B. Pharmacy 1st Semester - Pharmaceutical Analysis Notes

UNIT – 5: Electrochemical Methods of Analysis ⚡

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CONDUCTOMETRY 🔋

Introduction 📖

Conductometry is an electroanalytical technique that measures the electrical conductivity of solutions to determine the concentration of ionic species. This method is based on the fundamental principle that ionic solutions conduct electricity due to the movement of charged particles (ions) in the solution.

Conductometric titration operates on the principle of determining changes in conductivity that occur due to the replacement of one ion by other ions during chemical reactions. The conductivity of a solution is directly proportional to the concentration and mobility of ions present in the solution.

When two platinum electrodes are immersed in an electrolytic solution and connected to an electrical source, the current flow is governed by Ohm's law: **$I = E/R$**, where I is current, E is applied voltage, and R is electrical resistance.

Basic Concepts and Definitions 🔍

Conductance (G)

Conductance is the reciprocal of electrical resistance ($G = 1/R$). It represents the ability of a solution to conduct electrical current. The unit of conductance is Siemens (S), mhos, or ohm^{-1}.

Specific Conductance (κ)

Specific conductance, denoted by kappa (κ), is defined as the conductance of a cube of liquid solution with sides of 1 cm each. It is obtained by multiplying conductance with the cell constant. The unit is ohm^{-1} cm^{-1} or mho/cm.

Equivalent Conductance

Equivalent conductance is the specific conductance of a solution containing one gram equivalent of solute dissolved in 1000 ml of solution. The unit is mho cm^2/gram equivalent.

Molar Conductance (Λ)

Molar conductance is the conductance of a solution containing one mole of solute in 1000 ml of solution placed between two parallel electrodes 1 cm apart. It is denoted by capital lambda (Λ) and has units of siemens cm^2/mole.

Conductivity Cell and Instrumentation 🔧

Current Source

Alternating current (AC) source is employed in conductometers to prevent electrolysis and polarization effects. High-frequency AC generators are used to ensure accurate measurements.

Conductivity Cells

Two main types of conductivity cells are used:

- **Wide-mouthed cells** for general analytical work
- **Dip-type cells** for continuous monitoring

These cells are constructed from Pyrex or quartz glass to ensure chemical inertness and are fitted with platinum electrodes. Temperature control is maintained by placing cells in thermostated water baths.

Electrodes

Platinum electrodes are preferred due to their chemical inertness and stability. The electrode surfaces are coated with platinum black through platinization to:

- Increase the effective surface area
- Minimize polarization effects
- Improve measurement accuracy

The platinization process involves coating the electrodes with a solution containing 3% chloroplatinic acid and lead acetate.

Types of Conductometric Titrations 📊

Titration Type	Analyte	Titrant	Conductance Change
Strong Acid-Strong Base	HCl	NaOH	Decreases then increases
Strong Acid-Weak Base	HCl	NH_4OH	Decreases then constant
Weak Acid-Strong Base	CH_3COOH	NaOH	Slight decrease then sharp increase
Weak Acid-Weak Base	CH_3COOH	NH_4OH	Complex curve pattern

Acid-Base Titrations 🧪

Strong Acid-Strong Base Titrations: In these titrations, the conductance initially decreases as highly conducting H^+ ions are replaced by less conducting Na^+ ions. At the equivalence point, conductance reaches its minimum value. Beyond the equivalence point, excess OH^- ions cause a sharp increase in conductance.

Strong Acid-Weak Base Titrations: The conductance decreases until the equivalence point due to the neutralization of H^+ ions. After the equivalence point, the conductance remains relatively constant due to the common ion effect and the weak ionization of the base.

Weak Acid-Strong Base Titrations: Initially, the conductance decreases slowly as the weak acid is neutralized. At the equivalence point, there is a minimum in conductance, followed by a sharp increase due to excess OH^- ions from the strong base.

Weak Acid-Weak Base Titrations: These titrations show complex conductance curves due to the formation of salts and the weak ionization of both reactants. The equivalence point is often difficult to determine precisely.

Precipitation Titrations 💧

In precipitation titrations, one ion is replaced by another during the formation of a precipitate. The conductance change depends on the relative mobilities of the ions being exchanged. The equivalence point is indicated by a change in the slope of the conductance curve.

Complexometric Titrations 🔗

These titrations involve the formation of coordination complexes. The conductance changes are related to the binding of metal ions with complexing agents, resulting in species with different mobilities and charges.

Applications of Conductometry 🌍

Conductometric methods find extensive applications in various fields:

Environmental Analysis:

- Water pollution monitoring in rivers, lakes, and natural water resources
- Determination of water alkalinity and salinity
- Assessment of seawater conductivity for oceanographic studies

Food Industry:

- Estimation of ash content in sugar juices
- Quality control of food products
- Microbiological analysis for tracing microorganisms

Pharmaceutical Analysis:

- Purity assessment of distilled and deionized water
- Quality control of pharmaceutical formulations
- Analysis of ionic impurities

Research Applications:

- Determination of deuterium ion concentration in isotopic mixtures
- Solubility studies of sparingly soluble salts

- Atmospheric pollution monitoring (SO_2 determination)

POTENTIOMETRY 🔬

Introduction 📖

Potentiometry is a branch of electroanalytical chemistry that involves the measurement of electrical potential under conditions of zero current flow. This technique utilizes the relationship between the electrical potential of an electrochemical cell and the concentration of analyte species in solution.

The fundamental principle of potentiometry is based on the measurement of the electromotive force (EMF) of electrochemical cells. The potential difference develops as a result of free energy changes that would occur if the chemical reactions proceeded to equilibrium. These measurements provide quantitative information about the concentration of specific ions in solution.

Electrochemical Cells ⚡

An electrochemical cell consists of two electrodes immersed in electrolytic solutions, capable of producing electrical energy through chemical reactions. Each cell contains:

Oxidizing Electrode (Anode):

- Liberates electrons during oxidation reactions
- Undergoes oxidation at its surface
- Connected to the negative terminal

Reducing Electrode (Cathode):

- Accepts electrons during reduction reactions
- Site of reduction reactions
- Connected to the positive terminal

Electrode Potential and Nernst Equation 📈

Electrode Potential

Electrode potential (E) represents the electromotive force of a cell constructed with a standard hydrogen electrode on one side and the electrode of interest on the other side. It is measured in volts (V) and arises from:

- Transfer of charged species across the electrode-electrolyte interface
- Specific adsorption of ions at the interface
- Orientation of polar molecules including solvent molecules

Nernst Equation 🧮

The Nernst equation relates electrode potential to the concentrations of electroactive species:

$$\mathbf{E = E^\circ - (RT/nF) \ln Q}$$

Where:

- E = Electrode potential
- E° = Standard electrode potential
- R = Universal gas constant (8.314 J/(K·mol))

- T = Temperature in Kelvin
- n = Number of electrons transferred
- F = Faraday constant (96,485 C/mol)
- Q = Reaction quotient

Salt Bridge 🌉

A salt bridge is a crucial component that connects the oxidation and reduction half-cells of an electrochemical cell. It serves several important functions:

Functions:

- Maintains electrical neutrality in both half-cells
- Allows ion migration to complete the electrical circuit
- Prevents mixing of solutions from different half-cells
- Minimizes junction potentials

Types:

1. **Glass Tube Salt Bridge:** U-shaped glass tube filled with inert electrolyte (KCl or NaCl)
2. **Filter Paper Salt Bridge:** Filter paper soaked with inert electrolyte solution

Reference Electrodes 🔋

Reference electrodes provide a stable, known potential against which other electrode potentials can be measured. Ideal reference electrodes should possess the following characteristics:

Property	Requirement
Reversibility	Must obey Nernst equation
Stability	Constant potential with time
Recovery	Returns to original potential after small currents
Temperature	Minimal hysteresis with temperature changes

Standard Hydrogen Electrode (SHE)

The standard hydrogen electrode serves as the primary reference with an assigned potential of 0.000 V at all temperatures. It consists of:

Construction:

- Platinum wire or sheet coated with platinum black
- Immersed in solution with H^+ activity of unity
- Continuous hydrogen gas bubbling at 1 atm pressure
- Temperature maintained at 25°C

Half-Cell Reaction: $2H^+ + 2e^- \rightleftharpoons H_2$

Potential Equation: $E = -(RT/F) \ln(P\_H_2/[H^+]^2)$

Saturated Calomel Electrode (SCE)

The saturated calomel electrode is widely used in analytical chemistry due to its simplicity and reliability.

Construction:

- Inner tube containing platinum wire amalgamated with mercury

- Thick paste of metallic mercury, mercurous chloride (Hg_2Cl_2), and KCl
- Outer tube with porous asbestos fiber for solution contact
- Pin hole for electrolytic contact between tubes

Half-Cell Reaction: $Hg_2Cl_2 + 2e^- \rightleftharpoons 2Hg + 2Cl^-$

Potential: +0.244 V vs. SHE at 25°C

Silver-Silver Chloride Electrode (Ag-AgCl) 🟣

This electrode functions as a redox electrode with equilibrium between silver metal and its salt.

Construction:

- Silver wire coated with silver chloride
- Immersed in chloride-containing solution
- Simple and robust design

Half-Cell Reaction: $AgCl + e^- \rightleftharpoons Ag + Cl^-$

Nernst Equation: $E = E°(Ag^+/Ag) - (RT/F) \ln[Cl^-]$

Indicator Electrodes 📏

Indicator electrodes respond to changes in analyte concentration and generate potentials that vary with the concentration of the species being determined.

Metallic Indicator Electrodes

These electrodes are made from the metal involved in the electrochemical reaction. They provide direct response to the activity of their corresponding metal ions in solution.

Glass Electrode 🔬

The glass electrode is the most important indicator electrode for pH measurements.

Construction:

- Thin-walled glass bulb made from special low-melting-point glass
- Internal reference electrode (Ag-AgCl or calomel)
- Internal solution with known H^+ and Cl^- concentrations
- Sealed tube design

Principle: The glass membrane selectively responds to hydrogen ion activity, developing a potential proportional to the pH of the solution.

pH Response: $E = E^\circ - (2.303RT/F)\,\mathrm{pH}$

Types of Potentiometric Titrations 📊

Titration Type	Electrode System	Applications
Acid-Base	Glass electrode vs. SCE	pH determination, buffer analysis
Precipitation	Metal electrode vs. SCE	Halide analysis, $AgNO_3$ titrations
Complexometric	Metal electrode vs. SCE	Metal ion determination
Redox	Platinum electrode vs. SCE	Oxidation-reduction reactions

Oxidation-Reduction Titrations

These titrations utilize platinum or other inert electrodes that respond to the ratio of oxidized and reduced forms of redox couples. The potential changes dramatically near the equivalence point.

Acid-Base Titrations

Glass electrodes are used to monitor pH changes during neutralization reactions. The equivalence point corresponds to the steepest part of the potential-volume curve.

Precipitation Titrations

Metal electrodes respond to changes in metal ion concentration during precipitation reactions. The equivalence point is indicated by a sharp potential change.

Complexometric Titrations

These titrations involve the formation of metal-ligand complexes, monitored using metal indicator electrodes that respond to free metal ion concentrations.

Applications and Advantages 🌟

Applications:

- pH measurements in various industries
- Water quality analysis
- Pharmaceutical quality control
- Environmental monitoring
- Food industry analysis

Advantages:

- High precision and accuracy
- Suitable for colored and turbid solutions
- Wide concentration range
- Minimal sample consumption
- Real-time monitoring capability

POLAROGRAPHY 📊

Introduction and Principle 📖

Polarography is a specialized form of voltammetry that employs a dropping mercury electrode (DME) as the working electrode. This technique was developed by Jaroslav Heyrovský, who received the Nobel Prize for this groundbreaking work.

The fundamental principle involves the study of electrode processes through electrolysis using two electrodes: one polarizable (dropping mercury electrode) and one non-polarizable (reference electrode). Current-voltage relationships are recorded as the applied potential is gradually varied.

Polarography measures the current flowing through an electrochemical cell as a function of applied voltage. The resulting current-voltage curves (polarograms) provide both qualitative and quantitative information about electroactive species in solution.

Ilkovic Equation 🧮

The Ilkovic equation, named after Slovak chemist Dionýz Ilkovič, relates the diffusion current to various experimental parameters:

$$\mathbf{Id = 607\ n\ D^{(1/2)}\ C\ m^{(2/3)}\ t^{(1/6)}}$$

Where:

- **Id** = Diffusion current (μA)
- **n** = Number of electrons transferred
- **D** = Diffusion coefficient (cm^2/s)
- **C** = Concentration of electroactive species (mol/L)
- **m** = Mass flow rate of mercury (mg/s)
- **t** = Drop time (s)
- **607** = Constant incorporating fundamental constants

This equation demonstrates that the diffusion current is directly proportional to the concentration of the electroactive species, forming the basis for quantitative analysis.

Dropping Mercury Electrode (DME) 💧

Construction and Working 🔧

The dropping mercury electrode consists of:

- **Mercury reservoir** connected to a fine glass capillary
- **Capillary tube** with precisely controlled bore diameter
- **Mercury drops** that form and fall at regular intervals
- **Mercury pool** at the bottom serving as auxiliary electrode

Operating Characteristics:

- Drop formation rate: 0.2 Hz (approximately 5-30 drops/minute)
- Drop lifetime: 2-12 seconds
- Applied potential scan rate: 50-200 mV/minute
- Potential range: +0.4 V to -2.0 V vs. SCE

Advantages of DME ✅

Surface Renewal: The continuously forming fresh mercury surface eliminates problems associated with electrode poisoning and surface contamination that plague solid electrodes.

Reproducibility: Each mercury drop provides an identical, smooth surface, ensuring highly reproducible measurements and eliminating surface history effects.

Amalgam Formation: Mercury forms amalgams with many metals, enabling the analysis of various metallic species through reduction to their metallic state.

Immediate Steady State: The diffusion current reaches a stable value immediately after potential changes, providing reliable and reproducible analytical signals.

Calculable Surface Area: The electrode surface area can be precisely calculated from the drop weight and drop time, enabling accurate kinetic studies.

Disadvantages of DME ❌

Limited Anodic Range: At potentials more positive than +0.4 V vs. SCE, mercury oxidation occurs, producing interfering anodic waves that mask other electrochemical processes.

Restricted Applications: DME is primarily suitable for analyzing reducible species or easily oxidizable substances due to mercury's limited potential window.

Capillary Problems: The fine capillary is susceptible to blockage, requiring careful maintenance and regular cleaning procedures.

Toxicity Concerns: Mercury vapor and mercury compounds pose significant health hazards, requiring proper ventilation and waste disposal procedures.

Oxidation Sensitivity: Mercury is easily oxidized in the presence of oxygen, necessitating deoxygenation of solutions before analysis.

Rotating Platinum Electrode (RPE) ⚙️

Construction and Working 🔧

The rotating platinum electrode consists of:

- **Platinum wire** sealed in soft-glass tubing
- **Constant-speed motor** for rotation control
- **Bell-shaped glass tube** housing the electrode
- **Extended platinum wire** to the outer edge of the bell

Operating Principles:

- High-speed rotation (typically 1000-3000 rpm)

- Enhanced mass transfer through forced convection
- Reduced residual current due to absence of capacitive effects
- Lower hydrogen overpotential compared to mercury

Advantages of RPE ✅

Enhanced Mass Transfer: High-speed rotation creates efficient mass transport, resulting in well-defined limiting currents and sharp end-points in titrations.

Reduced Residual Current: The absence of continuously changing surface area eliminates capacitive current contributions, improving signal-to-noise ratios.

Wide Potential Range: Platinum electrodes can operate over a broader potential range compared to mercury electrodes, particularly in the anodic region.

Mechanical Stability: The solid electrode construction provides excellent mechanical stability and resistance to vibration.

Applications and Advantages of Polarography 🌟

Inorganic Analysis 🔬

Metal Analysis: Polarography excels in the determination of trace metals including zinc, cadmium, lead, copper, and other heavy metals. Detection limits often reach parts per billion levels.

Anion Analysis: Various anions such as dichromate, iodate, nitrate, and others can be analyzed through their characteristic reduction waves.

Speciation Studies: Different oxidation states of the same element can be distinguished and quantified simultaneously.

Organic Analysis 🧪

Functional Group Analysis: Specific organic functional groups produce characteristic polarographic waves:

- **Carbonyl groups** (aldehydes and ketones)
- **Nitro groups** in aromatic compounds
- **Azo groups** in dyes and pharmaceuticals
- **Peroxide linkages** in various compounds

Biochemical Applications: Polarography finds extensive use in biochemical analysis, including the determination of vitamins, enzymes, and other biologically active compounds.

Analytical Advantages 📈

Advantage	Description
Small Sample Volume	Requires only microliters of sample
Turbid Solutions	Unaffected by sample turbidity or color
Simultaneous Analysis	Multiple species can be determined in one run
High Sensitivity	Detection limits in parts per billion range
No Prior Separation	Direct analysis without sample pretreatment
Rapid Analysis	Quick measurements suitable for quality control

Quality Control Applications:

- Pharmaceutical analysis for active ingredients and impurities
- Environmental monitoring for toxic metals
- Food analysis for additives and contaminants
- Industrial process monitoring

Research Applications:

- Kinetic studies of electrode processes
- Mechanism elucidation of electrochemical reactions
- Thermodynamic parameter determination
- Corrosion studies and inhibitor evaluation

The versatility, sensitivity, and reliability of polarographic methods make them indispensable tools in modern analytical chemistry, particularly for trace analysis and quality control applications across various industries.