ANALYTICAL METHODS FOR THE ESTIMATION OF VARIOUS PHARMACEUTICAL DRUGS USING IR SPECTROSCOPY: A REVIEW

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ABSTRACT: Infrared spectroscopy also termed as vibrational spectroscopy is used for analysis and determination of different functional groups and compounds in different areas and mainly in pharmaceutical field. It is an easy and accurate method for functional group determination. Principle behind this is the measurement of the molecular bond vibrations of compounds, excited by radiation of a suitable frequency, when given the conditions for energy absorption by the molecules. Fourier transform infrared spectroscopy (FTIR) and Attenuated transmission reflectance (ATR) Spectroscopy are the new advancement in measurements of IR. Both can be used for qualitative and quantitative analysis of different substances. Here, we review the potential applications of FTIR and ATR for use in analysis of drugs. Vibrational spectroscopy has shown high potential as a novel method of analysis.

Key words: Attenuated transmission reflectance, Infrared Spectroscopy, Fourier Transform Infrared Spectroscopy, Quantitative Analysis of Drugs, Vibrational Spectroscopy.

INTRODUCTION

Infrared Spectroscopy involves the interaction of Infrared radiations with matter. It is used to identify and study chemicals both qualitatively and quantitatively. The sample which is used may be solid, liquid or gas. Instruments used as IR spectrophotometer for producing IR spectrum. Infrared radiation is electromagnetic radiation in the wavelength region ranges from 0.78 mm–1000 mm [Indian Pharmacopoeia.,1996]. Spectroscopy in the infrared range includes far IR regions from 4000-400cm^{-1}. Infrared spectrum is a graph between transmittance (or absorbance) *vs* wavenumber. The common laboratory instrument used in IR spectroscopy is Fourier transform infrared spectroscopy (FTIR) and Attenuated Total Reflectance (ATR) [Pavia et al., 2009].

FTIR is used for the identification of organic and inorganic materials, the quantitative determination of species in complex mixtures, molecular composition of surface species and the differentiation of structural and geometric isomers. Other applications are as in materials science for determination of key functional groups in organic polymers and a nondestructive method of analysis in ion sugar industry. It is also used to separate components along with chromatography, as a detector capable of molecular identification of unknown species and for characterization of nanomaterials as well as for forensic applications [Gaffeny et al., 2003]. This articles reviews the application of FTIR in analysis of drugs.

Another new method such as ATR **(**attenuated total reflectance) is a sampling technique used in conjunction with IR spectroscopy which enables sample to be directly analyzed in the solid or liquid state without further preparation. The advantage of ATR-IR over transmission-IR, is the limited path length into the sample that avoids the problem of strong attenuation of the IR signal in highly absorbing media like water. ATR-FTIR is also used to investigate protein/pharmaceutical interactions in detail. It produces difference spectra to study conformational changes of the proteins upon binding [Perkin et al., 2007].

ASSAY PERFORMED USING FTIR AND ATR

Analysis of Ciprofloxacin in Tablets

This method for analysis which involves least square treatment of FTIR spectrometric data of the wavenumber corresponding to the carbonyl group 1707cm^{-1}. The method involves the extraction of active ingredients with methanol followed by phosphate buffer pH 6.0.The excipient in the commercial preparation does not interfere with the results. The results involve determination of following parameters such as Linearity in range of 2-20 µg/ml with regression coefficient 0.998, Limit of Detection (LOD)- 0.068 µg/ml and Limit of Quantitation (LOQ)- 0.450 µg/ml. The precision obtained were as 1.16 and 0.73 % Relative Standard deviation (RSD). The percentage recovery obtained were 98.65%, 101.05%, 99.8%, 103.21% of market product of ciprofloxacin such as Cifran, Biosip, Cipsogen and Ciplox. Here statistical results were compared with other method of quantification of ciprofloxacin [Pandey et al., 2002].

Analysis of Folic Acid

Infrared analysis was conducted for pure folic acid which was weighted (0.5 -6.7) mg then mixed with potassium bromide to obtain total mixed weight. Calibration curve obtained from FTIR spectra between the weight of folic acid and the absorbance at a wave number and comparing the resulted correlation coefficient values for calibration curves. The relative percentage error (E%) and Recovery percentage (Rec. %) results for both methods proved that sampling procedure in FTIR technique for both pure and pharmaceutical samples was of more superiority beside being simple [Raouf et al., 2014].

Analysis of Lorazepam

Extraction of lorazepam with sonication and direct determination of peak height at 1704 cm^{-1} using baseline correction between 1850 and 1550 cm^{-1} is performed. This method provides a limit of detection of 0.0030 mg per tablet, a relative standard deviation of 2.65% for concentration

level of 1 mgg^{-1}. Results obtained by FTIR agrees with those obtained by a reference methodology based on UV spectrometry and hence, the developed method offers a good alternative for the determination of lorazepam in commercial products [Konoz et al., 2012].

Analysis of Clindipine

Cilnidipine is new and effective antihypertensive drug. Cilnidipine can also be determined by Fourier transform infrared spectrophotometric techniques. Here we measure the absorbance of carbonyl group (C=O) peak at 1697 cm^{-1}. This method is validated for pharmaceuticals in tablets and %RSD was found to be less than two with recovery levels 99.8-102.5 and 99.8- 101.4 as per absorbance and peak area respectively [Patel and kadam et al., 2015].

Analysis of 5-Fluorouracil

Gold nanoparticles are used as probes to detect 5-fluorouracil. The nature of binding between 5FU and gold nanoparticles *via* complexation is investigated using (FTIR). The 5FU-colloidal gold complex is observed to have antibacterial and antifungal activity against *Micrococcus luteus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Aspergillus niger*. Pure drug shows band at 3450 cm^{-1} corresponding to the stretching frequency of –NH group at 3534 cm^{-1} and other absorption bands at 1684 and 1420 $^{cm-1}$ are due to C-C and C–N stretching vibrations, respectively. Here the free –NH group is involved in binding on the gold nanoparticle surface as gold has a strong affinity towards amino groups. [Selvaraj et al., 2015]

Method to Investigate the Nature of Binding of Antibiotics.

Gold nanoparticles are effective for transporting large amount of antibiotics on their surface via electrostatic interaction between the amine group of drugs and gold nanoparticles [Grace et al., 2007]. The absorption peak at 1399 cm^{-1} was observed only for gold nanoparticles, attributed to symmetrical stretching vibration of carboxylate group [Kishore et al., 2009]. The amino-glycosidic antibiotics showed characteristic absorption bands corresponding to N–H bending frequency at 1600–1652 cm^{-1}.The distinctive NH_2 stretching frequencies of the amine groups were noticed at 3435, 3491, 3456 and 3482 cm^{-1} for the antibiotics streptomycin, kanamycin, neomycin and gentamicin, respectively [Tong et al., 2003]. It can be concluded that amino groups of the antibiotics are bound to gold nanoparticle surface. These IR data also confirms the coating of the nanoparticles by the protein BSA [Rastogi et al., 2012].

Identification of the Counterfeit Drug

ATR is also used for identification of counterfeit drugs. Here sample preparation is not required here and gives information on the spatial distribution of the components at the surface of the sample used. IR spectra obtained using focal plane array detector. The characteristic absorbance bands obtained at 1,750cm^{-1}, 1,055 cm^{-1}observed in genuine AS tablets to show the distribution of the active ingredient (AS) and several other compounds like artemisinin, dipyrone, paracetamol and calcium carbonate [Martin et al., 2012].

Methods for Determination of Drug Localized in the Skin

ATR-FTIR is used in conjunction with tape-stripping and ATR spectra's are obtained each within the stratum corneum. Here aqueous saturated solutions of C-labeled 4-cyanophenol were applied, in an appropriate delivery system, to the forearm surfaces of healthy human volunteers. After 15 min, the delivery system was removed and the treated skin was then harvested by tape stripping [Potts et al., 1985]. Each tape strip is analyzed for 4-cyanophenol, referring to calibration graph data and taking into account tape strip weight values, it was possible to determine the concentration depth profile for the permeant in the stratum corneum [Naik., 1995].

Analysis of Acetylsalicylic Acid

Here KBr-spectra were compared for the determination of active substance in drug preparations. The Beer-Lambert law and two chemo metric approaches, partial least squares (PLS) and principal component regression (PCR+) methods, were used in data processing. The Beer-Lambert law used for the quantitative determination of ASA in pharmaceutical products at 1605.49 cm^{-1} with regression coefficient(R) of 0.9886 [Benicia., 2006].

Determination of the Extent of Lipid Peroxidation in Plasma During Hemodialysis

FTIR-ATR spectroscopy used to determine primary peroxidation products. The proposed method was effective during the evaluation of changes in the extent of lipid peroxidation in plasma during a hemodialysis in sheep. A measurement using the FTIR-ATR showed an increase in plasma lipid peroxidation after 15 and 240 minutes of treatment. As FTIR-ATR spectroscopy showed lower reproducibility between different series of measurements than the TBARS method, which resulted in high standard deviation values, the lipid peroxidation test technique using FTIR ATR spectroscopy allowed for the determination of oxidative stress in plasma during hemodialysis [Oleszko et al., 2015].

Study of Chemical Intermediates by Means of ATR-IR

3,5-Diamino-1,2,4-triazole (DAT) is a significant energetic materials intermediate. Online attenuated total reflection infrared spectroscopy combined with the novel approach of hybrid hard- and soft-modelling multivariate curve resolution-alternating least squares (HS-MCR) analysis used to monitor and detect changes in structural properties of the intermediate. This study gives the basis for the optimization of synthesis process and technology of energetic materials and provides a strong technical support of research and development of energy material [Junxiu et al., 2017].

Method for Identification of Yeasts Isolated from Human and Animals.

This method involves determination of spectral differences between the various examined species of *Candida*, *Cryptococcus*, *Trichosporon*, *Rhodotorula* and *Geotrichum* isolated from different sources. This method confirmed that FTIR spectroscopy is a promising diagnostic tool, because of its sensitivity, rapidity and high differentiation capacity compared to conventional/molecular techniques [Taha at al., 2013].

CONCLUSION

It is clear that FT-IR spectrometry is capable of direct quantitative and qualitative determination of different substances used in pharmaceutical formulation and for other purposes. With the commercial software involving chemometric approaches, Beer-Lambert law, the methods proposed are simple, precise and not time-consuming compared to the other methods that exist in literatures.

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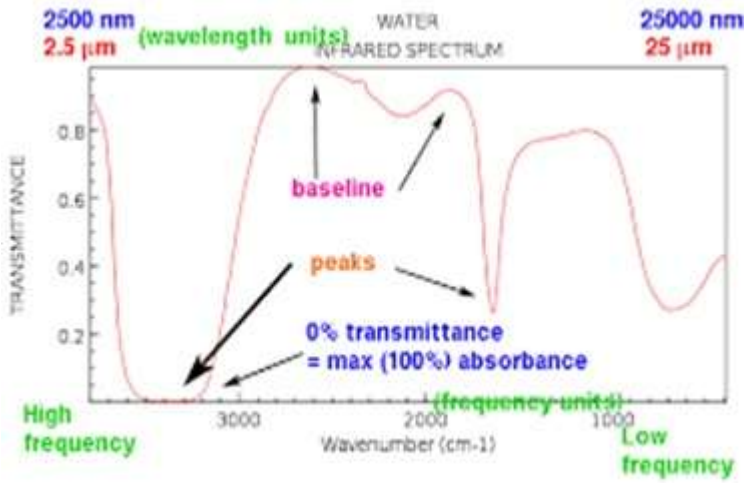

Fig1; Regions of IR spectrum

[Source;Masterorganicchemistry.com]

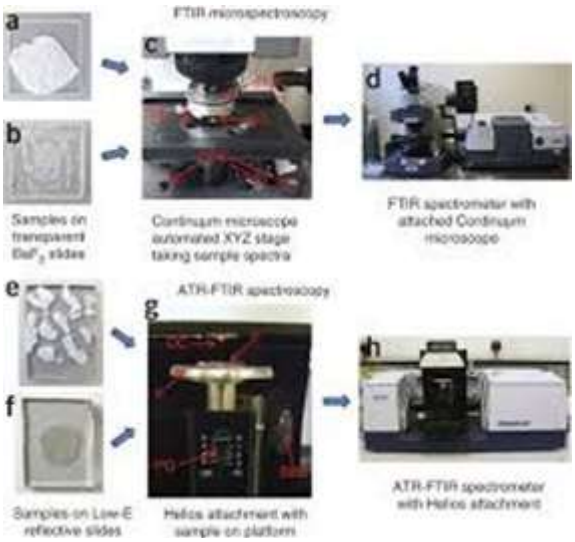

Fig2; Instruments used in FTIR [Source;http://www.nature.com/nprot/journal/v5/n11/images_article/nprot.2010.133-F3.jpg]

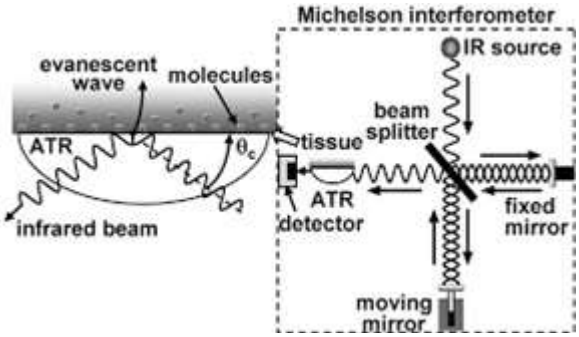

Fig3; Instrumentation In ATR

[Source; https://encryptedtbn0.gstatic.com/images?q=tbn:ANd9GcQZgqGBN_5sk3fDB9OQR7DU0OMFRwtiPAvy7hrGv-FnxqjpOBxHQ]