WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 3, 741-763. Review Article ISSN 2277– 7105

# A REVIEW ON GAS CHROMATOGRAPHY-MASS SPECTROMETRY (GC-MS)

**Sathe Komal Pramod*[1], Khedkar Amol Navnath[2] and Sathe Mahesh Pramod[3]**

[1,3]Hon. Shri. Babanrao Pachpute Vichardhara Trusts, Group of Institutions, College of Pharmacy Kashti, Shrigonda, Ahmednagar, Maharashtra, India-414701.

[2]Hon. Shri. Babanrao Pachpute Vichardhara Trusts, Parikrama Diploma in Pharmaceutical Sciences, Kashti, Shrigonda, Ahmednagar, Maharashtra, India-414701.

Article Received on
30 Dec. 2020,

Revised on 20 Jan. 2021,
Accepted on 10 Feb. 2021

DOI: https://doi.org/10.17605/OSF.IO/GAFMT

***Corresponding Author**
**Sathe Komal Pramod**
Hon. Shri. Babanrao Pachpute Vichardhara Trusts, Group of Institutions, College of Pharmacy Kashti, Shrigonda, Ahmednagar, Maharashtra, India-414701.

## ABSTRACT

Gas Chromatography- Mass Spectrometry (GC-MS) is an analytical method that combines the features of gas chromatography and mass spectrometry. As the name implies, it is actually two techniques that are combined to form a single method of analyzing mixtures of chemicals. It is one of the most accurate tools for analyzing environmental samples. GC-MS is used both for the qualitative identification and for the quantitative measurement of individual components in complex mixtures. GC/MS is the most mature chromatography mass spectrometry coupling technology, suitable for the analysis of metabolites with low polarity, low boiling point, or volatile after being derivatized. Applications of GC-MS include drug detection, fire investigation, explosives investigation, academic research, Astrochemistry and identification of unknown samples. It can identify trace elements in materials that were previously thought to have disintegrated beyond identification. Selected applications show that GC-MS is an integral and complimentary part of many field studies involving organic compound detection and determination. This article is prepared with an aim to review different aspects of GC-MS, such as principle, instrumentation, working, applications and advantages.

**KEYWORDS:** Gas chromatography, mass spectrometry, instrumentation, detectors, applications.

## INTRODUCTION

Chromatography is used to separate mixtures of substances into their components. Once isolated, the components can be evaluated individually. All forms of chromatography work on the same principle. They all have a stationary phase (a solid or a liquid supported on a solid) and a mobile phase (a liquid or a gas).In gas chromatography (GC), the mobile phase is an inert gas such as helium. The use of a mass spectrometer as the detector in gas chromatography was developed during the 1950s by Roland Gohlke and Fred McLafferty.[1] In 1996 the top-of-the-line high-speed GC-MS units completed analysis of fire accelerants in less than 90 seconds, whereas first-generation GC/MS would have required at least 16 minutes. This has led to their widespread adoption in a number of fields.

Gas chromatography (GC) is a widely applied technique in many branches of science and technology. For over half a century, GC has played a fundamental role in determining how many components and in what proportion they exist in a mixture. However, the ability to establish the nature and chemical structure of these separated and quantified compounds is ambiguous and reduced, and requires a spectroscopic detection system. The most used, is the mass spectrometric detector (MSD), which allows obtaining the "fingerprint" of the molecule, i.e., its mass spectrum. Mass spectra provide information on the molecular weight, elemental composition, if a high resolution mass spectrometer is used, functional groups present, and, in some cases, the geometry and spatial isomerism of the molecule.

Gas Chromatography/ Mass Spectrometry (GC/MS) is an analytical method that combines the features of gas chromatography and mass spectrometry to identify different substances within a test sample.[2] This instrument separates chemical mixtures (the GC component) and identifies the components at a molecular level (the MS component).[3] It is suitable for the analysis of metabolites with low polarity, low boiling point, or volatile after being derivatized. Gas chromatographic-mass spectrometry (GC-MS) is a very powerful analytical technique.[4] GC-MS has been regarded as a “gold standard” for forensic substance identification because it is used to perform a 100% specific test, which positively identifies the presence of a particular substance. A nonspecific test merely indicates that any of several in a category of substance is present. It is of particular note that the choice of the GC model depends on the research problem a researcher (geochemist, environmentalist, pharmacist, etc.) is trying to answer. The analyses can be run in different modes such as full scan, Total Ion Current (TIC), and Selected Ion Monitoring (SIM) modes to enhance signal-to-noise ratio

for weak peaks.[5] The present review discusses the analytical technique of gas chromatography mass spectrometry (GC-MS), specifically basic principles and instrumentations.

**Figure 1: GC/MS.[6]**

## Principle[7,8]

The mass spectrometer is a universal detector for gas chromatographs since any compound that can pass through a gas chromatograph is converted into ions in mass spectrometer. At the same time, the highly specific nature of mass spectrum makes the mass spectrometer a very specific gas chromatographic detector. Gas chromatography is an ideal separator, whereas mass spectrometry is excellent for identification. GC can well separate complex mixtures, and MS can detect these compounds. The combination of the two has a more favorite place, for example, both GC and MS can run in the gaseous state; thus, they can be connected directly, and the interface is very simple. Simply speaking, the performance of GC-MS is stable, and the reproducibility is good.[3] The aim of an interfacing arrangement is to operate both a gas chromatograph and a mass spectrometer without degrading the performance of either instrument. The problem is compatibility. One incompatibility problem is the difference in pressure required for the operation of a gas chromatograph and the mass spectrometer. Whereas the former operates at high pressures, the latter is designed to run under high vacuum. An associated problem is the presence of much carrier gas and little sample in the effluent from the gas chromatograph. If the gas chromatograph is using packed column the flow of carrier gas may be in excess of 30ml/min, which would collapse the vacuum of the mass spectrometer. Therefore carrier gas must be substantially removed and various designs have to be developed.[1]

### 1. Gas chromatography

Gas chromatography is a common type of chromatography used in analytical chemistry for separating and analyzing compounds that can be vaporized without decomposition.[9,10] It is the most powerful and applicable separation technique for complex mixtures of volatile chemicals. Gas chromatography uses a gaseous mobile phase, or eluent, to carry the analyte being analyzed through a column packed or coated with a stationary phase. Some GC columns are up to 100 meters long.[11] The stationary phase in gas chromatography is commonly a packing of inert, small diameter particles (such as diatomaceous earth) with a nonpolar liquid coating them, or just a liquid coating on the inner surface of the column. This liquid is very thin layer (0.1 to 5 µm). The mobile phase is an inert gas such as Argon, Helium or Nitrogen that only carries the analyte molecules through the column. The carrier gas does not interact with the analyte and column packing material. Helium remains the most commonly used carrier gas in about 90% of instruments although hydrogen is preferred for improved separations.[9,12] The sample is injected into a long tubular column, the chromatography column. Drugs in a sample are separated from each other because some take longer tome to pass through the column than others.

The *retention time*(time it takes to pass through the column) for an analyte is based on the time spent in the stationary phase vs. the mobile phase, with longer retention times for analytes with polarities closer to that of the stationary phase.

### 2. Mass spectrometry

Mass spectrometry (MS) is an analytical technique that ionizes chemical species and sorts the ions based on their mass-to-charge ratio. A mass spectrum measures the masses within a sample. Mass spectrometry is used in many different fields and is applied to pure samples as well as complex mixtures. A mass spectrometer consists of three components: an ion source, a mass analyzer, and a detector. The ionizer converts a portions of the sample into ions. There is a wide variety of ionization techniques, depending on the phase (solid, liquid, gas) of the sample and the efficiency of various ionization mechanisms for the unknown species.[13]

The detector records the charge induced or the current produced when an ion passes by or hits a surface. Typically, some type of electron multiplier is used, though other detectors including Faraday cups and ion-to-photon detectors are also used. Micro channel plate detectors are commonly used in modern commercial instruments.[14] The mass spectrum indicates the mass to charge ratio of the ions, not the molecular weight of the neutral species

(amu/e or Da/z Where, e is the charge on an electron, Da is Daltons (1 Da = 1 amu) and z is the number of positive charges).[4]

- **Ionization**[15,16]

The essence of a mass spectrometric method revolves around the process of ionization of the molecule, with or without subsequent cleavage or fragmentation. The ionization of a molecule is an energy consuming process, which can be supplied by accelerated or thermal electrons (electron impact or electron capture), by photons (photoionization, corona discharge, laser beam), by atoms or ions accelerated by a high electrostatic field gradient or thermal impact, among other mechanisms. A rather large number of methods have been developed to transfer energy for the ionization process, to thermolabile, high- or low-molecular weight, polar or non-polar molecules, in the gas phase (electron impact, EI, chemical ionization, CI, photoionization, PI, field ionization, FI) or in the condensed phase (field desorption, FD, laser desorption, LD, fast atom bombardment, FAB, plasma desorption, PD, secondary ion mass spectrometry, SIMS, matrix-assisted laser desorption ionization, MALDI). The ionization of neutral molecules is followed by fragmentation, or dissociative ionization, whose product ions can be separated with varying degrees of accuracy, depending on the "spectroscopic balance", i.e. analyzer used.

- **Mass analyzers**[15,17]

The mass selective detectors are divided into two groups. The first group corresponds to scanning analyzers. These include sector analyzers, e.g., magnetic deflection of single or double focus (when an electrostatic analyzer is added). The mass selective detectors are distinguished by their properties or specifications and analytical scope. The most important parameters include:

1. Resolution,
2. The maximum mass that can be measured, and
3. The ion transmission.

Ion transmission in mass analyzers is measured as the ratio between the ions formed in the ionization chamber and those which, after passing through the mass analyzer, reach the detector. Scanning analyzers (sector, quadrupole) have lower ion transmission values than the simultaneous transmission analyzers, i.e. TOF, orbitrap, FT-ICR-MS. The latter generally have a higher sensitivity.

TOF analyzer is the simplest analyzer, with high scanning speed, very high ion collection efficiency, wide mass range, a resolution of up to 40,000, and dynamic range of up to 105. TOF is very suitable for analyzing very complex metabolomics samples. It can quickly scan the whole spectrum and obtain qualitative information.

- **Tandem mass spectrometry**

The classic configuration of a tandem mass spectrometer is the connection in series of MS1, collision- activated chamber and MS2, followed by a system for the detection and measurement of ionic currents. Tandem mass systems are divided into two large groups depending on the types of mass analyzers involved.[18] The first group is made up of tandem-in-time mass spectrometers. These include linear and quadrupolar ion traps, orbital traps (orbitrap) and FTICR-MS. The second group of tandem mass (MS/MS) instruments is made up of the so-called tandem-in-space mass spectrometers. In these, at least 2 analyzers are separated in space.[15]

A tandem mass spectrometer is one capable of multiple rounds of mass spectrometry, usually separated by some form of molecule fragmentation. Tandem MS can also be done in a single mass analyzer over time, as in a quadrupole ion trap. There are various methods for fragmenting molecules for tandem MS, including collision-induced dissociation (CID), electron capture dissociation (ECD), electron transfer dissociation (ETD), infrared multiphoton dissociation (IRMPD), blackbody infrared radiative dissociation (BIRD), electron-detachment dissociation (EDD) and surface-induced dissociation (SID). The main tandem MS/MS scan modes are product ion, precursor ion, neutral loss, selected reaction monitoring, multiple reaction monitoring, and $MS^n$ scans.[19] An important application using tandem mass spectrometry is in protein identification.

- **Instrumentation and working of GC-MS[3,20,21,22]**

Different parts of GC-MS are shown in figure 2. The gas chromatograph utilizes a capillary column which depends on the column's dimensions as well as the phase properties (e.g. 5% phenyl polysiloxane) The difference in the chemical properties between different molecules in a mixture and their relative affinity for the stationary phase of the column will promote separation of the molecules as the sample travels the length of the column. The molecules are retained by the column and then elute from the column at different times and this allows the mass spectrometer downstream to capture, ionize, accelerate, and detect the ionized molecules separately. The mass spectrometer does this by breaking each molecule into

ionized fragments and detecting these fragments using their mass-to-charge ratio. Its instrumentation and functions are discussed below:

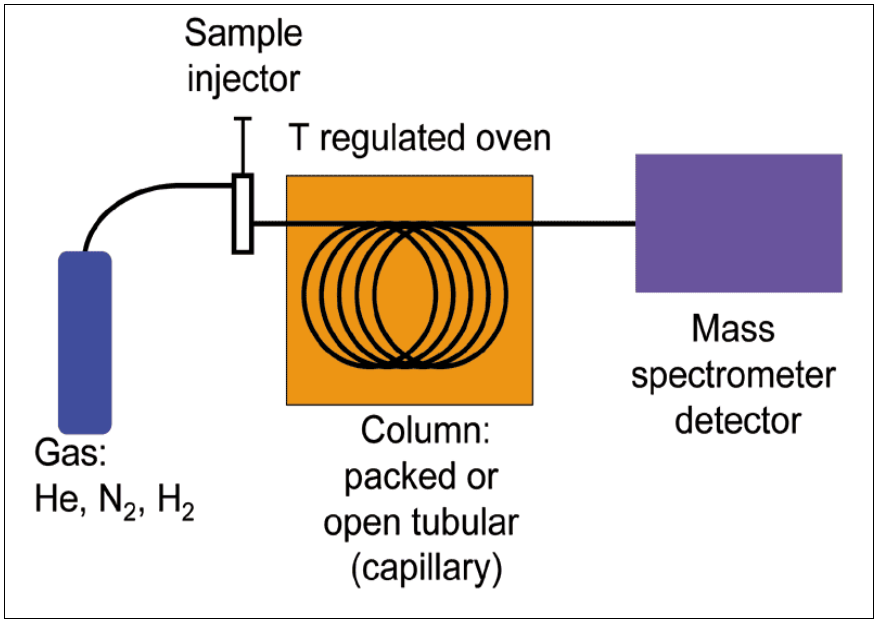


**Figure 2: GC-MS schematic.**[23]

**Gas supply**

Carrier gas is fed from the cylinders through the regulators and tubing to the instrument. It is usual to purify the gases to ensure high gas purity and gas supply pressure. Typically, Helium is used as carrier gas for hydrocarbon applications; however, hydrogen, argon and nitrogen are also used, depending on the application. A carrier gas must be dry, free of oxygen and chemically inert.

**Injector**

Here the sample is volatilized and the resulting gas entrained into the carrier stream entering the GC column. To inject the sample into the analytical flow path, the sample injection valve is actuated and the carrier gas is switched so as to push the sample out of the sample loop and into the first column.

**Column**

Gas Chromatography uses a gaseous mobile phase to transport sample components through columns eitherpacked with coated silica particles or hollow capillary columns containing, the stationary phase coated onto the inner wall. The columns separate the gas mixture into its individual components using some physical characteristic. As the gas sample moves through the column, components with lower boiling points move more slowly than the components

with higher boiling points. The speed at which this separation occurs is dependent on the temperature of the column. The length of the column determines the amount of separation of the components. Capillary GC columns are usually several meters long (10-120 m is typical) with an internal diameter of 0.10-0.50 mm, while packed GC columns tend to be 1-5 meters in length with either 2 or 4mminternal diameter.

The diameter of the capillary column and the thickness of the stationary phase determine the β value (the distribution ratio of substance between the gas phase and the stationary phase), that is, the amount of substances distributed in the gas phase and the stationary phase. Column with thick-film stationary phase (low β value) is typically used for the analysis of volatile compounds, and thin-film column is beneficial for the analysis of less volatile compounds with high boiling point.

**Detectors**[24]

After the components have been separated by the chromatograph columns, they then pass over the detector. The detector is the device located at the end of the column which provides a quantitative measurement of the components of the mixture as they elute in combination with the carrier gas. Several types of detectors are available for gas chromatographs, including flame ionization detectors (for ppm-level hydrocarbons) and flame photometric detectors (for ppb- to ppm-level sulphur detection), but the most common detector used for most hydrocarbon gas measurements is the thermal conductivity detector (TCD). The other detectors are Electron- capture detector, Atomic Emission detector, GC Chemiluminesence detector.

**Oven**

Gas chromatography have ovens that are temperature programmable, the temperature of the gas chromatographic ovens typically range from $5^0$C to $400^0$C but can go as low as -$25^0$C with cryogenic cooling. The oven is designed to insulate the components from the effects of ambient temperature changes and maintain a very stable temperature internally. The temperature at which the oven is controlled is dependent on the application: the heavier the expected hydrocarbon mixture, the hotter the oven temperature. Natural gas applications have a typical oven temperature setting of around $80^0$C.

**Mass spectrometer**

The separation of the phase ions is achieved within the mass spectrometer using electrical and/or magnetic fields to differentiate ions. Atoms and molecules can be deflected by magnetic fields- provided the atom or molecules is first turned into an ion.

- **Samples**

**State:** Organic compounds must be in solution for injection into the gas chromatograph. The solvent must bevolatile and organic (for example, hexane or dichloromethane).

**Amount:** Depending on the ionization method, analytical sensitivities of 1 to 100 pg per component are routine.

**Preparation:** Sample preparation can range from simply dissolving some of the sample in a suitable solvent to extensive cleanup procedures using various forms of liquid chromatography.

- **Analysis time**

In addition to sample preparation time, the instrumental analysis time usually is fixed by the duration of the gas chromatographic run, typically between 20 and 100 min. Data analysis can take another 1 to 20 hours (or more) depending on the level of detail necessary.

- **The data system**[25]

A custom GC-MS data system has been developed using the prototype file system. The 'accumulate mass chromatogram' is a unique example of distributed processing. The remote file system calculates chromatographic profiles locally and sends only the results to GC-MS data system.[26] The amount of data that can be produced during one GC-MS experiment is overwhelming. In a typical GC-MS experiment, the mass spectrometer might be scanned every 2 sec during a 90-min GC run, whether GC peaks are entering the mass spectrometer or not. There are two different rates within the system. There is a slow rate that times the start and stop of the mass spectrometer scan. This is usually set such that 10 to 15 mass spectra are obtained across a typical GC peak. Because these peaks are usually on the order of 20 to 30 sec wide, the mass spectrometer scan speed is usually set at 2 to 3 sec per spectrum. While this scan is going on, the computer must read the output of the electron multiplier at a rate fast enough to define the mass peak profile. In most commercial GC-MS data systems, the voltage output from the preamplifier on the electron multiplier is converted from an analog signal to a digital value (using an analog-to-digital converter) at a rate of 10,000 to 100,000 times per sec. This process generates large amounts of data: If the analog-to-digital converter

worked at 10,000 conversions/second, each minute of the GC-MS experiment would generate 600,000 numbers. This would quickly fill most bulk storage devices; thus, to avoid saving all of these data, most data systems find the mass peaks in real time and convert them into mass intensity pairs, which are then stored on the computer's hard disk. Once the most recent mass spectral scan is stored, this cycle is repeated until the end of the gas chromatogram is reached. Each of the spectra stored on the hard disk has a retention time associated with it, which can be related directly to the gas chromatogram itself. The latter is usually reconstructed by the GC-MS data system by integrating the mass spectrometer output. All modern GC-MS data systems are capable of displaying the mass spectrum on the computer screen as a bar plot of normalized ion abundance versus mass-to-change (m/z) ratio (often called mass). Like the other parts of the GC-MS instrument, the data system must be calibrated. Typically this is done by running a standard compound, such as perfluoro-tributylamine.

- **Applications**

**1. Medicine and Pharmaceutical applications[27]**

GC-MS can determinecompounds in urine even in minor concentration. These compoundsare normally not present but appear in individuals suffering frommetabolic disorders. This is easy, effective and efficient way to diagnosethe problem like in case of genetic metabolic disorders by a urine testat birth. Urine is analyzed for morphine, cocaine, and amphetamines by EMIT (Syva), with positives confirmed by GC-MS.[28] In combination with isotopic labeling of metabolite, the GC-MSis used for determining metabolic activity. Itisuseful to detect oils in creams, ointments, lotion etc.The application of GC/MS metabolic profiling in the area of toxicology is relatively underdeveloped as compared to NMR and LC/MS.[29]

GC-MS is widely used in pharmaceutical industries for analytical research and development, quality control, quality assurance,production, pilot plants departments for active pharmaceuticalingredients (API), bulk drugs and formulations. It is used for process and method development, identification of impurities in API. It is anintegral part of research associated with medicinal chemistry (synthesisand characterization of compounds), pharmaceutical analysis (stabilitytesting, impurity profiling), Pharmacognosy, pharmaceutical process control (Figure 3), pharmaceutical biotechnology etc.[30,31]

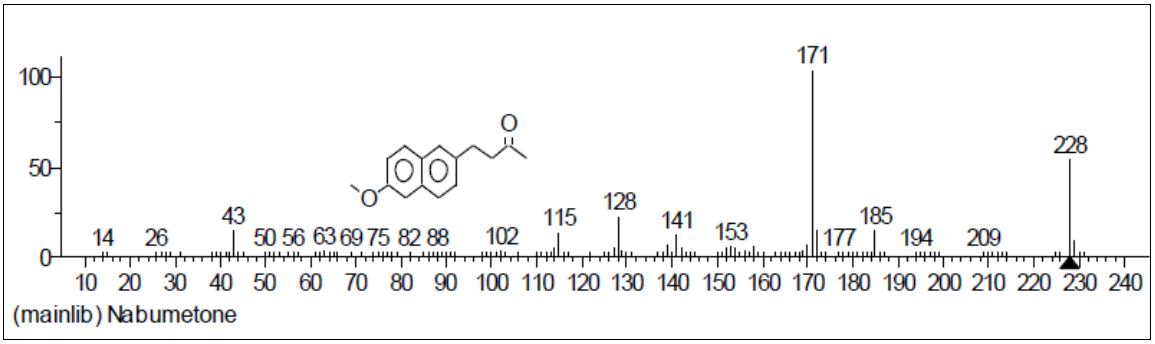


**Figure 3: The GC-MS spectrum of Nabumetone (Formula: $C_{15}H_{16}O_2$, MW: 228) with x-axis and y-axis as intensity.[32]**

GC-MS is the main tool used in sports anti-doping laboratories to test athlete's urine samples for prohibited performance- enhancing drugs, for example anabolic steroids.

GC-MS is used to analyze the metabolites of steroids hormones and their precursors. This technique can readily be utilized in comprehensive (full scan) and targeted (selected ion) mode. A "scanned" GC-MS run contains all steroids excreted and the data set can be searched for any required analyte even years after the analysis. Accurate values are generally being obtained for the first time, particularly in female and pediatric patients with low concentrations of androgens and estrogens although work is still necessary in improving reproducibility in laboratories.[33]

## 2. Energy and fuel applications[34]

Significantly enhanced molecular ions that are always observed, isomer and structurally significant mass spectral peaks and extended range of low volatilite hydrocarbons that are amenable for analysis including waxes up to $C_{74}H_{150}$ makes the GC-MS a most valuable technique. GC-MS is used for the analysis of aromatic solvents, sulphur, impurities in polypropylene, sulphur in menthane, natural gases, 1,3 butadiene, ethylene, gas oil, unleaded gasoline, polyethene, diesel oil, unleaded gasoline, polyethylene, diesel (figure 4A and 4B), modified biomass, grafted polymers etc.

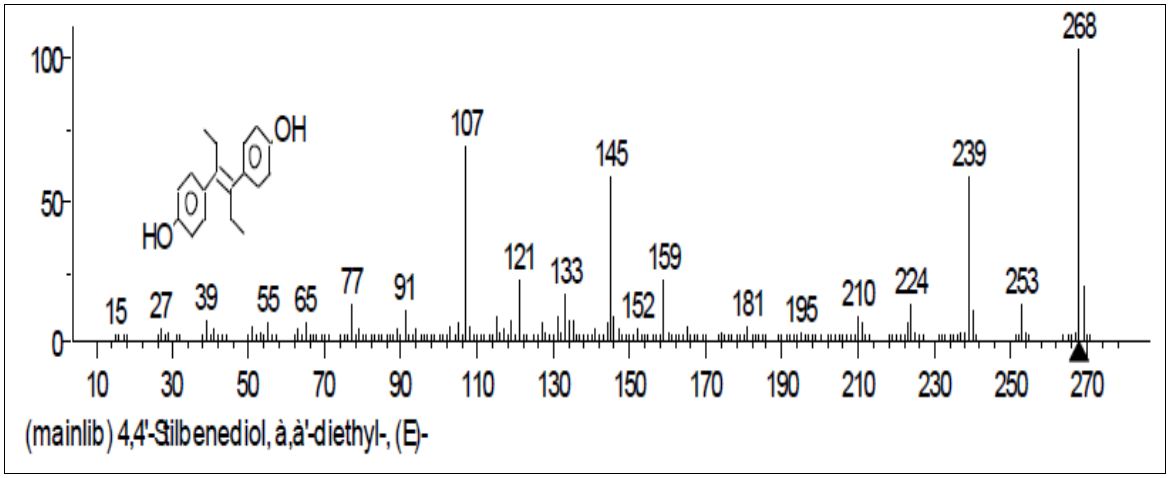


**Figure 4A: The GC-MS spectrum of Diesel (Formula: $C_{18}H_{20}O_2$, MW: 268) with x-axis m/z ratio and y-axis as intensity.[35]**

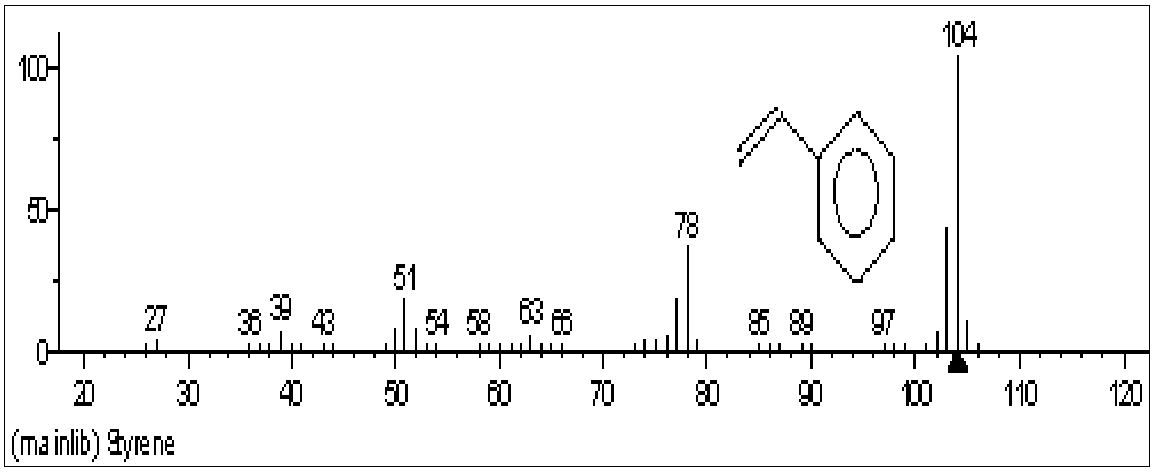


**Figure 4B: The GC-MS spectrum of Diesel (Formula: $C_8H_8$, MW: 104) with x-axis and y-axis as intensity.[36]**

### 3. Academic research[37,38]

As a unique and powerful technology the GC-MS provides a rare opportunity to perform the analysis of new compounds for characterization and identification of synthesized or derivatized compound. It is widely used in pure and applied sciences like Chemistry, Polymers, Nanotechnology and Biotechnology etc. It yields useful information that can be used in research publication internationally.

### 4. Astrochemistry[39,40]

A gas chromatograph uses a thin capillary fiber known as a column to separate different types of molecules, based on their chemical properties.[41]Several GC-MS have left earth. Two were brought to mars by the Viking program. Venera 11 and 12 and Pioneer Venus analyzed

the atmosphere of Venus with GC-MS. The Huygens probe of the Cassini- Huygens mission landed one GC-MS on Saturn's largest moon, Titan. The material in the comet 67P/Churyumov- Gerasimenko will be analyzed by the Rosetta mission with a chiral GC-MS in 2014.

GCMS records direct atmospheric measurements, including altitude profiles of the constituents, isotopic ratios, and trace species (including organic compounds).[42]

**5. Environmental analysis[43]**

For determination of trace concentrations of organics in environmental samples, the only real method of choice is gas chromatography- mass spectrometry. GC-MS is an effective technique for environmental analysis applications because of the tremendous separating power of modern fused silica wall- coated open- tubular (capillary) columns (FSOT), and because mass spectrometers are available that can detect from pictogram to femtogram quantities of organic molecules.

**6. Forensic (Arson, explosives, drugs, unknowns)[1]**

When it comes to forensic science, GC-MS is a powerful technique in any analyst's toolbox. Due to its simplicity, accuracy, sensitivity and versatility, GC-MS is often called the gold standard of analytical methodologies for many forensic tests. The use of GC-MS has expanded to numerous applications, and modern laboratories use the technique for everything from arson investigation, to crime scene testing, to forensic pathology and drugs-of-abuse screening, and beyond.[44]

GC-MS can analyze the particles from a human body in order to help link a criminal to a crime. Enhanced and trustworthy molecular ions, extended range of thermally labile compounds amenable for analysis including all the major labile explosives (figure 5), isotope abundance analysis software for improved sample identification, ChromatoProbe solid sample introduction device, Open Probe and ultra-fast GC-MS analysis make the Supersonic GC-MS the ideal Forensic GC-MS system. With the Supersonic GC-MS we could get a step closer to make the CSI (Crime Scene Investigation) TV scenes with GC-MS a reality. Touch the sample, push it inside the GC-MS and get in a few seconds an accurate answer on the type of mixture or compound analyzed.

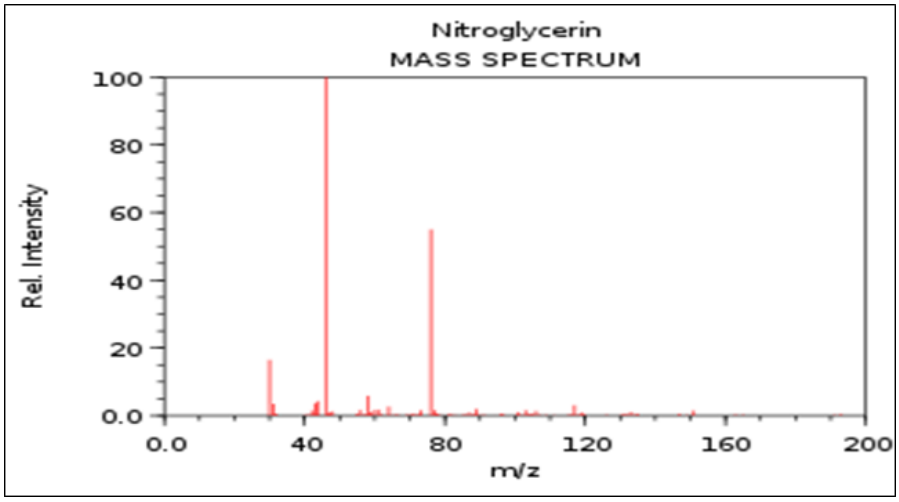


**Figure 5: The GC-MS spectrum of nitroglycerin.[45]**

## 7. Geochemical research[1]

Significantly enhanced molecular ions that are always observed (can be dominant for hopanes/stearanes), major isomer and structurally significant mass spectral peaks, extended range of low volatility hydrocarbons that are amenable for analysis and unique isotope ratio information (without combustion) and the ability to perform parent scans MS-MS of biomarkers make the Supersonic GC-MS a most valuable GC-MS for organic geochemical applications.

## 8. Law enforcement[2,20]

GC-MS is increasingly used for detection of illegal narcotics, and may eventually supplant drug- sniffing dogs. It is also commonly used in forensic toxicology to find drugs and/or poisons in biological specimens of suspects, victims, or the deceased.

## 9. Determination of organic compounds[46]

GC-MS is used for the analysis of unknown organic compound mixtures. One critical use of his technology is the use of GC-MS to determine the composition of bio-oils processed from raw biomass. Volatile organic compounds were detected by membrane inlet mass spectrometry in approximately 10 s. Headspace-GC-MS system is used to detect volatile organic compounds in water is described. This method corresponds to the performance requirements for the analysis of drinking water. A method was proposed for determination of trace organic compounds such as PCB, dioxin, hormone, waste plastic, explosive, agrochemicals, and medicine. The device comprises an UV-Vis spectrophotometer, a solid phase absorbent, and a detector. Silica gel or alumina was used as adsorbent for gathering the

target organic compounds. GC-MS, GC-electron capture detector, or GC-MS-electron capture detector was used for detection. The method could be used for monitoring the harmful compounds in natural water and waste water.

### 10. Detection of orellanine present in stomach content[47]

Gas chromatography-mass spectrometry with supersonic molecular beams (GC-MS with SMB) was used for the direct detection of Orellanine in the stomach fluids of rats after they were fed with food containing C. Orellanus. This method can be used as a platform for the future development of analytical procedures for the direct analytical detection of Orellanine in humans intoxicated by ingestion of toxic mush-rooms. Orellanine was detected in the chromatogram by MS as [M]+ ions with m/z 252 as a base signal. The fragmentation of Orellanine from the stomach content of an intoxicated rat was comparable to the spectrum and to spectra published in the literature. The mass spectrum of Orellanine showed intense signals at m/z 252 [M]+, moderate signals at m/z 235 and weaker signals at m/z 236 and m/z 220. The mass spectrum of standard Orellanine is shown in Figure 6 and is identical to that for Orellaninein biological samples.

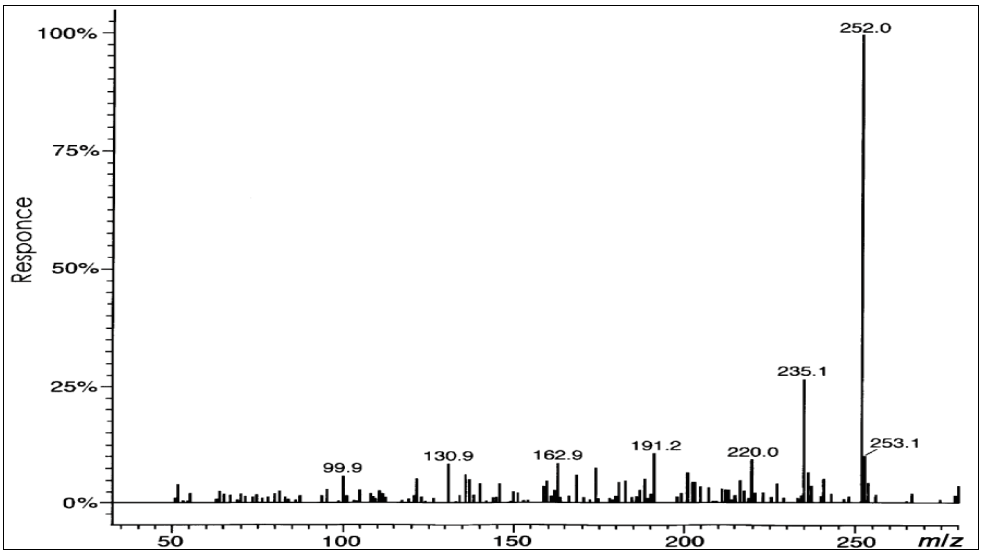


**Figure 6: Mass spectrum of the isolated toxin.**

### 11. Biological and Pesticides detections[27]

GC-MS is exclusively used in bio-analysis of blood, urine for the presence of barbiturates, narcotics, alcohols, and residual solvents, drugs like anesthetics, anticonvulsant (figure 7), antihistamine, anti-epileptic drug, sedative hypnotics, narcotics and food items. This technique could be used for detecting adulterations, fatty acid profiling in microbes, presence

of free steroids, blood pollutants, metabolites in serum, organo-chlorinated pesticides in river water, drinking water, soft drinks by head space, pesticides in sunflower oil etc.

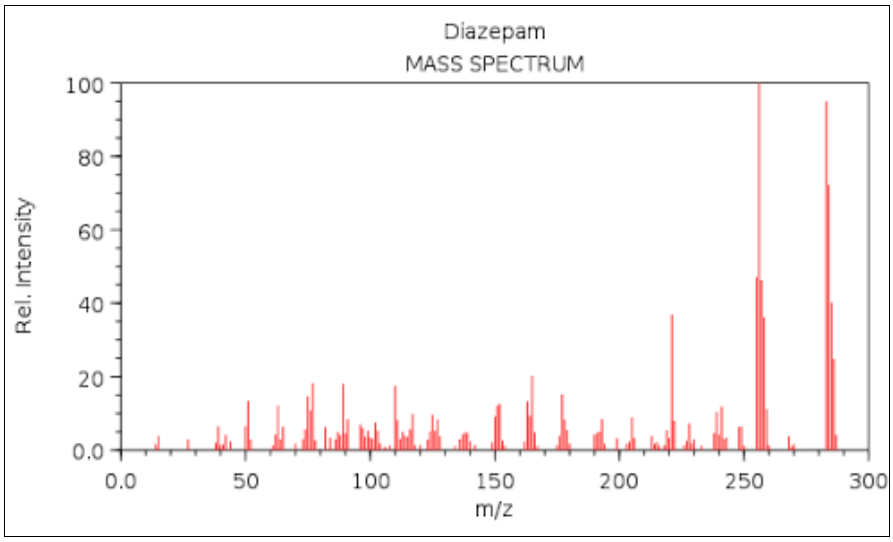


**Figure 7: Diazepam mass spectrum.[48]**

## 12. Applications in food science[21]

GC-MS applications in the food sector are among the fastest developing fields in science and industry. Its main strength is its high resolution separation and its broad usage by the food industry for analyzing target compounds, metabolomics and volatile compound profiling. Foods are complex mixtures of different components contained in varying amounts, making analysis a challenging task. GC-MS is in the forefront of this analytical challenge; being a unique tool for reliable characterization of complex mixtures. Its excellent figures of merit are a consequence of the combination of the separative power of gas chromatography to the power of mass spectrometry to identify molecular structure. It became possible to characterize any food at the molecular level.

The applications of GC-MS include monitoring for the formation of ethyl carbamate in foods and beverages that requires fermentation and detecting unwanted and/or toxic compounds like furan, acrylamide, and BPA (bisphenol A) in food products. The major complex mixture application is the detection and quantification of pollutants in foods, including residues of various pesticides which comprise the most common GC- mediated food safety issue.[49] Desirable and undesirable molecules are often routinely identified and quantified in various foods. GC–MS is useful analytical method which allows simultaneous assessment of a variety of components in complexmixtures such as foods.

GC-MS technique is used for Identification and quantification of volatile N-nitrosamines in meat products, Determination of melamine and cyanuric acid in dairy products, Detection of furan levels in foods, Quantification of inulin type-fructans, Screening, determination and confirmation of seafood, meat and honey, Pesticide residue analysis in routine food control, Optimizing the analysis of Acrylamide in food by quadrupole GC/MS, Detection of Chloropropanols.

**13. Airport security[50]**

When searching for explosive, GC-MS is commonly used for analyzing the volatile substances found in explosives. GC/MS can also be used in airport security to detect substances in luggage or on human beings. Additionally, it can identify trace elements in materials that were previously thought to have disintegrated beyond identification. In this a detector takes a sample of the air and runs a GC-MS on it- this can automatically detect explosives. Using these machines means a much higher percentage of passengers and bag can be screened.

**14. Analysis of essential oils[51]**

The essential oils obtained by hydrodistillation were analyzed by GC-MS. Identification of individual components of the essential oil was performed by computerized matching of the acquired mass spectra with those stored in the NIST21 and NIST107 mass spectral libraries of the GC-MS data system and by comparison of their retention times with those of authentic standards. The essential oil from the undamaged M. indica leaves obtained by hydrodistillation and analyzed via combined GC-FID and GC-MS contained 17 known compounds, making up 72.0% of the total composition. The main compound was diterpene labd-7.13-dien-15-ol, accounting for 26.8%,but the predominant class was sesquiterpenes (46.8%). The main sesquiterpenes identified were gymnomitrone (24.9%), 14-hydroxy-4,5-dihydro caryophyllene (9.3%) and caryophyllene oxide (1.2%).

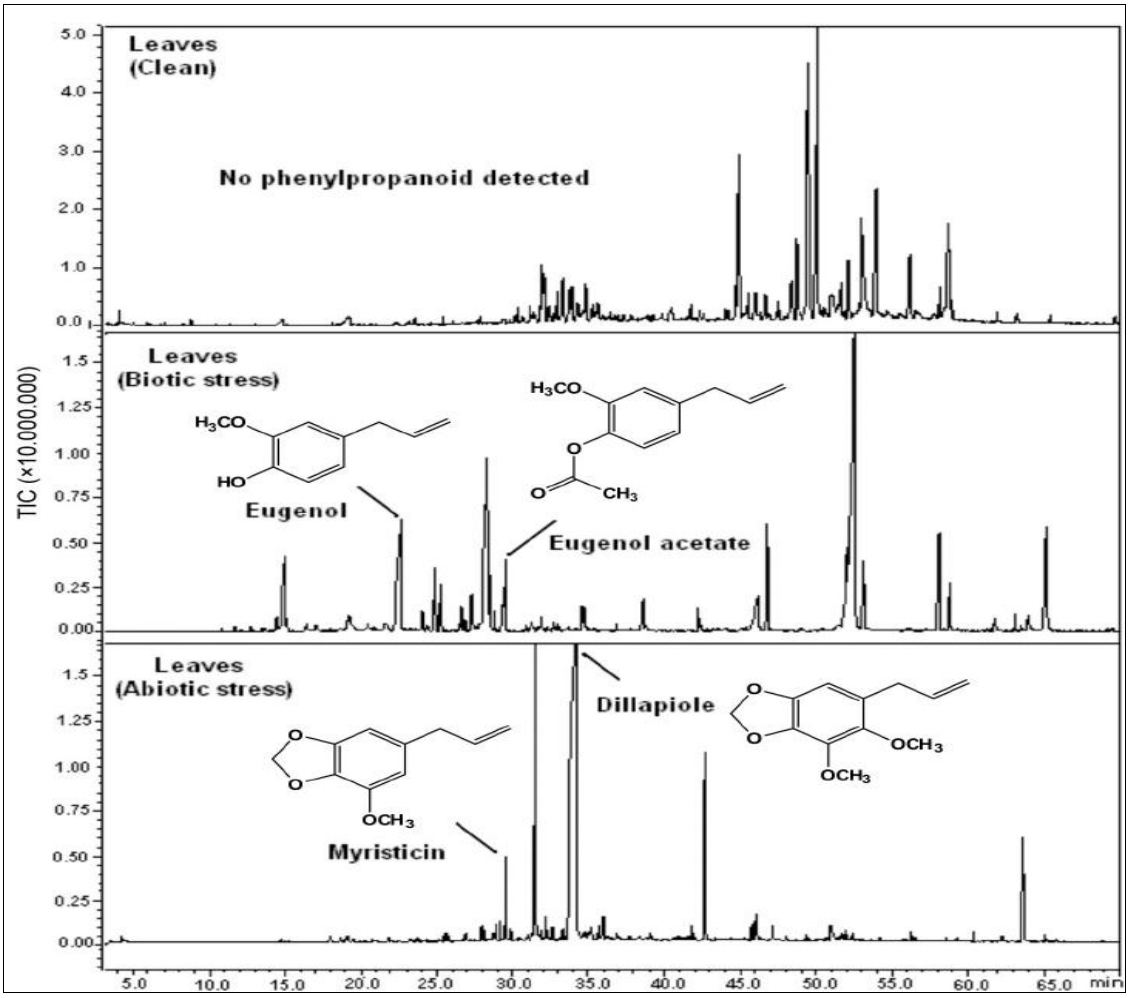


**Figure 8: GC-MS of essential oils of M. indica leaves.**

- **Advantages**[25,27,29,46,52]

When two separate techniques such as gas chromatography (GC) and massspectrometry (MS) are successfully combined to form gas chromatography- massspectrometry (GC-MS), the advantages become obvious.

1) GC-MC technique offers high chromatographic resolution, high sensitivity, and reproducibility,
2) Faster analysis,
3) Significantly increased range of thermally labile and low volatility samples amenable for analysis,
4) Improved sensitivity particularly for compounds that are hard to analyze,
5) Improved confidence in sample identification,
6) Structural determination of unknown organic compounds in complex mixtures both by matching their spectra with reference spectra and by a priori spectral interpretation,
7) Analysis of industrial products for quality control.

8) GC-MS is less expensive than LC-MS. A tank of helium gas can last for months.
9) Maintenance of GC-MS is also less expensive than LC-MS,
10) Determines trace levels of organic contaminations,
11) Quantitative analysis.

- **Limitations**[25,52]

**General:** Only compounds with vapor pressures exceeding about 10–10 torr can be analyzed by gas chromatography mass spectrometry (GC-MS). Many compounds with lower pressures can be analyzed if they are chemically derivatized (for example, as trimethylsilyl ethers). Determining positional substitution on aromatic rings is often difficult. Certain isomeric compounds cannot be distinguished by mass spectrometry (for example, naphthalene versus azulene), but they can often be separated chromatographically.

**Accuracy:** Qualitative accuracy is restricted by the general limitations cited above. Quantitative accuracy is controlled by the overall analytical method calibration. Using isotopic internal standards, accuracy of ±20% relative standard deviation is typical.

**Sensitivity and Detection limits:** Depending on the dilution factor and ionization method, an extract with 0.1 to 100 ng of each component may be needed in order to inject a sufficient amount. Atmospheric gases are challenging ($CO_2$, $N_2$, $O_2$, Ar, CO, $H_2O$).

## CONCLUSION

Gas chromatography (GC) is a widely applied technique in many branches of science and technology. The association of separation and mass spectrometric techniques is a key that opens up a rich and multidimensional analytical space for the investigation of complex mixtures with high sensitivity, selectivity and specificity. GC-MS offers improved confidence in sample identification, faster analysis, improved sensitivity particularly for compounds that are hard to analyze. This has led to their widespread adoption in a number of fields. It is often the analytical method of choice in toxicology, forensics, food science, academic research, detection of organic compounds and environmental research. The application of GC/MS metabolic profiling in the area of toxicology is relatively underdeveloped as compared to NMR and LC/MS. The only "conflict" (short-term and already resolved) between GC and MS, were the different working pressures, i.e., atmospheric at the GC column exit and low (10-5 - 10-6 Torr) in the ionization chamber, respectively. This drawback was overcome by technically introducing an efficient vacuum pump (turbo molecular and gas-jet pumps). This versatile GC-MS analytical technique could be explored for better prospects in future.

## REFERENCES


1. Kataria S, Beniwal P, Middha A, Sandhu P, Rathore D. Gas Chromatography- Mass Spectrometry: Applications. International Journal of Pharmaceutical & Biological Archives, 2011; 2(6): 1544-1560.
2. O. David Sparkman, Penton Z, Fulton G,Kiston.Gas Chromatography and Mass Spectrometry: A Practical Guide. Academic Press, 2011; ISBN 978-0-08-092015-3.
3. Xue Z,Duan LX, Xiaoquan Qi. Gas Chromatography Mass Spectrometry Coupling Techniques. Plant Metabolomics. Chemical Industry Press.
4. https://www.scribd.com/mobile/document/363060871/gcmshandout-000-pdf.
5. Akande WG. A review of experimental procedures of gas chromatography- mass spectrometry (gc-ms) and possible sources of analytical errors. Earth Science, 2012; 1(1): 1-9.
6. http://www.elcalabs.com/images/common/gas-analysis-01-big.jpg.
7. Philp RP. Geochemical Analysis: Gas Chromatography and GC-MS. Academic Press, 2000.
8. Hobart HW, Lynne LM. Instrumental Methods of Analysis. 6th ed., CBS Publishers & Distributors, 2011; 6: 569-571.
9. https://en.m.wikipedia.org/wiki/Gas-chromatography.
10. AL-Bukhaiti WQ, Noman A, Qasim AS, AL-Farga A. Gas Chromatography: Principles, Advantages and Applications in Food Analysis. International Journal of Agriculture Innovations and Research, 2017; 6(1): 123-128.
11. https://www.google.co.in/url?sa=t&source=web&rct=j&url=http://aerosol.chem.uci.edu/AirUCI_summer/PDFs/labs/2014_GCMS_Lab.pdf&ved=0ahUKEwilvdTBtObxAhWHwl8KHU4CCq4FggjMAA&usg=AOvVaw0jd-CUuzf3egTS-aR62tN5.
12. Dr. Grob K. Carrier Gases for GC.Restek Advantage, Restek Corporation, 1997; 3.
13. https://en.m.wikipedia.org/wiki/Mass_spectrometry.
14. Dubois F, Knochenmus R, Zenobi R, Brunelle A, Deprun C, Le Beyec Y. A comparison between ion-to-photon and Microchannel plate detectors.Rapid Communication in Mass Spectrometry, 1999; 13(9): 786-791.
15. Guo X. Advances in Gas Chromatography. In: Stashenko E, Jairo RM. Gas Chromatography-Mass Spectrometry, InTech Publisher, 2014; 1.
16. Ashcroft AE. Ionization Methods in Organic Mass Spectrometry. The Royal Society of Chemistry, 1997; 20-24.

17. El-Aneed A, Cohen A, Banoub J. Mass Spectrometry, Reviews of the Basics: Electrospray, MALDI, and Commonly Used Mass Analyzers. Applied Spectroscopy Reviews, 2009; 44(3): 210-230.
18. Kandiah M, Urban PL. Advances in Ultrasensitive Mass spectrometry of Organic Molecules. Chemical Society Reviews, 2013; 42: 5299-5322.
19. Hajšlová J, Cajka T. Gas chromatography- mass spectrometry (GC-MS). Food Toxicants Analysis, Elsevier BV, 2007; 419-473.
20. https://en.m.wikipedia.org/wiki/Gas_chromatography%E2%80%93mass_spectrometry.
21. Hussain SZ, Maqbool K. GC-MS: Principle, technique and its application in Food Science. Int J CurrSci, 2014; 13(E): 116-126.
22. http://instrumentationtools.com/working-principle-of-gas-chromatography/#.WhV2d9a3TqA.
23. https://en.m.wikipedia.org/wiki/Gas_chromatography%E2%80%93mass_spectrometry#/media/File%3AGcms_schematic.gif.
24. Pravallika S. Gas Chromatography a Mini Review. Research and Reviews Journal of Pharmaceutical Analysis, 2016; 5(2): 55-62.
25. Settle FA. Handbook of Instrumental Techniques for Analytical Chemistry In: Hites RA. Gas Chromatography Mass Spectrometry, Upper Saddle River, NJ: Prentice Hall PTR, 1997; 609-626.
26. Gemperline PJ, Megargle R. The implementation of a GC/MS data system using DISNET: a Distributed Instrument System NETwork. Journal of Automatic Chemistry, 1984; 6(4): 197-201.
27. Chauhan A, Goyal MK, Chauhan P. GC-MS Technique and its Analytical Applications in Science and Technology. Analytical and Bioanalytical Techniques, 2014; 5(6).
28. Ullucci PA, Cadoret R, Stasiowski, Martin HF. A comprehensive GC/MS Drug Screening Procedure. Journal of Analytical Toxicology, 1978; 2(2): 33-38.
29. Pasikanti KK, Ho PC, Chan ECY. Gas chromatography/mass spectrometry in metabolic profiling of biological fluids. Journal of Chromatography B, 2008; 202-211.
30. CDER Guidance for Industry Analytical Procedures and Methods Validation. FDA, 2000.
31. CDER (1994) Reviewer Guidance: Validation of Chromatographic Methods. FDA.
32. https://www.omicsonline.org/articles-images/analytical-bioanalytical-techniques-Nabumetone-5-222-g007.png.
33. Krone N, Haughes BA, […], Cedric HL, Shackleton. Gas chromatography/mass spectrometry (GC/MS) remains a pre-eminent discovery tool in clinical steroid

investigations even in the era of fast liquid chromatography tandem mass spectrometry (LC/MS/MS). J Steroid Biochem and MolBiol, 2010; 121(3-5): 496-504.

34. Grob RL, Barry EF. Modern Practice of Gas Chromatography. New Jersey; Wiley and Sons, 2004.
35. https://www.omicsonline.org/articles-images/analytical-bioanalytical-techniques-axis-intensity-5-222-g008a.png.
36. https://www.omicsonline.org/JABTimages/2155-9872-5-222-g008b.gif.
37. Kalachova. Analysis of emerging persistent organic pollutants using GCMS/ MS, SETAC, Berlin, 2012.
38. Ziegenhals K, Hübschmann HJ, Speer K, Jira W. Fast-GC/HRMS to quantify the EU priority PAH. J Sep Sci, 2008; 31: 1779-1786.
39. Krasnopolsky VA, Parshev VA. Chemical composition of the atmosphere of Venus. Nature International Journal of Science, 1981; 292: 610-613.
40. Goesmann F, Rosenbauer H, Roll R, Bohnhardt H. COSAC Onboard Rosetta: A Bioastronomy Experiment for the Short- Period Comet 67P/Churyumov- Gerasimenko. Astrobiology, 2005; 5(5): 622-631.
41. SEARCHING FOR LIFE ON MARS: The Development Of The Viking GCMS. NASA. Academy of program/ project and engineering leadership.
42. Niemann HB, Atreya SK, Bauer SJ, Carignan GR, Demick JE, Frost RL, Gautier D, Haberman JA, Harpold DN, Hunten DM, Israel G, Lunine JI, Kasprzak WT, Owen TC, Paulkovich M, Raulin F, Raaen F, Way SH. The abundances of constituents of Titan's atmosphere from the GCMS instrument on the Huygens probe. Nature International Journal of Science, 2005; 438: 779-784.
43. Kashyap SM, Pandya GH, Wachasunder SD, Kondawar VK. QA/QC aspects of GC-MS analytical instrument for environmental analysis. Indian J ChemTechnol, 2005; 12: 477-487.
44. https://www.forensicmag.com/article/2015/04/gold-standard-forensics-gcms-case-study.
45. http://webbook.nist.gov/cgi/cbook.cgi?Spec=C55630&Index=0&Type=Mass.
46. Sneddon J, Masuram S, Richert JC. Gas Chromatography-Mass Spectrometry-Basic Principles, Instrumentation and Selected Applications for Detection of Organic Compounds. Analytical Letters, 2007; 40(6): 1003-1012.
47. Brondz I, Nevo E, Solomon P, Wasser, Brondz A. A direct gas chromatography-mass spectrometry (GC-MS) method for the detection of orellanine present in stomach content (Part I). Journal of Biophysical Chemistry, 2012; 3(1): 29-34.

48. http://webbook.nist.gov/cgi/cbook.cgi?Spec=C439145&Index=0&Type=mass.
49. Mayer MJ. Emerging Techniques: Gas Chromatography Mass Spectrometry for Food Applications. Thermo Fisher Scientific, 2016.
50. https://www.chromatographytoday.com/news/gc-mdgc/32/breaking-news/airports-are-using-chromatography-to-detect-bombs-find-out-how/32854.
51. www.researchgate.net/figure/262626252_fig1_Figure-1-Chemical-profiles-GC-MS-of-essential-oils-of-M-indica-leaves-intact-leaves.
52. http://ezinearticles.com/?Gas-Chromatography-Mass-Spectrometry-Advantages-and-Disadvantages&id=9580518.