

Gas Chromatography (GC)

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Introduction to Gas Chromatography

- Gas Chromatography is a type of column chromatography in which the mobile phase is a gas (usually an inert carrier gas), and the stationary phase can be either a solid (in GSC) or a liquid (in GLC).
- The sample, when introduced into the GC system, is vaporized and carried by the inert gas through a column containing the stationary phase.
- Components in the sample mixture are separated based on their partitioning behavior between the mobile and stationary phases.
- **In pharmaceutical analysis, GC is primarily used for:**
 - Determination of residual solvents (as per ICH guidelines)
 - Analysis of drug substances and excipients
 - Identification of impurities
 - Quality control and stability testing

Theory of Gas Chromatography

Basic Principle

- GC operates on the principle of partition chromatography (in Gas-Liquid Chromatography) or adsorption chromatography (in Gas-Solid Chromatography).
- Components of a vaporized sample are separated based on their distribution between the stationary phase and the gaseous mobile phase.
- **The separation depends on:**
 - Boiling point of the analytes
 - Volatility
 - Polarity
 - Interaction with the stationary phase
- Each component in the sample moves through the column at different rates depending on its interaction with the stationary phase, leading to separation.

Retention Time (t_R)

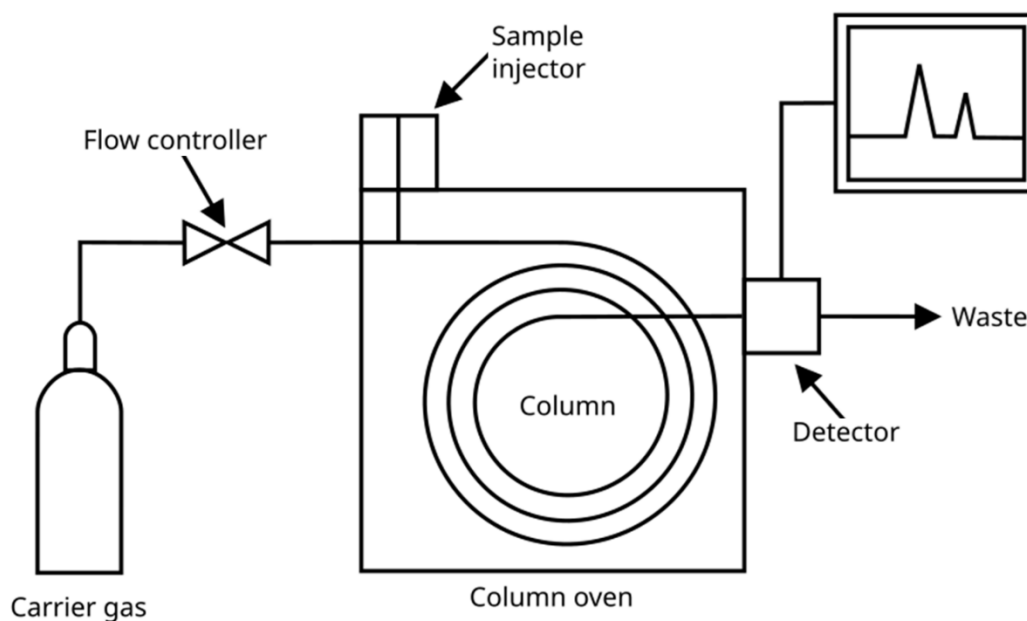
- The retention time is the time taken by a compound to travel from the injection port to the detector.
- It is a characteristic property and is used for qualitative identification.

Efficiency & Resolution

- **Theoretical plates (N):** A measure of column efficiency. Higher plate number means better separation.
- **Resolution (Rs):** Indicates how well two peaks are separated. For pharmaceutical analysis, $R_s \geq 1.5$ is usually considered acceptable.

Instrumentation of Gas Chromatography

A GC system typically consists of the following components:



A. Carrier Gas System (Mobile Phase)

- The carrier gas transports the sample through the column.
- It must be inert, pure, and non-reactive with the sample or stationary phase.

Common carrier gases:

- **Helium** (most common; excellent thermal conductivity, inert)
- **Nitrogen** (cheaper, lower efficiency than helium)
- **Hydrogen** (high efficiency, flammable—requires precautions)

Functions of carrier gas:

- Acts as the mobile phase
- Ensures proper sample transport
- Maintains consistent flow and pressure
- Carrier gas flow rate significantly influences retention time and resolution.

B. Sample Injection System

- Introduces the sample into the GC system.

- Must ensure rapid and complete vaporization.
- **Most commonly used:** split/splitless injection.

Split Injection:

- Only a portion of the sample enters the column.
- Used for high-concentration samples.

Splitless Injection:

- Entire sample enters the column.
- Used for trace analysis (e.g., impurities or residual solvents).
- Injection temperature must be above the boiling point of the sample to ensure complete vaporization.

C. Column and Column Oven

- The column is the heart of GC and is placed in a thermostatically controlled oven.

Types of GC Columns

1. Packed Columns:

- Larger diameter (2–4 mm)
- Shorter length (1–3 m)
- Packed with solid support coated with liquid stationary phase
- Used in preparative work and for gases

2. Capillary (Open Tubular) Columns:

- Narrow internal diameter (0.1–0.53 mm)
- Longer length (15–100 m)
- Superior resolution and efficiency
- **Types:**
 - Wall-coated open tubular (WCOT)
 - Support-coated open tubular (SCOT)

Column Oven

- Maintains a constant or programmed temperature
- Temperature programming improves separation of compounds with a wide boiling point range
- Crucial for reproducibility and sensitivity

D. Detector System

- Detectors identify and quantify the components as they elute from the column.

Common Detectors in Pharmaceutical GC:

1. Flame Ionization Detector (FID):

- Most widely used
- Sensitive to organic compounds
- High sensitivity, wide linear range
- Not responsive to inorganic gases or water

2. Thermal Conductivity Detector (TCD):

- Universal detector
- Lower sensitivity compared to FID
- Detects any compound that has a different thermal conductivity than the carrier gas

3. Electron Capture Detector (ECD):

- Highly sensitive for halogenated compounds
- Used in pesticide or solvent residue analysis

4. Mass Spectrometry (GC-MS):

- Combines separation of GC with identification power of MS
- Extremely useful in qualitative and quantitative analysis of unknowns and impurities

Types of Columns in Gas Chromatography

- Columns are where the actual separation of analytes occurs.
- They are classified primarily by their construction and internal phase configuration.

Types of Columns in Gas Chromatography



A. Packed Columns

Structure:

- Stainless steel, glass, or Teflon tubes filled with solid support particles coated with stationary phase (for GLC) or a solid adsorbent (for GSC).

Dimensions:

- Length: 1–5 meters
- Internal diameter: 2–4 mm

Use:

- Ideal for preparative or high-load analytical work.

Advantages:

- Simple construction
- Suitable for large sample sizes

Disadvantages:

- Lower efficiency (less resolution)
- Slower analysis compared to capillary columns

B. Capillary Columns (Open Tubular Columns)

Structure:

- Fused silica tubes with polyimide coating; inner wall coated or lined with stationary phase.

Types:

- **WCOT (Wall-Coated Open Tubular):** Liquid phase coated directly on the inner wall.
- **SCOT (Support-Coated Open Tubular):** Solid support layer holds the stationary phase on the wall.
- **PLOT (Porous Layer Open Tubular):** Inner wall coated with porous solid adsorbent (used in GSC).

Dimensions:

- Length: 15–100 meters
- Internal diameter: 0.1–0.53 mm

Advantages:

- Higher efficiency and resolution
- Faster analysis with small sample sizes

Disadvantages:

- Fragile
- More expensive than packed columns

Stationary Phases Gas Chromatography

Stationary Phases in Gas–Liquid Chromatography (GLC)

- In GLC, the stationary phase is a non-volatile liquid coated on a solid support or inner wall.
- Analytes are separated based on their partitioning between the mobile gas and liquid phase.

Characteristics of Ideal GLC Stationary Phases:



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