene was analyzed. . This technique
can help to identify the most significant changes occurring during the reaction and hence to optimize the reac tion[39]
. The combination of FTIR analysis and chemical chemometric analysis is a promising analytical tool that ai ms to reduce the complexity of drug analysis with green performance. Compared to traditional methods such as HPLC, it can help in reducing measurement, reducing problems, reducing work time and mobility, reducin g costs, reducing waste and improving user safety. Side-by-
side comparison of the potential of FTIR and HPLC techniques combined with PLS regression for quantitativ e identification of active compounds by green chemical analysis
Summary of the study by Kelani et al. [34].
The analysis of ketoprofen/scopolamine and benzocaine/dextromethorphan hydrobromide in binary mixtures and drug formulations using FTIR-
PLS regression shows superior performance as it provides less weight consumption, portability, less waste pr oduction, short working time. , reduces operating costs,
lower energy consumption, improved operator safety and easy integration with traditional chemical equipme nt here. antidote. This technique has several advantages, including the ability to control unfavorable reactions , improve mass conversion, improve reaction kinetics, and provide information about the behavior of the elec trochemical reaction of reactants. Overall, combining FTIR with other techniques provides an effective meth od for monitoring and optimizing reactions.

7. Use of FTIR spectroscopy in the medical industry for

Diseases and Treatments The development of diseases such as cancer and infectious diseases and the lack of appropriate, reliable, cost-effective and technology-
based high diagnostics necessitate the development of other diagnostic tests. FTIR spectroscopy is important for understanding many applications from chemical and quality control to biomedicine. This method is a rapi d, non-invasive, label-free, reagent-free and well-
reproducible method for the characterization of biomolecules
[It allows automated and reproducible analyses leading to objective analysis of samples. FTIR can reveal mo lecular structures and chemical elements such as proteins, lipids, nucleic acids and carbohydrates. It can also identify changes in the molecular composition associated with the disease by providing specific markers of bi ological materials such as tissues, cells and fluids The role of FTIR spectroscopy in the diagnosis of infectio us diseases[1] is studied by spectral changes, thus providing precise information about the stage of the diseas e. The study of genomic changes during the infection, known as MTP, will be important in the diagnosis of t he disease. FTIR spectroscopy can identify changes such as total cholesterol and immunoglobulins in serum after infection. Some studies have tried to develop new diagnostic methods for the 2019 coronavirus (COVI D-19) based on saliva and plasma vibration modes examined by ATR-

FTIR spectroscopy. They determined the biological fingerprints of COVID-
19 and followed the diagnosis of COVID-
19 using a multivariate linear regression model, which will help to develop diagnostic equipment faster and c heaper in the future. Lee-
Montiel and colleagues investigated the effectiveness of FTIR spectroscopy in identifying infectious diseases [126], using poliovirus (PV1) and buffalo green kidney cells. The results showed that the method worked be st at 8 h post-
infection and could identify virus titers ranging from 10 to 106 PFU/mL. According to the study, this method for identifying poliovirus and its composition could be applied to other diseases and adapted for use in water safety monitoring and pain testing. FTIR studies showed that, from an optical perspective, the intensity of ca rbohydrate peaks decreased with the growth of herpesvirus [35]. Decreases in cellular glucose content are use d as biomarkers of herpesvirus kinetics and can be used to develop spectroscopic methods to measure herpes virus growth. ATR-
FTIR spectroscopy has also been used to identify hepatitis C and B viruses caused by dengue arboviruses an d dengue fever . It is a tool for the detection and analysis of different types of cell death in leukemia
The results show that FTIR spectroscopy can distinguish between apoptosis and necrosis based on changes in DNA conformation and protein secondary structure. The B-
pattern is increased in association with apoptosis, while random coil formation is reduced during necrosis. St udies show that FTIR spectroscopy appears to be a promising method for in situ monitoring of cell death, as i t can provide unbiased biochemical information with minimal sample processing and without the need for rea gents.
There are reports on the use of FTIR spectroscopy to detect cancers: breast cancer breast cancer , lung cance r [cancer [36], etc. It measures urine such as protein, creatinine and urea. FTIR spectroscopy, which provides information about bone composition and molecular numbers, can be used to diagnose bone[37]-
related diseases. Using FTIR spectroscopy, researchers determined the contribution of minerals and collagen to the risk of stress fracture (SF) and determined the differences in biochemical markers between bone healt h and stress. According to comparative analysis and biochemical profiling, stress fractures show higher colla gen content, poor growth, texture, carbonate and acid alteration, and higher Crystallinity
compared to healthy bone.[38]

8. Conclusion

This review aimed to provide strong evidence of FTIR spectroscopy as a practical, fast and selective technique, with the advantage of requiring small samples, having a viable budget in terms of instrumentation, increasing the ability to identify or characterise complex structures, minimizing the handling of toxic materials, and reducing the generation of organic waste solvents.The primary contribution of this work is to show examples of ex situ and in situ FTIR applications for substance identification and analysis that can now also be utilised in chemical, pharmaceutical and medical fields, while being “greener” than existing procedures. FTIR spectroscopy may be conveniently employed in routine drug and chemical testing and quantification. Moreover, this valuable technique may be employed in disease identification.

In all industries, ex situ FTIR spectroscopy is a reliable tool formaterial identification, quality control, and stability assessment. Itsability to characterise contaminants, monitor crystallisation processes, and manage medication release patterns highlights itscritical role in product quality, safety, and efficacy. Furthermore, itsquantification capabilities lead to more efficient drug development,dosing methodologies, and quality control practices, while itsenvironmentally friendly characteristics are consistent with green

analytical practices. In situ FTIR spectroscopy, on the other hand,emerges as a novel tool for dynamic analysis, allowing for real-timemonitoring of molecular changes during reactions and processes.Its contributions range from monitoring drug release patterns and crystallisation dynamics to studying surface interactions andadsorption phenomena. The time-resolved examination of chemical reactions by in situ FTIR offers a unique perspective that complements ex situ approaches, leading to a better knowledge of molecular changes and material behaviour.Together, the precision of ex situ FTIR in characterising and quantifying, combined with the ability of in situ FTIR to capturedynamic changes, creates a comprehensive analytical frameworkfor advancing green practices, quality control and innovation inboth chemical and pharmaceutical sectors. With

their distinct advantages, these methodologies work in tandem to shape efficient,sustainable and effective analytical strategies for the growth of research and industry. Overall, the prospects for using FTIR in greening chemical and pharmaceutical processes are promising.However, further research is needed to explore the potential of FTIR in these fields fully and to develop new applications that can further enhance the sustainability of chemical and pharmaceutical processes.

Declaration of competing interest

The authors declare that there are no conflicts of interest.

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