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MATS CENTRE FOR DISTANCE & ONLINE EDUCATION

Basic Analytical Chemistry

**Bachelor of Science (B.Sc.)
Semester - 4**



SELF LEARNING MATERIAL



DSEC
Chemistry
(Basic Analytical Chemistry)
MATS University Chemistry
(Basic Analytical Chemistry)
CODE:ODL/MSS/BSCB/407

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Module Introduction

The course has four modules: Under this theme, we covered the following topics

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01	Module 1:	Qualitative and Quantitative Aspects of Analysis
	Unit 1.1	Analytical approaches
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	Unit 4.1	Laboratory hazards and safety precautions
	Unit 4.2	Criteria of purity
	Unit 4.3	

References

This course provides a comprehensive foundation in analytical chemistry, laboratory practices, and instrumental techniques. **Module 1** introduces the **qualitative and quantitative aspects of analysis**, covering analytical approaches, laboratory apparatus, chemical concentration, titration, physical constants, and distillation methods. **Module 2** focuses on **separation techniques**, including fundamental principles and applications of adsorption chromatography for isolating and purifying compounds. **Module 3** emphasizes **spectroscopic methods of analysis**, particularly UV-Visible and Infrared spectroscopy, enabling students to understand molecular interactions and structural identification. **Module 4** highlights essential **laboratory work**, with emphasis on safety protocols, handling laboratory hazards, and criteria of purity for chemical substances. The course integrates theory with practical skills, preparing students to apply analytical tools in research, quality control, and industrial applications. References are provided to support deeper learning and reinforce fundamental concepts. Overall, the curriculum blends conceptual knowledge with hands-on training for effective problem-solving in chemical sciences.



Module 1:

Qualitative and Quantitative Aspects of Analysis

Unit 1.1 Analytical approaches

Objectives

1. To understand the fundamental concepts of qualitative and quantitative analysis in chemistry.
2. To differentiate between classical and instrumental analytical techniques.
3. To explore the role of analytical methods in pharmaceutical drug discovery, development, and quality control.
4. To study qualitative techniques for the identification of organic and inorganic compounds.
5. To explain quantitative techniques such as volumetric, gravimetric, and instrumental methods.

1.1.1 Analytical Approaches

Analytical chemistry is the branch of chemistry that deals with the identification, separation, and quantification of chemical components in natural and artificial materials. Analytical approaches are broadly classified into two categories: qualitative analysis and quantitative analysis. Qualitative analysis is concerned with determining the presence or absence of a particular substance in a sample, while quantitative analysis involves measuring the exact amount of the substance present. In the context of pharmaceutical sciences, analytical approaches play a critical role in drug discovery, development, quality control, and regulatory compliance.

Qualitative analytical techniques are foundational to understanding the composition of unknown substances. These techniques involve observing physical and chemical properties such as color, odor, melting



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point, boiling point, and solubility. For example, in organic analysis, functional group identification through chemical tests can confirm the presence of alcohols, ketones, amines, and carboxylic acids. Instrumental methods like ultraviolet-visible (UV-Vis) spectroscopy, infrared (IR) spectroscopy, and nuclear magnetic resonance (NMR) are also employed in qualitative assessments by providing structural information about molecules. Inorganic qualitative analysis relies on precipitation reactions, complexation, and flame tests to detect cations and anions in a given sample. These classical and modern techniques ensure that a pharmaceutical compound has the correct identity before it is further processed.

Quantitative analysis, on the other hand, is aimed at determining the exact amount or concentration of a substance within a sample. There are several classical and instrumental methods used in quantitative analysis. Classical methods include volumetric and gravimetric techniques. In volumetric analysis, titration is the most common method, wherein a reagent of known concentration is added to a sample until a reaction is completed, often indicated by a color change. This method is simple, inexpensive, and reliable for routine analysis. Gravimetric analysis involves isolating and weighing a compound of known composition, often as a precipitate. Though accurate, it is more time-consuming and less suited for complex mixtures.

With advancements in science, instrumental methods of quantitative analysis have gained prominence. Spectrophotometry, chromatography, and electrochemical methods provide high precision and sensitivity. Spectrophotometric methods, like UV-Vis and atomic absorption spectroscopy (AAS), are based on the interaction of light with matter, measuring absorbance to calculate concentrations. Chromatographic techniques, such as high-performance liquid chromatography (HPLC) and gas chromatography (GC), are used for separating components in a mixture and quantifying each component based on peak area or height. These methods are especially crucial in pharmaceutical analysis, where detecting impurities, degradation



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products, and active pharmaceutical ingredients (APIs) is mandatory for safety and efficacy.

Another important analytical approach is potentiometry, which measures the voltage of electrochemical cells to determine the concentration of ions in a solution. This method is commonly used in pH measurement using glass electrodes, and in redox titrations. Conductometry, which involves the measurement of electrical conductivity, is also used to determine the endpoint of titrations involving ionic species. Coulometry and voltammetry are advanced electroanalytical methods that offer high sensitivity and are particularly useful in trace analysis of pharmaceuticals and biological samples.

Method development and validation are essential aspects of modern analytical approaches. An analytical method must be specific, accurate, precise, linear, and robust. These parameters are evaluated during method validation to ensure that the method is reliable and suitable for its intended purpose. Specificity refers to the ability of the method to measure the analyte in the presence of other components like impurities or degradation products. Accuracy indicates how close the measured value is to the true value, while precision reflects reproducibility. Linearity confirms that the method provides results that are directly proportional to the concentration of analyte within a given range. Robustness examines how small changes in analytical conditions affect the results.

In pharmaceutical analysis, various guidelines such as those provided by the International Council for Harmonisation (ICH) are followed to validate analytical methods. Regulatory agencies like the FDA (U.S. Food and Drug Administration) and EMA (European Medicines Agency) require validated methods for all analytical procedures involved in drug production. Quality control laboratories must consistently perform validated tests on raw materials, intermediates, and finished products to ensure conformity with specifications.



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Furthermore, sampling is a critical step in any analytical approach, as it directly affects the reliability of the analysis. An appropriate sampling method must ensure that the sample is representative of the whole batch or lot. Errors in sampling can lead to misleading conclusions. Sample preparation, which may involve filtration, centrifugation, extraction, or digestion, must be performed carefully to avoid contamination and loss of analyte.

The selection of an appropriate analytical approach depends on several factors including the nature of the sample, the required sensitivity and selectivity, time constraints, cost considerations, and available instrumentation. For instance, when analyzing trace levels of a toxic impurity in a drug formulation, a highly sensitive method like mass spectrometry coupled with chromatography may be used. On the other hand, routine testing of pH or moisture content may involve simpler techniques like pH meters or Karl Fischer titration.

In conclusion, analytical approaches form the backbone of research, development, and quality control in pharmaceutical and medicinal chemistry. They provide the necessary tools to ensure that pharmaceutical products are safe, effective, and of high quality. From the identification of raw materials to the final batch release of a drug, analytical methods are employed at every stage. The choice between qualitative and quantitative approaches, and classical versus instrumental techniques, must be made judiciously based on analytical goals, regulatory requirements, and the complexity of the sample. As technology evolves, analytical methods continue to become more precise, automated, and high-throughput, thereby enhancing the reliability and speed of pharmaceutical analysis.



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Summary

Analytical chemistry is essential for identifying, separating, and quantifying chemical components in natural and artificial samples, particularly in pharmaceutical sciences. Analytical methods are divided into qualitative (determining the presence/absence of substances) and quantitative (measuring exact amounts). Qualitative analysis uses physical/chemical properties (color, melting point, solubility) and instrumental methods (UV-Vis, IR, NMR) to confirm chemical identity.

Quantitative analysis includes classical methods like volumetric titrations and gravimetric analysis, and instrumental methods such as spectrophotometry, chromatography (HPLC, GC), and electroanalytical techniques (potentiometry, conductometry, voltammetry).

MCQs

1. Analytical chemistry primarily deals with:
 - a) Identification, separation, and quantification of substances
 - b) Only synthesis of chemical compounds
 - c) Measuring physical constants
 - d) None of the above

Answer (b)

2. Which of the following is a **qualitative** analysis method?
 - a) UV-Vis Spectroscopy
 - b) Titration
 - c) Gravimetric analysis
 - d) Conductometry

Answer (a)

3. The most common method in volumetric analysis is:
 - a) Gravimetry
 - b) Titration
 - c) Chromatography



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d) Electrolysis

Answer (b)

4. In pharmaceutical analysis, **HPLC** is mainly used for:

- a) Separating and quantifying mixture components
- b) Measuring melting points
- c) Measuring viscosity
- d) Identifying flame colors

Answer (a)

5. Which parameter of method validation reflects reproducibility?

- a) Specificity
- b) Accuracy
- c) Precision
- d) Linearity

Answer (c)

Short Questions

1. Define qualitative and quantitative analysis with examples.
2. Mention two instrumental techniques used in qualitative analysis.
3. What is the principle of volumetric analysis?

Long Questions

1. Differentiate between classical and instrumental methods of quantitative analysis.
2. Describe the importance of sampling and sample preparation in analytical approaches.
3. Explain chromatographic techniques (HPLC, GC) and their applications in pharmaceutical analysis

Unit 1.2

Laboratory apparatus and measuring equipment

Objectives

1. To identify common laboratory apparatus and their uses in scientific experiments.
2. To understand the principles of operation of measuring instruments used in laboratories.
3. To develop skills in handling and maintaining laboratory equipment safely.
4. To learn the importance of calibration and accuracy in measurement.
5. To relate laboratory apparatus with real-world scientific applications.

1.2.1 Laboratory Apparatus and Measuring Equipment

The modern chemical laboratory is a well-organized and equipped environment that requires a wide range of apparatus and measuring equipment for accurate and reproducible scientific work. Whether in research, industrial quality control, or academic laboratories, the selection and use of appropriate apparatus are critical for ensuring experimental success. In pharmaceutical and medicinal chemistry, precise measurement is essential in the preparation, analysis, and formulation of drugs. A thorough understanding of laboratory equipment is therefore fundamental to the training of chemistry professionals.

Glassware is one of the most common categories of laboratory apparatus and serves multiple purposes such as holding, mixing, heating, or measuring chemicals. Common glassware includes beakers, flasks, test tubes, and measuring cylinders. Beakers are generally used for mixing and rough volume measurements and are available in various capacities. Flasks, including Erlenmeyer flasks



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and volumetric flasks, are used for mixing solutions, titrations, or preparing standard solutions. While Erlenmeyer flasks have a conical shape and can be stoppered for shaking, volumetric flasks are calibrated precisely to a fixed volume and are used in preparing solutions of known concentrations. Test tubes are cylindrical containers used for qualitative reactions and heating small quantities of substances. Graduated cylinders are used to measure liquid volumes more precisely than beakers, but less accurately than volumetric glassware.



Figure 1.1: Volumetric flask, reagent bottles, and other glassware

For highly accurate volume measurements, burettes and pipettes are indispensable. Burettes are long, graduated tubes fitted with a stopcock at the bottom and are primarily used in titrations to deliver variable volumes of titrant. The volume of liquid delivered is read

from the graduations on the side. Pipettes, on the other hand, are used to transfer fixed volumes of liquids with high precision. Volumetric pipettes deliver a single, specific volume, while graduated pipettes can deliver a range of volumes. The correct use of pipettes requires skill in drawing and releasing the liquid, often using a pipette bulb or automatic pipetting device.

Among the solid apparatus used for measurement and transfer are balances. Analytical balances are crucial in pharmaceutical analysis, where the accurate weighing of substances to four or more decimal places is necessary. These balances are enclosed in a draft shield and are sensitive to very small weight differences. Top-loading balances are less precise but are used when high accuracy is not required. Calibration and proper handling of balances are vital. The balance must be level, placed on a vibration-free surface, and regularly calibrated using certified standard weights. Materials to be weighed should be placed in clean, dry containers like weighing boats or beakers to avoid contamination or loss.

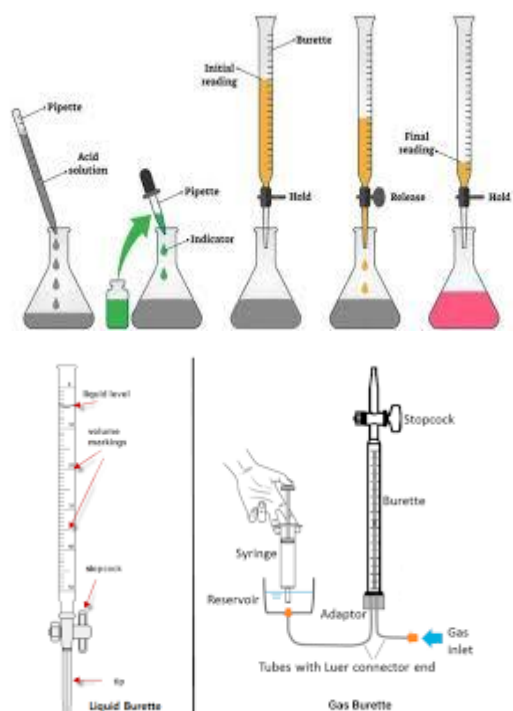


Figure 1.2: Titration process in a Laboratory



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Temperature regulation and measurement are also essential in laboratories, particularly for reactions sensitive to thermal changes. Heating devices such as Bunsen burners, hot plates, and heating mantles are widely used. Bunsen burners are traditional flame-based devices used for general heating but can pose fire risks. Hot plates provide controlled surface heating and are often used with magnetic stirrers for heating and mixing simultaneously. Heating mantles are used for round-bottom flasks and offer even heating without open flames, making them safer for flammable solvents. For temperature control, water baths and oil baths are employed. Water baths provide consistent temperatures for heating sensitive biological or chemical samples, while oil baths can reach higher temperatures for heating organic reactions.

Thermometers, both mercury and digital types, are used to monitor temperature during experiments. Digital thermometers with probes are increasingly preferred due to safety and accuracy. Some advanced labs use thermocouples and infrared thermometers, especially in automated setups. Temperature control and accuracy are crucial during pharmaceutical syntheses, crystallization processes, and stability studies, where even minor deviations can affect product quality.

Measuring pH is another important aspect of laboratory work, particularly in the pharmaceutical field where formulation stability, drug solubility, and bioavailability depend on the pH of a solution. The pH meter is an electronic device used to determine the acidity or alkalinity of a solution accurately. It consists of a pH-sensitive electrode and a reference electrode that measure the potential difference caused by hydrogen ion activity. Calibration of the pH meter using standard buffer solutions is essential before

measurement. Proper maintenance of the electrode, including regular rinsing and storage in appropriate solutions, is required to preserve its accuracy and lifespan.



Figure 1.3: pH meter

Filtration apparatus is essential for separating solids from liquids. This includes filter funnels, vacuum filtration setups, Buchner flasks, and sintered glass crucibles. Gravity filtration is typically used for simple separations using filter paper and funnels, while vacuum filtration provides faster and more efficient separation, especially when handling large volumes or viscous materials. Buchner funnels and flasks connected to vacuum pumps create suction that draws liquid through the filter rapidly. In pharmaceutical labs, filtration is used to remove particulate matter from solutions, separate precipitates, and purify reaction products.



Figure 1.4: Bukner funnel

To support experiments involving solution concentration and purification, evaporators and distillation setups are employed. The rotary evaporator, commonly called a rotavap, is used to remove solvents under reduced pressure. It consists of a rotating flask, a water or oil bath for heating, and a condenser connected to a vacuum pump. This setup allows gentle evaporation of solvents, preventing decomposition of heat-sensitive compounds. In contrast, distillation apparatus, including simple and fractional distillation columns, is used to separate mixtures based on boiling point differences. These setups are often essential in the purification of solvents, recovery of reaction products, and preparation of distilled water or solvents in the lab.

In analytical laboratories, spectroscopy instruments like UV-Vis spectrophotometers and IR spectrometers are also considered part of

essential measuring equipment. A UV-Vis spectrophotometer measures the absorbance or transmittance of a sample at specific wavelengths, allowing for concentration determination based on Beer-Lambert's law. IR spectrometers detect molecular vibrations and are used for structural elucidation. Similarly, chromatographic instruments like high-performance liquid chromatography (HPLC) and gas chromatography (GC) systems are used to separate, identify, and quantify components in complex mixtures. These instruments often incorporate detectors such as UV, refractive index, flame ionization, or mass spectrometers, each providing different types of information.



Figure 1.5 UV-Visible spectrophotometer



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CHEMISTRY Other commonly used laboratory apparatus include desiccators, drying ovens, and centrifuges. Desiccators are sealed containers used to keep materials moisture-free, often containing drying agents like silica gel. Ovens are used for drying glassware and samples,



Figure 1.6: High Performance Liquid Chromatography

typically at controlled temperatures. Centrifuges separate mixtures based on density by spinning samples at high speeds. In pharmaceutical labs, centrifugation is used in processes such as separating blood components, collecting precipitates, or clarifying solutions.

Proper maintenance, calibration, and safety precautions are essential when working with laboratory apparatus and measuring instruments. Equipment should be regularly checked for wear and damage. Glassware must be inspected for cracks or chips, and electronic instruments must be serviced according to manufacturer instructions.



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All users should be trained in the correct use of equipment to avoid errors and accidents. Labeling, documentation, and adherence to standard operating procedures (SOPs) ensure that measurements are reliable, traceable, and compliant with regulatory standards. In pharmaceutical analysis, where even minor deviations can have critical consequences, the integrity and accuracy of measuring instruments are paramount.

To conclude, laboratory apparatus and measuring equipment form the backbone of any scientific investigation, especially in pharmaceutical and medicinal chemistry. From simple glassware and balances to advanced chromatographic and spectroscopic systems, each tool has a distinct role in ensuring experimental precision and safety. A deep understanding of their working principles, proper usage, maintenance, and limitations is essential for every laboratory professional. As technology continues to advance, laboratories are increasingly moving toward automation and digital integration, making the future of laboratory measurement both efficient and sophisticated.

Summary

Laboratory apparatus and measuring equipment are essential tools in scientific research, teaching, and industry. Basic apparatus such as beakers, flasks, pipettes, burettes, and test tubes are used for preparing, transferring, and holding substances. Specialized instruments like balances, spectrophotometers, calorimeters, and pH meters help in precise measurement and analysis. Measuring equipment ensures accuracy and reliability, which is critical for reproducibility of experiments. Proper handling, calibration, and safety precautions are necessary to prevent errors and accidents. Mastery of laboratory equipment enhances experimental efficiency, accuracy, and credibility of results, forming the foundation of all scientific investigations.



Notes MCQs

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1. Which apparatus is used to measure the volume of liquids most accurately?

- a) Beaker
- b) Measuring cylinder
- c) Pipette
- d) Conical flask

Answer: c) Pipette

2. A burette is mainly used for:

- a) Heating substances
- b) Measuring pH
- c) Titration experiments
- d) Storing solutions

Answer: c) Titration experiments

3. The instrument used to measure the mass of a substance is:

- a) Hygrometer
- b) Balance
- c) Thermometer
- d) Barometer

Answer: b) Balance

4. Which equipment is best for measuring temperature in a laboratory?

- a) Barometer
- b) Thermometer
- c) Manometer



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d) Hygrometer

Answer: b) Thermometer

5. A spectrophotometer is used for:

a) Measuring light absorbance of solutions

b) Measuring temperature

c) Stirring solutions

d) Separating solids from liquids

Answer: a) Measuring the light absorbance of solutions

Short Answer Questions

1. Differentiate between a beaker and a measuring cylinder.
2. What is the function of a burette in titration?
3. State the importance of calibration in laboratory measuring instruments.
4. Write two safety precautions while handling glassware in the laboratory.
5. Why is a pipette considered more accurate than a beaker for volume measurement?

Long Answer Questions

1. Describe five commonly used laboratory apparatus, their functions, and precautions in handling them.
2. Explain the role of measuring equipment such as balances, thermometers, and pH meters in experimental accuracy.
3. Discuss the importance of proper maintenance and calibration of laboratory instruments with examples.



Notes

Unit 1.3

BASIC ANALYTICAL CHEMISTRY

Chemical Concentration

Objectives

1. To define chemical concentration and understand its importance in chemistry.
2. To differentiate between various units of concentration (molarity, molality, normality, mole fraction, % composition).
3. To calculate concentrations of solutions using appropriate formulas.
4. To apply concentration concepts to practical laboratory and industrial scenarios.
5. To relate concentration changes to dilution and mixing principles.

1.3.1 Chemical Concentration

The concept of chemical concentration lies at the heart of analytical and pharmaceutical chemistry. It defines the amount of a substance (solute) present in a given quantity of a solution or mixture.

Understanding and controlling chemical concentration is essential for preparing reagents, analyzing pharmaceutical products, formulating medications, and ensuring the safety and efficacy of drug compounds. Accurate knowledge of concentration not only helps in quantitative analysis but also influences reaction rates, equilibrium, and biological responses to therapeutic agents. Therefore, chemical concentration forms a foundational aspect of laboratory practice and theoretical studies.

The basic idea of concentration is derived from the ratio between the amount of solute and the quantity of solvent or solution in which the solute is dissolved. Several standard expressions are used to describe concentration, each suited to different experimental and practical

contexts. One of the most frequently used units in chemistry is molarity, defined as the number of moles of solute per liter of solution. Molarity is denoted by the symbol 'M' and is particularly useful in volumetric analysis and titration reactions. For example, a 1 M solution of sodium chloride contains one mole of NaCl in one liter of solution. Molarity is temperature-dependent because it involves volume, which can expand or contract with temperature.

Molarity	Molality
The ratio between the number of moles of solute and the volume of solvent in Liters	The ratio between the number of moles of solute and the solvent volume in kilograms
$M = \frac{\text{Moles of Solute}}{\text{Solution in liter}}$	$m = \frac{\text{Moles of Solute}}{\text{Solution in liter}}$

Another important measure is molality, which refers to the number of moles of solute per kilogram of solvent. Unlike molarity, molality does not change with temperature, making it useful for colligative property calculations, such as boiling point elevation and freezing point depression. Since it is based on mass, molality remains stable even when thermal expansion occurs. It is particularly beneficial in physical chemistry experiments where precise temperature control is necessary.

$$m = \frac{\left(\frac{W}{\text{Molar Mass}}\right) \text{ solute}}{\frac{W}{1000} \text{ gm solvent}}$$

$$m = \left(\frac{W}{\text{Molar Mass}}\right) \times \frac{1000}{W \text{ gm solvent}}$$



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Normality is another expression of concentration, defined as the number of gram equivalents of solute per liter of solution. It is represented by the symbol 'N' and is used in acid-base chemistry and redox titrations. The concept of equivalence is based on the reactive capacity of the substance. For acids, one equivalent is the amount that furnishes one mole of hydrogen ions (H^+), while for bases, it is the amount that supplies one mole of hydroxide ions (OH^-). In redox reactions, it refers to the number of electrons that a compound can donate or accept. Normality is highly context-specific, depending on the reaction involved, and is often used in titration calculations.

Normality, N

Formula

$$N = \frac{wt(g) \times 1000}{\text{Equivalent weight} \times V} \Rightarrow \frac{wt(g) \times 1000}{Eq. wt. \times V}$$

↓

$$\text{Equivalent weight} = \frac{\text{Molecular weight}}{\text{Number of } H^+ \text{ in acid or } OH^- \text{ in base}} \Rightarrow \frac{M. W}{n}$$

Percentage concentration is commonly used in pharmaceutical and industrial settings. It is expressed in different forms such as weight/weight (w/w), weight/volume (w/v), or volume/volume (v/v) percentages. For example, a 10% w/v solution of glucose means 10 grams of glucose are present in 100 mL of solution. This method is intuitive and easy to understand for practical applications, especially in clinical formulations and over-the-counter medicines. It allows for quick assessment of the active ingredient's strength in a given product.

Percentage Concentration

$$\bullet \% (w/w) = \frac{\text{mass solute}(g)}{\text{mass solution}(g)} \times 100$$

• W is weight same as mass

$$\bullet \% (w/v) = \frac{\text{mass solute}(g)}{\text{volume solution}(mL)} \times 100$$

$$\bullet \% (v/v) = \frac{\text{volume solute}(mL)}{\text{volume solution}(mL)} \times 100$$

Parts per million (ppm) and parts per billion (ppb) are used when the concentration of a substance is very low, such as in environmental analysis or impurity testing in pharmaceuticals. These units express the ratio of solute to solution in parts per million or billion, often without specifying a mass or volume basis, although it is typically assumed to be weight/weight. For example, one ppm corresponds to one milligram of solute in one liter of water (assuming the density of water is 1 g/mL). These units are vital in ensuring that drug impurities or toxic contaminants remain within permissible limits set by regulatory authorities.

1. Mass Basis:

$$\text{ppm} = \left(\frac{\text{mass of solute}}{\text{mass of solution}} \right) \times 10^6$$

2. Volume Basis (for gases):

$$\text{ppm} = \left(\frac{\text{volume of solute}}{\text{volume of solution}} \right) \times 10^6$$

3. Molar Basis (for solutions):

$$\text{ppm} = \left(\frac{\text{moles of solute}}{\text{moles of solution}} \right) \times 10^6$$

In the laboratory, preparing solutions of desired concentration requires an accurate understanding of solute mass, solution volume, and unit conversion. To prepare a molar solution, one calculates the required number of moles using the molecular weight of the solute and then



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precision. For example, to prepare 1 liter of a 0.5 M sodium chloride solution, one would weigh 29.22 grams of NaCl (molecular weight = 58.44 g/mol), dissolve it in a small amount of water, and then dilute it to exactly 1 liter in a volumetric flask.

Dilution is a common process used to reduce the concentration of a solution by adding more solvent. The relationship between concentration and volume during dilution is governed by the formula $C_1V_1 = C_2V_2$, where C_1 and V_1 are the initial concentration and volume, and C_2 and V_2 are the final concentration and volume. This formula is widely used in analytical chemistry and pharmaceutical practices to prepare working solutions from stock solutions. It ensures that while the volume increases, the total amount of solute remains unchanged.

In pharmaceutical laboratories, chemical concentration is crucial for dosage accuracy. Drugs must be formulated in such a way that the correct amount of active ingredient is delivered to the patient. Too little of a drug may result in therapeutic failure, while too much can lead to toxicity. Quality control laboratories routinely measure the concentration of active pharmaceutical ingredients (APIs) in bulk materials and finished dosage forms using methods such as spectrophotometry, chromatography, and titration. These analytical techniques are sensitive enough to detect minute concentration changes that could impact product quality.

Chromatographic methods such as high-performance liquid chromatography (HPLC) and gas chromatography (GC) are widely employed to quantify substances in complex mixtures. These instruments measure concentration based on peak area or peak height

relative to calibration standards. Spectroscopic techniques like UV-visible and infrared spectroscopy measure absorbance, which can be related to concentration using Beer-Lambert's law. This law states that absorbance is directly proportional to the concentration of the absorbing species and the path length of the sample cell. Calibration curves are constructed to determine unknown concentrations by comparing sample absorbance with those of known standards.

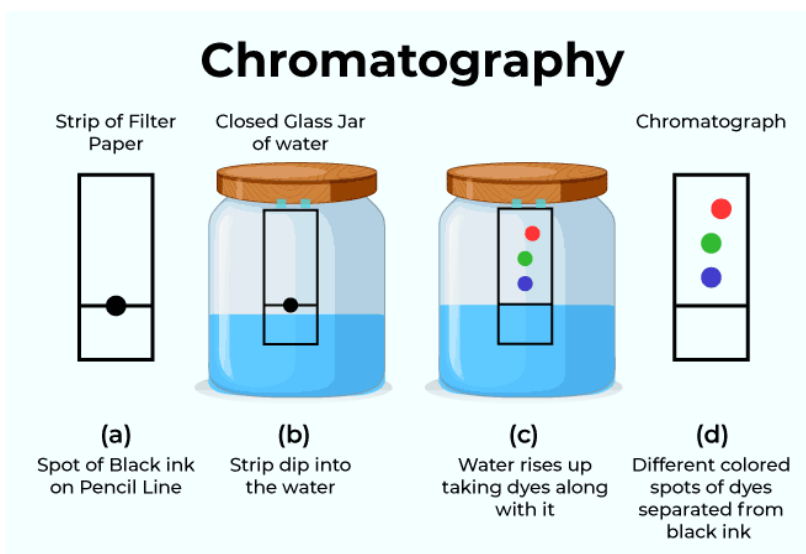


Figure 1.7: Chromatography equipment

$$R_s = \underbrace{\frac{k}{k+1}}_{\text{Retention}} \times \underbrace{\frac{a-1}{a}}_{\text{Selectivity}} \times \underbrace{\frac{\sqrt{N}}{4}}_{\text{Efficiency}}$$

Regulatory bodies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) place strict requirements on concentration determination during drug development and manufacturing. The concentration of active ingredients, excipients, and impurities must fall within established limits for a product to be approved for clinical or commercial use. Analytical methods used for concentration measurements must be validated according to guidelines provided by the International Council for Harmonisation (ICH). These guidelines require



Notes on Evaluation of method accuracy, precision, specificity, linearity, and
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robustness to ensure reliability.

In biochemical applications, concentration also plays a role in enzyme kinetics, buffer preparation, and protein quantification. Enzyme activity is influenced by substrate concentration, which must be optimized to study reaction rates effectively. Buffer solutions, which maintain stable pH levels during reactions, are prepared using specific concentrations of weak acids and their conjugate bases. The Henderson-Hasselbalch equation is often used in this context. Protein concentrations are determined using colorimetric assays such as the Bradford or Lowry method, which involve generating standard curves based on known protein concentrations.

In conclusion, chemical concentration is a fundamental parameter in scientific experimentation and pharmaceutical applications. Its accurate determination and control are vital for achieving reproducibility, safety, and effectiveness in chemical and biological systems. Whether preparing standard solutions, performing titrations, or analyzing drug formulations, the concept of concentration is central to laboratory practice. A sound understanding of different concentration units, methods of preparation, and techniques for analysis empowers chemists and pharmaceutical scientists to carry out reliable and compliant analytical work. As instrumentation and analytical techniques continue to evolve, the precision with which concentrations can be measured and controlled will further enhance the quality and safety of pharmaceutical products.

Summary

Chemical concentration refers to the amount of a substance (solute) present in a given quantity of solvent or solution. It is a key parameter in analytical chemistry, reaction kinetics, and solution chemistry. The choice of concentration unit depends on the nature of



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the chemical process. For example, molarity is commonly used in titration, while molality is preferred when temperature variation is significant. Understanding concentration is essential for preparing accurate solutions, carrying out quantitative analysis, and ensuring correct stoichiometric relationships in reactions.

MCQ

1. Molarity is defined as:
 - a) Moles of solute per kg of solvent
 - b) Moles of solute per liter of solution
 - c) Mass of solute per liter of solution
 - d) Equivalents of solute per liter of solution**Answer: b**

2. Which unit of concentration does not change with temperature?
 - a) Molarity
 - b) Molality
 - c) Normality
 - d) % Volume**Answer: b**

3. The mole fraction of a solute is always:
 - a) Greater than 1
 - b) Equal to 0
 - c) Between 0 and 1
 - d) Undefined**Answer: c**

4. Normality is used mostly in:
 - a) Thermodynamics
 - b) Titration reactions
 - c) Molecular orbital calculations



Notes d) Gas law problems

BASIC ANALYTICAL CHEMISTRY **Answer: b**

5. A solution contains 1 mol NaCl in 1 L water. Its molarity is:

- a) 0.5 M
- b) 1 M
- c) 2 M
- d) 0.1 M

Answer: b

4. Short Answer Questions

1. Define molarity and molality. How are they different?
2. Why is molality preferred over molarity when working at varying temperatures?
3. Write the formula for mole fraction and explain with an example.
4. What is the significance of normality in acid–base titration?
5. A solution is prepared by dissolving 5 g of NaOH in 100 g of water. Calculate molality.

5. Long Answer Questions

1. Explain different methods of expressing chemical concentration with suitable examples.
2. Discuss the importance of concentration in industrial and pharmaceutical applications with examples.
3. Describe the effect of dilution on concentration and explain how to prepare standard solutions in the laboratory.

Unit 1.4**Titration****Objectives**

1. To understand the fundamental principles of titrations as a quantitative analytical method.
2. To differentiate between various types of titrations (acid–base, redox, complexometric, precipitation).
3. To learn how to select appropriate indicators for different titrations.
4. To calculate unknown concentrations using titration data.
5. To apply titration techniques in pharmaceutical, environmental, and industrial analysis.

1.4.1 Titration

Titration is one of the most fundamental and widely used analytical techniques in chemistry. It is a quantitative chemical analysis method employed to determine the unknown concentration of a solution by reacting it with a solution of known concentration. Titration, also known as volumetric analysis, is especially crucial in pharmaceutical laboratories for the accurate determination of drug content, purity analysis, and quality control. Its precision, simplicity, and broad applicability make it an essential technique in both research and industrial environments.

The underlying principle of titration involves a chemical reaction between the analyte (the substance whose concentration is to be determined) and a standard solution called the titrant, which has a precisely known concentration. This reaction proceeds until it reaches the equivalence point, the stage at which the quantity of titrant added is stoichiometrically equivalent to the quantity of analyte in the sample. The completion of this reaction is usually indicated by a



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is used to signal the endpoint — a visual cue that approximates the equivalence point.

There are several types of titration, each tailored to specific chemical reactions. One of the most commonly used is acid-base titration, which involves the neutralization reaction between an acid and a base. In this process, a strong acid may be titrated with a strong base, or vice versa.

Alternatively, weak acids or bases may be titrated with their strong counterparts, which requires the selection of an appropriate pH indicator. Phenolphthalein, for example, is commonly used when titrating a strong acid with a strong base because of its sharp color transition near pH 8.3. Methyl orange is more suitable for strong acid–weak base titrations due to its transition in the acidic pH range.

Another important class is redox titration, which is based on oxidation-reduction reactions. In redox titrations, electrons are transferred from one substance to another. These titrations are particularly useful for determining concentrations of oxidizing and reducing agents. Potassium permanganate, which acts as a self-indicating titrant due to its intense purple color, is often used in redox titrations to determine the amount of reducing substances in a solution. Iodometric and iodimetric titrations are also common, involving iodine as either the titrant or the analyte. These titrations are especially useful in pharmaceutical assays involving the estimation of compounds like ascorbic acid and certain alkaloids.

Precipitation titrations involve reactions in which an insoluble product is formed during the titration. A classical example is the titration of chloride ions with silver nitrate, forming a white precipitate of silver



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chloride. The endpoint of such titrations is detected using indicators like potassium chromate, which changes color once all chloride has precipitated and silver ions begin reacting with chromate to form red silver chromate. Precipitation titrations are useful in water analysis, pharmaceutical salt testing, and determining halide concentrations in various formulations.

Complexometric titrations are employed for the quantitative analysis of metal ions using complexing agents such as ethylenediaminetetraacetic acid (EDTA). These titrations are vital in water hardness analysis, pharmaceutical raw material testing, and chelation studies. In a typical EDTA titration, a metal ion reacts with EDTA to form a stable, colorless complex. Indicators like Eriochrome Black T are used to signal the endpoint by changing color when the metal ions are completely complexed. The ability of EDTA to form strong 1:1 complex with metal ions makes complexometric titration a preferred method in many analytical procedures.

The apparatus used in titration includes a burette, which accurately dispenses the titrant; a pipette for measuring the analyte; a conical flask in which the reaction takes place; and a suitable indicator. The burette is clamped vertically and filled with the standard solution. The analyte is pipetted into the flask, and a few drops of indicator are added. The titrant is then slowly added from the burette to the analyte with constant swirling until the endpoint is observed. The volume of titrant used is recorded, and using the stoichiometry of the reaction, the concentration of the analyte is calculated.

To ensure accurate titration results, several precautions must be taken. All glassware should be clean and free from contaminants. The burette should be rinsed with the titrant before filling, and the pipette should be rinsed with the solution it will deliver. During titration, the addition of titrant should be slow near the endpoint to avoid overshooting. The endpoint must be recorded precisely, and multiple trials should be



Notes performed to obtain concordant readings. Environmental factors such as temperature and light may also affect the reaction and should be controlled or accounted for.

Titration calculations are based on the concept of stoichiometry, which involves balanced chemical equations. For acid-base titrations, the formula used is $M_1V_1 = M_2V_2$, where M and V refer to the molarity and volume of acid and base, respectively. For reactions involving different stoichiometric coefficients, the balanced equation must be used to determine the exact mole ratio. For example, if two moles of base are required to neutralize one mole of acid, the calculations must reflect this relationship. In redox titrations, equivalent weights and n-factor (number of electrons exchanged per mole) are used in calculations. Precision in these computations is crucial in pharmaceutical analysis, where regulatory standards require strict conformity to label claims.

In pharmaceutical laboratories, titration plays a central role in quality control and formulation development. It is used for the standardization of reagents, assay of bulk drugs, estimation of preservatives, and pH adjustment in formulations. For instance, sodium hydroxide solution is commonly standardized against potassium hydrogen phthalate, and hydrochloric acid is standardized using sodium carbonate. The standardized solutions are then used for routine titrations to assay pharmaceutical compounds such as aspirin, sodium benzoate, and various vitamins. The reproducibility and traceability of titration results are essential for compliance with Good Laboratory Practice (GLP) and pharmacopoeial standards.

Pharmacopoeias such as the United States Pharmacopeia (USP), British Pharmacopoeia (BP), and Indian Pharmacopoeia (IP) describe official titration procedures for numerous pharmaceutical substances.



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These include specifications for titrant concentration, choice of indicators, sample preparation, and permissible result ranges. Validation of titration methods is required to ensure accuracy, precision, linearity, and specificity. In some cases, automated titrators are used to improve consistency and reduce human error. These instruments can detect endpoints by potentiometric or conductometric means and are especially useful in non-colored or turbid solutions where visual indicators are ineffective.

In educational laboratories, titration is a standard experiment used to introduce students to quantitative analysis. It provides hands-on experience in measurement, observation, and calculation. It also reinforces the principles of stoichiometry, solution chemistry, and acid-base theory. By performing titration experiments, students learn critical laboratory skills such as accurate pipetting, burette reading, and data interpretation. Beyond its academic value, titration lays the groundwork for advanced analytical methods and fosters an appreciation for precision in scientific work.

In conclusion, titration is a powerful and versatile analytical technique that plays a vital role in both academic and professional chemical analysis. Its applications in acid-base chemistry, redox reactions, complexometric, and precipitation analysis make it indispensable in pharmaceutical quality control, environmental testing, and chemical research. By enabling the accurate determination of unknown concentrations, titration helps ensure the safety, effectiveness, and consistency of chemical and pharmaceutical products. Mastery of titration techniques is therefore essential for any chemist or analyst working in the field of medicinal or analytical chemistry.



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Summary

Titration is a volumetric analytical technique used to determine the unknown concentration of a solution by reacting it with a standard solution of known concentration. The reaction is monitored until the equivalence point, where stoichiometrically equal amounts of

reactants have combined. Indicators or instrumental methods are used to detect the endpoint, which approximates the equivalence point.

Types of titrations include:

- **Acid–Base Titrations** (neutralization, use of pH indicators).
- **Redox Titrations** (involving oxidation-reduction reactions).
- **Complexometric Titrations** (formation of stable complexes, e.g., EDTA titrations).
- **Precipitation Titrations** (formation of a precipitate as endpoint).

Titrations are widely used in laboratories for purity testing, pharmaceutical assays, water hardness determination, and food analysis.

MCQs

1. The point at which the titration reaction is chemically complete is called:
 - a) Endpoint
 - b) Equivalence point
 - c) Neutral point
 - d) Half-neutralization point

Answer: b) Equivalence point



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2. The indicator commonly used in strong acid–strong base titrations is:

- a) Phenolphthalein
- b) Methyl orange
- c) Potassium dichromate
- d) Starch

Answer: a) Phenolphthalein

3. EDTA is used in titrations for determination of:

- a) Water hardness
- b) Acidity
- c) Chloride content
- d) Oxidizing agents

Answer: a) Water hardness

4. In iodometric titration, starch is used as an indicator because it forms a complex with:

- a) Sodium
- b) Iodine
- c) Sulfate
- d) Hydroxide

Answer: b) Iodine

5. Which type of titration involves precipitation as a basis of measurement?

- a) Redox titration
- b) Acid–base titration
- c) Complexometric titration



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d) Mohr's method

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Answer: d) Mohr's method

Short Answer Questions

1. Define titration and its purpose in analytical chemistry.
2. Differentiate between endpoint and equivalence point.
3. Give two examples each of acid–base and redox titrations.
4. Why is phenolphthalein not suitable for titrating strong acid with weak base?
5. What is the role of EDTA in complexometric titrations?

Long Answer Questions

1. Explain the principle, procedure, and applications of acid–base titrations with examples of suitable indicators.
2. Describe the different types of titrations (acid–base, redox, precipitation, and complexometric) with examples and applications.
3. Discuss the criteria for selecting a suitable indicator in titrations.
4. Explain the procedure of EDTA titration for the determination of water hardness, along with calculations.
5. Compare and contrast iodometry and iodimetry with suitable reactions and uses.



Unit 1. 5

Physical Constants

Objectives

1. To understand the concept of physical constants and their importance in science.
2. To identify fundamental constants such as the speed of light, Planck's constant, Avogadro's number, etc.
3. To explain the role of physical constants in defining units of measurement (SI units).
4. To appreciate the universality and invariance of physical constants across nature.

1.5.1 Physical Constants

In the realm of chemical and pharmaceutical sciences, physical constants are indispensable tools that provide a reliable foundation for theoretical understanding, experimental design, and practical calculations. These constants are fixed values representing fundamental properties of matter and energy, and they recur throughout all branches of physical science. In both research and industry, accurate knowledge and application of physical constants allow scientists to perform precise calculations, standardize procedures, and interpret experimental results in a consistent and reproducible manner.

A physical constant is defined as a physical quantity whose value is generally assumed to be universal in nature and unchanging in time. These constants can be classified into two major types: universal physical constants and substance-specific physical constants.



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Universal constants, such as the speed of light, Planck's constant, the gas constant, and Avogadro's number, are the same for all systems and materials.

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materials. On the other hand, substance-specific constants include properties such as melting point, boiling point, refractive index, density, and solubility. These constants vary from one compound to another but remain consistent for a given pure substance under defined conditions.

In pharmaceutical and medicinal chemistry, universal physical constants are frequently employed in thermodynamic and kinetic calculations. The gas constant (R), which links pressure, volume, temperature, and the number of moles in the ideal gas law, is crucial for understanding gas behavior, calculating enthalpy changes, and working with equations of state. Its value in SI units is $8.314 \text{ J/mol} \cdot \text{K}$. Avogadro's number, which defines the number of particles in one mole of a substance ($6.022 \times 10^{23} \text{ particles/mol}$), is fundamental in stoichiometric calculations, molar relationships, and molecular weight determination. Planck's constant, central to quantum mechanics, is important in spectroscopy and photochemistry, influencing how we understand the energy levels of electrons and the interaction of light with matter.

Substance-specific physical constants have more direct applications in pharmaceutical practice. One of the most commonly encountered is the melting point, the temperature at which a solid turns into a liquid under atmospheric pressure. This property is crucial in the identification and purity analysis of organic and inorganic compounds. A pure compound typically has a sharp and well-defined melting point, while impurities cause depression and broadening of the melting range. Pharmaceutical compounds must meet specific melting point standards to ensure their identity and quality. Similarly, the boiling



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point is the temperature at which a liquid's vapor pressure equals atmospheric pressure. It is essential in processes like distillation, solvent recovery, and the preparation of volatile drugs or intermediates.

Density, another fundamental physical constant, refers to the mass of a substance per unit volume and is usually expressed in grams per cubic centimeter (g/cm^3) or kilograms per liter (kg/L). It is vital for the formulation of liquid dosage forms, including syrups, suspensions, and injections. Accurate density measurements allow the conversion between mass and volume, which is necessary when preparing solutions based on weight-in-volume or volume-in-volume percentages. In addition, density is an important quality control parameter and is used to detect adulteration or variation in raw materials.

Refractive index is a physical constant that measures how much light is bent, or refracted, when it passes from one medium into another. This property is extensively used in the characterization of liquids, especially oils and solvents. It is temperature-dependent and specific to the wavelength of light used in measurement. In the pharmaceutical industry, refractometry is used to identify substances and determine their purity. For example, essential oils, glycerin, and alcohols have specific refractive indices, and any deviation may indicate contamination or degradation.

Another important physical constant in pharmaceutical analysis is the partition coefficient, which expresses the ratio of concentrations of a compound in a two-phase system consisting of two immiscible solvents, usually octanol and water. This constant reflects a compound's lipophilicity and influences its absorption, distribution, metabolism, and excretion (ADME) properties. Drugs with high partition coefficients tend to cross biological membranes more easily but may accumulate in fatty tissues. Thus, understanding and



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Measuring the partition coefficient is critical in drug design and
BASIC ANALYTICAL system development.
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Vapor pressure, yet another significant constant, is the pressure exerted by a vapor in equilibrium with its liquid or solid phase at a given temperature. It provides insight into the volatility of a substance. In pharmaceutical formulations, controlling vapor pressure is essential in the manufacture and packaging of volatile substances like aerosols, sprays, and inhalation products. Volatile anesthetics and solvent-based drugs must be carefully handled to avoid loss or alteration due to vaporization.

Specific heat capacity, the amount of heat required to raise the temperature of a unit mass of a substance by one degree Celsius, is also a relevant physical constant. It affects the energy requirements for heating and cooling substances during pharmaceutical processing, including crystallization, drying, and sterilization. Compounds with high specific heat require more energy for temperature changes, which influences the choice of heating methods and temperature regulation in production.

Electrical conductivity and dielectric constant are important in the evaluation of ionic solutions and polar compounds. Conductivity measures a substance's ability to conduct electric current, and it is directly related to the concentration of ions in solution. This is useful in the quality control of electrolyte solutions, saline infusions, and buffer systems. The dielectric constant reflects the ability of a material to store electrical energy in an electric field and is significant in the formulation of emulsions and colloidal systems, where electrostatic interactions play a role in stability.

In physical chemistry and pharmaceutical kinetics, the rate constant is a critical parameter that governs the speed of chemical reactions. It is



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influenced by temperature, pressure, and the presence of catalysts. The Arrhenius equation, which relates the rate constant to temperature, contains the activation energy and the pre-exponential factor—both of which are considered physical constants for a given reaction. These parameters help predict the stability and shelf life of pharmaceutical products, ensuring they retain potency throughout their intended duration of use.

In analytical chemistry, spectroscopic constants are frequently used. For example, the molar absorptivity or molar extinction coefficient is a constant that describes how strongly a substance absorbs light at a particular wavelength. It is integral to Beer-Lambert's law, which relates absorbance to concentration and path length. This constant is specific for each compound and is used in UV-Vis spectrophotometry to determine the concentration of drugs, vitamins, and other analytes in pharmaceutical formulations.

Pharmacopoeias and scientific literature provide standardized values for these physical constants, which are used globally in laboratory calculations and regulatory submissions. Their reliability ensures that experiments and manufacturing processes can be reproduced accurately across different labs and facilities. The use of these constants supports the standardization and validation of analytical methods, contributing to the integrity and safety of pharmaceutical products.

In conclusion, physical constants are essential components of scientific understanding and technological application in pharmaceutical and medicinal chemistry. They serve as the backbone for countless equations, calculations, and experimental procedures. Whether universal or substance-specific, these constants enable chemists to describe, predict, and control the behavior of materials with precision. Mastery of these constants allows professionals to



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ensure quality, compliance, and innovation in pharmaceutical research and production. As science progresses, the measurement of these constants becomes increasingly accurate, reinforcing their role as foundational pillars of physical science and applied chemistry.

Summary

Physical constants are quantities in nature that remain fixed and universal, independent of time, place, or experimental conditions. They provide the foundation for scientific laws and equations. Examples include the speed of light in vacuum ($c = 3.0 \times 10^8 \text{ m/s}$), Planck's constant ($h = 6.626 \times 10^{-34} \text{ J}\cdot\text{s}$), Avogadro's number ($N_a = 6.022 \times 10^{23} \text{ mol}^{-1}$), Boltzmann constant ($k = 1.38 \times 10^{-23} \text{ J/K}$), and elementary charge ($e = 1.602 \times 10^{-19} \text{ C}$). These constants are essential in defining the SI unit system and play a vital role in quantum mechanics, thermodynamics, electromagnetism, and relativity. Without physical constants, scientific predictions and calculations would lack precision and universality.

MCQs

1. The speed of light in vacuum is:

- a) $3.0 \times 10^6 \text{ m/s}$
- b) $3.0 \times 10^8 \text{ m/s}$
- c) $3.0 \times 10^{10} \text{ m/s}$
- d) $3.0 \times 10^{12} \text{ m/s}$

Answer: b)

2. Planck's constant has the unit:

- a) J/K
- b) J·s
- c) C



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d) $\text{N}\cdot\text{m}$

Answer: b)

3. Avogadro's number refers to the number of:

- a) Molecules in 1 g of substance
- b) Atoms in 1 mol of substance
- c) Particles in 1 mol of substance
- d) Electrons in 1 atom

Answer: c)

4. Boltzmann constant relates:

- a) Pressure and volume
- b) Temperature and energy
- c) Charge and mass
- d) Force and acceleration

Answer: b)

5. Which physical constant is fundamental in Einstein's mass-energy relation?

- a) h
- b) G
- c) c
- d) k

Answer: c)

Short Answer Questions

1. Define physical constants with suitable examples.
2. Write the value and significance of Planck's constant.
3. How does Avogadro's number help in chemical calculations?
4. Give the unit of Boltzmann constant and its role in thermodynamics.
5. Differentiate between universal and material-dependent constants.



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Long Answer Questions

1. Discuss the importance of physical constants in scientific measurements and laws. Give examples.
2. Explain how physical constants define SI units with reference to the speed of light, Planck's constant, and Avogadro's number.
3. Describe at least five fundamental constants, their values, units, and applications.

Unit 1.6

Distillation

Objectives

1. To understand the fundamental principles of distillation and its role in separation processes.
2. To study the differences between simple, fractional, and steam distillation techniques.
3. To learn how volatility and boiling points influence separation efficiency.
4. To explore the applications of distillation in pharmaceutical, petrochemical, and chemical industries.
5. To analyze the advantages, limitations, and operational considerations of different distillation methods.

1.6.1 Distillation

Distillation is one of the most fundamental and widely used separation techniques in chemistry and chemical engineering. It is a physical process employed to separate components of a mixture based on differences in their boiling points. The underlying principle of distillation relies on the vaporization of the more volatile component in a liquid mixture followed by condensation, resulting in its physical separation from the less volatile components. This process finds extensive application in laboratories, pharmaceutical industries, petrochemical refineries, beverage production, and in the purification of organic solvents and chemicals.

At its core, distillation involves heating a liquid to form vapor and then cooling the vapor to recover it as a purified liquid, known as the distillate. The process typically requires a distillation apparatus



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consisting of a heat source, a distillation flask or boiler, a condenser to condense the vapors, and a receiver to collect the distillate.

The efficiency of distillation depends upon the difference in boiling points between the components, the design of the apparatus, and the operational parameters such as temperature control and rate of heating. For a simple binary mixture, the component with the lower boiling point vaporizes first and can be separated effectively from the component with the higher boiling point.

There are several types of distillation techniques, each suited to specific purposes and material properties. The most basic form is simple distillation, used when separating a volatile liquid from non-volatile impurities or when the boiling point difference between two liquids is large, typically greater than 40°C. In this process, the mixture is heated in a distillation flask until the more volatile component vaporizes and passes through a condenser where it is converted back to the liquid phase and collected separately. Simple distillation is commonly used in the purification of solvents, distillation of water, and recovery of low-boiling-point organic liquids.

When the boiling point difference between components is small, fractional distillation is employed. This technique uses a fractionating column placed between the distillation flask and the condenser. The column is packed with materials such as glass beads or structured packing, which provide a large surface area for repeated condensation and vaporization cycles, known as theoretical plates. These multiple equilibrium stages enhance the separation of closely boiling components by enriching the vapor in the more volatile substance as it ascends the column. Fractional distillation is widely applied in the separation of hydrocarbons in petroleum refining, alcohol purification, and separation of essential oils.



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Vacuum distillation is another important variation, particularly useful when dealing with high-boiling-point or thermally unstable compounds. By reducing the pressure within the distillation apparatus, the boiling points of substances are lowered, allowing distillation to occur at lower temperatures. This minimizes the risk of decomposition and is suitable for substances such as glycerol, plant extracts, vitamins, and certain pharmaceutical intermediates. The equipment for vacuum distillation includes a vacuum pump and pressure gauge along with the standard distillation setup.

Steam distillation is a technique specifically suited for the extraction of temperature-sensitive volatile compounds that are immiscible with water, such as essential oils and aromatic compounds from plant materials. In this method, steam is introduced into the distillation flask containing the plant material or compound, and the steam carries the volatile components into the condenser. Since the total vapor pressure is the sum of the individual pressures of water and the volatile component, the boiling point is effectively reduced, allowing distillation at temperatures below 100°C . This gentle process preserves the chemical integrity of the distillates and is widely used in the cosmetic, perfume, and herbal industries.

Azeotropic distillation is employed to separate mixtures that form azeotropes, which are constant-boiling mixtures with a fixed composition and cannot be separated by ordinary distillation. In this method, a third component called an entrainer is added to break the azeotrope by forming a new azeotrope or changing the volatility of the mixture. This technique is essential in separating ethanol from water, where benzene or cyclohexane may be used to alter the volatility characteristics. Although effective, azeotropic distillation often requires careful consideration of safety, toxicity, and environmental impact due to the nature of entrainers.



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Molecular distillation, also known as short-path distillation, is a highly specialized technique used to purify high-value, heat-sensitive compounds at very low pressures and short distances between evaporator and condenser. It minimizes residence time and thermal degradation, making it ideal for purifying complex organic molecules such as vitamins, fatty acids, steroids, and other biologically active compounds. The process is carried out in high-vacuum environments, and the distillate travels only a few centimeters before condensation, thus reducing exposure to heat.

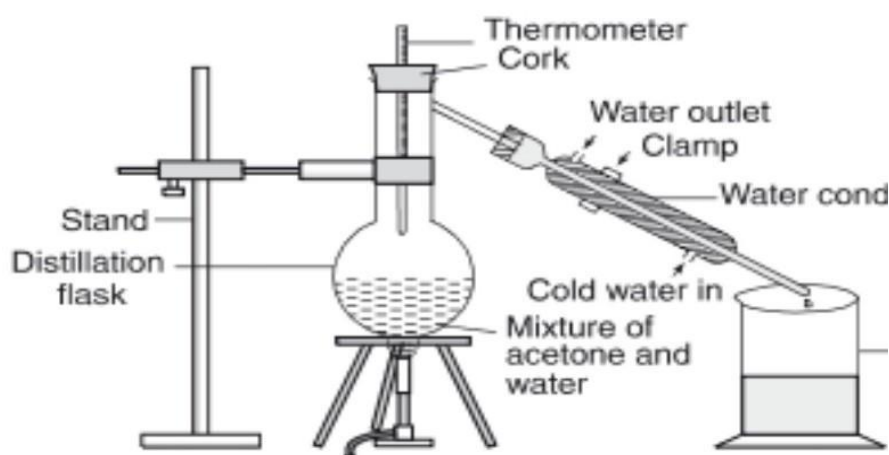
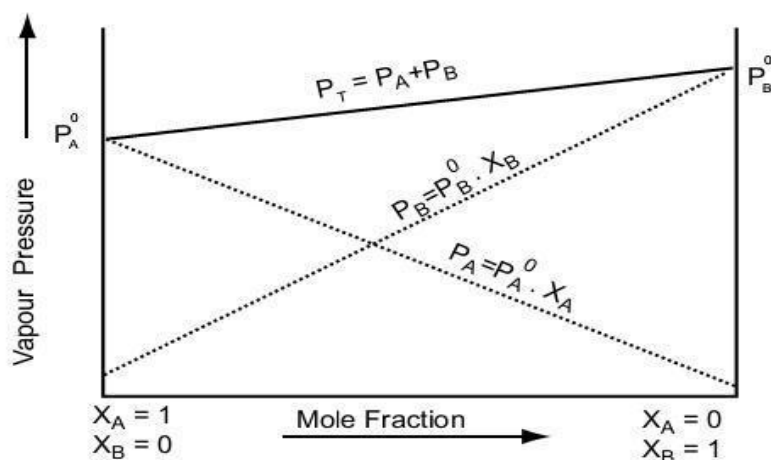


Figure: Distillation process in the Laboratory

The distillation process is governed by Raoult's law and Dalton's law, which describe the vapor pressures of individual components and the composition of vapor in equilibrium with a liquid mixture. The efficiency of a distillation process is often measured in terms of the number of theoretical plates and the reflux ratio. Reflux refers to the portion of condensed vapors returned to the column to maintain the temperature gradient and enhance separation. Higher reflux ratios

generally improve the purity of the distillate but increase energy consumption and operational time.



Vapour Pressure Diagram for Ideal Solution

In pharmaceutical and medicinal chemistry, distillation serves multiple purposes. It is instrumental in the purification of organic solvents, preparation of pure water, recovery of volatile drugs, isolation of active ingredients from natural sources, and formulation of certain dosage forms such as tinctures and elixirs. Additionally, it plays a role in analytical laboratories for sample preparation, residue analysis, and quality control testing. Regulatory agencies often require the use of high-purity solvents and excipients, necessitating the use of distillation techniques in their production and validation.

The effectiveness of distillation depends not only on the type of distillation chosen but also on the design and condition of the equipment, control of operating parameters, and purity of input materials. Laboratory-scale distillation may involve round-bottom flasks, Liebig condensers, and water baths, while industrial-scale operations use large distillation towers, reboilers, and condensers made from corrosion-resistant materials. Process automation, temperature sensors, pressure controls, and computer monitoring systems have greatly enhanced the efficiency, safety, and



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reproducibility of distillation operations in modern pharmaceutical plants. Environmental and energy considerations are also important in the context of distillation. Since distillation is an energy-intensive process, particularly in fractional and vacuum distillations, optimizing energy usage and heat recovery is crucial for sustainability. Advances in green chemistry have led to the development of more efficient distillation techniques such as pervaporation, membrane distillation, and reactive distillation that aim to reduce solvent loss, energy consumption, and chemical waste.

To summarize, distillation is a vital and versatile technique for the separation and purification of chemical substances based on volatility differences. From simple liquid purification to complex fractionation of chemical mixtures, distillation remains a cornerstone technique in laboratories and industries alike. Its wide range of applications, coupled with adaptability and scalability, make it indispensable in pharmaceutical development, chemical synthesis, quality assurance, and environmental analysis. As technology evolves, innovations in distillation design and process control will continue to enhance its utility, safety, and environmental compatibility, ensuring its relevance in both traditional and emerging areas of chemical science.

Summary

Quantitative and Qualitative Chemical Analysis are two fundamental approaches in analytical chemistry used to study the composition of substances. Qualitative analysis focuses on identifying the presence or absence of particular elements, ions, or compounds in a sample. It answers the question “What is present?” and is often the first step in chemical examination. This analysis uses physical observations such as color change, precipitate formation, flame tests, and characteristic reactions, as well as instrumental methods like spectroscopy,



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chromatography, and mass spectrometry to detect and confirm specific chemical species. On the other hand, Quantitative analysis determines the exact amount or concentration of a component in a sample, answering “How much is present?”. It involves precise measurements and calculations using classical methods such as gravimetric analysis, where the mass of an analyte or its derivative is measured, and volumetric analysis, where the volume of a titrant required to react completely with the analyte is recorded. Modern techniques such as UV–Vis spectroscopy, atomic absorption spectroscopy, and chromatography with detectors also provide highly accurate quantitative data. Both approaches are complementary—qualitative analysis ensures correct identification, while quantitative analysis measures the amount for quality control, research, and regulatory purposes. In practice, analytical chemists often perform qualitative testing before quantitative determination to avoid errors from misidentification. Together, these methods form the basis for applications in pharmaceuticals, environmental monitoring, food quality testing, forensic investigations, and industrial process control, ensuring that products and materials meet safety and quality standards.

MCQs

1. Distillation is based on the difference in:
 - a) Melting point
 - b) Boiling point
 - c) Density
 - d) SolubilityAnswer: b) Boiling point
2. Fractional distillation is used when:
 - a) Liquids have very large boiling point differences
 - b) Liquids have close boiling points
 - c) Solids are dissolved in liquids



Notes d) Non-volatile substances are present

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Answer: b) Liquids have close boiling points

3. Steam distillation is suitable for:

- a) Volatile liquids only
- b) Heat-sensitive compounds
- c) Inorganic salts
- d) Gaseous mixtures

Answer: b) Heat-sensitive compounds

4. Which part of a distillation setup improves separation in fractional distillation?

- a) Condenser
- b) Fractionating column
- c) Distillation flask
- d) Receiver

Answer: b) Fractionating column

5. Vacuum distillation is performed to:

- a) Increase boiling point
- b) Reduce boiling point
- c) Increase purity
- d) Separate solids

Answer: b) Reduce boiling point

Short Answer Questions (2–5 Marks)

1. Define qualitative analysis.
2. What is meant by quantitative analysis?
3. Differentiate between accuracy and precision.
4. What is the role of a standard solution in analysis?
5. State the difference between volumetric and gravimetric analysis.
6. What do you understand by the term "limit of detection"?



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7. Name two examples each of qualitative and quantitative tests.
8. What is the significance of blank determination?
9. Define the term “analytical chemistry.”
10. Explain the term “error” in chemical analysis.

Long Answer Questions (10–15 Marks)

1. Explain in detail the differences between qualitative and quantitative analysis with suitable examples.
2. Describe the steps involved in a typical quantitative analysis process.
3. Discuss various types of errors in analytical chemistry and their impact on results.
4. Explain the concepts of accuracy, precision, sensitivity, and specificity in chemical analysis.
5. Elaborate on the importance and methods of calibration in quantitative analysis.
6. Describe gravimetric and volumetric methods of quantitative analysis. Compare their advantages and limitations.
7. Discuss the significance of standard solutions and the process of standardization in volumetric analysis.
8. Explain the principles and applications of titrimetric methods in quantitative analysis.
9. Describe how instrumental methods have enhanced the precision of qualitative and quantitative analysis.
10. Give a detailed account of the steps involved in the validation of an analytical method.



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Module 2

Separation Techniques

Unit 2.1 General Aspects of Chromatography

Objectives

1. To understand the fundamental principles of separation techniques used in chemistry and allied sciences.
2. To classify separation methods into physical, chemical, and chromatographic techniques.
3. To learn the applications of separation techniques in analytical and industrial processes.
4. To evaluate the advantages, limitations, and suitability of different separation methods.
5. To develop problem-solving skills for selecting appropriate techniques in pharmaceutical, food, and environmental analysis.

2.1.1 General Aspects of Chromatography

Chromatography is a powerful and versatile analytical and preparative technique used extensively in chemistry, biochemistry, pharmaceutical sciences, and materials science for the separation, identification, purification, and quantification of components within a mixture. The word "chromatography" originates from the Greek words "chroma," meaning color, and "graphein," meaning to write. The term was initially coined in the early 20th century by the Russian botanist Mikhail Tswett, who used it to separate plant pigments. Today, chromatography encompasses a wide range of techniques that have evolved far beyond simple pigment separation and are integral to research and industrial laboratories worldwide.



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The fundamental principle of chromatography involves the distribution of components between two phases: a stationary phase and a mobile phase. The stationary phase is an immobile material that interacts with the mixture's components through various physical or chemical means, while the mobile phase is a fluid—either liquid or gas—that carries the mixture through or over the stationary phase. As the components travel with the mobile phase, they interact differently with the stationary phase based on their physical and chemical properties, such as polarity, molecular weight, charge, or volatility. These differential interactions cause the components to move at different rates, leading to their separation.

Chromatographic techniques are broadly classified based on the physical state of the mobile phase, the mechanism of separation, and the configuration of the system. Based on the mobile phase, chromatography can be categorized into gas chromatography (GC), which uses a gaseous mobile phase, and liquid chromatography (LC), which employs a liquid mobile phase. Furthermore, the mechanism of separation leads to classifications such as adsorption chromatography, partition chromatography, ion-exchange chromatography, size-exclusion chromatography, and affinity chromatography. Each of these techniques leverages different molecular properties to achieve separation and is suited to specific types of analytes and applications. In adsorption chromatography, separation is based on the differential adsorption of compounds onto the surface of a solid stationary phase. Components that adhere strongly to the surface move more slowly, while those with weaker interactions travel faster. This method is commonly used in column and thin-layer chromatography. In partition chromatography, separation occurs based on the solubility of compounds between two immiscible liquid phases—one stationary and one mobile. High-performance liquid chromatography (HPLC) often utilizes this principle, where analytes partition between a liquid

stationary phase bonded to a solid support and a flowing liquid mobile phase.

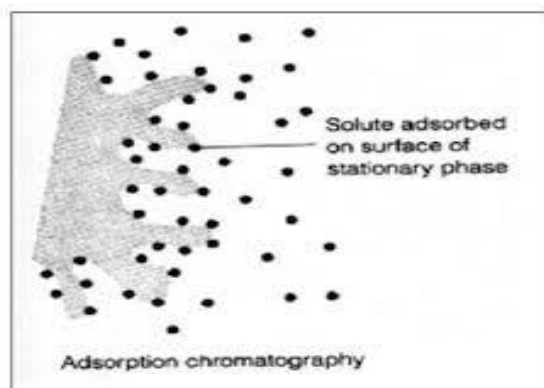
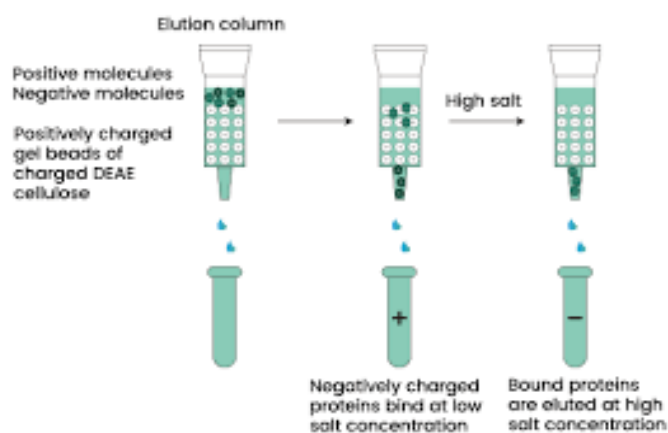


Figure 2.1 Adsorption Chromatography

Ion-exchange chromatography separates components based on their charge. The stationary phase is composed of charged resins that attract oppositely charged ions. Cation-exchange resins bind positively charged molecules, while anion-exchange resins bind negatively charged ones. By changing the ionic strength or pH of the mobile phase, bound ions can be selectively eluted. This technique is especially useful in protein purification, water treatment, and analysis of ionic species. Size-exclusion chromatography, also known as gel filtration chromatography, separates molecules based on size. Porous beads in the stationary phase allow smaller molecules to enter the pores and thus elute later than larger molecules, which are excluded from the pores and pass through more quickly.



Affinity chromatography is a highly specific technique that utilizes the unique biological affinity between molecules such as enzyme-



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substrate, antigen-antibody, or receptor-ligand interactions. The stationary phase is functionalized with a molecule that selectively binds the target analyte, allowing non-target components to be washed away. The bound molecule can then be eluted using a specific elution buffer. This method is widely used in biotechnology and pharmaceutical research for purifying biomolecules such as proteins, enzymes, and antibodies.

Chromatographic systems may be planar or columnar in configuration. In planar chromatography, such as paper chromatography and thin-layer chromatography (TLC), the stationary phase is arranged on a flat surface, and the mobile phase moves through capillary action. Paper chromatography uses cellulose filter paper as the stationary phase, while TLC employs a layer of silica gel or alumina spread on a glass, metal, or plastic plate. These methods are simple, inexpensive, and suitable for rapid qualitative analysis. In contrast, column chromatography uses a cylindrical column packed with stationary phase particles, through which the mobile phase is passed under gravity, pressure, or with the aid of a pump. This configuration allows greater control over flow rate, resolution, and scalability.

High-performance liquid chromatography (HPLC) and gas chromatography (GC) are advanced forms of column chromatography that offer high resolution, sensitivity, and quantitative accuracy. HPLC employs a high-pressure pump to push the mobile phase through a tightly packed column, enabling fast and efficient separation of complex mixtures. It is applicable to both polar and non-polar analytes, including pharmaceuticals, environmental pollutants, and food additives. GC, on the other hand, uses an inert gas as the mobile phase and a coated capillary column as the stationary phase. The sample is vaporized and carried by the gas through the column, where components separate based on volatility and interaction with the column coating. GC is particularly suitable for volatile organic



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compounds and is widely used in forensic analysis, petrochemical testing, and fragrance quality control.

Detection and quantification of components in chromatography are achieved using various detectors tailored to the nature of the analyte and the technique. In HPLC, common detectors include UV-Vis detectors, fluorescence detectors, refractive index detectors, and mass spectrometers. GC often employs flame ionization detectors (FID), thermal conductivity detectors (TCD), or electron capture detectors (ECD). These detectors provide information about the identity and concentration of eluted compounds and can be coupled with data acquisition systems for automated analysis.

The effectiveness of a chromatographic separation is evaluated using parameters such as retention time, resolution, capacity factor, and selectivity. Retention time refers to the time a component takes to travel from the injection point to the detector. A shorter retention time indicates weaker interaction with the stationary phase, while a longer time suggests stronger interaction. Resolution measures the degree of separation between adjacent peaks and is crucial for the clarity of analysis. The capacity factor reflects the retention of a component relative to an unretained compound, and selectivity indicates the relative separation of two analytes.

Chromatography has become indispensable in pharmaceutical quality control, drug development, and clinical diagnostics. It is used to assess the purity of drug substances, detect impurities, analyze formulation components, and monitor the stability of pharmaceuticals. In biotechnology, chromatography is critical for the separation and purification of biomolecules such as proteins, peptides, nucleic acids, and hormones. Environmental analysis uses chromatography to detect pollutants, pesticides, and hazardous chemicals in water, soil, and air. Food and beverage industries apply chromatographic methods to verify authenticity, detect adulterants, and ensure compliance with safety standards.

The choice of chromatographic technique depends on the nature of the sample, the separation goal, and available instrumentation. While simple techniques such as paper and TLC are ideal for quick and cost-effective screening, more advanced methods like HPLC and GC offer greater precision and are essential for regulatory compliance and research. Innovations in stationary phase chemistry, miniaturization, automation, and hyphenated techniques such as LC-MS and GC-MS continue to expand the scope and capability of chromatography. These developments allow faster analysis, better resolution, and the ability to detect and identify compounds at trace levels.

Thin Layer Chromatography

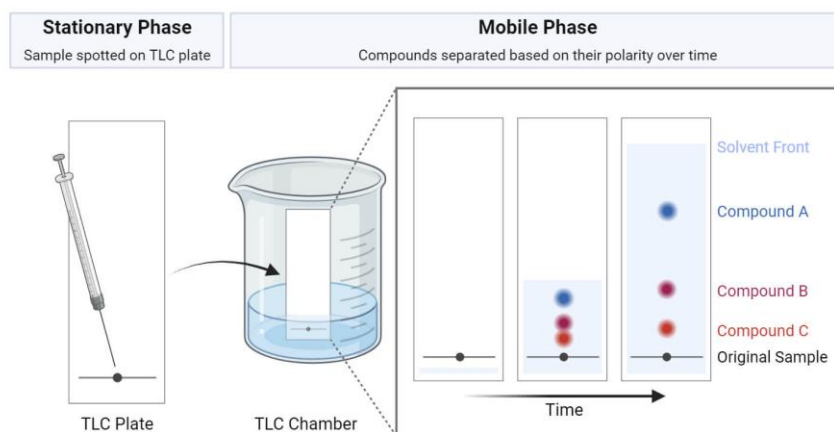


Figure 2.2 Thin-layer Chromatography

In conclusion, chromatography is a cornerstone analytical tool that continues to evolve in response to scientific and industrial demands. Its general aspects—encompassing principles of separation, types of interactions, configurations, and applications—form the basis for a multitude of specialized techniques. A deep understanding of these fundamentals enables scientists to choose and optimize chromatographic methods for a wide array of analytical challenges. As the complexity of modern chemical and biological systems increases, chromatography remains central to discovery, quality assurance, and technological progress.



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Summary

Separation techniques are essential methods in analytical chemistry for isolating and purifying components from complex mixtures. These techniques can be broadly categorized into physical methods (filtration, distillation, centrifugation), chromatographic methods (paper, thin-layer, column, gas, liquid chromatography), and advanced methods (electrophoresis, dialysis, ultrafiltration). Each technique is based on differences in physical or chemical properties, such as solubility, particle size, density, polarity, or volatility. Separation techniques are widely applied in pharmaceuticals, food analysis, clinical diagnostics, and environmental monitoring. The choice of method depends on the nature of the sample, the sensitivity required, and the purpose of the analysis.

Multiple Choice Questions (MCQ)

1. Which separation technique is based on differences in boiling points?
 - a) Filtration
 - b) Distillation
 - c) Chromatography
 - d) Centrifugation

Answer: b) Distillation

2. Paper chromatography separates compounds based on:
 - a) Solubility differences
 - b) Molecular weight
 - c) Density differences
 - d) Boiling point differences

Answer: a) Solubility differences

3. The principle of centrifugation is based on:
 - a) Density differences
 - b) Solubility
 - c) Adsorption
 - d) Melting point

Answer: a) Density differences



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4. Which of the following is NOT a chromatographic technique?

- a) Gas chromatography
- b) TLC
- c) Paper chromatography
- d) Distillation

Answer: d) Distillation

5. Dialysis is mainly used to separate:

- a) Proteins from salts
- b) Liquids from gases
- c) Organic solvents
- d) Insoluble solids

Answer: a) Proteins from salts

Short Answer Questions

1. Define separation techniques with examples.
2. Differentiate between filtration and centrifugation.
3. State the principle of paper chromatography.
4. Write two applications of electrophoresis.
5. Why is distillation important in the pharmaceutical industry?

Long Answer Questions

1. Discuss in detail the principles, procedure, and applications of chromatography techniques.
2. Explain distillation, types of distillation, and its role in industrial and laboratory practices.
3. Compare physical, chemical, and chromatographic separation techniques with suitable examples.
4. Describe centrifugation and its applications in clinical and industrial laboratories.
5. Elaborate on advanced separation methods such as electrophoresis and dialysis with their biomedical significance.



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Unit 2.2

Adsorption Chromatography

Objectives

By the end of this topic, learners should be able to:

1. Understand the principle of adsorption chromatography.
2. Differentiate between stationary phase and mobile phase.
3. Explain the factors affecting adsorption.
4. Identify different types of adsorption chromatography (column, thin-layer, paper).
5. Apply adsorption chromatography in qualitative and quantitative analysis.

2.2.1 Adsorption Chromatography

Adsorption chromatography is one of the oldest and most fundamental chromatographic techniques used for the separation of compounds based on their differential affinities towards a solid stationary phase and a mobile phase. It was first introduced in the early 1900s by Mikhail Tswett, who demonstrated its utility by separating plant pigments. Since then, adsorption chromatography has developed into a widely employed analytical and preparative method in laboratories across chemistry, pharmaceuticals, and biochemistry.

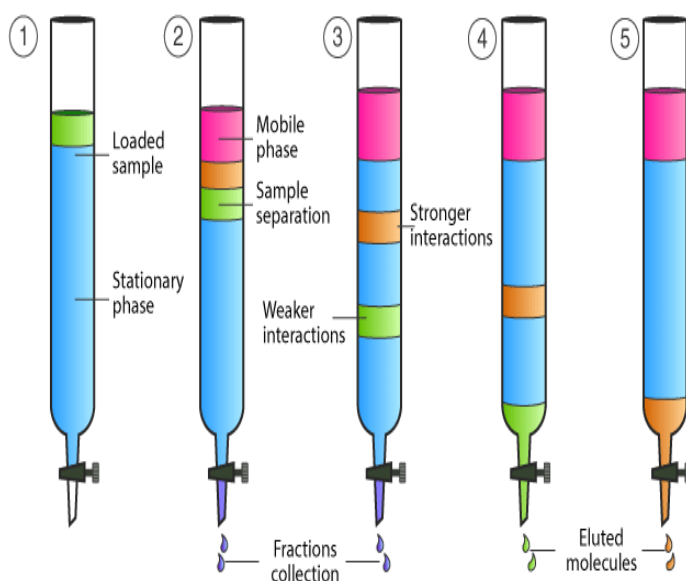


Figure 2.3: Adsorption chromatography

The basic principle of adsorption chromatography lies in the competition between the components of a mixture and the mobile phase molecules for active binding sites on the surface of a solid adsorbent. The stationary phase in this technique is a finely divided solid with a large surface area and high adsorption capacity, while the mobile phase is either a liquid or a gas that carries the sample through the stationary phase. As the sample passes over the adsorbent, its components interact with the surface to different extents depending on their polarity, molecular size, and functional groups. Compounds with a stronger affinity for the stationary phase are adsorbed more firmly and thus move more slowly, whereas those with weaker interactions travel faster. This differential rate of movement leads to separation.

Adsorption occurs due to physical or chemical interactions between the analyte molecules and the surface of the adsorbent. Physical adsorption, which is most common in chromatography, involves van der Waals forces, hydrogen bonding, dipole-dipole interactions, and electrostatic forces. The extent of these interactions is determined by the nature of both the analyte and the adsorbent surface. Polar compounds tend to adhere more strongly to polar adsorbents, while



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non-polar compounds interact more with non-polar materials. This concept is exploited in both normal-phase and reverse-phase adsorption chromatography.

The stationary phases commonly used in adsorption chromatography include silica gel, alumina (Al_2O_3), and activated carbon. Silica gel is the most widely used adsorbent due to its high surface area, controlled pore size, and polar surface rich in hydroxyl groups. It effectively interacts with polar compounds through hydrogen bonding and dipole-dipole interactions. Alumina is another polar adsorbent that can be acidic, basic, or neutral, depending on its preparation. Activated carbon is particularly useful for the separation of non-polar organic compounds and pigments. The physical form of the stationary phase is usually a powder or granules packed into a chromatographic column or spread as a thin layer in thin-layer chromatography.

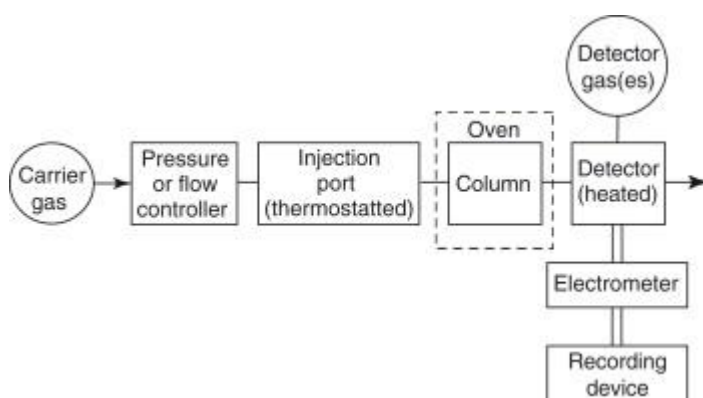
The mobile phase in adsorption chromatography is selected based on the solubility of the analytes and the desired degree of interaction with the stationary phase. In liquid-solid adsorption chromatography, solvents such as hexane, chloroform, methanol, acetone, or mixtures thereof are used. The polarity of the mobile phase can be gradually increased in a process called gradient elution, which helps to sequentially elute components based on their adsorption strength. In gas-solid chromatography, an inert gas such as nitrogen or helium acts as the mobile phase and carries volatile analytes over the solid adsorbent, which is packed into a column.

Several configurations are used in adsorption chromatography, including column chromatography, thin-layer chromatography (TLC), and gas-solid chromatography (GSC). Column chromatography is a widely practiced form where the adsorbent is packed in a vertical glass or plastic tube, and the sample is introduced at the top. The mobile phase is then passed through the column under gravity or pressure, allowing components to move down the column at different rates. The effluent is collected in fractions, which can be further analyzed or

combined based on the separation achieved. Column chromatography is often used for preparative separations, natural product isolation, and compound purification in synthetic chemistry.

Thin-layer chromatography is a planar technique where the adsorbent, typically silica gel or alumina, is coated as a thin layer on a glass, metal, or plastic plate. The sample is spotted near the bottom, and the plate is placed vertically in a developing chamber containing the solvent. The solvent ascends the plate by capillary action, and as it moves upward, it carries the components at different rates. After development, the separated spots are visualized under UV light or by using a detecting reagent. TLC is widely used for monitoring reactions, checking purity, and rapid qualitative analysis.

Gas-solid chromatography is a type of gas chromatography where the stationary phase is a solid adsorbent rather than a liquid-coated support. It is particularly suitable for the separation of gaseous or highly volatile compounds. Since physical adsorption interactions are generally weak, the resolution in GSC depends on precise temperature control and the surface properties of the adsorbent. Applications include analysis of permanent gases, hydrocarbons, and environmental pollutants.



One of the important theoretical aspects of adsorption chromatography is the adsorption isotherm, which describes the relationship between the amount of solute adsorbed on the stationary phase and its



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concentration in the mobile phase at constant temperature. The most commonly used models are the Langmuir and Freundlich isotherms. The Langmuir isotherm assumes a monolayer adsorption on a finite number of identical sites and no interaction between adsorbed molecules. In contrast, the Freundlich isotherm is empirical and describes adsorption on heterogeneous surfaces. The shape of the isotherm influences the efficiency and capacity of the chromatographic process and is essential in understanding retention behavior and peak broadening.

Another important factor in adsorption chromatography is the selectivity and resolution between analytes. Selectivity is governed by the differential adsorption energies of compounds and can be manipulated by changing the stationary phase, mobile phase composition, or operating conditions such as temperature and flow rate. High selectivity results in better separation, which is quantified by the resolution parameter. Efficiency, on the other hand, is influenced by column packing, particle size, and flow rate. Smaller particle size and uniform packing generally enhance separation efficiency by reducing band broadening.

Applications of adsorption chromatography are vast and diverse. In the pharmaceutical industry, it is used for isolating active ingredients from natural sources, purifying intermediates and final products, and separating isomers. It plays a critical role in the preparation of reference standards and active pharmaceutical ingredients (APIs). In environmental analysis, adsorption chromatography helps in detecting and quantifying organic pollutants, pesticides, and hydrocarbons in soil and water samples. It is also employed in the food industry for the analysis of additives, preservatives, and contaminants, and in forensic science for the examination of drug residues, toxins, and explosives.

One of the key advantages of adsorption chromatography is its simplicity and cost-effectiveness. It does not require sophisticated equipment and can be performed using basic glassware and commonly



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available adsorbents. This makes it accessible to laboratories with limited resources. Additionally, it offers good resolving power for a wide range of organic compounds, especially those with differences in polarity or molecular interaction potential. However, adsorption chromatography also has limitations. Strongly retained compounds may be difficult to elute, leading to long retention times or irreversible adsorption. This can be addressed by using a more polar mobile phase or by modifying the surface of the adsorbent.

Recent advancements in adsorption chromatography include the development of modified adsorbents with enhanced selectivity and stability. Functionalized silica and alumina, carbon nanotubes, and metal-organic frameworks (MOFs) are being explored as novel stationary phases with tailored properties. These materials offer improved surface area, pore structure, and interaction capabilities, thereby expanding the applicability of adsorption chromatography. Automation and instrumentation of column chromatography, such as flash chromatography systems, have also improved speed, reproducibility, and safety in laboratory operations.

In conclusion, adsorption chromatography is a foundational technique in analytical and preparative chemistry. Its working principle, based on the differential adsorption of compounds onto a solid phase, underpins its effectiveness in separating complex mixtures. With applications spanning pharmaceuticals, environmental science, natural products, and forensic analysis, it remains an indispensable tool for chemists and researchers. A thorough understanding of its theory, components, and operational variables enables optimal utilization of this technique and fosters innovations in separation science.

Summary

Adsorption chromatography is a separation technique based on the differential adsorption of compounds on a solid stationary phase. Molecules in a mixture interact with the surface of the stationary phase



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through weak physical forces (van der Waals, hydrogen bonding, dipole–dipole interactions). The mobile phase, usually a liquid or gas, carries the analytes through the stationary phase. Components with stronger adsorption remain longer, while weakly adsorbed molecules move faster, enabling separation. The method is widely used in pharmaceutical, biochemical, and environmental studies for separating pigments, drugs, and other complex mixtures. Factors influencing adsorption include polarity of the solvent, nature of the adsorbent (e.g., silica gel, alumina), temperature, and flow rate of the mobile phase.

MCQ

1. Adsorption chromatography separates compounds based on:

- a) Boiling point
- b) Adsorption affinity
- c) Solubility in water
- d) Molecular weight

Answer: b) Adsorption affinity

2. Common stationary phases used in adsorption chromatography include:

- a) Silica gel and alumina
- b) Sodium chloride
- c) Mercury
- d) Copper sulfate

Answer: a) Silica gel and alumina

3. In adsorption chromatography, the component that travels fastest has:

- a) Strongest adsorption
- b) Weakest adsorption



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c) Highest boiling point

d) Lowest polarity

Answer: b) Weakest adsorption

4. Thin Layer Chromatography (TLC) is an example of:

a) Partition chromatography

b) Adsorption chromatography

c) Ion-exchange chromatography

d) Gel filtration chromatography

Answer: b) Adsorption chromatography

5. The efficiency of separation in adsorption chromatography mainly depends on:

a) Size of the container

b) Type of mobile phase

c) Rate of evaporation

d) Temperature of the room

Answer: b) Type of mobile phase

Short Answer Questions

1. Define adsorption chromatography.
2. Name two common adsorbents used in this technique.
3. Why do polar compounds generally have stronger adsorption than non-polar ones?
4. Differentiate between stationary phase and mobile phase.
5. Mention two applications of adsorption chromatography in pharmaceuticals.



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Long Answer Questions

1. Explain the principle, working, and applications of adsorption chromatography with suitable diagrams.
2. Discuss factors affecting adsorption chromatography and how they influence separation.
3. Compare adsorption chromatography with partition chromatography.
4. Describe the role of adsorbent and solvent polarity in adsorption chromatography.
5. Explain the procedure of column chromatography as a form of adsorption chromatography.



Module 3:

Spectroscopic Methods of Analysis

Unit 3.1 UV-Visible Spectroscopy

Objectives

1. To understand the principles and working of UV-Visible spectroscopy.
2. To study the electronic transitions responsible for UV-Visible absorption.
3. To differentiate between chromophores and auxochromes.
4. To interpret absorption spectra using Beer-Lambert's law.
5. To apply UV-Visible spectroscopy in qualitative and quantitative analysis.
6. To recognize applications of UV-Visible spectroscopy in pharmaceutical, chemical, and biological sciences.

3.1.1 UV-Visible Spectroscopy

Ultraviolet-visible (UV-Vis) spectroscopy is one of the most widely used analytical techniques for qualitative and quantitative analysis of compounds that absorb in the ultraviolet and visible regions of the electromagnetic spectrum. The method is based on the absorption of radiation in the range of 190 to 800 nanometers by electrons in a molecule. This absorption leads to electronic transitions, primarily involving π to π^* and n to π^* excitations. The intensity and wavelength of absorbed light can provide valuable information about the molecular structure, concentration, and chemical environment of a substance.



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The fundamental principle of UV-Visible spectroscopy is governed by the Beer-Lambert Law, which states that the absorbance of a solution is directly proportional to the concentration of the absorbing species and the path length through which the light passes. Mathematically, it is represented as $A = \epsilon cl$, where A is the absorbance, ϵ is the molar absorptivity coefficient, c is the concentration of the analyte, and l is the path length of the cuvette, usually 1 cm. This linear relationship makes UV-Visible spectroscopy particularly useful for determining the concentration of solutions containing chromophores—functional groups capable of absorbing UV or visible light.

Electronic transitions occur when electrons in a molecule absorb energy and move from a lower energy orbital to a higher energy orbital. The type of transition observed depends on the electronic structure of the molecule. In organic compounds, the most common transitions include σ to σ^* , n to σ^* , π to π^* , and n to π^* . Among these, the π to π^* and n to π^* transitions are typically observed in the UV-Visible region. Compounds with conjugated double bonds and aromatic rings generally exhibit strong π to π^* transitions and are thus excellent candidates for UV-Vis analysis. On the other hand, compounds with lone pair electrons on heteroatoms like oxygen or nitrogen may exhibit n to π^* transitions, which are generally weaker in intensity.

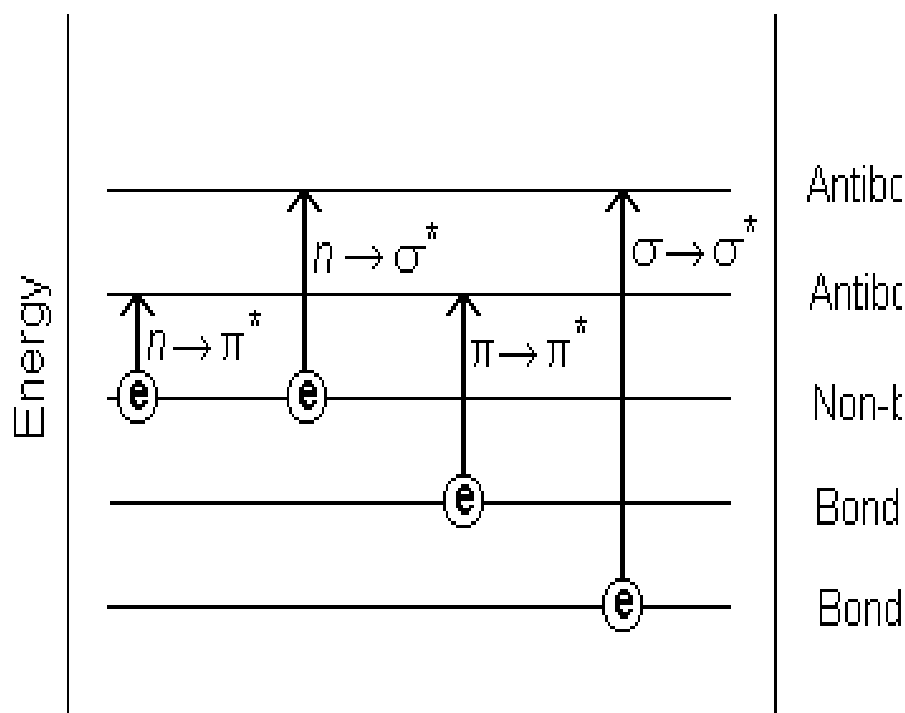
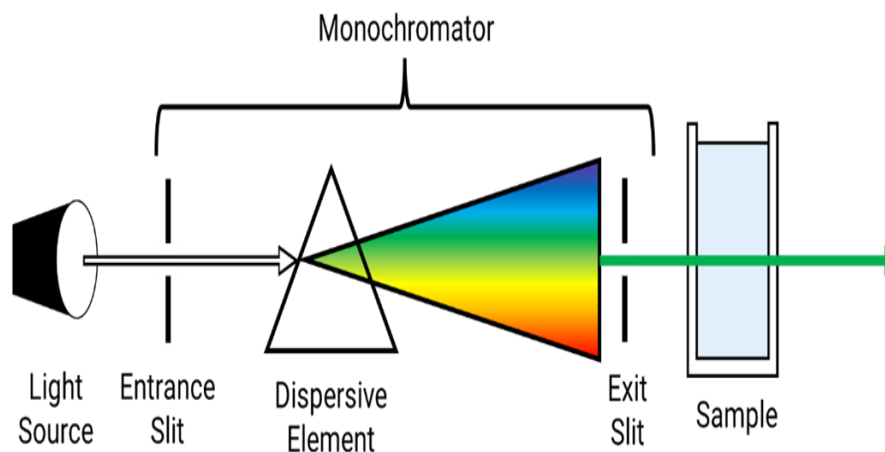


Figure 3.1 π to π^* transitions

The instrumentation of UV-Visible spectroscopy consists of several essential components: a radiation source, monochromator, sample holder, detector, and a data processing system. The light source typically used for UV radiation is a deuterium lamp, while a tungsten filament lamp is employed for the visible region. These sources provide a continuous spectrum of radiation over their respective wavelength ranges. The monochromator, which can be a prism or diffraction grating, serves to isolate a narrow band of wavelengths from the broad spectrum emitted by the source. The selected wavelength is directed through the sample solution placed in a quartz or glass cuvette, depending on the region of interest.



After passing through the sample, the transmitted light is collected by a detector, which converts the light signal into an electrical signal. Common detectors include photodiodes and photomultiplier tubes, which are highly sensitive and capable of detecting low levels of light intensity. The electrical signal is processed by a computer to produce an absorption spectrum, which displays absorbance as a function of wavelength. This spectrum can be analyzed to determine the maximum wavelength of absorption (λ_{max}), which provides information about the chromophores present in the molecule, and the absorbance values, which are used for quantitative calculations.

UV-Visible spectroscopy is particularly valuable in qualitative analysis by allowing identification of compounds based on their characteristic absorption spectra. Each molecule exhibits a unique spectral fingerprint, and by comparing the λ_{max} and the shape of the absorption band to known standards, one can infer the structural features of unknown compounds. Moreover, the presence of conjugated systems, aromatic rings, and functional groups such as carbonyls, nitro groups, and amines can be confirmed by the position and intensity of absorption bands.

In quantitative analysis, UV-Vis spectroscopy is widely used for determining the concentration of analytes in solution. A calibration curve is constructed by measuring the absorbance of standard solutions of known concentration and plotting absorbance versus



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concentration. The absorbance of the unknown sample is then measured and its concentration is interpolated from the calibration curve. This method is highly accurate and reproducible for samples that obey the Beer-Lambert Law within the working range. Deviations from linearity can occur due to instrumental limitations, high analyte concentrations leading to intermolecular interactions, or chemical changes in the sample upon dilution.

Solvent effects play a significant role in UV-Visible spectroscopy. The choice of solvent can affect the position and intensity of absorption bands due to solvent-solute interactions. Polar solvents, for example, can stabilize excited states differently than ground states, causing bathochromic or hypsochromic shifts in the absorption maxima. Common solvents used include ethanol, methanol, water, and acetonitrile, and their transparency in the UV-Vis region must be ensured to avoid interference in the measurements. Solvents themselves must be UV-transparent over the wavelength range of interest.

An important aspect of UV-Visible spectroscopy is the use of derivative and difference spectroscopy techniques. Derivative spectroscopy involves the mathematical manipulation of the absorption spectrum to obtain first, second, or higher derivatives, which enhances the resolution of overlapping bands and improves sensitivity for complex mixtures. Difference spectroscopy, on the other hand, compares the absorbance of a sample under two different chemical or physical conditions, such as pH changes, redox state variations, or ligand binding, to provide insights into molecular interactions and structural changes.

Applications of UV-Visible spectroscopy span across various scientific disciplines. In pharmaceutical analysis, it is used for drug identification, assay, and dissolution testing. For example, active pharmaceutical ingredients (APIs) that possess chromophores can be



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easily quantified in tablets and capsules using this technique. In environmental chemistry, UV-Vis spectroscopy helps monitor pollutants such as nitrates, phosphates, and phenols in water samples. In biochemical studies, it is used to study enzyme kinetics, protein-ligand interactions, and the concentration of biomolecules like DNA, RNA, and proteins, which have characteristic absorbance at specific wavelengths—typically at 260 nm for nucleic acids and 280 nm for proteins.

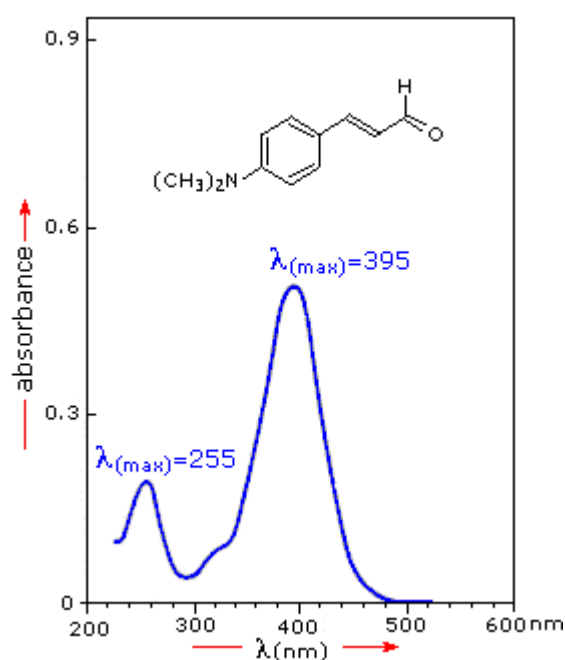
A key application of UV-Vis spectroscopy is in the determination of transition metal complexes, which exhibit intense colors due to d-d electronic transitions and charge transfer bands. The absorption spectra of such complexes are often used to study ligand field strength, geometry of coordination compounds, and redox properties. This has significant implications in inorganic and coordination chemistry, as well as catalysis and material science. Additionally, the study of conjugated organic dyes and pigments using UV-Vis spectroscopy provides insight into their electronic structures and color properties.

In modern analytical laboratories, UV-Visible spectroscopy is increasingly automated, with software integration for data acquisition, analysis, and reporting. Multiwavelength scanning, spectral storage, peak analysis, and library comparison are routine features in advanced spectrophotometers. Furthermore, fiber-optic UV-Vis probes enable real-time, in situ monitoring of chemical processes, allowing chemists and engineers to track reaction progress and optimize conditions without interrupting the system.

Despite its many advantages, UV-Visible spectroscopy has limitations. It is suitable only for compounds that absorb in the UV or visible region, and thus compounds lacking chromophores cannot be analyzed directly. In such cases, derivatization with chromogenic reagents may be necessary. The method is also sensitive to impurities and stray light, which can affect accuracy. Matrix effects, such as scattering or fluorescence, may interfere with absorbance readings. Nevertheless,

these challenges can often be mitigated through careful sample preparation, baseline correction, and the use of blanks.

In conclusion, UV-Visible spectroscopy is a cornerstone of analytical science due to its simplicity, cost-effectiveness, and versatility. Its ability to provide rapid, non-destructive analysis makes it indispensable for both routine quality control and advanced research applications. Whether identifying organic and inorganic compounds, monitoring reaction kinetics, or quantifying biomolecular concentrations, UV-Visible spectroscopy continues to play a pivotal role in modern laboratories across chemistry, biology, medicine, and environmental science. With continual advancements in instrumentation and data processing, the scope and sensitivity of UV-Visible spectroscopic analysis are expected to expand further, reinforcing its value as a fundamental analytical tool.



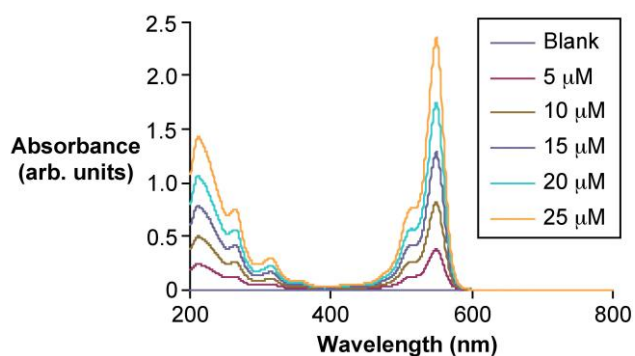


Figure 3.3: UV-Visible spectrophotometer

Summary

UV-Visible spectroscopy is an important analytical technique based on the absorption of electromagnetic radiation in the ultraviolet (200–400 nm) and visible (400–800 nm) regions. It involves transitions of electrons from lower-energy molecular orbitals to higher-energy orbitals ($\sigma \rightarrow \sigma^*$, $n \rightarrow \sigma^*$, $\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$). The amount of light absorbed by a sample is governed by **Beer-Lambert's law**, which relates absorbance to concentration and path length. Chromophores are groups responsible for absorption, while auxochromes modify absorption by shifting the wavelength (bathochromic/hypsochromic shift). This technique is widely applied

in determining drug purity, concentration, structural elucidation, and monitoring chemical reactions. It is fast, non-destructive, and highly sensitive, making it essential in research and industry.

MCQs

1. UV-Visible spectroscopy is based on:

- a) Nuclear transitions
- b) Vibrational transitions
- c) Electronic transitions
- d) Rotational transitions

Answer: c) Electronic transitions

2. Beer-Lambert's law relates absorbance to:

- a) Concentration and wavelength
- b) Concentration and path length
- c) Path length and molar mass
- d) Solvent polarity

Answer: b) Concentration and path length

3. Which transition requires the highest energy?

- a) $\pi \rightarrow \pi^*$
- b) $n \rightarrow \pi^*$
- c) $n \rightarrow \sigma^*$
- d) $\sigma \rightarrow \sigma^*$

Answer: d) $\sigma \rightarrow \sigma^*$

4. A bathochromic shift is also called:

- a) Blue shift
- b) Red shift
- c) Hypochromic shift
- d) Hyperchromic shift

Answer: b) Red shift

5. The range of UV region is:

- a) 400–800 nm



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b) 200–400 nm

c) 800–2500 nm

d) 2–10 nm

Answer: b) 200–400 nm

Short Answer Questions

1. Define chromophore and auxochrome with examples.
2. State Beer-Lambert's law and its mathematical expression.
3. Differentiate between hypsochromic and bathochromic shifts.
4. Mention two pharmaceutical applications of UV-Visible spectroscopy.
5. Explain why quartz cuvettes are used in UV spectroscopy.

Long Answer Questions

1. Explain the principle, instrumentation, and working of UV-Visible spectroscopy.
2. Describe different types of electronic transitions observed in UV-Visible spectroscopy.
3. Discuss Beer-Lambert's law. What are its limitations and deviations?
4. Explain the role of chromophores and auxochromes in UV absorption spectra with examples.
5. Write a detailed note on the applications of UV-Visible spectroscopy in pharmaceutical and chemical sciences.

Unit 3.2

Infrared Spectroscopy

Objectives

By the end of this unit, students will be able to:

1. To understand the basic principle of IR spectroscopy and its interaction with molecular vibrations.
2. To identify the regions of the IR spectrum and their applications in chemical analysis.
3. To differentiate between stretching and bending vibrations.
4. To interpret IR absorption bands for functional group identification.
5. To apply IR spectroscopy in qualitative and quantitative analysis, especially in pharmaceutical and chemical industries.

3.2.1 Infrared Spectroscopy

Infrared (IR) spectroscopy is a powerful analytical technique used for identifying organic and inorganic compounds based on their vibrational transitions. Unlike ultraviolet-visible spectroscopy, which involves electronic transitions, infrared spectroscopy involves the absorption of infrared radiation by molecules, leading to vibrational and rotational changes in the bonds of atoms within the molecules. The IR region of the electromagnetic spectrum spans wavelengths from approximately 2.5 to 25 micrometers, corresponding to wavenumbers from about 4000 to 400 cm^{-1} . When infrared radiation is passed through a sample, specific frequencies are absorbed by the sample depending on the functional groups present, creating a characteristic absorption spectrum that serves as a molecular fingerprint.

The fundamental principle of IR spectroscopy is based on the interaction of infrared radiation with matter, causing vibrational transitions. Molecules absorb IR radiation when the frequency of the radiation matches the natural frequency of vibration of a bond in the



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molecule. These vibrations occur only if there is a change in the dipole moment of the molecule during vibration, a necessary condition for IR activity. The most common types of molecular vibrations include stretching and bending. Stretching vibrations occur when the distance between two atoms increases or decreases along the axis of the bond, while bending vibrations involve changes in the angle between bonds. Bending can be classified further into scissoring, rocking, wagging, and twisting modes.

Each type of bond and functional group in a molecule absorbs infrared radiation at specific characteristic frequencies, which appear as peaks in the IR spectrum. These peaks are often expressed in terms of wavenumber, measured in reciprocal centimeters (cm^{-1}). For example, O-H stretching vibrations typically appear in the range of 3200–3600 cm^{-1} , while C=O stretching vibrations occur around 1650–1750 cm^{-1} . By examining the pattern of absorption bands in an IR spectrum, one can identify the functional groups present in a molecule. This makes IR spectroscopy particularly useful for structural elucidation and verification of organic compounds, especially in the context of pharmaceutical quality control and synthetic chemistry.

An IR spectrometer consists of several key components. The infrared radiation source, typically a heated inert solid such as a Nernst glower or globar, emits radiation over a broad range of wavelengths. The radiation is directed through a monochromator, which isolates a narrow band of wavelengths using prisms or diffraction gratings. The selected IR radiation is then passed through the sample, which may be prepared as a thin film, solution, or pressed pellet, depending on its physical properties. After interacting with the sample, the transmitted radiation is detected by sensors such as thermocouples, bolometers, or pyroelectric detectors, which convert the infrared signal into an electrical signal. This signal is then processed and converted into a spectrum, which displays the percentage transmittance or absorbance as a function of wavenumber.



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Sample preparation for IR spectroscopy is critical and varies depending on whether the sample is a solid, liquid, or gas. Solids are often ground with potassium bromide (KBr) and compressed into pellets for transmission measurements. Alternatively, they may be analyzed using attenuated total reflectance (ATR), a method that requires minimal preparation and is suitable for surface analysis. Liquids are typically placed between two sodium chloride or potassium bromide plates to form a thin film, while gases are measured in specialized gas cells with long path lengths. ATR has become increasingly popular due to its convenience and compatibility with a wide range of sample types, including biological tissues, polymers, and pharmaceutical tablets.

The IR spectrum is typically divided into three regions: the near-IR (14000–4000 cm^{-1}), mid-IR (4000–400 cm^{-1}), and far-IR (400–10 cm^{-1}) regions. The mid-IR region is most commonly used in analytical applications because it contains the fundamental vibrational frequencies of most functional groups. The fingerprint region, located between 1500 and 400 cm^{-1} , is particularly important for compound identification, as it contains complex absorption patterns unique to each molecule. This region is less influenced by individual functional groups and more by the entire molecular structure, allowing for highly specific identification when compared to reference spectra.

Quantitative analysis using IR spectroscopy is possible but less common compared to qualitative applications. The absorbance of a particular peak is proportional to the concentration of the analyte, provided that Beer's Law is obeyed. However, factors such as baseline drift, overlapping bands, and matrix effects can complicate quantitation. Despite these challenges, quantitative IR methods are employed in certain contexts, such as determining water content in pharmaceuticals, assessing polymer composition, or analyzing complex mixtures using chemometric techniques. Calibration curves



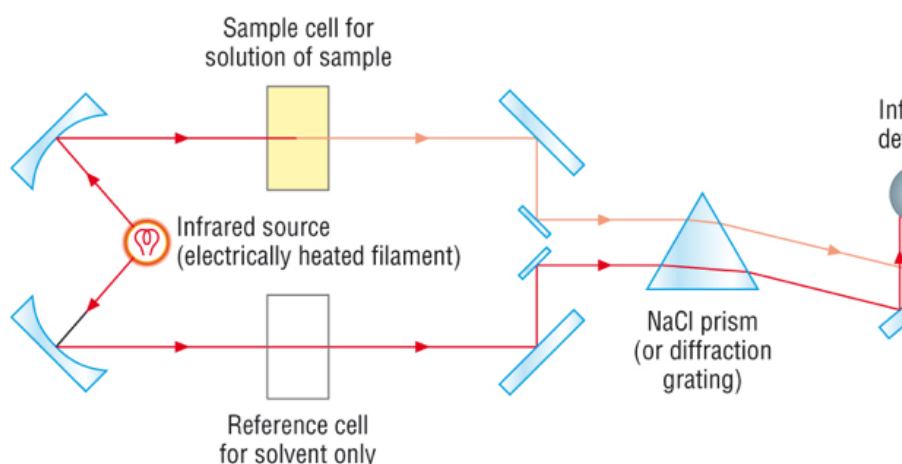
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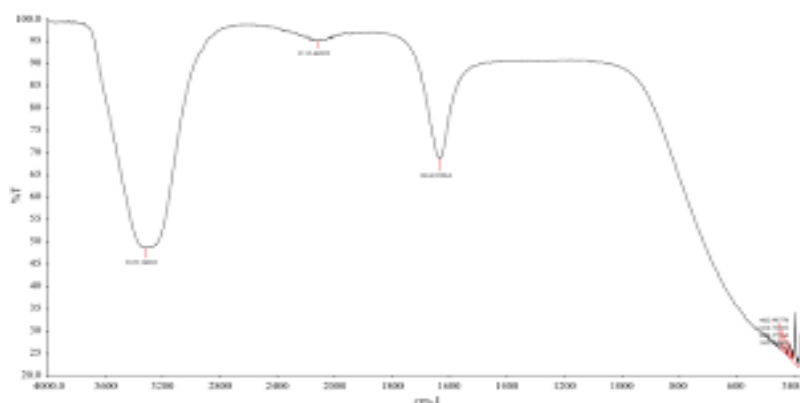
and multivariate statistical methods can enhance the accuracy and reliability of quantitative IR analysis.

Infrared spectroscopy has found extensive applications in both research and industrial settings. In the pharmaceutical industry, IR spectroscopy is used for identifying raw materials, verifying the identity and purity of drug substances, and analyzing finished dosage forms. It is also applied in studying drug-excipient compatibility, monitoring chemical degradation, and verifying the formation of polymorphs and hydrates. In forensic science, IR spectra can be used to identify unknown substances such as narcotics, explosives, and fibers. In environmental analysis, IR spectroscopy helps detect pollutants in air, water, and soil. In biochemistry and molecular biology, IR spectra provide insights into protein secondary structure, lipid organization, and carbohydrate composition.

One of the most significant advancements in IR spectroscopy is the development of Fourier Transform Infrared (FTIR) spectroscopy. FTIR instruments differ from traditional dispersive IR spectrometers in that they collect all spectral data simultaneously using an interferometer. The result is a high-resolution spectrum with better signal-to-noise ratio and faster data acquisition. FTIR spectroscopy allows for more precise identification of functional groups, improved sensitivity, and the ability to conduct time-resolved studies. FTIR instruments are often coupled with microscopes, gas chromatographs, or thermal analyzers for expanded functionality. FTIR microscopy, in particular, allows for spatially resolved chemical analysis of microscopic samples, which is invaluable in fields such as materials science and pathology.



Another modern advancement is the use of infrared imaging and hyperspectral mapping, which combines IR spectroscopy with imaging technology to create spatial maps of chemical composition. This technique is particularly useful in the pharmaceutical industry for quality assurance and uniformity assessment of tablets and coatings. Additionally, portable and handheld IR spectrometers have made the technique accessible in field applications, enabling on-site analysis in industries ranging from agriculture and food safety to law enforcement and customs.



Despite its strengths, IR spectroscopy does have limitations. It cannot easily distinguish between structural isomers with identical functional groups, and it may struggle with highly complex mixtures where overlapping bands occur. The technique is also limited to molecules that are IR-active, meaning they exhibit a change in dipole moment during vibration. Homonuclear diatomic molecules such as nitrogen



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(N₂) and oxygen (O₂) do not show IR absorption. Moreover, sample handling and environmental factors such as moisture can influence the quality of the spectra. Water and carbon dioxide from the atmosphere absorb in the IR region and can introduce interference, so care must be taken to minimize these effects, often by purging the instrument with dry air or nitrogen.

In conclusion, infrared spectroscopy remains an essential tool in the analytical chemist's repertoire, providing detailed information about molecular vibrations and functional groups. Its ability to identify and characterize a wide range of chemical substances quickly and non-destructively makes it indispensable across many disciplines. With the advent of FTIR technology and innovations in sampling and data analysis, the applications of IR spectroscopy have expanded tremendously. From routine quality control to cutting-edge research, IR spectroscopy continues to evolve and contribute to advancements in science, industry, and healthcare.

Summary

Infrared spectroscopy is a vibrational spectroscopic technique based on the absorption of infrared radiation by molecules, causing vibrational transitions. The IR region ranges from 4000–400 cm⁻¹ (mid-IR being the most widely used). When molecules absorb IR radiation, their vibrational modes—stretching or bending—change according to the energy absorbed. Each functional group shows characteristic absorption bands, making IR spectroscopy a valuable tool for structural elucidation and compound identification. It is extensively applied in organic and pharmaceutical chemistry for detecting functional groups, verifying purity, and monitoring reactions.

Multiple Choice Questions (MCQs)

1. The region commonly used in IR spectroscopy is:

- a) 4000–400 cm⁻¹



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- b) 10^5 – 10^3 cm^{-1}
- c) 200 – 50 cm^{-1}
- d) 10^7 – 10^5 cm^{-1}

Answer: 4000 – 400 cm^{-1}

2. IR radiation mainly causes:

- a) Electronic transitions
- b) Vibrational transitions
- c) Nuclear transitions
- d) Rotational transitions

Answer: Vibrational transitions

3. The absorption band near 1700 cm^{-1} is characteristic of:

- a) –OH group
- b) C=O group
- c) C–H stretching
- d) N–H bending

Answer: C=O group

4. Which type of vibrations are possible in IR spectroscopy?

- a) Stretching and bending
- b) Rotational only
- c) Electronic transitions
- d) Nuclear resonance

Answer: Stretching and bending

5. Fingerprint region in IR spectrum lies in:

- a) 4000 – 2500 cm^{-1}
- b) 2500 – 1500 cm^{-1}



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c) $1500\text{--}400\text{ cm}^{-1}$

d) $6000\text{--}5000\text{ cm}^{-1}$

e) **Answer:** $1500\text{--}400\text{ cm}^{-1}$

Short Answer Question

◆ Short Answer Questions (2–5 Marks)

1. What is spectroscopy?
2. Differentiate between UV and IR spectroscopy.
3. What is a chromophore?
4. Define the term absorbance.
5. What is the basic principle of spectroscopic analysis?
6. Mention any two applications of UV-Visible spectroscopy.
7. What is the role of a monochromator in a spectrophotometer?
8. Define transmittance and give its mathematical expression.
9. What are vibrational and rotational spectra?
10. Give an example of a molecule that is IR-active.

Long Answer Questions (10–15 Marks)

1. Describe the working principle of UV-Visible spectroscopy. Discuss its instrumentation and applications.
2. Explain the principle and instrumentation of infrared (IR) spectroscopy. How is it used in functional group analysis?
3. Compare and contrast UV, IR, and NMR spectroscopy based on principle, instrumentation, and applications.
4. Discuss the Beer-Lambert Law. Derive its equation and explain its significance in spectroscopic measurements.



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5. Describe various components of a typical spectrophotometer and explain the function of each.
6. Explain the interaction of electromagnetic radiation with matter and how it forms the basis of spectroscopic techniques.
7. Write a detailed note on the qualitative and quantitative applications of spectroscopic methods in pharmaceutical analysis.
8. Explain the types of transitions that occur in UV-visible spectroscopy with suitable examples.
9. Discuss how molecular vibrations are detected and analyzed using IR spectroscopy.
10. Describe how spectroscopic methods are employed in the structural elucidation of organic compounds.



Module 4: Laboratory Work

Unit 4.1: Laboratory hazards and safety precautions

Objectives

By the end of this topic, students should be able to:

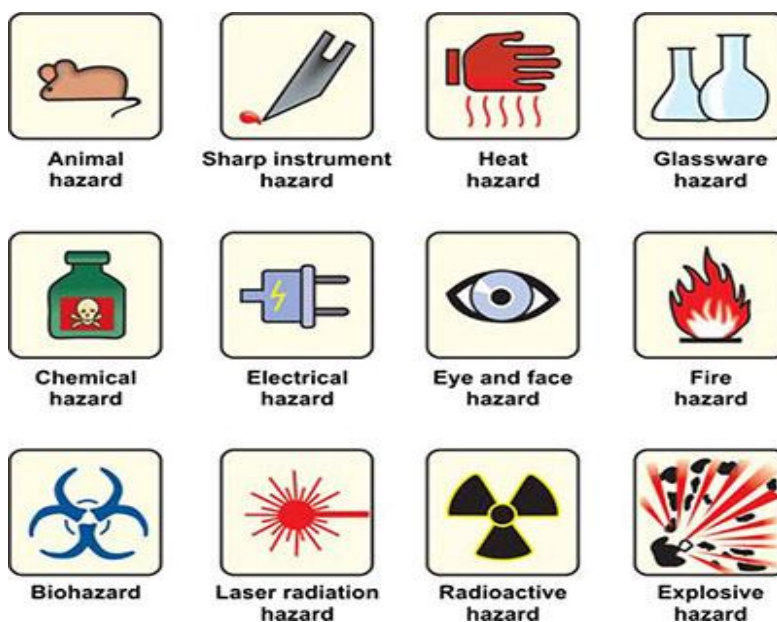
1. To identify common laboratory hazards in chemical, biological, and physical contexts.
2. To understand and apply standard safety precautions in laboratory practices.
3. To demonstrate knowledge of personal protective equipment (PPE) and its correct use.
4. To follow proper procedures for handling chemicals, glassware, and equipment.
5. To recognize emergency protocols such as fire safety, chemical spill management, and first aid.

4.1.1 : Laboratory hazards and safety precautions

Laboratories are vital spaces for scientific inquiry and experimentation, but they also contain numerous potential hazards that can endanger human health and safety if not managed properly. The importance of maintaining a safe laboratory environment cannot be overstated, as even minor negligence can lead to significant injuries, property damage, or chemical contamination. Understanding the various types of hazards and the measures required to minimize their risks is a fundamental aspect of laboratory work, especially for students and professionals in the fields of chemistry, biology,

pharmacy, and engineering. Effective laboratory safety practices are rooted in knowledge, vigilance, and the consistent implementation of established protocols.

Laboratory hazards can be broadly classified into chemical, biological, physical, mechanical, and electrical categories. Chemical hazards are perhaps the most common and involve exposure to substances that can be toxic, corrosive, flammable, explosive, or reactive. Chemicals such as concentrated acids, organic solvents, and heavy metals pose significant risks through inhalation, skin contact, ingestion, or accidental splashes. Proper handling, storage, and disposal of these chemicals are crucial in preventing exposure. Chemical labeling and documentation using systems like Material Safety Data Sheets (MSDS) or Safety Data Sheets (SDS) help identify the properties, hazards, and first aid measures associated with each compound, ensuring that all personnel are informed and prepared.



Biological hazards are primarily encountered in laboratories engaged in microbiological or biomedical research. These hazards arise from the use of infectious agents such as bacteria, viruses, fungi, or parasites that can cause diseases in humans. The risk level depends on the biosafety classification of the organism, ranging from Level 1 (minimal risk) to Level 4 (extreme risk). To contain these hazards, laboratories must employ strict aseptic techniques, biosafety cabinets, personal protective equipment, and sterilization procedures. Biological waste, including cultures, contaminated gloves, pipettes, and sharps, must be autoclaved or chemically disinfected before disposal. The importance of vaccination, incident reporting, and post-exposure protocols also forms a core component of biological safety.

HCS PICTOGRAMS & HAZARDS

Health Hazard  • Carcinogen • Mutagenicity • Reproductive Toxicity • Respiratory Sensitizer • Target Organ Toxicity • Aspiration Toxicity	Flame  • Flammables • Pyrophorics • Self-Heating • Emits Flammable Gas • Self-Reactives • Organic Peroxides	Exclamation Mark  • Irritant (skin and eye) • Skin Sensitizer • Acute Toxicity (harmful) • Narcotic Effects • Respiratory Tract Irritant • Hazardous to Ozone Layer (Non Mandatory)
Gas Cylinder  • Gases under pressure	Corrosion  • Skin Corrosion/ burns • Eye Damage • Corrosive to Metals	Exploding Bomb  • Explosives • Self-Reactives • Organic Peroxides
Flame over Circle  • Oxidizers	Environment (Non-mandatory)  • Aquatic Toxicity	Skull & Crossbones  • Acute Toxicity (fatal or toxic)

Physical hazards refer to injuries caused by environmental or operational conditions in the laboratory. These include slips,



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trips, and falls due to wet floors or cluttered workspaces, as well as burns from open flames, hot surfaces, or heated equipment like ovens and autoclaves. Sharp instruments such as scalpels, glass pipettes, and broken glassware can cause cuts or puncture wounds. Noise from machines like centrifuges and UV exposure from sterilization units or lasers also present significant concerns. Maintaining a clean, well-organized lab environment, using protective barriers, and ensuring adequate ventilation and lighting are basic strategies to reduce physical hazards.

Mechanical hazards are associated with the operation of laboratory machinery and equipment. Improper use or maintenance of devices such as centrifuges, stirrers, vacuum pumps, and hydraulic presses can lead to serious accidents. Rotating parts may catch loose clothing or hair, and pressurized systems may cause explosions or implosions. Equipment should be operated only by trained personnel and should be regularly inspected for wear, alignment, and calibration. Emergency shut-off switches and fail-safe systems must be functional and easily accessible. Users must also be alert to potential noise pollution, vibration, and ergonomic risks when using heavy or repetitive motion devices.

Electrical hazards occur due to the widespread use of electrical equipment in laboratories. These hazards include the risk of shock, burns, fires, or explosions caused by faulty wiring, damaged cords, exposed contacts, or improper grounding. Wet conditions, flammable solvents, and metal



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surfaces can significantly increase the likelihood of electrical accidents. It is essential to use equipment with proper insulation, overload protection, and grounded outlets. All electrical devices must be unplugged before servicing or cleaning. Regular inspection, labeling of high-voltage areas, and the use of surge protectors are additional safeguards. Personnel should never handle electrical devices with wet hands or operate them in damp environments without appropriate insulation and grounding.

In light of these varied hazards, safety precautions must be an integral part of all laboratory operations. The foundation of laboratory safety begins with comprehensive training. All students and workers must be thoroughly trained in laboratory protocols, chemical hygiene, emergency procedures, and waste management. Training should be refreshed periodically and updated whenever new equipment or procedures are introduced. Familiarity with the locations and proper use of emergency exits, eye wash stations, fire extinguishers, safety showers, and first aid kits is crucial for effective incident response. Laboratories must have clearly posted safety signage, including hazard warnings and evacuation routes, to guide and inform users at all times.

Personal protective equipment (PPE) serves as a frontline defense against laboratory hazards. Depending on the activity, appropriate PPE may include lab coats, gloves, safety goggles, face shields, respirators, or aprons. Lab coats provide general protection from spills and splashes, while gloves protect against chemical and biological exposure.



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Goggles and face shields are essential when dealing with reactive substances or during procedures such as centrifugation, blending, or heating volatile compounds. The selection of PPE should be based on the risk assessment of the specific task, and it must be worn consistently and correctly. Reusable protective gear should be properly cleaned and maintained, while disposable items must be discarded according to hazardous waste protocols.

Proper laboratory practices and behavior also play a critical role in minimizing risk. Eating, drinking, smoking, and applying cosmetics in the lab are strictly prohibited. Unauthorized experiments, horseplay, or careless handling of materials can quickly escalate into accidents. Chemical containers must always be labeled with the substance name, hazard class, and date of preparation. Storage of chemicals must follow compatibility guidelines to prevent unintended reactions. Flammable materials should be stored in flame-proof cabinets, and oxidizers must be kept away from organics and reducers. Segregated storage and use of fume hoods or laminar flow cabinets for volatile or toxic chemicals ensure that inhalation risks are minimized.

Waste disposal in the laboratory must be systematic and environmentally responsible. Chemical, biological, and sharps waste must be collected in clearly marked containers and disposed of through certified hazardous waste management services. Drains should never be used to dispose of chemicals unless explicitly permitted by safety guidelines. Broken glassware, though not chemically hazardous, poses a



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physical hazard and should be disposed of in designated puncture-resistant containers. Documentation and tracking of waste generation help ensure compliance with environmental regulations and facilitate audits and inspections.

Emergency preparedness is an essential component of laboratory safety. All personnel should be trained in the use of fire extinguishers, emergency alarms, and first aid techniques. Regular emergency drills, such as fire or chemical spill response simulations, help reinforce readiness. Laboratories should develop and maintain a written Chemical Hygiene Plan or Biosafety Manual outlining roles, responsibilities, and procedures for dealing with various emergencies. Quick response and correct action during an emergency can prevent escalation and save lives. For example, in the event of chemical exposure to the eyes, the affected individual must immediately proceed to the eye wash station and rinse for at least 15 minutes while others call for medical assistance.

In recent years, digital tools and software have been introduced to enhance laboratory safety. Inventory management systems can track chemical quantities and expiration dates, while electronic logs can document incidents and corrective actions. Smart sensors and alarms provide real-time monitoring of conditions such as temperature, humidity, gas leaks, and chemical spills. Safety audits and checklists integrated into laboratory management systems improve compliance and accountability. However, while technology is helpful, it cannot replace the



fundamental responsibility of individual users to act safely and responsibly.

In conclusion, laboratory safety is a shared responsibility that depends on knowledge, discipline, and adherence to established protocols. The presence of multiple types of hazards in a laboratory requires a multi-faceted approach involving training, engineering controls, PPE, safe behavior, and emergency preparedness. Cultivating a strong culture of safety ensures that laboratories remain productive, secure, and compliant environments where innovation and discovery can flourish without undue risk. By embedding safety into every aspect of laboratory work, scientists and students can protect themselves, their colleagues, and the integrity of their research.

Summary

Laboratory hazards refer to potential risks that may cause harm to people, equipment, or the environment in laboratory settings. They can be classified as **chemical hazards** (toxic, corrosive, flammable substances), **biological hazards** (pathogens, microorganisms), **physical hazards** (sharp objects, fire, radiation, electrical risks), and **ergonomic hazards** (improper posture, repetitive strain).

To minimize these risks, laboratories implement **safety precautions** such as the use of PPE (gloves, goggles, lab coats), proper storage and labeling of chemicals, use of fume hoods, safe handling of glassware, and maintaining good housekeeping. Emergency measures, including first aid kits,



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fire extinguishers, eye wash stations, and spill kits, are essential. Training, adherence to standard operating procedures (SOPs), and safety audits further ensure a secure environment. Overall, laboratory safety is a shared responsibility, aimed at protecting both individuals and scientific integrity.

Multiple Choice Questions (MCQ)

1. Which of the following is a **biological hazard**?

- a) Flammable solvents
- b) Pathogenic bacteria
- c) Broken glassware
- d) High voltage wires

Answer: b) Pathogenic bacteria

2. PPE stands for:

- a) Personal Protective Equipment
- b) Professional Protective Equipment
- c) Public Protection Essentials
- d) Personal Prevention Essentials

Answer: a) Personal Protective Equipment

3. The first step in handling a chemical spill is to:

- a) Call emergency services immediately
- b) Neutralize the chemical
- c) Alert others and evacuate the area if necessary
- d) Continue working carefully

Answer: c) Alert others and evacuate the area if necessary



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4. The “fire triangle” includes:

- a) Heat, Fuel, Oxygen
- b) Gas, Liquid, Solid
- c) Light, Spark, Energy
- d) Heat, Water, Electricity

Answer: a) Heat, Fuel, Oxygen

5. Fume hoods are used primarily to:

- a) Store flammable chemicals
- b) Ventilate and remove hazardous vapors
- c) Provide sterile conditions
- d) Protect samples from light exposure

Answer: b) Ventilate and remove hazardous vapors

Short Questions

1. Define laboratory hazards.
2. Mention any two types of physical hazards in the laboratory.
3. What is the importance of labeling chemicals properly?
4. Write two uses of a fume hood.
5. What should be done if corrosive chemicals splash into the eyes?

Long Questions



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1. Discuss different types of laboratory hazards with suitable examples.
2. Explain the role and importance of personal protective equipment (PPE) in laboratory safety.
3. Describe the general safety precautions to be followed in a chemistry laboratory.
4. What are the emergency measures to be taken in case of:
 - a) Fire accident
 - b) Chemical spill
 - c) Glassware injury
5. Elaborate on the significance of developing a safety culture in laboratories, with preventive and corrective strategies.

Unit 4.2

Criteria of purity

Objectives

By the end of this topic, students should be able to:

1. Understand the concept of purity and its importance in chemical, pharmaceutical, and industrial applications.
2. Identify different criteria used to determine the purity of a substance.
3. Differentiate between chemical and physical criteria of purity.
4. Explain the role of melting point, boiling point, refractive index, and other physical constants in assessing purity.
5. Apply purity criteria in practical laboratory situations for analysis and quality control.

4.2.1 Criteria of Purity

Purity is a fundamental requirement in the chemical and pharmaceutical sciences, where the integrity of substances greatly influences the accuracy of results, safety of use, and efficacy of medicinal products. The concept of purity refers to the degree to which a substance is free from any foreign material, contaminants, or impurities. A pure compound consists solely of one type of molecule, with no detectable quantities of other substances. Evaluating the purity of a substance is a vital part of quality control, especially in the synthesis of chemical compounds, drug formulation, analytical procedures, and manufacturing processes. Since absolute purity is almost impossible to achieve, purity is often defined within acceptable limits, determined through established analytical and physical criteria.

One of the most widely used methods for determining the purity of a solid substance is through its melting point. A pure compound exhibits a sharp and narrow melting point range, typically within one to two degrees Celsius. Impurities in a compound tend to disrupt the crystalline structure, resulting in a depression and broadening of the



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melting range. Thus, if a compound melts at a defined temperature and in a narrow range consistent with literature values, it is presumed to be pure or nearly pure. However, while the melting point provides a quick and inexpensive method for preliminary purity checks, it does not identify the nature of the impurity nor its quantity. Therefore, it is often supplemented with other analytical techniques for confirmation.

In the case of liquids, the boiling point serves as an analogous criterion of purity. A pure liquid boils at a specific temperature under standard atmospheric pressure. The presence of impurities alters the intermolecular interactions within the liquid, which may raise or lower the boiling point. Similar to melting point analysis, boiling point measurements are generally used for identification and preliminary purity estimation. However, mixtures of volatile substances or azeotropes can complicate interpretation. Additionally, impurities with very different volatilities may go undetected, necessitating more sophisticated techniques such as distillation under controlled conditions or gas chromatography for a more accurate assessment.

Refractive index is another important physical property used in evaluating the purity of both solids and liquids. The refractive index measures the degree to which light is bent, or refracted, when it passes through a substance. This value is specific to a compound and sensitive to changes in composition. Any deviation from the expected refractive index of a pure compound suggests the presence of impurities. Refractive index determination is particularly useful for colorless liquids where visual inspection is difficult. Modern refractometers provide rapid and precise readings, although the method requires careful temperature control since refractive index is highly temperature-dependent.

Spectroscopic techniques are powerful tools for assessing chemical purity. Ultraviolet-visible (UV-Vis) spectroscopy is often used to detect and quantify impurities that absorb light in the UV or visible region. The presence of absorbance peaks not corresponding to the expected



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spectrum of the pure compound can signal contamination. Infrared (IR) spectroscopy provides information about functional groups in a compound. Extra peaks in an IR spectrum may indicate the presence of foreign functional groups, thereby suggesting the presence of impurities. Similarly, Nuclear Magnetic Resonance (NMR) spectroscopy offers a detailed insight into the molecular structure of compounds. Impurities manifest as unexpected signals or distortions in the spectral pattern, allowing chemists to both detect and sometimes quantify impurities with high accuracy.

Chromatographic methods are among the most definitive techniques for evaluating chemical purity. Techniques such as Thin Layer Chromatography (TLC), High-Performance Liquid Chromatography (HPLC), and Gas Chromatography (GC) are routinely employed in pharmaceutical and analytical laboratories. In TLC, a pure substance typically produces a single spot on a chromatographic plate under given conditions, while the presence of multiple spots indicates impurities. HPLC and GC provide more quantitative data, offering high-resolution separation and detection of components within a mixture. The purity of a compound can be expressed as a percentage, determined by integrating the area under the peaks in a chromatogram. These methods also allow for the identification and retention time comparison of known impurities, thus offering comprehensive purity profiling.

Another technique frequently used in determining the purity of organic compounds is elemental analysis. This method involves the quantitative determination of carbon, hydrogen, nitrogen, and sometimes sulfur and oxygen in an organic compound. The experimental values are compared with theoretical values calculated from the molecular formula of the expected compound. A close match between the observed and calculated values indicates a high degree of purity. Significant discrepancies suggest the presence of contaminants or an incorrect molecular structure. While elemental analysis is highly useful



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in academic and research settings, it requires specialized equipment and is not typically used for routine purity checks.

Inorganic compounds and salts often require different approaches for purity determination. Gravimetric and titrimetric analyses are commonly employed for this purpose. These classical methods involve quantitative precipitation or volumetric reaction with known reagents. The end results are compared with theoretical values derived from stoichiometric calculations. For example, purity of sodium chloride may be determined by precipitation with silver nitrate and weighing the resulting silver chloride. Titration with standard acid or base can also be used to estimate the purity of acidic or basic salts. These methods are reliable but time-consuming and require careful control of experimental conditions.

Thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) are modern thermal methods used in determining purity, especially in polymers and pharmaceuticals. TGA measures changes in mass with temperature, which helps identify volatile impurities or decomposition products. DSC detects endothermic and exothermic transitions such as melting, crystallization, or degradation. Pure compounds display sharp and characteristic thermal transitions, while impurities result in broad or shifted thermal events. These methods are particularly valuable in pharmaceutical industries where thermal behavior can impact drug stability and shelf-life.

Electrical conductivity and pH measurement can also be useful indicators of purity, particularly for aqueous solutions and ionic compounds. For example, deionized water should ideally have very low electrical conductivity, and any deviation might suggest ionic contamination. Similarly, the pH of a buffer solution can indicate the presence of acidic or basic impurities if it differs significantly from expected values. These measurements are quick and require minimal sample preparation, making them suitable for routine quality control checks.



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Purity assessment is especially critical in pharmaceutical formulations, where the presence of even trace amounts of impurities can affect drug safety, efficacy, and stability. Impurities may originate from raw materials, manufacturing processes, degradation, or storage conditions. Regulatory agencies such as the USFDA, EMA, and ICH have established stringent guidelines for permissible impurity levels in drug substances and products. Impurity profiling, which includes identification, quantification, and control of impurities, forms a cornerstone of pharmaceutical quality assurance. Analytical methods must be validated to ensure accuracy, precision, specificity, linearity, and sensitivity. The use of reference standards and internal standards further strengthens the reliability of purity assessments.

In summary, the determination of purity is a multidimensional process involving a variety of physical, chemical, and instrumental methods. Each method provides unique insights and serves different purposes depending on the nature of the compound and the intended application. Physical properties like melting point, boiling point, and refractive index offer simple and rapid assessments, while spectroscopic and chromatographic methods provide detailed structural and quantitative data. Elemental analysis, titrimetry, and thermal techniques add further dimensions to the evaluation. By combining multiple methods, scientists can obtain a comprehensive understanding of a substance's purity, ensuring compliance with quality standards and supporting safe and effective use in research, manufacturing, and therapeutics. The importance of purity assessment lies not just in meeting regulatory requirements but also in maintaining scientific integrity and public trust in chemical and pharmaceutical products.

Summary

The criteria of purity refer to the parameters used to evaluate whether a substance is pure or contaminated with impurities. In chemistry, a pure substance has definite and characteristic physical and chemical properties. The physical constants most commonly used as purity



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indicators are melting point, boiling point, refractive index, specific gravity, and optical rotation. A pure substance shows sharp and fixed values of these properties, while the presence of impurities usually broadens or shifts them. For example, a pure crystalline solid has a sharp melting point, whereas impurities cause melting over a range. Chemical methods, such as titration and chromatographic techniques, also serve as criteria for assessing purity. These criteria are crucial in pharmaceuticals, food chemistry, and material sciences, ensuring safety, efficacy, and quality standards.

MCQs

1. The most reliable criterion for the purity of a crystalline solid is:

- a) Boiling point
- b) Melting point
- c) Density
- d) Refractive index

Answer: b) Melting point

2. A pure organic liquid is expected to have:

- a) Constant boiling point
- b) Broad boiling range
- c) Constant melting point
- d) Variable optical rotation

Answer: a) Constant boiling point

3. Impurities in a solid usually:

- a) Raise the melting point
- b) Lower and broaden the melting point
- c) Sharpen the melting point
- d) Have no effect on melting point

Answer: b) Lower and broaden the melting point

4. Which of the following is **not** a physical criterion of purity?

- a) Refractive index
- b) Specific gravity



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c) Melting point

d) Titration

Answer: d) Titration

5. Optical rotation is mainly used as a criterion of purity for:

a) Inorganic salts

b) Colored compounds

c) Chiral compounds

d) Metals

Answer: c) Chiral compounds

Short Answer Questions

1. Define “criteria of purity” with examples.
2. Why is melting point considered a good test of purity for solids?
3. Mention two chemical and two physical methods used to determine purity.
4. What is the effect of impurities on boiling point?
5. Explain the significance of refractive index in assessing purity.

Long Answer Questions

1. Discuss the various physical criteria used for determining the purity of organic compounds. Give suitable examples.
2. Explain the importance of purity in pharmaceuticals and how it is assessed using different techniques.
3. Compare chemical and physical criteria of purity with examples.
4. Describe the role of melting point and boiling point as criteria of purity. What changes occur in their values when impurities are present?
5. Explain how chromatographic techniques can be applied to assess the purity of a compound.



Titration and chromatography

Objectives

1. To understand the principle and procedure of titration as a volumetric analytical method.
2. To study different types of titrations (acid-base, redox, complexometric, precipitation).
3. To understand the principles and applications of chromatography for separation and analysis.
4. To compare different chromatographic techniques (paper, thin-layer, column, gas, and HPLC).
5. To develop problem-solving and analytical skills in identifying unknown compounds using titration and chromatography.

4.3.1 Titration and Chromatography

Titration and chromatography are two essential analytical techniques widely applied in chemical laboratories, pharmaceutical industries, clinical diagnostics, and environmental analysis. Both methods serve critical roles in qualitative and quantitative analysis, helping determine the concentration and identity of unknown substances. Titration, a classical method of volumetric analysis, involves the gradual addition of a standard reagent to a solution until a reaction is complete, while chromatography is a separation technique that exploits differences in the physical or chemical properties of substances. Understanding both these techniques in detail is fundamental for students and professionals engaged in analytical science.

Titration, often referred to as titrimetry or volumetric analysis, is a process used to determine the unknown concentration of an analyte by reacting it with a titrant of known concentration. The titrant is added gradually from a burette to the analyte solution until the reaction reaches its equivalence point, which is the point at which the number of moles of titrant equals the number of moles of analyte. An indicator, which changes color near the equivalence point, is often employed to



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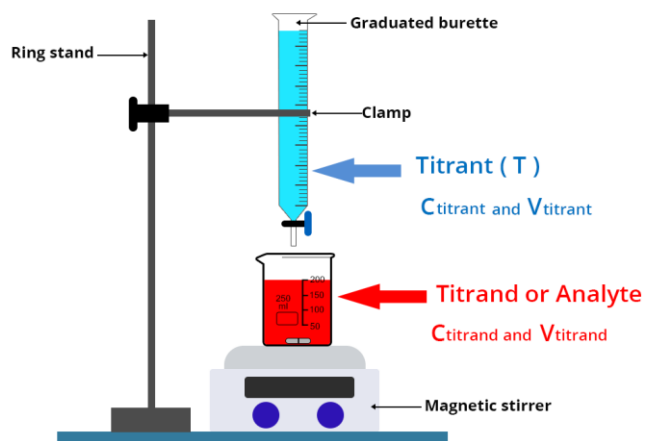
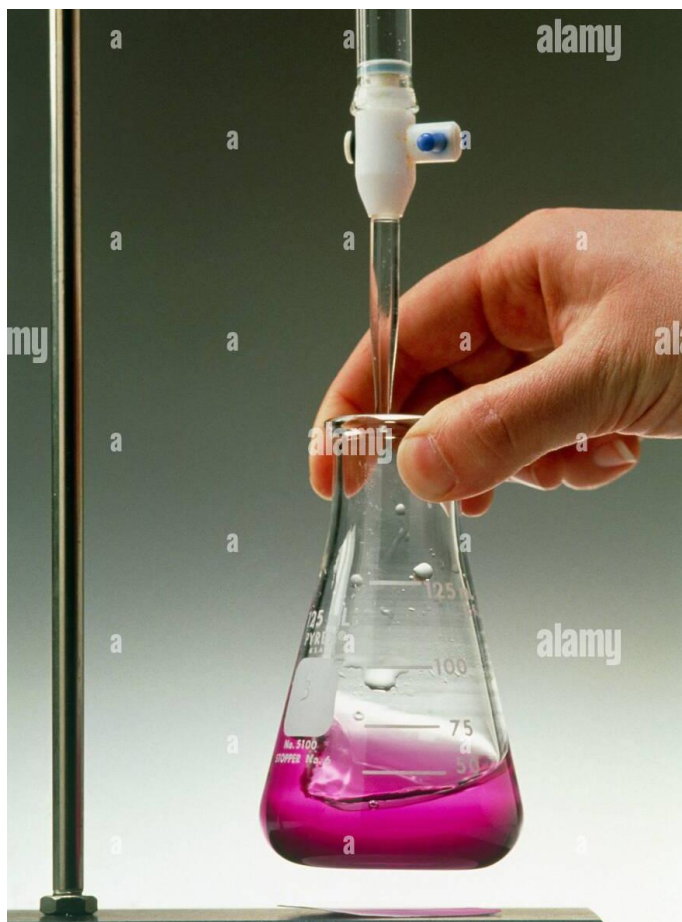
detect the end point of the titration. Titration is characterized by its simplicity, accuracy, and precision when performed correctly. It is widely used in various fields including pharmaceutical quality control, food chemistry, environmental monitoring, and clinical laboratories.

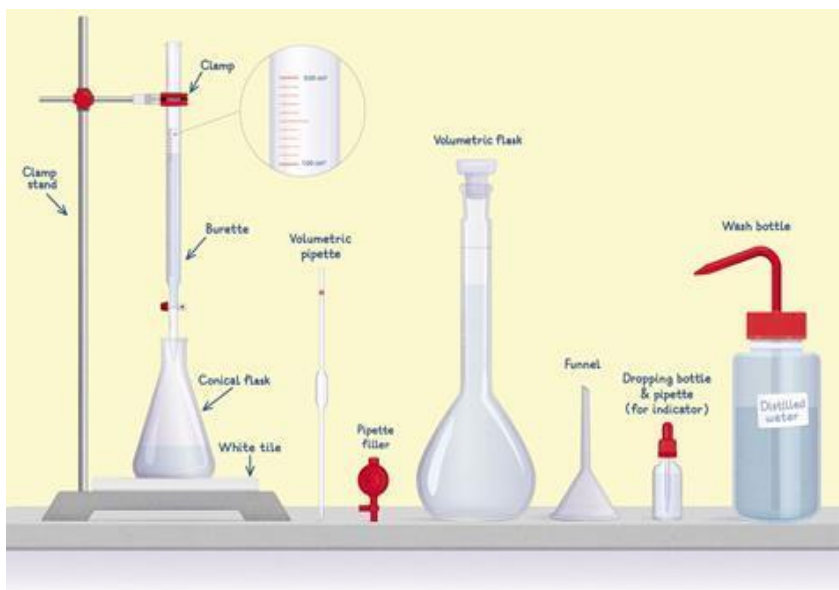
There are several types of titration, each designed to suit the nature of the analyte and the chemical reaction involved. Acid-base titrations are the most common, used to determine the concentration of acidic or basic solutions. These titrations involve neutralization reactions and typically use indicators such as phenolphthalein or methyl orange to signal the end point. Redox titrations involve oxidation-reduction reactions and use redox-sensitive indicators or self-indicating titrants like potassium permanganate. Complexometric titrations, often used in water hardness analysis, rely on the formation of a colored complex between metal ions and chelating agents like EDTA. Precipitation titrations involve the formation of an insoluble precipitate and are often used for halide ion determination with silver nitrate. Each titration type requires an understanding of the stoichiometry of the reaction and the properties of the analyte and titrant.



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The procedure of titration typically involves careful preparation of the analyte solution, filling the burette with the standard solution, and adding the titrant dropwise while continuously stirring the mixture. The progress of the reaction is monitored visually or with the help of pH meters or potentiometers. As the reaction approaches completion, the titrant is added more slowly until the end point is reached. At this stage, the volume of titrant used is recorded, and calculations are performed using the known concentration of the titrant and the reaction equation. Errors in titration can arise from incorrect burette readings, use of impure reagents, or imprecise detection of the end point, and thus careful technique and calibration are essential for accurate results.

In contrast to titration, chromatography is a separation and analysis technique based on the differential distribution of components in a mixture between a stationary phase and a mobile phase. Chromatography plays a crucial role in isolating, identifying, and quantifying compounds present in complex mixtures. The technique relies on the fact that different substances move at different rates through a medium under the influence of a solvent or carrier gas. As the components travel, they interact differently with the stationary phase, leading to separation based on polarity, molecular weight, charge, or other chemical properties. Chromatography has become indispensable



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in pharmaceutical analysis, biochemical research, forensic science, and environmental testing due to its versatility, sensitivity, and ability to handle complex samples.

There are several forms of chromatography, each tailored to specific analytical needs. Thin Layer Chromatography (TLC) uses a thin layer of adsorbent, usually silica gel, coated onto a glass or plastic plate as the stationary phase, and a solvent as the mobile phase. When a small amount of the sample is spotted on the plate and the solvent rises via capillary action, components separate based on their affinity to the stationary phase. TLC is a simple and rapid technique used for monitoring reactions, checking the purity of compounds, and preliminary identification. Paper Chromatography operates on similar principles but uses cellulose paper as the stationary phase, making it useful for the separation of pigments and amino acids. Column Chromatography involves packing a column with adsorbent material and pouring the sample on top. The mobile phase is passed through, eluting the components at different times depending on their interactions with the stationary phase.

More advanced forms of chromatography include High-Performance Liquid Chromatography (HPLC) and Gas Chromatography (GC). HPLC uses a liquid mobile phase under high pressure to push the sample through a packed column. It is highly efficient and capable of separating, identifying, and quantifying substances with high precision. HPLC is especially suited for thermally labile or non-volatile compounds and is widely used in drug analysis and quality assurance. Gas Chromatography, on the other hand, uses an inert gas such as helium as the mobile phase and requires the analytes to be volatile. GC is known for its excellent resolution and is commonly employed in environmental analysis, food testing, and detection of toxins. Both HPLC and GC are often equipped with detectors like UV, fluorescence, or mass spectrometers for enhanced sensitivity and specificity.



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In practical applications, chromatography provides both qualitative and quantitative information. The identity of components is inferred from the retention time or R_f values (in TLC), while the concentration is determined from the peak area or height in instrumental chromatograms. Standard curves constructed from known concentrations of reference standards help in quantifying unknowns. The versatility of chromatography lies in its adaptability; by changing the mobile phase, stationary phase, temperature, or flow rate, analysts can tailor the method to achieve optimal separation. This flexibility makes chromatography a powerful tool for method development, impurity profiling, and pharmacokinetic studies.

When titration and chromatography are compared, several distinctions emerge. Titration is best suited for single-component analysis when the stoichiometry of the reaction is well known. It provides highly accurate quantitative results with simple instrumentation. However, titration cannot be used for mixtures with unknown composition or components that do not undergo well-defined reactions. Chromatography, in contrast, excels in separating and analyzing complex mixtures. It provides both qualitative and quantitative information and can handle a wide range of substances. Although more resource-intensive and requiring sophisticated equipment in advanced forms, chromatography offers unmatched analytical power in modern laboratories.

In many analytical workflows, titration and chromatography are used in a complementary manner. For instance, a pharmaceutical chemist may use titration to determine the active content of a bulk drug substance and chromatography to profile impurities. In quality control, chromatographic methods are often validated against titrimetric methods to ensure consistency and compliance with pharmacopeial standards. Both techniques require careful calibration, appropriate selection of reagents or mobile phases, and strict adherence to protocols to ensure reliable results. The precision of titration depends on factors like reagent standardization and endpoint detection, while the success



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of chromatography hinges on method optimization and instrument maintenance.

As both titration and chromatography continue to evolve, new developments in automation, miniaturization, and data analysis have significantly enhanced their capabilities. Automatic titrators now allow for precise addition of titrant and real-time monitoring of pH or redox changes, improving accuracy and reducing operator error. Similarly, advances in chromatography such as ultra-high-performance liquid chromatography (UHPLC), multidimensional chromatography, and hyphenated techniques like LC-MS and GC-MS have expanded the analytical horizons. These innovations enable the detection of trace-level substances, characterization of complex biological samples, and support for regulatory compliance in high-stakes industries.

In conclusion, titration and chromatography are two foundational pillars of analytical chemistry. While titration offers a classical, cost-effective, and accurate approach for quantitative analysis of known substances, chromatography provides an advanced, adaptable, and powerful method for separating and characterizing complex mixtures. A deep understanding of these techniques, including their principles, procedures, applications, and limitations, is essential for students and practitioners in the chemical sciences. Mastery of both methods not only strengthens analytical capabilities but also fosters critical thinking, precision, and scientific rigor in all aspects of experimental work.

Summary

Titration and chromatography are fundamental analytical techniques used in chemistry and pharmaceutical sciences. **Titration** is a quantitative method where a solution of known concentration (titrant) is added to a solution of unknown concentration until the reaction reaches an endpoint, often indicated by a color change or an instrument reading. Common titrations include acid-base, redox, precipitation, and complexometric titrations.

Chromatography is a qualitative and quantitative separation technique based on the distribution of components between a stationary phase and a mobile phase. It allows the separation, identification, and sometimes quantification of mixtures. Major types include paper chromatography, thin-layer chromatography (TLC), column chromatography, gas chromatography (GC), and high-performance liquid chromatography (HPLC).

Together, titration provides accurate quantitative results, while chromatography helps in separation and identification of complex mixtures. Both methods are widely applied in pharmaceuticals, environmental testing, food analysis, and research.

Multiple Choice Questions (MCQs)

1. The point at which the reaction is complete in a titration is called:
 - a) Neutral point
 - b) Equivalence point
 - c) End point
 - d) Standard point
2. Which indicator is used in a strong acid–strong base titration?
 - a) Phenolphthalein
 - b) Methyl orange
 - c) Both a and b
 - d) None
3. In complexometric titration, the most common reagent is:
 - a) KMnO_4
 - b) I_2
 - c) EDTA
 - d) AgNO_3

Answer: b) Equivalence point

Answer: c) Both a and b

Answer: c) EDTA



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4. In chromatography, the phase that moves is called:

- a) Stationary phase
- b) Mobile phase
- c) Solute phase
- d) Adsorption phase

Answer: b) Mobile phase

5. Retention factor (R_f) in chromatography is defined as:

- a) Distance travelled by solvent $\div$ distance travelled by solute
- b) Distance travelled by solute $\div$ distance travelled by solvent
- c) Solute mass $\div$ solvent mass
- d) Solvent volume $\div$ solute volume

Answer: b) Distance travelled by solute $\div$ distance travelled by solvent

Short Answer Questions

- 1. Define titration and explain its importance in quantitative analysis.
- 2. What is the difference between the equivalence point and end endpoint in titration?
- 3. State the principle of chromatography.
- 4. Mention two differences between TLC and paper chromatography.
- 5. Write two applications of titration and two of chromatography.

Long Answer Questions

- 1. Explain the procedure of an acid-base titration with an example, including indicators used and calculation of results.
- 2. Describe in detail the principles, types, and applications of chromatography.
- 3. Discuss the differences between gas chromatography and HPLC in terms of principle, apparatus, and applications.



4. Explain the role of complexometric titrations in water hardness determination.
5. Describe the factors affecting the separation efficiency in chromatography.

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