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A Review Article on Advancements in GC-MS

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ABSTRACT: GC-MS is a powerful technique method for the analyze of small & volatile molecules. This technique is well-recognized for its ability in unknown compound analysis. This article represents GC-MS principle, Applications, Instrumentation & Approaches. GC-MS are quite similar in a way that it involves gaseous compounds and high temperature. GC-MS is used for the both qualitative identification and quantitative measurement of individual compounds which is presents in complex mixtures.

KEYWORDS: GC-MS, Molecules, Gas, Liquid

I. INTRODUCTION

Gas chromatography–mass spectrometry (GC-MS) is one of the so-called hyphenated technique that combines the features of gas-chromatography and mass spectrometry to distinguish various substances inside a test. GC-MS is used as an incorporate medication location, fire examination, ecological examination, explosives examination, examples, including that of material examples acquired from planet Mars during test missions as ahead of schedule as the 1970s.Analytical technique that combines the separationproperties of gas-liquid chromatography with the detection feature of mass spectrometry to identify different substances within a test sample. GC is used to separate the volatile and thermally stable substitutes in a sample whereas GC-MS fragments the analyte to be identified based on its mass. The further addition of mass spectrometer in it leads to GC-MS/MS. Superior performance is achieved by single and triple quadrupole modes.

Schematic Diagram Of Gas Chromatography-Mass Spectroscopy

Compatibility with the chromatographic environment [3]

Most chemical derivatizations are performed to convert the analytes to chemical forms that are more compatible with the chromatographic environment. The bringing about of the compatibility may be mandatory or simply to improve performance characteristics.

Drugs are often chemically derivatized prior to their GC-MS analysis for the following reasons:

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(a) to bring the analytes to the chemical forms that are more compatible to the chromatographic environment;
(b) to create a separation mechanism or to maximize resolution efficiency
(c) to improve detection or structural elucidation effectiveness
(d) to make use of the analytes' specific structural features for analytical needs
Analytes that are strongly acidic, basic or with functional groups, that may not vaporize or may interact with (irreversibly or reversibly) silanol groups or contaminating compounds present in the chromatographic system, can be more effectively analyzed after chemical derivatization.

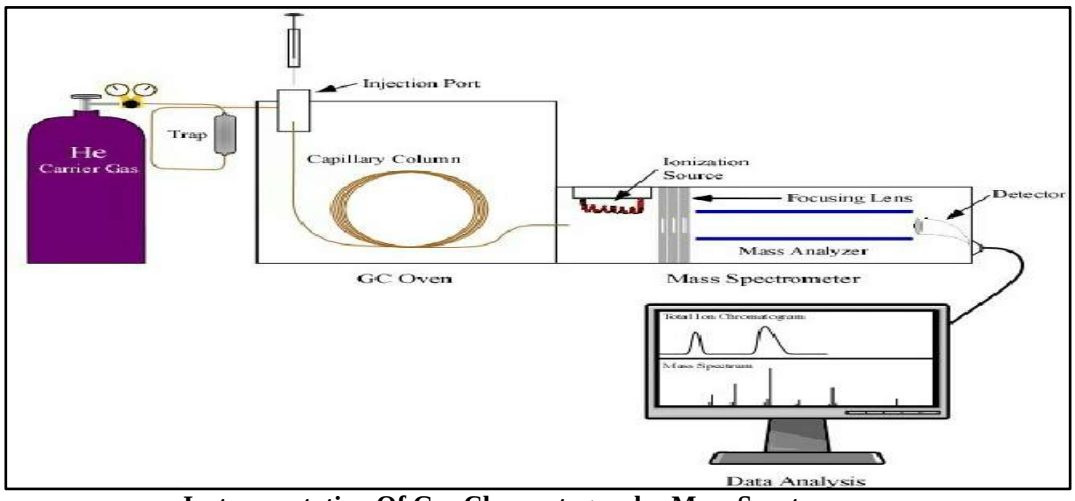
2 Dimensional GC-MS [7]

It is a hyphenated technique.MS is most often coupled to GC × GC allowing another dimension to classify compounds. MS ensures high selectivity throughout the chromatogram and provides structural information for unambiguous identification. Comprehensive two-dimensional gas chromatography-mass spectrometry (GC×GC-MS) uses two GC columns, usually connected via a thermal modulator. The second column is typically much shorter than the first (i.e., 1–2 m as opposed to 30–60 m for the first column) with a different stationary phase and is generally operated at a higher temperature. GC×GC-MS can provide superior chromatographic peak capacity, selectivity, and lower detection limit for the analysis of small molecules.

PRINCIPLE [4]

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 favourite 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. 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 must be developed.

INSTRUMENTATION



Instrumentation Of Gas Chromatography-Mass Spectroscopy

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Instrument components:

1.Carrier gas
2.Injector
3.Coloumn
4.Detectors
5.Oven
6.Mass spectrometer

1.Carrier gas

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.

2.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.

3.Coloumn

Gas Chromatography uses a gaseous mobile phase to transport sample components through columns either packed 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.

4.Detectors

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 Chemiluminescence detector.

5.Oven

Gas chromatography have ovens that are temperature programmable, the temperature of the gas chromatographic ovens typically range from 50C to 4000C but can go as low as -250C 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

6.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.

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION [5]

- **Analytical method development**

The number of drugs introduced into the market is increasing every year. These drugs may be either new entities or partial structural modification of the existing one, very often there is a time lag from the date of introduction of a drug into the market to the date of its inclusion in pharmacopoeias. This happens because of the

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possible uncertainties in the continuous and wider usage of these drugs, reports of new toxicities (resulting in their withdrawal from the market), development of patient resistance and introduction of better drugs by competitors.

Under these conditions, standards and analytical procedures for these drugs may not be available in the pharmacopoeias. It becomes necessary, therefore to develop newer analytical methods for such drugs.

→ Basic criteria for new method development of drug analysis:

- The drug may not be official in any pharmacopoeias.
- A proper analytical procedure for the drug may not be available in the literature due to patent regulations.
- Analytical methods may not be available for the drug in the form of a formulation due to the interference caused by the formulation excipients.
- Analytical methods for the quantification of the drug in biological fluids may not be available.
- Analytical methods for a drug in combination with other drugs may not be available.
- The existing analytical procedures may require expensive reagents and solvents. It may also involve cumbersome extraction and separation procedures and these may not be reliable.

➢ **Analytical method validation**

Analytical Method Validation is "the collection and evaluation of data, from the process design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products." Validation is an act of proving that any procedure, process, equipment, material, activity, or system performs as expected under given set of conditions and give the required accuracy, precision, sensitivity, ruggedness, etc. The biggest advantage of method validation is that it builds a degree of confidence, not only for the developer but also to the user.

Validation parameters:

The various parameters according to the ICH Guidelines as follows.

1. Accuracy
2. Precision
3. Selectivity
4. Sensitivity
5. Reproducibility
6. Stability

APPROACHES TO FAST GC-MS [6]

Fast gas chromatography–mass spectrometry (GC–MS) has the potential to be a powerful tool in routine analytical laboratories by increasing sample throughput and improving laboratory efficiency. However, this potential has rarely been met in practice because other laboratory operations and sample preparation typically limit sample throughput, not the GC–MS analysis.

The five main current approaches to fast GC–MS are described.

1. Short, microbore capillary GC columns
2. Fast temperature programming
3. Low-pressure GC–MS
4. Supersonic molecular beam for MS at high GC carrier gas flow
5. Pressure-tunable GC–GC

ADVANTAGES OF GC-MS [2,4]

- GC-MS represents the mass of a given particle (Da) to the number (z) of electrostatic charges (e) that the particle carries. The term m/z is measured in DA/e.
- GC-MS commonly uses electron impact (EI) and chemical ionization (CI) techniques.
- The main features of enhanced molecular ion, improved confidence in sample identification, significantly increased range of thermally labile, much faster analysis, improved sensitivity particularly for compounds that are hard to analyse and the many other features and options provide compelling reasons to use the GC-MS in broad range of areas.
- GC-MC technique offers high chromatographic resolution, high sensitivity, and reproducibility,
- Faster analysis,
- Significantly increased range of thermally labile and low volatility samples amenable for analysis,
- Improved sensitivity particularly for compounds that are hard to analyze,
- Improved confidence in sample identification,
- Structural determination of unknown organic compounds in complex mixtures both by matching their spectra with reference spectra and by a priori spectral interpretation,
- Analysis of industrial products for quality control.

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- GC-MS is less expensive than LC-MS. A tank of helium gas can last for months.

II. LIMITATIONS

- **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 (CO2, N2, O2, Ar, CO, H2O).

III. APPLICATIONS

1. **Environmental monitoring:** GC-MS has become a highly recommended tool for monitoring and tracking organic pollutants in the environment. The cost of GCMS equipment has decreased whereas the reliability has markedly increased. The determination of chloro-phenols in water and soil, polycyclic aromatic hydrocarbons (PAH), unleaded gasoline, dioxins, dibenzofurans (Figure 2), organo-chlorine pesticides, herbicides, phenols, halogenated pesticides, sulphur in air is very convenient to be screened by this technique. It can be used to screen the degradation products of lignin in bio-mass research, pesticides in spinach. Analysis of decacyclene, ovalene and even C60 degradation analysis of carbamazepine and its metabolites in treated sewage water and steroid can be done without derivatization.
2. **Food, beverage, and perfume analysis:** Nourishments and refreshments contain various sweet-smelling intensifies, some normally present in the crude materials and some framing during handling.GC-MS is broadly utilized for the examination of these mixes which incorporate esters, unsaturated fats, alcohols, aldehydes, terpenes and so on.It is likewise used to distinguish and gauge contaminants from decay or debasement which might be hurtful and which are frequently constrained by legislative offices, for instance pesticides.70
3. **Medicine:** Many innate metabolic infections otherwise called intrinsic blunders of digestion (IEM) are presently perceptible by infant screening tests, particularly the testing utilizing gas chromatography–mass spectrometry. GC-MS can decide mixes in pee even in minor focus. These mixes are ordinarily not present however show up in people enduring with metabolic disarranges. This is progressively turning into a typical method to analyze IEM for prior finding and foundation of treatment in the long run prompting a superior result. In mix with isotopic naming of metabolic aggravates, the GC-MS is utilized for deciding metabolic action. Most applications are based on the use of 13C as the labelling and the measurement of 13C-12C ratios with an isotope ratio mass spectrometer (IRMS); an MS with a detector designed to measure a few select ions and return values as ratios.
4. **Biological and pesticides detections:** GC-MS is exclusively used in bio-analysis of blood, urine for the presence of barbiturates, narcotics, alcohols, residual solvents, drugs like anaesthetics, anticonvulsant, antihistamine, anti-epileptic drug, sedative hypnotics, narcotics and food items (Figure 5). 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.
5. **Sports anti-doping analysis:** GC-MS is the fundamental apparatus utilized in sports hostile to doping research centers to test competitors' pee tests for disallowed execution improving medications, for instance anabolic steroids.
6. **Criminal forensics:** GC-MS can examine the particles from a human body so as to help connect a criminal to a wrongdoing. The examination of fire flotsam and jetsam utilizing GC-MS is settled, and there is even a set up American Society for Testing and Materials (ASTM) standard for fire trash

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investigation.GC-MS/MS is particularly valuable here as tests regularly contain complex lattices and results, utilized in court, should be exceptionally precise.

IV. CONCLUSION

GC-MS is used to separate gas liquid different substances. It is widely used in industry and there are many applications like environmental monitoring, medicine, criminal forensics, sports anti-doping analysis. It contains different instrument contents and also some approaches.

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