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Innovations in Drug Spectroscopy Methods for Pharmaceutical Compounds

Huda Faeq Hasan Aldabag[1], Abdullah Kamaluldeen[2], Saif Ali Ahmed[3], Talib abbas Alzurfi[4]
[1] Ministry of Water Resourses
[2] Department of Biomedical Engineering, College of Materials Engineering, Islamic Azad University, Najafabad branch, Isfahan, Iran
[3] Department of chemistry, Ilam University, , Iran
[4] Department of chemistry, Mazndran University, Iran

Email: hdaldbagh@gmail.com[1], Kamaluldeen.a@gmail.com[2], saifail3181987@gmail.com[3], abbastalib376@gmail.com[4]

Abstract. General Background: Spectroscopy is a pivotal analytical technique in pharmaceutical research, enabling precise analysis of molecular structures and compositions through the interaction of light with matter. Specific Background: Spectroscopic methods have significantly advanced pharmaceutical analysis since the mid-20th century, addressing challenges like drug resistance and the need for improved drug purity and stability. Techniques such as UV-Visible, Fourier Transform Infrared (FTIR), and Nuclear Magnetic Resonance (NMR) spectroscopy are widely employed for drug discovery, quality control, and structural elucidation. Knowledge Gap: Despite their extensive use, limitations persist, such as spectral complexity, overlapping bands, and the need for costly instrumentation, leaving room for improvement in sensitivity, efficiency, and cost-effectiveness. Aims: This study aims to consolidate the principles, applications, and advancements of key spectroscopic methods in pharmaceutical analysis while highlighting emerging trends to overcome existing limitations. Results: The analysis demonstrates that UV-Visible spectroscopy provides high-speed, non-destructive analysis for drug quantification; FTIR offers qualitative and quantitative insights into functional groups; and NMR remains unparalleled for structural determination. Recent advancements include the integration of spectroscopy with machine learning for enhanced data interpretation and the development of hybrid techniques to improve sensitivity. Novelty: The study underscores the evolution of spectroscopy into a cornerstone of modern pharmaceutical analysis, driven by technological innovation and regulatory emphasis on accurate, reliable methods. Novel applications in drug design, impurity profiling, and real-time monitoring further exemplify its versatility. Implications: These findings emphasize the necessity of continued research into cost-effective, automated spectroscopic techniques to enhance pharmaceutical quality and safety, meeting the growing demands of global healthcare. Spectroscopy's integration into regulatory frameworks and novel drug development processes cements its role as a critical tool for advancing pharmaceutical science.

Highlights:

1. Spectroscopy ensures drug quality, purity, and safety in pharmaceuticals.
2. UV-Vis, FTIR, and NMR are key for structural and impurity analysis.
3. Innovations improve accuracy, efficiency, and broaden applications in drug analysis.

Keywords: pectroscopy, Pharmaceutical Analysis, UV-Vis, FTIR, NMR

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Introduction to Drug Spetroscopy

Spectroscopy is the branch of science concerned with the investigation and interpretation of the molecular structure and composition of substances by the study of differences in the radiant energy absorbed or emitted when the substance is irradiated (Baiz et al.2020). In the field of pharmaceutical analysis, drug spectroscopy plays an important role in carrying out a thorough investigation of pharmaceutical compounds, and it is applied in a variety of pharmaceutical stages such as method validation, impurity profile, pharmacokinetics, pharmacodynamics, and so on. A spectroscopic method is considered to be the primary and important technique of analysis due to its accuracy, reproducibility, verifiability, and the international regulatory agencies recommend a spectroscopic method as one of the preferred methods and reject a non-spectroscopic method for the estimation of the composition of pharmaceutical compounds (Li et al., 2021). The present era has witnessed immense advancement in the drug field because many new technological aspects have emerged to confront the problems of the pharmaceutical field, including increasing drug resistance, biopharmaceutical problems, and so on that define the demand to innovate in the field of drug analysis too (Arden et al.2021).

The spectrophotometric methods emerged last century for the determination of drug compounds in the 1940s and 1950s, evolving from very modest beginnings to high precision and excellent quantification, consolidating several decades of continuous research effort. Over time, many spectroscopic methodologies have been reported, most of which are becoming the norm for drug assay methods (Raal et al.2020). Nevertheless, for drugs and medical substances, spectra constitute a characteristic property based on various physical mechanisms observed by pharmacists and pharmaceutical scientists, involving volumes of hydrodynamic properties, adsorptive characteristics, moieties of functional groups, and molecular structures. Standardized methods are thus essential tools for examiners and experts to select the proper analytical tool and usage, knowing that further evolved methods operate according to protocols already qualified based on discoveries and innovations achieved in the standard mode, thus extending to new exclusive fields (Baiz et al.2020).

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Importance of Drug Spectroscopy in Pharmaceutical Analysis

Pharmaceutical analysis plays a critical role in proving the acceptance criteria for drug substances and drug products. Marketed pharmaceutical products should contain specified levels of the active drug ingredients and pose no health risks if synthetic pathways are not ideal. For these reasons, the maximum limits were imposed for the levels of individual and total organic impurities in the guidelines for drug products and substances. In recent years, many analytical methods based mainly on modern chromatography systems such as gas chromatography, high-performance liquid chromatography, and thin-layer chromatography have been established for the identification and quantification of the active drug substances and their organic impurities (Badawy et al.2022). Since the structure determination or identification of unknown chemicals has become more important in pharmaceutical products, many spectroscopy methods, including those based on ultraviolet, infrared, nuclear magnetic resonance, Raman, and mass spectrometry, were also developed by researchers and pharmaceutical industries (Rolinger et al., 2020).

However, only the specified spectroscopy methods have been considered in this text. These spectroscopy methods are important analytical quality control tools due to their speed, simplicity, and accuracy. These methods with compact instrumentation account for the identification of drug substances with high accuracy. The regulatory agencies also strongly recommend the calibration curves based on the spectroscopy data because correlations between the HPLC and spectroscopy drug concentrations were conducted to compare the quality of the food and drug substances. Regulatory agencies believe that the currently available analytical methods employing spectroscopy technologies are powerful enough to ensure that test results are within the specified limits. Spectroscopy methods also play an active role in drug discovery as well as during the new processes for existing drug substance production (Beć et al., 2022). Since the middle of the 1950s, industry and researchers have been interested in the use of spectroscopy techniques to analyze and control drug purity. A UV spectrophotometer is mainly used to analyze the analyte using a wavelength between 190 and 380 nm. A near-infrared spectrometer is capable of providing a spectral wavelength between 780 and 2500 nm. A spectrofluorometer is widely used in drug estimation and has a spectral range of less than 80 to 800 nm. Recent studies and analytical procedures for the

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estimation of pharmaceuticals using different spectroscopy parameters also consolidated the fact that the spectroscopy method is a reliable analytical tool. Although the existing methods have enough sensitivity, selectivity, and analytical characteristics, reliable, quick, and low-cost spectroscopic techniques that are alternatives to the existing methods are still of great interest in the field of drug analysis (Rolinger et al., 2020).

Principles of Spectroscopy

Spectroscopy is about how the interaction between light and matter results in an excited state. It provides a great foundation for data, both quantitative and qualitative, on samples. Typically, a light source is directed onto a sample, and the resulting updated state of the light is measured. The change in the light source after the sample interaction is measured by optical detection: absorbance in UV-Vis spectroscopy, transmittance in FTIR, or emission in fluorescence. Only one of the different kinds of spectroscopy will be discussed here: UV-Vis, FTIR, and Raman spectroscopy (Beć et al.2021).

The basic principle of UV-Visible spectrophotometry is a measurement of light transmittance with a dual beam system. The light source goes through a monochromator, and a sample solution placed in a quartz cuvette goes through to the light detector. As the sample molecules absorb some of the light, it will result in a reduction in the intensity of the incident light, where the radiation is then determined by calculating the absorbance. FTIR spectroscopy, in comparison with the Fourier Transform technique with infra-red radiation, is based on efficient background suppression for decreased absorbance of light in molecular bonds within an optically dense measurement sample and subsequently allows for lower detection limits in the molecules of interest. The IR radiation travels through a sample, resulting in radiation absorbance from the molecular vibrations within the sample. As radiation is absorbed only by specific vibrational absorbance, a plot of absorbance against wavenumbers in the range of interest will result in a unique spectrum for each investigated molecule. FTIR spectroscopy measures the concentration of a solute in a solvent, from which the concentration of an API in a pharmaceutical formulation can be deduced (Zhuang et al., 2020).

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UV-Visible Spectroscopy

UV-visible (UV-Vis) spectroscopy is the most extensively used analytical technique in pharmaceutical research. Analytical applications of ultraviolet and visible light in the pharmaceutical field are based on the absorption spectrum of drugs. The absorption of ultraviolet and visible light by the drug compound directly depends on the extent of the π-electron cloud in the compound. The costlier the drugs, the bigger the π-electron cloud, and the larger the incoming ultraviolet or visible light would be absorbed. From the above aspect, the Beer-Lambert law can be formulated as follows (Guemari et al.2022):

A = εlc where A is the absorbance, ε is the molar absorptivity of the drug, l is the path length, and c is the concentration. The λmax for a particular pharmaceutical compound is used to measure the concentration of the drug by UV-Vis spectroscopy.

The λmax is the wavelength at which the absorbance is maximum for the drug compound. UV-Vis spectrophotometry is particularly suitable for the study of pharmaceutical compounds in different fields. It is used in almost every quantitative study of pharmaceutical formulations, including the assay of pharmaceutical dosage forms, various analytical methods, dissolution studies, content uniformity studies, determination of drugs in biological fluids, forced degradation studies, and photostability studies (Mofavvaz et al., 2020). UV-Vis spectroscopy is currently used due to its high speed of analysis, simplicity, and non-destructive analysis. However, there are some limitations associated with the development, validation, and analysis of a drug and dosage form using the UV-Vis spectrophotometric method. Validation of minutest details is very important, particularly if they are planned to fit with the official guidance of agencies/organizations, including method validation as per guidelines. The concentration of the drug must reside in the straight line equation within the limits of linearity as well (Guo et al., 2020).

The UV-Vis spectra are complicated by overlapping spectra, matrix interference, dilution error, and stray light, and hence this method is not readily acceptable for utilization in solving complex matrices, including pharmaceuticals. Anyhow, the UV-Vis technique has offered explicit advantages in identifying catechol derivatives in urine due to catalysis. Regression analysis of UV-Vis spectral data is successfully carried out by partial least squares and principal component regression calibration, which could be

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applied to enzyme kinetics. Thus, one of the traditional spectroscopic methods that exhibit λmax with maximum absorbance of the pharmaceutical compounds has colossal significance in pharmaceutical research (Costa et al.2021).

Infrared Spectroscopy

Infrared (IR) or vibration spectroscopy is a spectroscopic technique for the analysis and characterization of pharmaceutical compounds based on their molecular vibrational transitions (changes in vibrations). Functional groups that are present in a pharmaceutical compound often undergo a change in dipole moment when they move, due to stretching, bending, and other movements, thereby causing vibrational transitions to occur. Each type of vibration has its own characteristic frequency, and IR bonding modes are characteristic for specific types of compounds such as drugs or polymers. From an IR absorption spectrum, the presence or absence of these characteristic absorption bands can be determined, meaning presence or knowing the groups in the sample (Beć et al., 2020).

Spectroscopy in the area of the infrared (IR) region has been used extensively in the pharmaceutical area for many years due to it being a relatively simple and low-cost analytical technique. Infrared spectroscopy has the capability of providing both quantitative and qualitative data. The qualitative advantages are significant; spectral interrogation can indicate the presence or absence of important characteristics of a sample. This technique will identify excipients in a drug formulation, provenance of a material, and the presence of an impurity. It can also provide structural information or 'fingerprinting' characteristics of an active molecule. These functions and characteristics are valuable in quality control, research, development, and formulation (Beć et al., 2020). Traditional instruments use dispersive scanning monochromators, but Fourier-transform infrared (FTIR) instruments have become more common; these provide for rapid analysis with minimum sample handling. In most cases, little or no sample preparation is required, and the size of the sample is compatible with microscopy. However, the use of IR spectroscopy in the pharmaceutical industry has been limited in the quantitation of low concentrations of drugs in formulations. The main disadvantages of spectroscopy in the IR region are: the spectra are complex and require interpretation; complex spectra result in continuous or broad bands with little information; overlap of bands in formulators' spectra is quite common; expertise is required for deploying the

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technique. There is ongoing research investigating combinations of spectroscopy in the mid-IR and NIR regions combined with another technique to make univariate predictions of drug concentration. As drug concentration and solvent composition have a complex non-linear relationship, NIR spectroscopy remains an instrument for expert users (Beć et al., 2020).

Nuclear Magnetic Resonance (NMR) Spectroscopy

Nuclear Magnetic Resonance (NMR) is a technique that is superior for the structural determination of pharmaceutical compounds. The basic NMR phenomena include rearrangement of precessions and the rotation of nuclear magnetization. These phenomena are related to the spin angular momentum of nuclear particles and their interaction with the applied magnetic field. When a small spin angular momentum is placed in a strong magnetic field, a resonance condition is reached when the frequency of rotation between the two states is equal. In NMR, the nuclear spin quantum number is the whole-number value determined by the formula $I = 2I + 1$, where I is the integer (0, 1/2, 1, 3/2 ...). The value of I determines whether or not a nucleus is magnetically active and therefore can give an NMR spectrum (Li et al., 2021).

NMR is the only tool available to study not only the actual structure of a compound but also to study the dynamics of the molecule's motion in its chemical environment. In an NMR experiment, the NMR signal is acquired in the frequency domain as well as in the time domain. The uniqueness of NMR among spectroscopic tools is due to its ability to provide high resolution and high-quality spectra even on mixtures as complex as biological fluids that contain hundreds of compounds. An NMR spectrum allows the direct observation of the number of different chemical components within a molecule and the average local or sub-molecular environment of the atoms in the molecule. No other technique can do this; and because having this kind of information can help design new drugs, NMR technology is being applied throughout the drug design and development process. In the NMR experiment, the sample is not destroyed. Most NMR experiments are performed on samples dissolved in solution, making NMR suitable for biomedical testing and imaging (Salo-Ahen et al.2020). The disadvantage of NMR is the need for expensive instrumentation, and since the NMR signal is weak, NMR requires a larger sample size and is less sensitive than other techniques for certain analyses

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Recent Technological Advances in Drug Spectroscopy

Recent technological advances provide traditional drug spectroscopy methods with novel capabilities. On one side, miniaturization enables the use of infrared and Raman-derived techniques as portable and handheld devices, facilitating analyses at the point of care, in the field, or during industrial manufacturing processes. This not only permits rapid examination of pharmaceutical compounds and products without sample destruction, but also reduces analysis time, cost, and resources. On the other side, the development of robust and user-friendly chemometrics and machine learning approaches allows improved interpretation of the obtained spectroscopic data. In addition, automation and robotics are being integrated into workflows, increasing reproducibility and decreasing analytical error. This technological advancement has the potential to revolutionize all aspects of drug analysis, although further development is still needed to make the obtained results compliant with regulatory scrutiny and patient safety, as well as the current Good Manufacturing Practices (Beć et al., 2020).

Further research in the development of miniaturized systems should also be accompanied by a proviso for the development and adaptation of multivariate algorithms in order to transform spectroscopic data into useful and valuable chemical and pharmaceutical information. Ideally, this transformation should be continuous and immediate, thus allowing feedback during on-site testing and manufacturing, as well as real-time process monitoring. Several of the latest miniature spectroscopy methods and their chemical applications are shown in the development of specialized data analysis. Emerging spectroscopic techniques, along with their major components and applications in on-site drug spectroscopy, separate works, and in-line/off-line process evaluation, are also being explored and are presented as potential future alternatives in drug analysis (Beć et al.2021).

Miniaturization and Portable Spectroscopy Devices

Miniaturization – Small Size, Big Potential. XRF, LIBS, and Raman spectroscopy provide the 'holy trinity' of miniaturized spectroscopic technology with a device that is fit for purpose in terms of portability, ease of use, and cost of purchase and maintenance. Such a device can revolutionize how drug analysis is carried out, expanding from specialist laboratories to be present and usable on-site in pharmaceutical and clinical testing, thus granting accessibility to those who work directly with drugs. Hospitals,

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pharmacies, and similar entities all have service demands that require accurate result generation immediately, enabling informed decisions without the need to send samples to a centralized testing location followed by waiting for the results (Singh et al., 2023). The reduced demand on a centralized laboratory can free staff to carry out more in-depth testing or handle more samples in the same timeframe, increasing efficiency in an area that is already contracted.

In addition, field testing benefits from a device that can travel with the operator without being bulky, fragile, heavy, or needing external power supplies or skilled operating staff. Being portable also allows for routine randomized inspection of broader geographical areas, such as wholesalers for counterfeits and substandards. The reduction in size leads to a reduction in costs. There is the obvious advantage in not having to fill a large laboratory with each separate device, but also to make the technique more affordable in areas that may require its use, where a decentralized approach is needed to service client area demands. Such devices depend far less on consumable items and routine maintenance kits, further reducing costs and expertise required for operation (Alonzo et al.2022). Though sensitive and more accurate than traditional eyeballing phone apps, the miniaturized offerings do not yet possess the required sensitivity and accuracy to confidently match traditional laboratory analysis instrumentation. Some have been successfully used, however, in scenario-wide confidence studies. Careful statistical studies into the device's sensitivity, when carefully validated for reproducibility and repeatability both in studies that include more than one operator and when switched on and off in succession to study durability, are still very much lacking. In addition, the 'best' type of apparatus is not concrete, and as such, no legislation goes into specificity in how test results obtained from a portable device should conform (Beć et al., 2022). However, guidance on what can be expected with a purchase of such a device is provided in relevant standards.

Enhanced Data Analysis Techniques

Advanced data analysis techniques have played a significant role in the evolution of drug spectroscopy. The analysis of drug products requires more sophisticated data interpretation. Chemometrics, from the more traditional methods to newer multi- or univariate statistical approaches, have thus become standard practice in the spectroscopically oriented field. Optimal selection of proper variables for predictive model

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development is essential, particularly when handling datasets containing so-called "big data" in the thousands. Machine Learning and Artificial Intelligence used in prediction-rich data consist of enhanced mathematical algorithms to extract meaningful chemical information available in the spectral data of drug substances and drug products, including their corresponding raw materials. The use of both Machine Learning and Artificial Intelligence in combination with spectroscopy has become extensively popular. The enhanced accuracy they deliver is most likely due to evaluating a large number of variables (Houhou & Bocklitz, 2021).

One of the key benefits of using Machine Learning and Artificial Intelligence is the development of automated iterative algorithms capable of handling the complete principle to practical use concept. They use machine model techniques to identify the best potential variable combinations to generate a model with a sufficient level of predictive power that is robust to the sample set. Modern sophisticated development of products with Machine Learning and Artificial Intelligence can screen more than 10,000 spectra in a matter of hours, which is a considerable amount of time when compared to conventional drug product development. Furthermore, commercially available software prepares the visual presentation of data, model development, validation, interpretation, and reporting, thus resulting in a one-day timeframe (Weis et al.2022). As a result, Machine Learning and Artificial Intelligence are helping solve unexpected physical and operational material science problems with relatively easy handling, visualization, and interpretation of both raw data and derived spectroscopic analytical results. Therefore, it is believed that the number of reported implementations of Machine Learning and Artificial Intelligence applications in spectroscopy and data analysis will continue to rise. The importance of these tools is highlighted in a variety of case studies dealing with pharmaceutical formulations, analytical development, and production that relate to real-time release testing. Scientific challenges, bottlenecks, and solutions are described, as well as tools provided for dealing with big spectroscopic data. More and more scientists involved in modern spectroscopic techniques development for drug substances and drug products should carefully evaluate the potential benefits of Machine Learning and Artificial Intelligence and, if these are deemed sufficient, acquire a sufficient level of expertise to apply and draw sound conclusions and make informed decisions. The concept itself is especially focused on the fact that it is the development of the product

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rather than a specific algorithm or mathematical method that makes further headway, thus establishing even more potential for dramatically increasing the industry (Meza et al.2021). At the same time, Machine Learning, Artificial Intelligence, the principles of digitalization, robotics, and automation have markedly become mature. In summary, more than half of this article focuses on advanced big spectroscopic data processing methods, pinpointing case studies and breaking the glass ceiling for other processing and digitization challenges in the analysis of materials.

Applications of Drug Spectroscopy in Pharmaceutical Research

Spectroscopic techniques are used in the pharmaceutical world and have become increasingly significant and vital for pharmaceutical research and development. The continued development and invention of new drugs and their delivery systems are the primary aim of pharmaceutical research. The authorities investigated the use of spectroscopic methods and declared that these techniques are important to pharmaceutical quality control. They aid in understanding the structure of pure drugs, identify unknown impurities, and provide validation data for unknown impurity limits in toxicology studies. The assays most commonly perform analyses to validate the results obtained using chromatographic methods. Furthermore, spectroscopy has a wide range of practical applications when it is employed in formulation development, particularly for photostability and chromatographic interference studies (Balekundri & Mannur, 2020).

A test for the analysis of polymorphic forms by measuring the resonance frequency and producing NMR data of the amilocaine drug is currently being investigated, as well as the de-mixing process of solid dosage forms. This is not only a viable method of distinguishing between different forms, but also a rapid, non-destructive method for revealing variability in the hydration state of monohydrate active pharmaceutical ingredients. Absorption and reflectance methods have been developed to quantify the complexation capacity of ion exchange resins and the encapsulation potential of microcapsule preparation. Pharmacokinetic and drug delivery research continue to use spectroscopy as well. Newly developed UV methods for the estimation and discovery of drugs such as flavonoids based on nano-fluids, matrices, and micro-emulsions have recently been reported and validated. The latest trends in the clinical

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implications of attenuated total reflectance spectroscopy and real-time spectroscopy are discussed. In vitro drug release tests, the development of solid lipid nanoparticles and nano-disperse systems, the optimization of equal dosage forms, and the assessment of the effects of impurities in product batches are all examples of formulations used in bioinformatics (Malvandi et al.2022). Formulation development and bioavailability studies can also benefit from the application of these types of protocols.

Quality Control and Assurance

Quality control and assurance is an important application for drug spectroscopy. Such applications help in determining safety, efficacy, and quality attributes of raw materials, pharmaceutical intermediates, and drug products. It is important to minutely check for the existence of any possible impurities, even at trace levels, in the final formulation. The low-level impurities, such as genotoxic impurities, are supposed to occur at concentrations lower than 1.5 µg per day or 0.1% in the final formulation dose, such as toxins and solvents in the formulations. They play a major role in controlling the drug quality using advanced analytical techniques. There are several dedicated spectroscopic methods that can strongly detect impurities, diluents, and quantify drug substances or parts used in drug formulations in a coherent and proficient way. Hence, the quality assurance of the final drugs involves a combination of analytical tests, including physicochemical, performance, and integrity checks (Silge et al.2022).

It encompasses attaining analytical testing procedures to confirm compliance of pharmaceuticals with established standards. The perfection of identity, purity, and strength is signified in drug spectroscopy chromatography, Fourier transform infrared spectroscopy (FTIR), and X-ray diffraction. Commonly used examples of spectroscopy in quality control are IR spectroscopy in combination with microscopy. In quality control applications, the best-known method is vibrational spectroscopy using Fourier transform Raman spectroscopy (FT-Raman). Real-life case studies indicate that successful spectroscopy tools continue to become an integral part of the validation of the quality of drugs used in new formulas and in the marketing of previous ones. The continuous change in quality control requirements is a hurdle. However, the quality control system will always be required because the control is not only for the new syntheses, but good quality is always a goal for the drugs. The need for a continuous methodology confirms that the method always inspects during validation (Fiore and Pellerito2021).

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Manufacturing practices are necessary to properly utilize the spectroscopy drugs referenced from previous validation. In general, spectroscopy works and depends on the drug mass, so the approach of using drugs with a small molecular weight limit is a viable alternative. Our intention was to contribute in this mini-review to demonstrate many practical applications of molecular spectroscopy in drug development and spectral therapy in the analysis of drugs and pharmaceuticals with a reduced amassing number. We have briefly highlighted some studies currently referred to and for the purpose of dosage techniques and the manufacture of drugs (Tamara et al., 2021). Several functions in drug substances have been measured, including, but not limited to, dose precision, robustness, performance verification, and process validation in production industries. Perhaps the most practical solution was the application of low molecular weight drug analytes.

Formulation Development

Formulation development is the process of combining varied chemical entities called excipients together to manufacture a final medicinal product that possesses a wide array of favorably acceptable physical, chemical, and biological performances. Spectrophotometric and spectroscopic techniques play a key role in the formulation development for these pharmaceutical products. They are the most important analytical tests in the formulation of the dosage form as well as in the preformulation stage. In the optimization of the pharmaceutical formulation, the selection of excipients and their compatibility studies with drug substances is fundamental. These tests give valuable information about the developed formulations, likely degradation sites in the gastrointestinal tract, and help to predict the bioavailability and stability of the drug. The analytical methods are usually developed and optimized for different dosage forms like tablets, capsules, injections, gels, creams, and liquid oral dosage forms such as syrups and solutions, as well as inhalation dosage forms, small or large volume parenterals (Christodoulou et al.2022).

A spectroscopic technique, such as infrared spectroscopy, Raman spectroscopy, or NMR spectroscopy, is generally used to investigate the interaction between components in the formulation. This approach can be extended to any type of excipient, including the controlled release, such as HPMC, carbopol, and chitosan. Initial spectroscopic methods are developed at the research scale and then applied to the

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development scale. There are many pharmaceutical formulations present in the market that were developed with the use of spectroscopy (Li et al., 2021). There is also increasing research in the area of excipient properties to optimize formulation properties, including in vitro dissolution.

Pharmacokinetic Studies

Pharmacokinetics aims to understand the time course of how the body interacts with a drug following administration to a patient or experimental animal. There are four general processes that contribute to drug behavior in the body, and it is their measurement and understanding that is the subject of a pharmacokinetic study: the absorption of the drug from the site of administration, the distribution of the drug in the body once it has entered, the metabolism of the drug into more polar or chemically reactive species, and excretion from the body, which includes both reversible back entrance into the bloodstream as well as ultimate irreversible removal from the body. Spectroscopy is playing a vital role in these areas by using an in vivo, non-invasive method to track the drug at any sites in the body following an extended time period (Coelho et al., 2021). This technique is rapidly growing due to advancements in the field and also because of the use of advanced instruments.

The next generation intelligent spectroscopes are the most advanced techniques used for pharmacokinetic studies, especially for preclinical and clinical studies. As just a finger prick of blood is required, they can measure different kinetic parameters such as Tmax, Cmax, Kin, Kout, Ka, K, AppV, F, and Tmax. Furthermore, using new biological tissues' optical properties, one can calculate the concentration of various constituents of the organs within the body. With the use of these techniques, the information obtained is very reliable and accurate, including various pharmacokinetic studies. There is also a rise in non-invasive drug estimations since the development of more advanced spectroscopes, particularly using a Fourier transformation system (Alshawwa et al.2022). Many reports demonstrate successful applications in this area. Clinical examples and case studies of in vivo therapeutic drug monitoring have also been successfully demonstrated using these new techniques. However, the major challenges currently being faced are the need for high sensitivity and specificity, and not all drugs can be determined using spectroscopy (Beć et al., 2020).

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Future Directions and Emerging Trends in Drug Spectroscopy

The trend in drug spectroscopy, looking to the future, is more sensitive spectroscopy suitable for drug detection in the clinic for the full range of drugs used in interesting practices, with a strong emphasis on intrinsically biomedical spectroscopy. The possibility of pursuing multimodal approaches is also an intriguing future possibility. These developments are likely to be strongly aided by the currently burgeoning area of machine learning and artificial intelligence. The future development of high-sensitivity techniques might also be possible from emerging areas in materials such as nanoparticles and nanocarbons. Furthermore, with the increasing importance of handheld Raman and IR spectroscopy for medical diagnoses, technological improvements in these devices seek to further miniaturize and protect instruments from environmental conditions, making data collection faster, more accurate, more reproducible, and more instrument-agnostic (Gergeroglu et al., 2020). Many differences exist between standard drug analysis and drug detection in clinical contexts. One perspective suggests that developments in the future will guarantee that this work will proceed; increasing amounts of interesting biomedical data from the early successes of new techniques will direct science down these emerging channels. Rather, one area that might facilitate the achievement of these future advances appears to be coordinating and collaborating the needs of different sectors of the spectroscopic community (Beć et al., 2020). For example, with dedicated biomedically aligned meetings from analytical and vibrational fields. It will also be important to discuss these plans and findings in some of the literature. In convincing funders of the increased importance of this work, or in discussing approaches with companies with the capability to produce reliable miniaturized equipment, it may be of interest to drug regulatory bodies to keep abreast of progress in spectroscopy.

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