5. INFRARED SPECTROSCOPY (IR)

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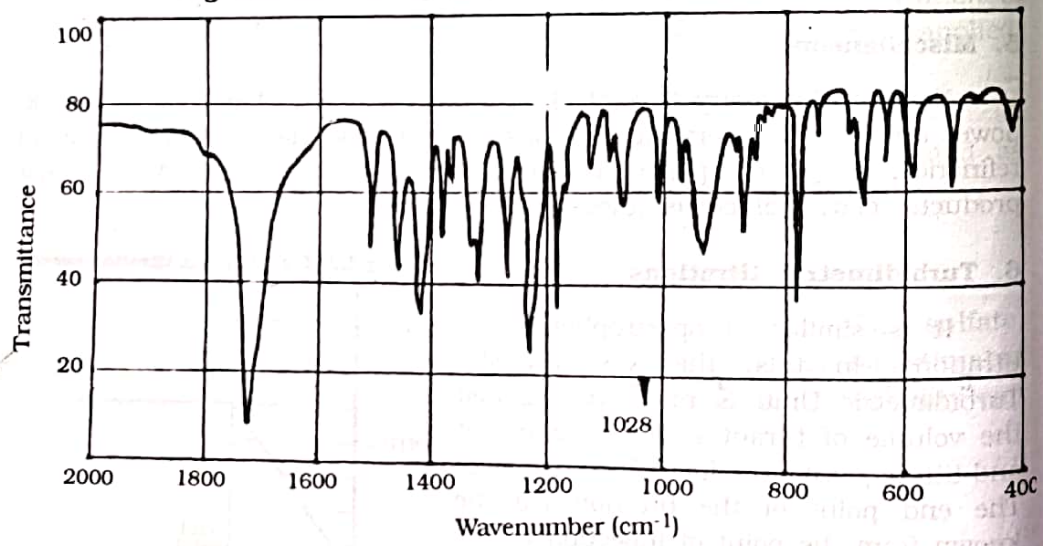
Fig 5.0. Infrared Spectra of Ibuprofen (KBr disc)



INTRODUCTION

Infrared spectroscopy or vibrational spectroscopy is concerned with the study of absorption of infrared radiation, which results in vibrational transitions. IR spectra is mainly used in structure elucidation to determine the functional groups. It is already known that,

Energy of a molecule = Electronic energy + Vibrational energy + Rotational energy

In this chapter, the study is focussed towards the changes in the vibration of molecule or absorption of energy due to vibrations.

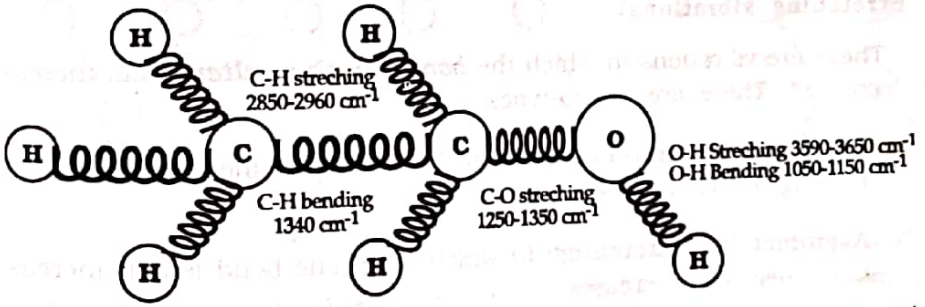
PRINCIPLE

In any molecule, it is known that atoms or groups of atoms are connected by bonds. These ***bonds*** are ***analogous*** to ***springs*** (Fig 5.1) and not rigid in nature. Because of the continuous motion of the molecule, they maintain some vibrations with some frequency, characteristic to every portion of the molecule. This is called the ***Natural frequency of vibration.*** When energy in the form of infrared radiation is applied and when,

Applied infrared frequency = Natural frequency of vibration,

absorption of ***IR*** radiation takes place and a ***peak is observed.***

Fig 5.1. Infrared vibrations of Ethanol



Every bond or portion of a molecule or functional group requires different frequency for absorption. Hence characteristic peak is observed for every functional group or part of the molecule. In other words, IR spectra is nothing but a finger print of a molecule. Eg. IR spectra of Ibuprofen is given in Fig 5.0.

In Pharmaceutical analysis, we use infrared radiation (mid-IR) of wavelength 25μ to 2.5μ or wavenumbers from ***400cm^{-1} to 4000cm^{-1}***. There are other regions like near-IR (0.8μ to 2.5μ) and far-IR (25μ to 1000μ) which are not used in Pharmacy.

In IR spectra, we use wave numbers instead of wavelengths for mentioning the characteristic peak, because wave numbers are larger values and easy to handle than wavelengths which will show only small differences between functional groups.

Wave number is nothing but the number of waves present per cm, which can be calculated from the wavelength.

$$\frac{1}{\text{wavelength in } \mu} \times 10^4 = \text{wavenumber per cm or } cm^{-1}$$

Criteria for a compound to absorb IR radiation

1. Change in ***dipole moment***.
2. ***Applied IR frequency*** should be ***equal*** to the ***natural frequency*** of radiation.
   Otherwise compounds do not give IR peaks.

TYPES OF VIBRATIONS

There are different types of vibrations (Fig.5.2)

1. Stretching vibrations

These are vibrations in which the ***bond length*** is ***altered*** i.e. increased or decreased. There are 2 sub-types:

a. **Symmetrical stretching:** in which two bonds increase or decrease in length, symmetrically.

b. **Asymmetrical stretching:** in which when one bond length increases, the other one decreases.

2. Bending vibrations

a. **In-plane bending:** In these vibrations, there is ***change*** in ***bond angle***. Bending of bonds takes place ***within the same plane.***

(i) **Scissoring:** in which bond angle decreases

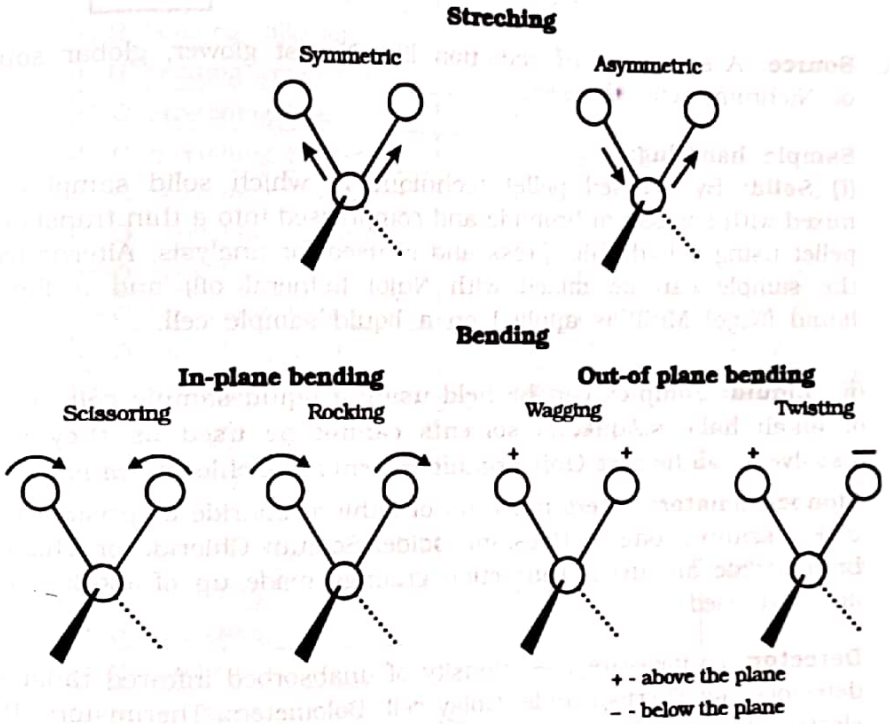
(ii) **Rocking:** in which bond angle is maintained, but both bonds moves within the plane

b. **Out-of-plane bending**: (outside the plane of molecule)

(i) **Wagging:** in which both atoms move to one side of plane.

(ii) **Twisting:** in which one atom is above the plane and the other is below the plane.

Fig 5.2. Different types of vibrations in a molecule



If a molecule contains 'n' atoms, the total number of fundamental vibrations can be expressed as

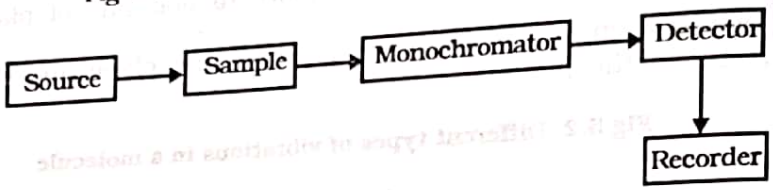
(3n-6) in a Non-linear molecule

(3n-5) in a Linear molecule

But sometimes, it will not be possible to obtain the predicted number of peaks, because of spectral overlapping, low resolution or due to weak peaks etc.

INSTRUMENTATION

Fig 5.3. Schematic diagram of IR spectrophotometer



1. **Source:** A source of IR radiation like Nernst glower, globar source or Nichrome wire is used.

2. **Sample handling:**
   (i) Solid: By pressed pellet technique in which solid samples are mixed with Potassium bromide and compressed into a thin transparent pellet using a hydraulic press and is used for analysis. Alternatively, the sample can be mixed with Nujol (mineral oil) and a film of liquid (Nujol Mull) is applied on a liquid sample cell.

   (ii). **Liquid:** Samples can be held using a liquid sample cell made of alkali halides.Aqueous solvents cannot be used as they will dissolve alkali halides.Only organic solvents like chloroform is used.

3. **Monochromator:** Filters made up of Lithium flouride or prisms made of Potassium bromide, Caesium iodide, Sodium Chloride or Thallium bromoiodide are used. Diffraction gratings made up of alkali halides are also used.

4. **Detector:** To measure the intensity of unabsorbed infrared radiation, detectors like Thermocouple, Golay cell, Bolometers, Thermistors, Pyro electric detectors are used.

5. **Recorder/Plotter:** They are used to record the IR spectrum, on white paper or transparent sheets.

6. **Types of instruments:** Single beam IR spectrophotometer and Double beam IR spectrophotometers are available. Also FT-IR (Fourier

Transform) Infrared Spectrophotometers with advanced features like matching of spectra, identification of functional group/compound using library databases and software are available. The advantages of FT-IR over dispersive instrument is that it is rapid, more sensitive, accurate and has more computational capabilities.

Table 5.1
ABSORPTIONS OF COMMON FUNCTIONAL GROUPS

Group	Range (cm^{-1})
C-H Stretching (alkane)	2960-2850
C-H Stretching (alkene)	3040-3010
C-H Stretching (aromatic)	3030
C-H bending (alkane)	1340
C-H bending (aromatic)	700-850
C=C Stretching (alkene)	1680-1620
C≡C Stretching (alkyne)	2100-2200
C=C Stretching (aromatic)	1450-1600
C=O Stretching (ketone)	1705-1725
C=O Stretching (aldehyde)	1720-1740
C=O Stretching (ester)	1735-1750
C=O Stretching (acid)	1700-1725
C=O Stretching (amide)	1650-1700
O-H Stretching (Free)	3590-3650
O-H bending (alcohols)	1050-1150
O-H bending (phenols)	1200
C-O stretching (alcohols)	1250-1350
C-O Stretching (phenols)	1310-1410
N-H Stretching	3400-3500
N-H bending	1500-1650
C-N vibrations	1000-1400
C≡N Stretching	2240-2260
C=N Stretching	1630-1690
N=N Stretching	1575-1630
S-H Stretching	2500-2600
C=S Stretching	1050-1200
S=O Stretching	1050-1400

APPLICATIONS

1. **Identification of functional group and Structure elucidation:** The entire IR region is divided into

   Group frequency region - $4000cm^{-1}$ to $1500cm^{-1}$

   Finger print region - $1500cm^{-1}$ to $400cm^{-1}$

In the ***group frequency region***, the ***peaks*** corresponding to different ***functional groups*** can be observed. (eg.) Amino group, alcoholic group etc. ***Table 5.1*** lists some of the common groups and their absorption region.

Every part of the molecule has different atoms and are connected by bonds. Each bond requires different IR region for absorption and so characteristic peaks are observed. Hence this region of IR spectrum is called as the ***finger print region*** of a molecule.

2. **Identification of drug substance:** IR spectrum of sample and standard can be compared to identify a substance. If the spectra are same, then the identity of the sample can be confirmed. This technique is called as ***spectral matching***. Eg. The IR spectra of sample Ibuprofen is compared with the standard as in Fig 5.0.

3. **Identifying the impurities in a drug sample:** Impurities have different chemical nature when compared to the pure drug. Hence these impurities give rise to additional peaks than that of the pure drug. By comparing these, we can identify the presence of impurity.

4. Study of hydrogen bonding - whether it is of intermolecular or intramolecular type.

5. Study of polymers.

6. Ratio of Cis-trans isomers in a mixture of compounds.

7. **Quantitative analysis**: The quantity of a substance can be determined either in pure form or as a mixture of 2 or more components. In this, the peak which is characteristic for the drug is chosen and a comparison of the extinction ($\log I_o/I_t$) of peaks for standard and sample is done. This method is called as Baseline technique and is thus used to determine the quantity of a substance.