UNIT 1

History of Pharmacopoeia

Definition of Pharmacopoeia:

A **pharmacopoeia** is an **official compilation of drug standards**—it contains **monographs** of drugs that describe their **identity, purity, strength, quality, tests, and assay methods**. It serves as a **legal and scientific reference** for the manufacture and quality control of pharmaceutical substances and formulations.

Historical Development of Pharmacopoeia:

1. Ancient Beginnings:

- The concept of documenting medicinal substances dates back to **ancient civilizations** like **Egypt**, **China**, **India**, and **Greece**.
- **Charaka Samhita** and **Sushruta Samhita** in India (around 1000 BC) described several medicinal preparations.
- **Hippocrates** (460–377 BC) and **Galen** (130–200 AD) of Greece were early contributors to systematic drug preparation.

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2. First Pharmacopoeia (Middle Ages):

- The earliest recognized pharmacopoeia was **"Antidotarium Nicolai"** (circa 1100 AD), written by **Nicolaus Myrepsus**, a court physician in Constantinople.
- The **first official pharmacopoeia** is considered to be the **"Nuovo Receptario"** (1498), published in Florence, Italy, authorized by the city government and prepared by the Medical College.

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3. British Pharmacopoeia (BP):

- The **first edition** of the **British Pharmacopoeia** was published in **1864**, combining the pharmacopoeias of London, Edinburgh, and Dublin.
- It is regularly revised and updated by the **British Pharmacopoeia Commission** under the UK Medicines and Healthcare products Regulatory Agency (MHRA).
- BP serves as a standard in many Commonwealth nations and is widely respected internationally.

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4. United States Pharmacopoeia (USP):

- First published in **1820** by a group of physicians in Washington, D.C.
- It became legally enforceable in the USA under the **Federal Food, Drug, and Cosmetic Act of 1938**.
- Published by the **United States Pharmacopeial Convention**, the USP sets standards not only for drugs but also for dietary supplements and food ingredients.

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5. Indian Pharmacopoeia (IP):

- India's first official pharmacopoeia, **The Indian Pharmacopoeia**, was published in **1955** by the **Indian Pharmacopoeia Committee** under the **Ministry of Health and Family Welfare**.
- It sets the **standards for drugs manufactured and marketed in India**.
- **Revised editions** were published in 1966, 1985, 1996, 2007, 2010, 2014, 2018, and the **latest version in 2022**.
- The **Indian Pharmacopoeia Commission (IPC)**, Ghaziabad, is responsible for its publication and maintenance.

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6. International Pharmacopoeia (Ph. Int.):

- Published by the **World Health Organization (WHO)** since 1951.
- Aims to provide **global standards** for quality control of medicines, especially for use in countries that do not have their own national pharmacopoeia.

Other Notable Pharmacopoeias:

- **European Pharmacopoeia (Ph. Eur.):** First published in **1969**, applicable in EU member states.
- **Japanese Pharmacopoeia (JP):** First edition in **1886**, revised every five years.
- **Chinese Pharmacopoeia (ChP):** Covers both modern and traditional Chinese medicines.

Sources and types of impurities

Impurities:

An **impurity** is any component present in a pharmaceutical substance other than the desired **active pharmaceutical ingredient (API)** or **excipients**, that arises during **manufacture, storage, or handling**, and may affect the **safety, efficacy, or quality** of the product.

According to the Indian Pharmacopoeia and ICH guidelines, impurities can be organic, inorganic, or residual solvents.

Sources of Impurities:

1. **Raw Materials Used in Manufacturing:**
    - Impurities in **chemicals or solvents** used for synthesis.
    - Impurities in **water** (e.g., calcium, magnesium, chlorides).
2. **Manufacturing Process:**
    - **Incomplete reactions** leading to unreacted starting materials.
    - **By-products** from side reactions.
    - **Decomposition products** due to heat, pH, or light.
3. **Reagents and Catalysts:**
    - Traces of **acids, bases, metal catalysts** (e.g., palladium, copper).
    - Use of impure **intermediate compounds**.
4. **Atmospheric Contaminants:**
    - **Dust**, carbon dioxide, and microorganisms.
    - Vapors from **acids, alkalis, solvents** in the production environment.
5. **Storage Conditions:**
    - **Oxidation, hydrolysis, polymerization** during storage.
    - **Reaction with container materials** (glass, plastic).
6. **Cross-Contamination:**
    - Contamination from **other products** or **inadequate cleaning** of manufacturing equipment.
7. **Solvents Used in Crystallization or Purification:**
    - **Residual solvents** may remain in the final product.
8. **Packaging Materials:**
    - Leaching of **plasticizers, lubricants**, or **stabilizers** into the drug from packaging.

Types of Impurities:

1. Organic Impurities:

- **Process-related impurities**: starting materials, by-products, intermediates.
- **Degradation products**: formed during storage (e.g., oxidation, hydrolysis).
- Examples: aldehydes, ketones, acids, esters, amines.

2. Inorganic Impurities:

- Arise from the manufacturing process or raw materials.
- Examples:
    - **Reagents**: acids, bases, drying agents.
    - **Catalysts**: heavy metals.
    - **Filter aids**: silicates, carbon.

3. Residual Solvents:

- Volatile organic compounds used during synthesis or purification.
- Classified based on toxicity (ICH Q3C):
    - **Class I**: to be avoided (e.g., benzene, carbon tetrachloride).
    - **Class II**: limited use (e.g., methanol, acetonitrile).
    - **Class III**: low toxic potential (e.g., ethanol, acetone).

4. Foreign Particulate Matter:

- Physical contaminants like **fibers, glass particles, dust**, etc.

5. Enantiomeric Impurities:

- Undesired **optical isomers** in chiral drugs.

Impact of Impurities:

- May **alter therapeutic efficacy**.
- Can cause **toxicity, allergic reactions**, or **adverse effects**.
- May affect **stability, solubility**, or **appearance** of the drug.

Control of Impurities:

- **Good Manufacturing Practices (GMP)**.
- Use of **validated processes** and **analytical methods**.
- **Limit tests** (e.g., for lead, arsenic, iron).

Principle involved in the limit test for Chloride, Sulphate, Iron, Arsenic, Lead and Heavy metals, modified limit test for Chloride and Sulphate

1. Limit Test for Chloride

Principle:

The test is based on the **precipitation reaction** between chloride ions (Cl^-) and **silver nitrate ($AgNO_3$)** in the presence of **dilute nitric acid (HNO_3)**, forming **silver chloride (AgCl)** as a **white turbidity**. The acid prevents precipitation of other interfering silver salts such as carbonates or phosphates.

This turbidity is visually compared with a **standard chloride solution** that contains a known amount of chloride, usually from **sodium chloride (NaCl)**. The comparison is done in **Nessler cylinders** under similar conditions.

Reaction:

$Cl^- + AgNO_3 \rightarrow AgCl\downarrow + NO_3^-$

Inference:

If the test solution produces **less or equal turbidity** compared to the standard, it passes the limit test.

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2. Modified Limit Test for Chloride

Principle:

The modified method improves sensitivity by **conducting the test in a white porcelain dish** instead of a Nessler cylinder, ensuring **uniform background and better light reflection**, making visual comparison of turbidity more accurate.

The chemistry remains the same, but the **visual clarity** and **reproducibility** are improved. This is especially useful when dealing with very low chloride levels.

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3. Limit Test for Sulphate

Principle:

This test is based on the **precipitation of sulphate ions (SO_4^{2-})** with **barium chloride ($BaCl_2$)** in the presence of **acetic acid (CH_3COOH)**, forming **barium sulphate ($BaSO_4$)** as a **white turbidity**. Acetic acid is used to maintain a slightly acidic pH, preventing interference by other ions.

The turbidity produced is compared with that of a **standard sulphate solution** (usually potassium sulphate, K_2SO_4).

Reaction:

$SO_4^{2-} + BaCl_2 \rightarrow BaSO_4 \downarrow + 2Cl^-$

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4. Modified Limit Test for Sulphate

Principle:

In the modified method, **ethanol** is included along with **barium chloride and dilute hydrochloric acid** to enhance precipitation. The reaction is performed in a **white porcelain dish** to improve visualization.

Ethanol reduces the solubility of barium sulphate, promoting finer and more uniform turbidity. This makes comparison against the standard more sensitive and precise.

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5. Limit Test for Iron

Principle:

This test detects traces of **ferric iron (Fe^{3+})**, which forms a **purple-colored complex** with **thioglycolic acid** in the presence of **ammonia buffer** at alkaline pH. Thioglycolic acid acts both as a **reducing agent** and **complexing agent**.

At alkaline pH, ferrous ions (Fe^{2+}) formed from the reduction of ferric ions react with thioglycolic acid to give a colored complex. The color intensity is compared with a standard solution of **ferric ammonium sulphate**.

Reaction:

Fe^{3+} + Thioglycolic acid undergoes reduction gives

$Fe^{2+} \rightarrow$ Purple complex

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6. Limit Test for Arsenic

Principle:

The test is based on the conversion of **arsenic (As^{3+})** in the sample into **arsine gas (AsH_3)** by reaction with **zinc and hydrochloric acid** in a specially designed apparatus. The arsine gas reacts with **mercuric chloride paper**, producing a **yellow to brown stain** due to the formation of **mixed arsenic–mercury halides**.

The intensity of the stain is compared with that of a standard arsenic solution prepared from **arsenic trioxide (As_2O_3)**.

Reactions:

1. Formation of arsine:

   $As^{3+} + 3Zn + 6H^+ \rightarrow AsH_3 \uparrow + 3Zn^{2+}$

2. Arsine reacting with mercuric chloride:

   $AsH3+3HgCl2 \rightarrow$ Brown stain (Hg-As compounds)

   This is a **highly sensitive test** and must be conducted in a **closed apparatus** to prevent toxicity.

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7. Limit Test for Lead

Principle:

Lead is detected by **precipitating it as lead sulfide (PbS)** in the presence of **alkaline tartrate solution and hydrogen sulfide (H_2S)**. This forms a **brown to black color**, which is compared with a standard lead solution of known concentration.

The test is performed in **slightly alkaline medium** using **ammonium citrate buffer**, which helps to dissolve interfering metal ions by forming soluble complexes.

Reaction:

$Pb2++H2S \rightarrow PbS\downarrow+2H+$

The intensity of color or precipitate is observed and compared visually.

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8. Limit Test for Heavy Metals

Principle:

This test is designed to detect **a group of heavy metals** like **lead, mercury, cadmium, arsenic, antimony**, etc. The metal ions are precipitated as their **sulfides** in the presence of **hydrogen sulfide (H_2S)** under acidic conditions (using acetic acid).

The test is done using **thioacetamide** as a sulfur source in some IP versions. The resulting **colored sulfide precipitates or turbidity** is compared with a standard solution prepared using **lead nitrate**, which serves as a reference for total heavy metal content.

Reaction:

$Mn^{+}+H_2S \rightarrow MS\downarrow+nH^{+}$

Where M = metal ion (e.g., Pb^{2+}, Hg^{2+}, Bi^{3+})

This is a **semi-quantitative test**, and different pharmacopoeias may specify limits in **parts per million (ppm)**.

1. Sodium Chloride (NaCl)*

1. General Method of Preparation:

Sodium chloride occurs naturally in large quantities as rock salt and in sea water. It can be obtained by:

- **Evaporation of sea water**, a process widely used in coastal regions. Seawater is allowed to stand in shallow ponds and evaporate under sunlight.
- **Mining of rock salt** (halite) deposits underground.
- **Synthetic method** (rare in practice): By neutralization of **hydrochloric acid** with **sodium hydroxide**.

  NaOH+HCl→NaCl+H2O

2. Assay Method: ***(As per IP)***

Volhard's method – an indirect titration (residual silver nitrate is back-titrated).

- Sodium chloride is reacted with excess **standard silver nitrate ($AgNO_3$)** to form a white **silver chloride precipitate**.
- Unreacted $AgNO_3$ is titrated with **ammonium thiocyanate (NH_4SCN)** using **ferric ammonium sulfate** as indicator.
- Endpoint: Formation of a red ferric thiocyanate complex.

  $Ag^+ + Cl^- \rightarrow AgCl\downarrow$

  $Ag^+ + Cl^- \rightarrow AgCl\downarrow$ $Fe^{3+} + SCN^- \rightarrow [FeSCN]^{2+}$(red)

3. Properties:

- **Physical:**
  - White crystalline powder or colorless crystals
  - Soluble in water, insoluble in alcohol
  - Neutral pH
- **Chemical:**
  - Stable under normal conditions
  - Decomposes only at very high temperatures

4. Medicinal Uses:

- Used in preparation of **normal saline (0.9%)** for IV fluid replacement
- Maintains **osmotic balance and electrolyte level** in the body
- Used in **oral rehydration salts (ORS)**

- Component of various **eye and nasal drops**
- **Flavor enhancer** in pharmaceutical formulations

2. Calcium Gluconate ($C_{12}H_{22}CaO_{14}$)

1. General Method of Preparation:

- Prepared by **neutralizing gluconic acid or gluconolactone** with **calcium carbonate ($CaCO_3$)** or **calcium hydroxide ($Ca(OH)_2$)**.
- The reaction is done in aqueous medium and followed by crystallization.

$CaCO3+2C6H12O7 \rightarrow Ca(C6H11O7)_2+CO2+H2O$

2. Assay Method: ***(As per IP)***

- **Complexometric titration with disodium EDTA**.
- Medium: Alkaline buffer (pH ~12), indicator: **Murexide**
- Endpoint: Color change from pink to purple

$Ca^{2+}+EDTA4- \rightarrow Ca^{-}EDTA$ complex

3. Properties:

- **Physical:**
  - White crystalline powder or granules
  - Sparingly soluble in water
  - Odorless, tasteless
- **Chemical:**
  - Slightly hygroscopic
  - Compatible with most drugs and fluids

4. Medicinal Uses:

- Used in **treatment of hypocalcemia** and **calcium deficiency**
- Used in **tetany** caused by vitamin D deficiency
- Given orally or parenterally (10% injection)
- Also used in **cardiac resuscitation** to counteract magnesium toxicity

3. Ammonium Chloride (NH_4Cl)*

1. General Method of Preparation:

Ammonium chloride is typically prepared by the **direct neutralization reaction** between **ammonia (NH_3)** and **hydrogen chloride (HCl)**:

$NH3+HCl \rightarrow NH4Cl$

Alternatively, it can be obtained as a **byproduct** in the **Solvay process** during the manufacture of sodium carbonate (Na_2CO_3).

In laboratory-scale preparations, **aqueous ammonia** is reacted with **hydrochloric acid**, and the solution is then evaporated to yield crystals of ammonium chloride.

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2. Assay Method: ***(As per Indian Pharmacopoeia)***

Ammonium chloride is assayed by an **indirect acid-base titration** method. Here's how it works:

- Ammonium ions (NH_4^+) do not act as bases directly.
- To make them titratable, **formaldehyde (HCHO)** is added to the solution to **fix ammonia** by forming hexamethylenetetramine.
- This reaction liberates equivalent **hydrochloric acid**, which is then titrated with standard **sodium hydroxide (NaOH)**.

$NH4^+ + HCHO \rightarrow (CH2)_6N4 + 4H^+$

The liberated acid is titrated with NaOH using **methyl red** as an indicator.

Endpoint: Color change from red to yellow

3. Properties:

- **Physical Properties:**
    - White, crystalline powder or colorless crystals
    - Slightly hygroscopic
    - Readily **soluble in water**
    - Slightly **cooling and salty taste**
    - pH of solution: slightly **acidic**
- **Chemical Properties:**
    - On heating, it **sublimes** without melting ($NH_4Cl \rightarrow NH_3 + HCl$)
    - In aqueous solution, acts as a **weak acid** due to hydrolysis

4. Medicinal Uses:

- **Systemic Acidifier:** Used in conditions like **metabolic alkalosis** to acidify the body.
- **Expectorant:** Promotes the secretion or expulsion of respiratory mucus by mildly irritating the gastric mucosa, which in turn stimulates bronchial secretions via a vagal reflex.
- **Diuretic action:** Occasionally used in **edema** or **urinary alkalosis**.
- **Electrolyte replenishment:** Sometimes included in **oral rehydration** or **electrolyte replacement therapies**.

4. Sodium Bicarbonate ($NaHCO_3$)*

1. General Method of Preparation:

Sodium bicarbonate is prepared industrially by the **Solvay process**, involving the following steps:

$NH3+CO2+NaCl+H2O \rightarrow NaHCO3+NH4Cl$

In the lab, it can also be prepared by bubbling **CO_2 gas** through a **cold solution of sodium carbonate (Na_2CO_3)**:

$Na2CO3+CO2+H2O \rightarrow 2NaHCO3$

2. Assay Method: ***(As per IP)***

Acid-base titration:

- Sodium bicarbonate reacts with **sulfuric acid** or **hydrochloric acid**, and the liberated CO_2 is an indicator of the reaction.

$NaHCO3+HCl \rightarrow NaCl+CO2\uparrow+H2O$

- The titration is done using **methyl orange** as the indicator.
- Endpoint: Color change from yellow to pink/red

3. Properties:

- **Physical**:
    - White crystalline powder
    - Slightly alkaline in aqueous solution
    - Soluble in water but insoluble in alcohol
- **Chemical**:
    - Decomposes on heating to give **sodium carbonate**, **CO_2**, and **water**

- Reacts with acids to release **carbon dioxide** (effervescence)

4. Medicinal Uses:

- Used as a **systemic antacid** to neutralize stomach acid in hyperacidity and GERD
- **Alkalizer** in metabolic acidosis
- Used in **effervescent granules**
- Component of **toothpastes** and **mouthwashes**
- Used in **alkaline urine therapy** and to treat **uric acid kidney stones**

5. Aluminum Hydroxide Gel [$Al(OH)_3$]

1. General Method of Preparation:

Prepared by **precipitating** aluminum ions from **aluminum salts** (such as aluminum chloride or sulfate) using an alkali like **ammonium hydroxide**:

$Al3^{+}+3NH4OH \rightarrow Al(OH)_3 \downarrow +3NH4^{+}$

The precipitate is washed and suspended in water to prepare the gel.

2. Assay Method: ***(As per IP)***

- Assayed **indirectly** by **acid-base back titration**.
- A known excess of **standard HCl** is added to dissolve $Al(OH)_3$.
- The unreacted HCl is then titrated with **NaOH** using **methyl orange**.

$Al(OH)3+3HCl \rightarrow AlCl3+3H2O$

3. Properties:

- **Physical**:
  - White viscous gel
  - Tasteless and odorless
  - Insoluble in water and alcohol
  - Amorphous in nature
- **Chemical**:
  - Reacts with acids to form soluble aluminum salts
  - Acts as a **weak base**

4. Medicinal Uses:

- Used as an **antacid** to relieve hyperacidity, gastritis, peptic ulcers

- **Slow-acting**, but provides **long-lasting effect**
- Also used to **bind phosphate** in chronic kidney disease to prevent hyperphosphatemia
- Component of **antidiarrheal** combinations
- May cause **constipation** with long-term use

6. Magnesium Hydroxide Mixture

1. General Method of Preparation:

Magnesium hydroxide mixture is prepared by the **precipitation reaction** of **magnesium salt (usually magnesium sulfate or chloride)** with **sodium hydroxide**:

$MgCl2+2NaOH \rightarrow Mg(OH)_2\downarrow+2NaCl$

The precipitated **magnesium hydroxide** is washed and **suspended in purified water** to form a uniform mixture.

2. Assay Method: ***(As per IP)***

- It is assayed **indirectly** by **acid-base back titration**.
- A known excess of **standard hydrochloric acid** is added to react with $Mg(OH)_2$, forming **$MgCl_2$**.
- The unreacted acid is back titrated with **sodium hydroxide** using **methyl orange** indicator.

$Mg(OH)_2+2HCl \rightarrow MgCl2+2H_2O$

3. Properties:

- **Physical**:
    - White, odorless, tasteless thick suspension
    - Practically insoluble in water
    - Settles on standing, requires shaking before use
- **Chemical**:
    - Acts as a **weak base**
    - Reacts with acids to form **magnesium salts**

4. Medicinal Uses:

- Used as a **fast-acting antacid** to relieve heartburn and acid indigestion
- Also used as a **saline laxative** in higher doses due to osmotic water retention in intestines

- Provides **synergistic effect** when combined with **aluminum hydroxide**
- Used in **dyspepsia** and **gastritis**

7. Magnesium Sulphate ($MgSO_4 \cdot 7H_2O$)

1. General Method of Preparation:

Prepared by neutralizing **magnesium oxide (MgO)** or **magnesium carbonate ($MgCO_3$)** with **dilute sulfuric acid (H_2SO_4)**:

$MgO + H_2SO_4 \rightarrow MgSO_4 + H_2O$

The solution is crystallized to obtain **heptahydrate** ($MgSO_4 \cdot 7H_2O$), known as **Epsom salt**.

2. Assay Method: ***(As per IP)***

- **Complexometric titration** using **EDTA**.
- The magnesium ions form a complex with EDTA.
- **Eriochrome Black T** is used as the indicator.
- Endpoint: Color changes from **wine red to blue**.

3. Properties:

- **Physical**:
    - Colorless or white crystalline powder
    - Odorless, with a cool, saline, bitter taste
    - Freely soluble in water
    - Slightly soluble in alcohol
- **Chemical**:
    - Neutral salt
    - Loses water of crystallization on heating

4. Medicinal Uses:

- Used as a **saline cathartic (laxative)** in constipation
- Administered intravenously in **eclampsia** and **preeclampsia** as a **CNS depressant**
- Also used to correct **magnesium deficiency**
- Externally used in **baths and compresses** for muscle relaxation
- Used as an **anticonvulsant**, **antiarrhythmic**, and **tocolytic** agent in specific clinical settings

8. Sodium Orthophosphate (Na_3PO_4)

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1. General Method of Preparation:

Sodium orthophosphate is prepared by **neutralizing phosphoric acid (H_3PO_4)** with **sodium carbonate (Na_2CO_3)** or **sodium hydroxide (NaOH)**:

H3PO4+3NaOH→Na3PO4+3H2O\text{H}_3\text{PO}_4 + 3\text{NaOH} \rightarrow \text{Na}_3\text{PO}_4 + 3\text{H}_2\text{O}H3PO4+3NaOH→Na3PO4+3H2O

OR

2Na2CO3+2H3PO4→2Na3PO4+3CO2+3H2O2\text{Na}_2\text{CO}_3 + 2\text{H}_3\text{PO}_4 \rightarrow 2\text{Na}_3\text{PO}_4 + 3\text{CO}_2 + 3\text{H}_2\text{O}2Na2CO3+2H3PO4→2Na3PO4+3CO2+3H2O

The product is purified by crystallization.

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2. Assay Method:

- It is assayed **gravimetrically** or by **complexometric titration**.
- One method involves precipitation of magnesium ammonium phosphate and weighing the residue after ignition.
- Alternative titration method involves **acid-base titration** after hydrolysis.

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3. Properties:

- White, crystalline powder
- Hygroscopic in nature
- Freely soluble in water, insoluble in alcohol
- Alkaline in nature due to hydrolysis in water

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4. Medicinal Uses:

- Used as a **saline cathartic**
- Employed in **enemas** and **bowel cleansing** before diagnostic procedures
- Sometimes used as a **buffering agent** in pharmaceutical formulations
- In combination with sodium biphosphate in **oral phosphates** for colon cleansing

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9. Kaolin

1. General Method of Preparation:

Kaolin is a **naturally occurring hydrated aluminum silicate** clay. It is obtained from natural deposits and purified by washing with water to remove impurities like sand, iron oxide, and other soluble salts.

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2. Assay Method:

Kaolin is **not assayed by conventional titration methods** due to its **insolubility** and **inorganic nature**. However, it is standardized for **fineness, adsorptive power**, and **purity** as per pharmacopoeial specifications.

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3. Properties:

- Fine, white to greyish-white powder
- Odorless and tasteless
- Insoluble in water and organic solvents
- Chemically inert and non-toxic

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4. Medicinal Uses:

- Acts as an **adsorbent** and **protective agent** in gastrointestinal disturbances like **diarrhea**
- Formerly used in **anti-diarrheal mixtures** (now less common due to more effective alternatives)
- Used externally in **dusting powders** for skin protection and to absorb moisture
- Used as a **diluent** or **base** in pharmaceutical preparations such as **calamine lotion**

10. Bentonite

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1. General Method of Preparation:

Bentonite is a **naturally occurring colloidal hydrated aluminum silicate** derived from **volcanic ash**. It is purified by suspending it in water, decanting off impurities, drying, and milling the remaining sediment into a fine powder.

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2. Assay Method:

- Bentonite is not assayed by conventional titrimetric methods.
- It is evaluated based on **swelling index**, **viscosity**, **adsorptive power**, and **pH**.
- Quality parameters such as **grittiness**, **fineness**, and **gel-forming ability** are important as per pharmacopoeial standards.

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3. Properties:

- Greyish-white or cream-colored, odorless fine powder
- Swells significantly in water to form a gel-like mass
- Insoluble in water and organic solvents
- pH is slightly alkaline

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4. Medicinal Uses:

- Acts as a **suspending agent** and **emulsifying agent** in pharmaceutical formulations
- Used as a **bulk-forming laxative**
- Applied externally as **protective** and **absorbent** in pastes and poultices
- Has **adsorbent** properties and can absorb toxins and bacteria in the GIT

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11. Potassium Permanganate ($KMnO_4$)

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1. General Method of Preparation:

Prepared by **oxidation of manganese dioxide (MnO_2)** in an **alkaline medium (KOH)** with **air or potassium nitrate**, forming potassium manganate (K_2MnO_4), which is then **disproportionated** upon boiling or acidification:

$3K2MnO4+2H2O \rightarrow 2KMnO4+MnO2\downarrow+4KOH$

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2. Assay Method:

- Assayed by **redox titration**.
- A known amount is titrated with a standard solution of **oxalic acid** or **sodium thiosulphate** under acidic conditions.
- Acts as a **self-indicator** (deep purple color disappears upon reduction).

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3. Properties:

- Dark purple, crystalline powder
- Odorless, has a metallic, sweetish taste
- Freely soluble in water forming a deep purple solution
- Powerful oxidizing agent, especially in acidic medium

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4. Medicinal Uses:

- Used as a **topical antiseptic** and disinfectant (0.01% to 0.1% solution)
- Employed in treatment of **wounds, ulcers**, and **fungal infections**
- Used in **gargles** and **douches** at low concentrations
- Acts by **oxidizing bacterial cell components**

12. Boric Acid (H_3BO_3)

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1. General Method of Preparation:

Prepared by **acidifying borax (sodium tetraborate)** with **hydrochloric acid** or **sulfuric acid**:

$Na2B4O7+2HCl+5H2O \rightarrow 4H3BO3+2NaCl$

The solution is filtered and cooled to crystallize **boric acid**.

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2. Assay Method:

- Assayed by **acid-base titration** using **mannitol** as a complexing agent to enhance the acidity of boric acid.
- The titration is carried out with **standard NaOH** using **phenolphthalein** as the indicator.

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3. Properties:

- White, crystalline, or granular powder
- Odorless with a slightly bitter taste
- Slightly soluble in cold water, more soluble in hot water and glycerin
- Weak monobasic acid (acts as a Lewis acid)
- pH ~ 5.0 in aqueous solution

4. Medicinal Uses:

- Used as a **mild antiseptic** and **antifungal** agent in eye washes, mouth rinses, and skin lotions
- Used in **dusting powders**, **ointments**, and **creams**
- Employed in **buffering** ophthalmic and otic solutions
- Overdose or prolonged use may cause **toxicity**, especially in infants

13. Hydrogen Peroxide (H_2O_2)

1. General Method of Preparation:

Industrially prepared by the **anthraquinone process** or by **acidifying barium peroxide** with sulfuric acid:

$BaO2+H2SO4 \rightarrow BaSO4\downarrow+H2O2$

2. Assay Method:

- Assayed by **permanganate titration** in acidic medium.
- $KMnO_4$ acts as an oxidizing agent and oxidizes H_2O_2 to oxygen.
- Endpoint: **Pink color** persists due to unreacted $KMnO_4$.

$5H2O2+2KMnO4+3H2SO4 \rightarrow 2MnSO4+K2SO4+8H2O+5O25$

3. Properties:

- Colorless, clear liquid with a slightly acidic taste
- Miscible with water in all proportions
- Decomposes on exposure to light or heat, releasing oxygen
- Stabilizers (e.g., sodium stannate) are added to prevent decomposition

4. Medicinal Uses:

- Used as a **mild antiseptic** and **disinfectant** (3% solution)
- Applied to clean wounds, ulcers, and mouth infections
- Used in ear drops and **tooth whitening preparations**
- Higher concentrations used in laboratory or industrial disinfection

14. Chlorinated Lime ($Ca(OCl)Cl \cdot H_2O$)

Also known as **Bleaching Powder**

1. General Method of Preparation:

Chlorinated lime is prepared by **passing chlorine gas over dry slaked lime ($Ca(OH)_2$):**

$Ca(OH)2+Cl2 \rightarrow Ca(OCl)Cl+H2O$

This reaction yields a **mixture of calcium hypochlorite and calcium chloride** with water of hydration.

2. Assay Method:

- Assayed by **iodometric titration**.
- The available chlorine content is determined by reaction with **potassium iodide** in acidic medium, liberating iodine, which is titrated against **standard sodium thiosulphate**:

$Cl2+2KI \rightarrow 2KCl+I2$

$I_2+2Na_2S_2O_3 \rightarrow 2NaI+Na_2S_4O_6$

3. Properties:

- White or grayish-white powder with a **chlorine-like odor**
- Decomposes on exposure to air and light
- Slightly soluble in water
- Strong oxidizing and bleaching agent

4. Medicinal Uses:

- Used as a **disinfectant** for water, hospital floors, and equipment
- Employed in **sanitation** during epidemics
- Acts by **liberating nascent oxygen and chlorine**
- Useful in **sterilizing surfaces, wounds**, and **treating infections**

15. Iodine and Its Preparations

1. General Method of Preparation:

Iodine is extracted from **natural brine** or **seaweed ashes**. It is liberated by oxidation of iodide salts (e.g., sodium iodide) using oxidizing agents like chlorine:

$2NaI+Cl2 \rightarrow 2NaCl+I2\downarrow$

2. Assay Method:

- Assayed by **iodometric titration**.
- Iodine is titrated with **standard sodium thiosulphate** using **starch** as the indicator.

- The endpoint is the **disappearance of blue color**.

3. Properties:

- Shiny, violet-black crystals with a characteristic **pungent odor**
- Slightly soluble in water, more soluble in alcohol and potassium iodide solution
- Volatile and sublimes easily

4. Medicinal Uses:

- Used as a **topical antiseptic** in tincture or povidone-iodine forms
- Effective against **bacteria, fungi, viruses**, and **spores**
- Iodine preparations:
    - **Tincture of Iodine** (Iodine in alcohol)
    - **Lugol's Iodine** (Aqueous solution with potassium iodide)
    - **Povidone-Iodine** (Iodine complexed with povidone for sustained release)

16. Potassium Iodide (KI)

1. General Method of Preparation:

Prepared by **reacting iodine with hot concentrated potassium hydroxide**, followed by crystallization:

$3I_2+6KOH \rightarrow 5KI+KIO_3+3H_2O$

Then, potassium iodide is purified by **recrystallization**.

2. Assay Method:

- Assayed **iodometrically** by titrating with **standard potassium iodate (KIO_3)** in presence of **acid**, which liberates iodine.
- The liberated iodine is titrated with **sodium thiosulphate** using **starch** as indicator.

3. Properties:

- White crystalline powder, **odorless** and **salty in taste**
- Freely soluble in water and glycerin
- Sensitive to air and light (may oxidize to iodine)
- Has good **stability in dry air**, but not in moist conditions

4. Medicinal Uses:

- Acts as an **expectorant** (enhances respiratory secretion)

- Used as an **iodine supplement** to prevent **goiter**
- Component of **Lugol's solution** for thyroid conditions
- Also used in **radioactive iodine prophylaxis** during nuclear exposure

17. Ammonium Chloride (NH_4Cl)

1. General Method of Preparation:

Prepared by **neutralizing ammonia** with **hydrochloric acid**:

$NH3+HCl \rightarrow NH4Cl$

The solution is crystallized and dried to obtain **ammonium chloride**.

2. Assay Method:

- Assayed by **acid-base titration**:
- Sample is dissolved in water and titrated with **standard NaOH** using **methyl red** as an indicator.
- Ammonia is liberated and titrated:

$NH4^{+}+OH^{-} \rightarrow NH3\uparrow+H2O$

3. Properties:

- White crystalline powder or granules
- Odorless, **cooling saline taste**
- Soluble in water, slightly soluble in alcohol
- Slightly **acidic** solution in water

4. Medicinal Uses:

- Used as an **expectorant** (lowers surface tension of respiratory secretions)
- Acts as a **systemic acidifier** and **diuretic**
- Occasionally used as a **component in cough syrups**
- Also used in **urinary acidification**

18. Copper Sulphate ($CuSO_4 \cdot 5H_2O$)

Also known as **Blue Vitriol**

1. General Method of Preparation:

Prepared by **dissolving copper metal** in **dilute sulfuric acid** with the help of an oxidizing agent like nitric acid or air:

Cu+2H2SO4→CuSO4+SO2+2H2O\text{Cu} + 2\text{H}_2\text{SO}_4 \rightarrow \text{CuSO}_4 + \text{SO}_2 + 2\text{H}_2\text{O}Cu+2H2SO4→CuSO4+SO2+2H2O

Alternatively:

CuO+H2SO4→CuSO4+H2O\text{CuO} + \text{H}_2\text{SO}_4 \rightarrow \text{CuSO}_4 + \text{H}_2\text{O}CuO+H2SO4→CuSO4+H2O

The solution is concentrated and allowed to crystallize to obtain **$CuSO_4 \cdot 5H_2O$**.

2. Assay Method:

- Assayed by **iodometric titration**.
- Copper(II) ions oxidize iodide to iodine, which is then titrated with **sodium thiosulphate**:

2Cu2++4I−→2CuI↓+I2

$6I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S\text{-}O_6$

3. Properties:

- Blue crystalline powder
- Efflorescent in dry air
- Soluble in water, slightly soluble in alcohol
- Turns white on heating (due to loss of water of crystallization)

4. Medicinal Uses:

- Used as an **emetic** (induces vomiting, though rarely used now)
- Also used **externally** as an **astringent** and **antiseptic**
- Employed in **veterinary medicine** for parasitic infections

19. Sodium Potassium Tartrate ($KNaC_4H_4O_6 \cdot 4H_2O$)

Also known as **Rochelle Salt**

1. General Method of Preparation:

Prepared by **neutralizing tartaric acid** with equimolar quantities of **sodium carbonate** and **potassium carbonate**, then crystallizing:

C4H6O6+Na2CO3+K2CO3→KNaC4H4O6+2CO2+2H2O

2. Assay Method:

- Assayed by **complexometric titration** with **EDTA**, where calcium or magnesium is displaced from the tartrate complex.
- Endpoint detected using **Eriochrome Black T**.

3. Properties:

- Colorless or white, efflorescent crystals
- Slightly alkaline in nature
- Soluble in water, insoluble in alcohol
- Forms a **complexing agent** with metal ions

4. Medicinal Uses:

- Used as a **mild saline cathartic (laxative)**
- Acts as a **sequestering agent** in complexometric titrations
- Sometimes used in **buffered solutions** for chemical reactions

20. Ferrous Sulphate ($FeSO_4 \cdot 7H_2O$)

Also known as **Green Vitriol**

1. General Method of Preparation:

Prepared by **dissolving iron filings or granules** in **dilute sulfuric acid**, followed by crystallization:

$Fe + H2SO4 \rightarrow FeSO4 + H2\uparrow$

The solution is cooled and allowed to crystallize to obtain **ferrous sulphate heptahydrate**.

2. Assay Method:

- Assayed by **redox titration** using **potassium permanganate ($KMnO_4$)** as the titrant in acidic medium.
- Reaction:

$5Fe^{2+} + MnO4^- + 8H^+ \rightarrow 5Fe^{3+} + Mn2^{+} + 4H2O5$

The pink color of $KMnO_4$ disappears at the endpoint.

3. Properties:

- Pale green crystalline powder with **metallic astringent taste**
- Efflorescent in air, oxidizes slowly to **ferric sulphate**
- Soluble in water; aqueous solution turns brown on exposure to air

4. Medicinal Uses:

- Used as a **haematinic** to treat **iron-deficiency anemia**
- Also acts as a **tonic** and general iron supplement
- Commonly used in combination with folic acid or multivitamins

21. Ferrous Gluconate ($C_{12}H_{22}FeO_{14}\cdot 2H_2O$)

1. General Method of Preparation:

Prepared by reacting **gluconic acid or sodium gluconate** with **ferrous carbonate or ferrous sulphate**, followed by purification and crystallization.

$FeCO3+2C6H11O7Na \rightarrow C12H22FeO14+Na2CO3$

2. Assay Method:

- Assayed by **complexometric titration** using **EDTA** in the presence of **ascorbic acid** to prevent oxidation of Fe^{2+} to Fe^{3+}.
- Endpoint is determined using a suitable metal indicator like **sulphosalicylic acid** or **phenanthroline**.

3. Properties:

- Yellowish to grey-green powder
- Slightly soluble in water, with **mild metallic taste**
- Less irritating to the gastrointestinal tract compared to ferrous sulphate

4. Medicinal Uses:

- Used as an **oral iron supplement** in iron-deficiency anemia
- Preferred over ferrous sulphate in patients with **gastric sensitivity**
- Also used in **pediatric formulations** and **iron tonics**

22. Sodium Thiosulphate ($Na_2S_2O_3\cdot 5H_2O$)

Also known as **Hypo**

1. General Method of Preparation:

Prepared by **boiling a solution of sodium sulphite (Na_2SO_3)** with **sulphur**:

$Na2SO3+S \rightarrow Na2S2O3$

Crystallization yields the **pentahydrate form**, $Na_2S_2O_3 \cdot 5H_2O$.

2. Assay Method:

- Assayed **iodometrically** by titrating with **iodine solution**.
- Reaction:

$2Na2S2O3+I2 \rightarrow Na2S4O6+2NaI$

Endpoint is detected using **starch indicator** which forms a blue complex with excess iodine.

3. Properties:

- Colorless crystalline powder with **cooling, saline taste**
- Soluble in water, **efflorescent** in dry air
- Decomposes on heating and in acidic medium
- Acts as a **reducing agent**

4. Medicinal Uses:

- Used as an **antidote** in **cyanide poisoning** (converts cyanide to thiocyanate)
- Acts as an **antioxidant** and **detoxifying agent**
- Employed in **iodometric titrations** as a standard reducing agent

23. Activated Charcoal (Activated Carbon)

1. General Method of Preparation:

Prepared by **carbonizing organic substances** like coconut shells or wood at high temperature, followed by **activation** using steam or carbon dioxide at ~900°C to increase surface area and porosity.

2. Assay Method:

- No standard pharmacopoeial assay.
- Quality is assessed by **adsorptive capacity tests**, such as:
    - **Decolorizing power**
    - **Adsorption of iodine or methylene blue**

3. Properties:

- Black, odorless, tasteless, fine powder

- Insoluble in water and most solvents
- Extremely **high surface area** and **porosity**
- Adsorbs a wide variety of substances

4. Medicinal Uses:

- Used as a **universal antidote** in poisoning by adsorbing toxic substances in the GIT
- Used to **reduce flatulence and bloating**
- Employed in **filtering and purification** processes in pharmaceutical and chemical industries

24. Sodium Nitrite ($NaNO_2$)

1. General Method of Preparation:

Prepared industrially by **reducing sodium nitrate ($NaNO_3$)** using heat in the presence of **lead or other reducing agents**, or by absorption of **nitrogen oxides** in alkaline solution:

NaNO3→heatNaNO2+12O2

2. Assay Method:

- Assayed by **redox titration**.
- Sodium nitrite is oxidized by **potassium permanganate ($KMnO_4$)** in acidic medium:

5NaNO2+2KMnO4+6H2SO4→5NaNO3+2MnSO4+K2SO4+3H2O

- Endpoint is the **permanent pink color** of $KMnO_4$.

3. Properties:

- White to slightly yellow crystalline powder
- Hygroscopic and soluble in water
- Mildly toxic and should be handled with care
- Acts as a **reducing agent**

4. Medicinal Uses:

- Used as an **antidote in cyanide poisoning**, often with sodium thiosulphate
- Converts hemoglobin to **methemoglobin**, which binds cyanide
- Also used as a **vasodilator** and **preservative** in some formulations (with restrictions)

25. Zinc Sulphate ($ZnSO_4 \cdot 7H_2O$)

1. General Method of Preparation:

Prepared by **dissolving zinc metal** or **zinc oxide** in **dilute sulfuric acid**, followed by crystallization:

$Zn + H_2SO_4 \rightarrow ZnSO_4 + H_2\uparrow$

Or

$ZnO + H_2SO_4 \rightarrow ZnSO_4 + H_2O$

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2. Assay Method:

- Assayed by **complexometric titration** with **EDTA**, using **Eriochrome Black T** as indicator in a buffered solution:

$Zn^{2+} + EDTA^{4-} \rightarrow [Zn\text{–}EDTA]^{2-}$

3. Properties:

- Colorless or white crystalline powder
- Soluble in water, insoluble in alcohol
- Astringent and metallic taste
- Efflorescent on exposure to air

4. Medicinal Uses:

- Used as an **astringent** and **antiseptic**
- Commonly used in **eye drops and lotions**
- Also used as a **nutritional supplement** in zinc deficiency