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HYPHENATION OF RAMAN SPECTROSCOPY WITH MASS SPECTROSCOPY: A REVIEW

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Keywords:

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ABSTRACT: A spectroscopic method called Raman spectroscopy is frequently employed to discover the vibrational modes of molecules. Raman spectroscopy is frequently used in chemistry to give compounds a unique structural fingerprint. Using mass spectroscopy, one or more molecules present in a sample can have their mass to charge ratio (m/z) measured. It is frequently possible to estimate the precise molecular weight of the sample's constituent parts using these measures. Raman spectroscopy and mass spectroscopy are complimentary analytical methods that are used to offer details on the chemical make-up and functional groups of the target analytes. Each device offers particular chemical data. When the raman spectroscopy is hyphenated with mass spectroscopy the interface used is a small piece of tissue paper. Biological Sample Analysis, New medication chemical analysis, to distinguish between positional isomers. The hyphenated approach makes it simple to get analytical findings such as molecular weights, chemical structures, and functional groups.

INTRODUCTION: Raman Spectroscopy is a molecular spectroscopic method for studying the properties of materials by taking use of the interaction between light and matter [1, 2]. Raman spectroscopy uses light scattering to produce the data it collects. Raman spectroscopy may be used to identify compounds since it produces a spectrum that is representative of the precise vibrations of a molecule (molecular fingerprinting) [3, 4]. In the analytical process of mass spectroscopy, chemical compounds are recognized by classifying gaseous ions in magnetic and electric fields according to their mass to charge ratio (m/z) [5, 6].

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Combining two techniques together with a hyphen is known as coupling. The independent analytical methods of mass spectroscopy (MS) and Raman spectroscopy are utilized to offer details on the chemical composition and functional groups of the target analytes. Each device offers particular chemical data. In-depth structural data may be concurrently gathered from the target substances that use these two analytical instruments online without missing any crucial quantitative data[7, 8, 9, 10]. The online hyphenation of Raman spectroscope and mass spectrometer is performed using a little strip of tissue paper. Moreover, it can make surface-enhanced Raman spectroscopy easier [11, 12, 13, 14].

Principle: The fundamental idea behind Raman spectroscopy is that the preponderance of photons that scatter or disperse when light interacts with molecules in a gas, liquid, or solid have the same strength as the input photons. This is referred as the

Rayleigh scattering or elastic scattering. Around 1 photon in every 10 million of such photons will scatter at a frequency distinct from the incoming photon. Inelastic scattering or the Raman Effect is the name of this mechanism [15, 16]. A stream of highly intense electrons is used to blast the molecules in mass spectroscopy. Ionization and fragmentation of the molecules result in the creation of many positive ions, among other types of components. Every type of ion has a unique mass to charge value, or m/z. As the majority of ions have a charge of 1, m/z is just the ion's molecular mass [17, 18, 19].

Instrumentation: The components of Raman spectroscopy are **Fig. 1.**

- Laser source
- Sample cell
- Wavelength selector
- Radiation transducer
- Detector
- Computer data system

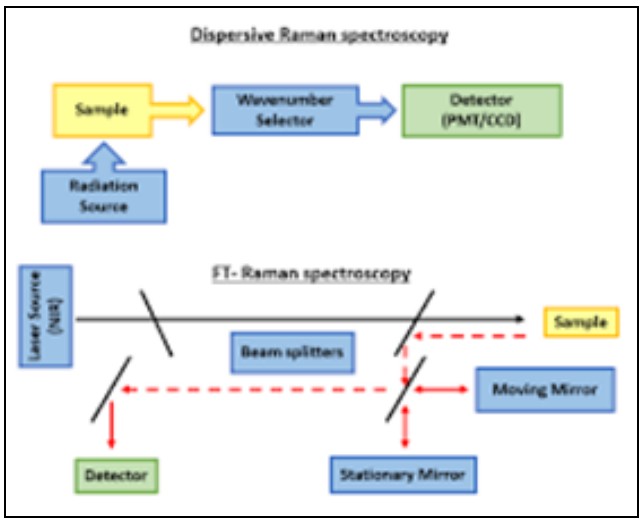

FIG. 1: BLOCK DIAGRAM OF RAMAN SPECTROSCOPY

Source: It makes usage of a monochromatic light source, often a laser that emits light in the visible, near-infrared, or near-ultraviolet ranges [20, 21, 22].

Laser Type	Wavelength (nm)
Argon ion, Krypton ion	488 or 514.5, 530.9 or 647.1
Helium neon, Diode Nd-YAG	632.8, 785 or 830 1064

Wavelength Selector (Filter or Spectrometer): A single laser beam can be isolated using band pass filters, a wavelength selection (Filter or Spectrometer). Often these dispersive instruments use a notch filter and a high-quality grating monochromator in conjunction. To distinguish between strong Rayleigh scattered radiations and comparatively weak Raman lines, techniques including double or triple grating monochromators, super notch filters, rejection filters, holographic notch or edge filters, and holographic filters are utilized [20, 21, 23, 24].

Radiation Transducer: A radiation transducer transforms a light-based optical signal into an electrical signal (current or voltage).

Detectors:

Photomultiplier Tube: The PMT, or photomultiplier tube, is a tool used for photon detection. By fusing the photoelectric effect with secondary emission, the photomultiplier turns light into an electrical signal. The photoelectric effect allows a photomultiplier to absorb light and then reemit it as electrons. A scintillation detector's photomultiplier tube is an essential component. The PMT absorbs the light that the scintillator emits. Because of its high quantum efficiency and strong amplification, this is the preferred option for photon detection[21].

Components of PMT **Fig. 2**.

Photocathode: There is a photocathode immediately following a little entering window. Materials with weakly bound valence electrons are used to create photocathode. It has a large cross section for the photoelectric effect, which transforms photons into electrons.

Dynodes: With the help of a voltage potential, the groups of initial electrons generated are electrostatically accelerated and concentrated so that they hit the first dynode with enough force to release more electrons. There are a number of dynodes set up that are operated at progressively higher potentials and built of materials with fairly modest work functions. At the dynodes, secondary emission multiplies electrons. As the electrons are released from the first dynode, they are directed towards the following one, which has a greater voltage. At each dynode, 3–4 electrons are emitted

for each incident electron, and since 6–14 dynodes are connected together in series, the total gain will be close to 104–107 when the electrons reach the anode. Operating voltages typically fall between 500 and 3000 V. Enough electrons are available at the last dynode for further amplification to start a pulse that is strong enough. The pulse generated contains data on the radiation's initial incidence energy. The number of pulses produced per unit time can be used to determine the radiation's intensity [25].

Principle of Operation:

- The material in the scintillator is exposed to ionizing radiation as it enters. The electron is elevated to an excited state as a result of its interactions with the substance.
- The track for the charged particles is the particle's own journey. Gamma rays are uncharged particles that have energy that is transformed to energetic electrons *via* Compton scattering, pair creation, or the photoelectric process.
- As the atoms and molecules of the scintillator material quickly return to the ground state, they produce a photon in the visible or near-visible light spectrum. It is claimed that the substance fluoresces. The energy generated is directly related to the energy that the ionizing atom has left behind. The three types of phosphorus that are employed are plastic phosphorus, inorganic crystals, and organic crystals.
- Photocathode is part of a photomultiplier tube. A maximum of one photoelectron per photon is released when the light from the scintillator hits the photocathode.
- This set of initial electrons is electrostatically speeded up and focused and use a voltage potential so that they may strike the first dynode with sufficient force to liberate further electrons.
- These secondary electrons are drawn to a second dynode, where they hit, producing further electrons. In the photomultiplier tube, this is the process that takes place.
- There is a current amplification impact at each step of the dynode as a result of the additional electrons produced by every one of these successive dynode collisions. Each stage has a larger potential than the preceding one in order to create the accelerating field.
- The first or primary signal is amplified, and this process of amplification is carried out for an additional 10 to 12 steps.
- At the last dynode, there will be adequate electrons accessible for additional intensification to produce a pulse with the necessary strength. This pulse conveys information on the radiation's initial incidence energy. The amount of pulses each for a unit of time could also be employed to determine knowledge concerning radiation intensity [26, 27].

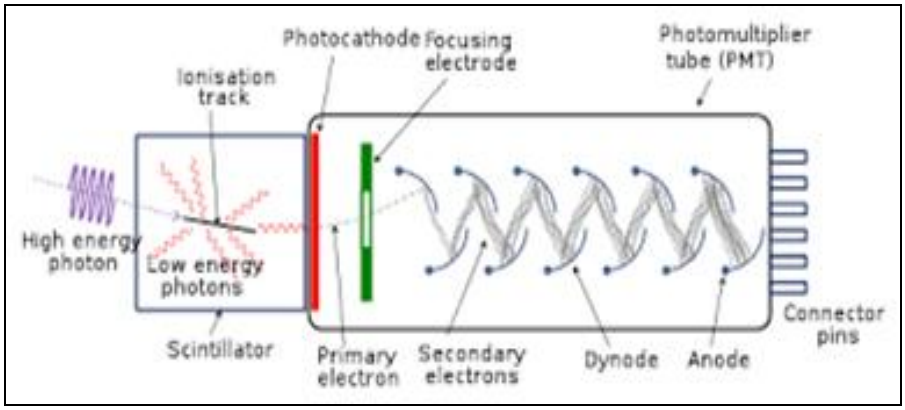

FIG. 2: PMT (PHOTO MULTIPLIER TUBE)

Charge Coupled Device: It may be characterized as a light-sensitive integrated circuit that has been imprinted on a silicon surface to create light-sensitive components known as pixels, each of which is transformed into an electrical charge [23, 24] **Fig. 3**.

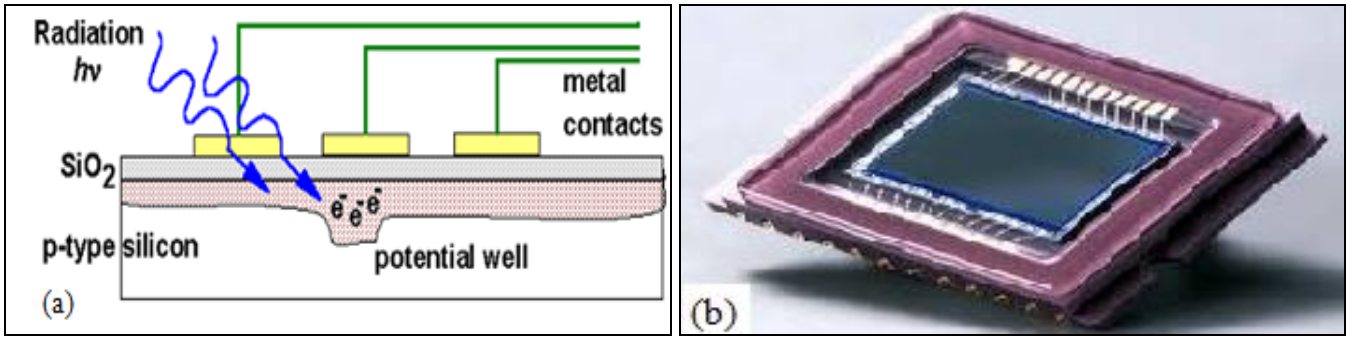

FIG. 3: (A) OPERATION OF CCD, (B) CHARGE COUPLED DEVICE

Raman Spectrum: The y-axis of the Raman spectrum represents intensity, while the x-axis is the frequency of the "Raman Shift." The difference in frequency between dispersed light and laser light is known as the Raman shift [20, 22, 28] **Fig. 4.**

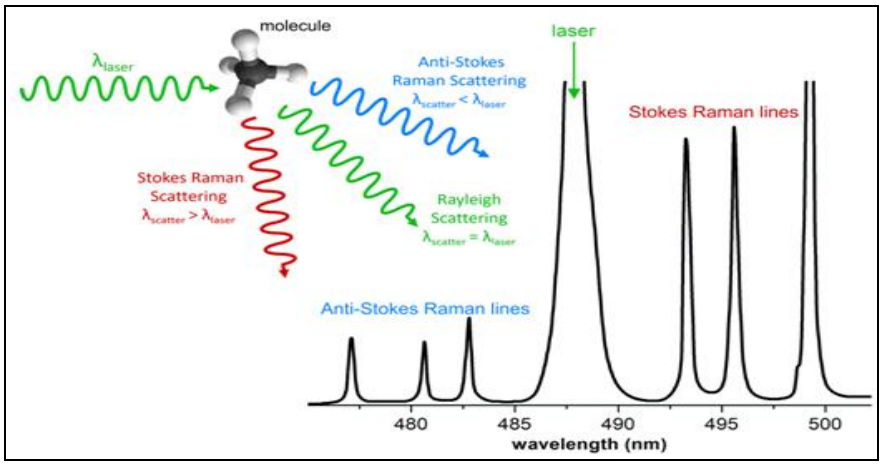

FIG. 4: RAMAN SPECTRUM

Mass Spectroscopy: Using the analytical method of mass spectroscopy, chemical compounds are recognized by classifying gaseous ions in both magnetic and electric fields as per their mass-to-charge ratios [29].

The major components of mass spectroscopy are **Fig. 5**.

1. Ion source
2. Analyzers
3. Detectors

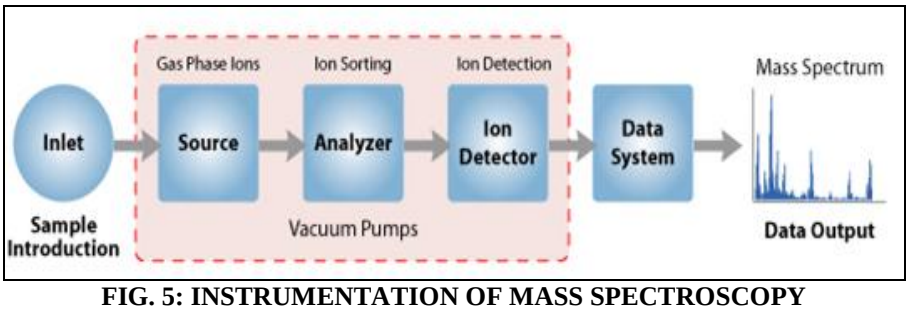

FIG. 5: INSTRUMENTATION OF MASS SPECTROSCOPY

Ion Source: As the mass analyzer exclusively uses gaseous ions, the production of gaseous analyte charged particles serves as the analysis's preliminary step. When non-volatile substances are subjected to analysis, they will be first transformed into the gaseous phase, and the ions are then created from the gaseous material. This procedure is performed in a chamber resembling a box called an ion source. The mass analyzer receives the supercharged ions created in the ion source [30, 31].

The ion source used as interface/for coupling raman spectroscopy with mass spectroscopy is electron spray ionization (ESI) [32].

Electron Spray Ionization (ESI): Through the utilization of electric energy, ESI facilitates the ion transport from aqueous to vapor form. This is done prior to them being analyzed using a mass spectrometer. As a result, ESI-MS may be utilized to more accurately and sensitively evaluate the ionic compounds in solution. It is also possible to examine neutral substances using ESI-MS. The mechanism of cationization/protonation transforms neutral substances into ionic species or in vapor form [32].

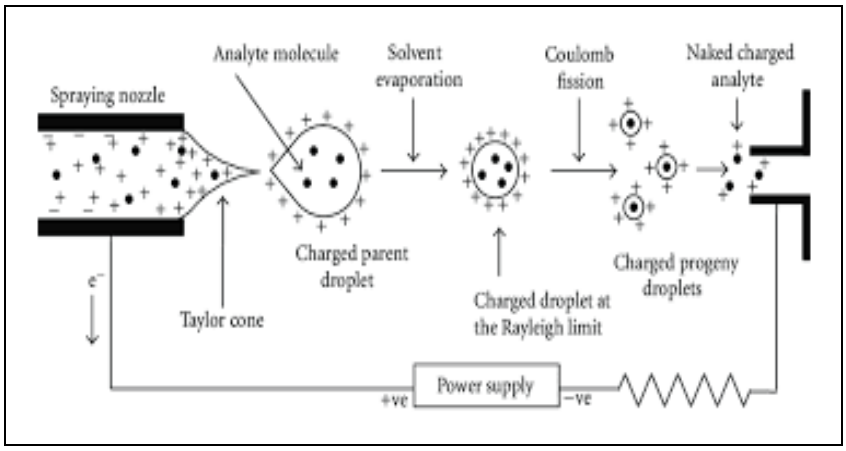

FIG. 6: ELECTRON SPRAY IONIZATION

The process of moving ionic species from liquid to gaseous form entails three steps:

1. Fine spraying of charged aerosols
2. Evaporation of solvent
3. Expulsion of ions from the highly charged aerosols

The adjacent chamber tube's surface is kept at quite a 2.5-6.0kv. High-voltage drops that possess the same polarity as that the capillary voltage form a mist. In order to increase the material rate of flow, nitrogen would be employed as the nebulizing gas since it shears around the sample solution that has been eluted. Charged droplets are created at the electrospray tip's exit and travel along a differential pressure and potential difference into the mass analyzer area.

The charged droplets are constantly shrunk in size by evaporation of the solvent with the use of a higher Electrospray ionization temperature and/or another stream of drying gas, such as nitrogen, which results in a rise in surface charge density and a decrease in droplet radius. Eventually, the electric field intensity inside the charged droplet reaches a threshold value at which the ions may be energetically and kinetically expelled into the gaseous phase on the droplet's surface. A sampling skimmer cone takes samples of the released ions. They are then propelled into the mass analyzer where the molecular mass is analyzed after the ion intensity is measured.

Analyzers: The part of the mass spectrometer known as the mass analyzer distinguishes ionized masses depending on charge - to - mass proportions before sending the separated masses to the detector to be recognized and eventually transformed into a digital signal.

Quadrapole Mass Analyzer: The quadrupole is constructed from four parallel metal poles that are positioned in opposition to one another. These opposing rod pairs are each electrically linked. A radio frequency (RF) voltage is generated to one set of rods although a direct current (DC) current is delivered to the other. Those ions with a specific m/z value exhibit a steady pathway and may be delivered to the detector at a specified RF and DC configuration. Due to the infinite intensity of their oscillation, other ions with unsteady paths are prevented from passing the road. The ions with varied m/z values may be sent to the detector each one at a time at a set proportion by varying the RF and DC through time [33, 34] **Fig. 7**.

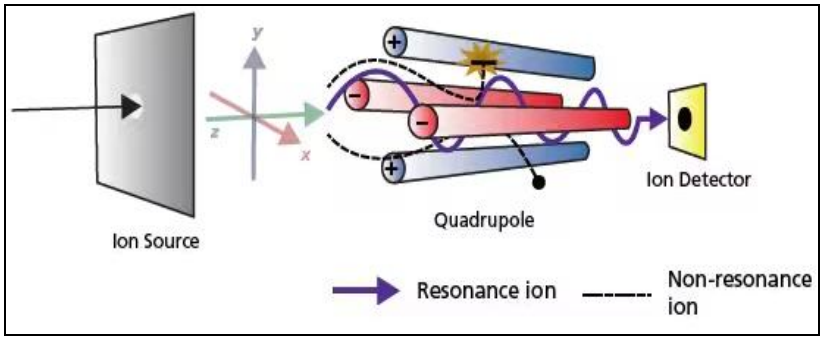

FIG. 7: QUADRAPOLE MASS ANALYZER

Time of Flight: A continuous wave ion source, an acceleration grid, a field-free flight pipe, and a detector make up a time of flight analyzer. Throbbing of the ionization chamber is necessary to prevent the concurrent introduction of ions with various m/z values reaching the detector.

A reflection with a succession of circular electrodes with a high voltage is inserted at the tip of the flight tube since all of the ions with identical m/z values at greater mass do not travel at their optimum velocities. The ion is reflected as in opposite way as a result of high voltage. Faster ions enter reflections more thoroughly than slower ones for ions with the same m/z value. The slow and rapid ions, which have the same m/z value, arrive at the detector simultaneously in this manner. The reflection boosts resolution by limiting the bandwidth range of flight durations for a particular m/z value [35] **Fig. 8.**

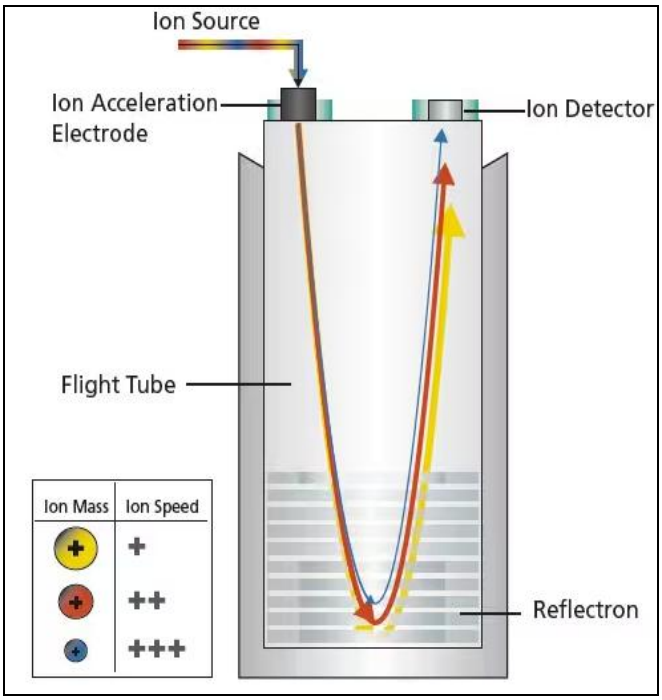

FIG. 8: TIME OF FLIGHT

Detectors:

Faraday Cup Detector: The cylindrical electrode detector, popularly known as the Faraday cup, is fairly straightforward. The incoming ion hits the dynode surface & discharges electrons, which is the primary idea at play. As a result, a current is produced that is intensified and captured. GaP, BeO, or CsSb are examples of secondary emissive materials used to construct the dynode electrode. The Faraday cup is an exceptionally reliable but still quite insensitive detector. It is perfect for IRMS and isotopic analysis **Fig. 9**.

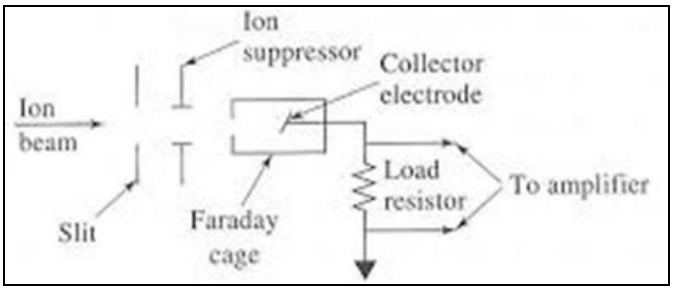

FIG. 9: FARADAY CUP DETECTOR

Electron Multiplier Tube: Because of its incredibly high amplification and minimal noise, electro multipliers represent the most widely utilized detectors. A solitary ion entering the multiplier's front can cause approximately one million electrons to depart from the rear. The principles underlying dynodes as well as secondary emission form the basis for how an electron multiplier detector works. Dynodes are essentially electrodes that are available in vacuum. Whenever a electron or ion that has enough kinetic energy strikes the dynode, it discharges electrons. Secondary emission describes this technique of releasing electrons. The secondary emission process is repeated in the electron multiplier, which contains a succession of dynodes to increase the quantity of electrons geometrically at each stage [30] **Fig. 10.**

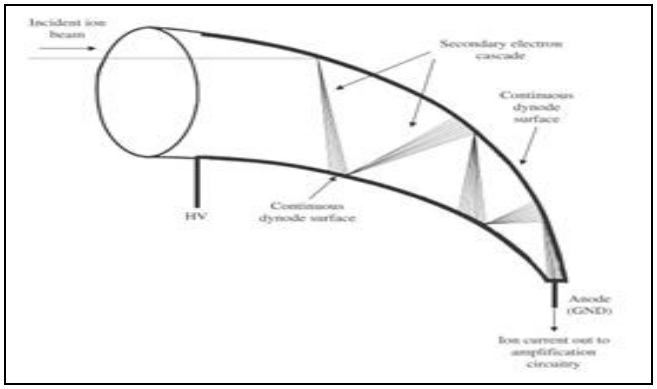

FIG. 10: ELECTRON MULTIPLIER

Mass Spectrum: The graph seen between relative intensity on the y-axis and the m/z ratio on the x-axis represents a mass spectrum [36, 37] **Fig. 11**.

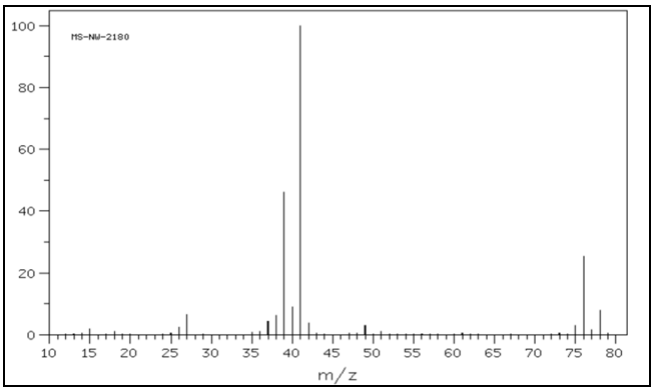

FIG. 11: MASS SPECTRUM

Coupling Raman Spectroscopy with Mass Spectroscopy: A little strip of tissue paper functions as the interface for ongoing hyphenation of a mass spectrometer and a Raman spectroscope. The material performs many functions, including loading substrate for samples and emitter for electrospray. In order to boost analyte information in Raman spectra, it can additionally assist surface-enhanced Raman spectroscopic analysis [38, 39, 40, 41] **Fig. 12**.

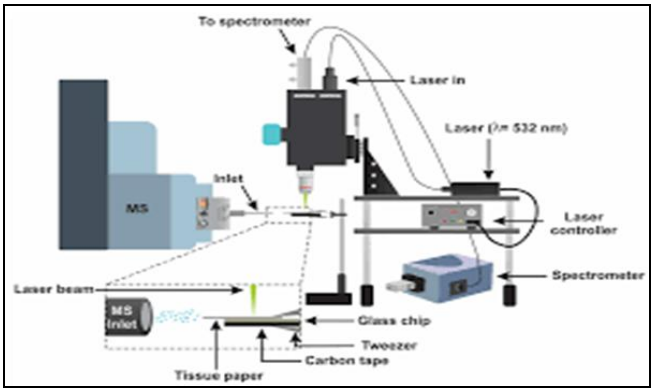

FIG. 12: RAMAN SPECTROSCOPY COUPLED WITH MASS SPECTROSCOPY

Applications:

1. Analysis of Biological Samples.
2. Chemical Analysis of new drugs.
3. To differentiate positional isomers.
4. The hyphenated approach makes it simple to get analytical findings such as molecular weight range, structural characteristics, and functional groups [42].

CONCLUSION: Hyphenation of Raman spectroscopy with Mass is easy, simple and useful analytical methods. They are complimentary analytical methods that are used to offer details on the chemical make-up and functional groups of the target analytes. Any kind of sample can be analyzed by Raman spectroscopy whereas Mass can analyze samples in gaseous state. Therefore the interface used while coupling Raman with mass is electron spray ionization (ESI). Coupling Raman spectroscopy with Mass spectroscopy we can obtain all the information regarding any kind of sample during its analysis.

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