Noteskarts
Smart Notes, Bright Future

B.PHARM SEMESTER I

# Pharmaceutical Inorganic and Analytical Chemistry

(Course Code: BP106T)

◆ ◆ ◆

## UNIT V

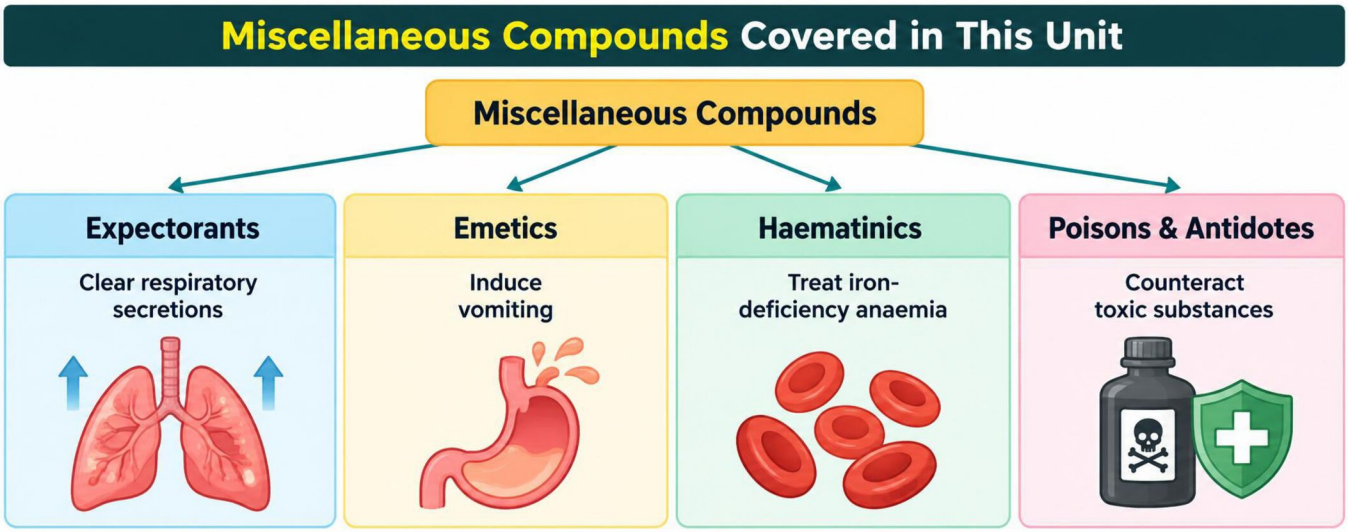
*Miscellaneous Compounds*

**SHORT NOTES**

Condensed Study Notes for Quick Revision (PCI Syllabus, NEP 2020)

**www.noteskarts.com**

Short notes for Unit V, covering expectorants, emetics, haematinics, and poison/antidote. Condensed bullets, tables and key diagrams for fast revision.



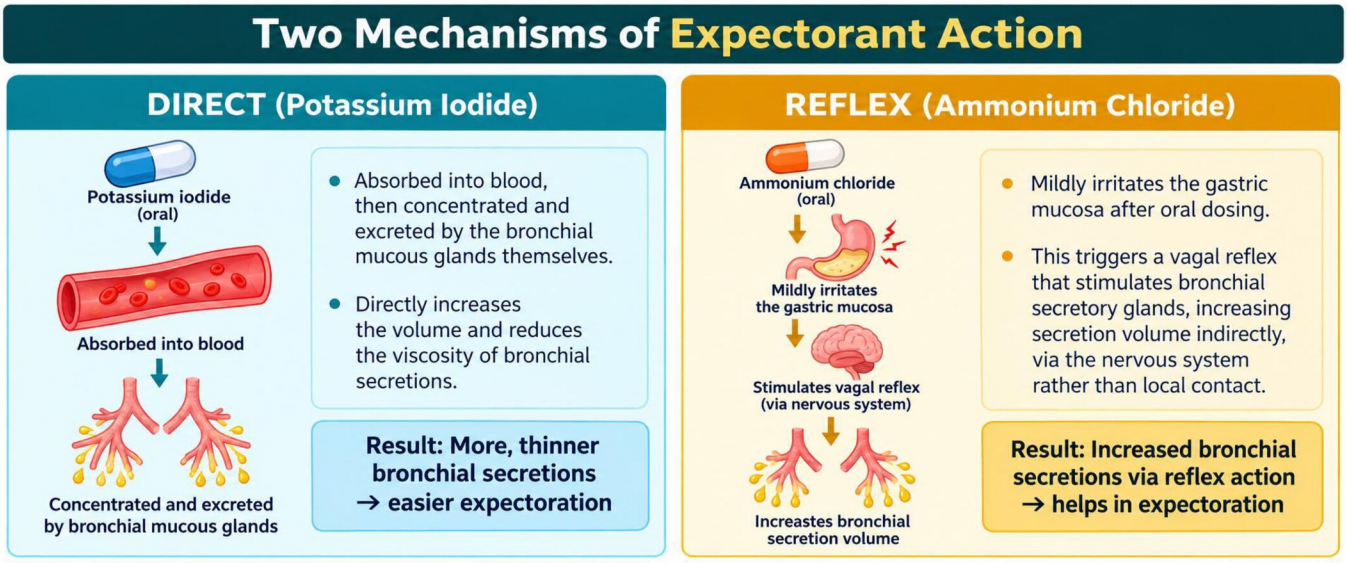

*The four groups of compounds covered in this unit*

## 5.1 Expectorants

# 5.1 Expectorants



- **Expectorants** are drugs that help in the **removal of mucus and respiratory secretions** from the airways.
- They make thick and sticky mucus **easier to cough up**, thereby helping to clear the respiratory tract.
- They may act by:
  - **Increasing the volume of respiratory secretions**, making mucus more dilute.
  - **Reducing the viscosity of mucus**, making it less thick and easier to expel.
- Expectorants are mainly used for the symptomatic relief of **productive (wet) cough**, in which mucus or phlegm is present.
- They may be useful in conditions such as:
  - **Common cold**
  - **Acute bronchitis**
  - Other respiratory conditions associated with **thick or retained secretions**
- Expectorants generally **do not suppress the cough reflex**. Instead, they help make coughing more effective by facilitating the removal of mucus.




*The two mechanisms of expectorant action*

## Potassium Iodide

- **Potassium iodide (KI)** is a **direct-acting expectorant** used to help loosen and clear thick respiratory secretions.

**ADVERSE EFFECTS**

Iodism: metallic taste, coryza, salivation, skin eruptions.

Thyroid dysfunction: Wolff-Chaikoff effect (hypothyroidism) or Jod-Basedow phenomenon (hyperthyroidism in susceptible patients).

Avoided in pregnancy (crosses placenta, affects fetal thyroid) and known thyroid disease.



### Precautions

- Use requires caution in patients with **known thyroid disease**.
- Potassium iodide is generally avoided during **pregnancy unless specifically indicated**, because iodide crosses the placenta and can affect fetal thyroid function.
- Medical supervision is important when KI is used for prolonged periods or at high doses.

### Other Important Uses

- **Thyroid blocking during a radioactive iodine emergency:**
  - A large dose of stable potassium iodide saturates the thyroid's iodine-uptake mechanism.
  - This reduces the uptake of **radioactive iodine-131 ($^{131}I$)** by the thyroid.
  - It is used only when recommended by appropriate public-health or radiation-safety authorities.

### Preparations

- Available as:
  - **Saturated solution of potassium iodide (SSKI)**
  - Tablets
  - Syrups

- KI has a **strong salty/metallic taste**, which is often masked with flavouring.

### Stability

- KI solutions may slowly release **free iodine** during prolonged storage or exposure to light.
- Formation of free iodine may cause the solution to become **yellow to brown**, indicating possible degradation.

### ▸ Classification of Expectorants

Expectorants can be classified according to **how they help in the removal of respiratory mucus**:

1. **Direct Expectorants**
   - Act **after systemic absorption**.
   - The drug or its active ion is excreted through the **bronchial glands**.
   - It directly stimulates bronchial secretion and helps make mucus easier to expel.
   - **Example:** Potassium iodide (KI).
2. **Reflex (Indirect) Expectorants**
   - Act through a **reflex mechanism**, usually after irritating the gastric mucosa.
   - Gastric stimulation produces a reflex increase in **bronchial secretion**.
   - The drug does **not need to reach the bronchial tree directly**.
   - **Example:** Ammonium chloride ($NH_4Cl$).
3. **Mucolytics**
   - A related but **distinct class** of respiratory medicines.
   - They do not primarily increase the volume of respiratory secretions.
   - Instead, they **break down or disrupt mucus glycoprotein structure**, reducing mucus viscosity.
   - This makes thick mucus easier to cough up.
   - **Examples:** Bromhexine and N-acetylcysteine (NAC).



## Ammonium Chloride

Ammonium chloride is a reflex expectorant. Taken orally, it mildly irritates the gastric mucosa, and this local gastric irritation triggers a vagal reflex that stimulates secretion from the bronchial glands, increasing the volume of respiratory secretions indirectly, through the nervous system, rather than by any direct local action on the airway itself. It also has a mild systemic acidifying action once absorbed: the ammonium ion is converted to urea in the liver, and the chloride ion is left associated with hydrogen ion, contributing a small acid load.

**PRECAUTIONS**

Used cautiously in hepatic impairment (impaired urea formation → ammonia accumulation) and renal impairment (impaired acid excretion → systemic acidosis).

Excessive doses can themselves produce systemic (hyperchloraemic) metabolic acidosis.

| Feature | Potassium Iodide | Ammonium Chloride |
|---|---|---|
| Mechanism | Direct (bronchial glands) | Reflex (gastric irritation → vagal reflex) |
| Key risk | Iodism; thyroid dysfunction | Systemic acidosis |
| Avoided in | Thyroid disease, pregnancy | Hepatic/renal impairment |

**WORKED EXAMPLE — AMMONIUM CHLORIDE ACID LOAD**

A dose contains 250 mg $NH_4Cl$ (mol. wt. 53.5). Estimate the acid load.

Moles = 250/53.5 = 4.67 mmol → acid load ≈ 4.67 mEq (small at recommended doses).

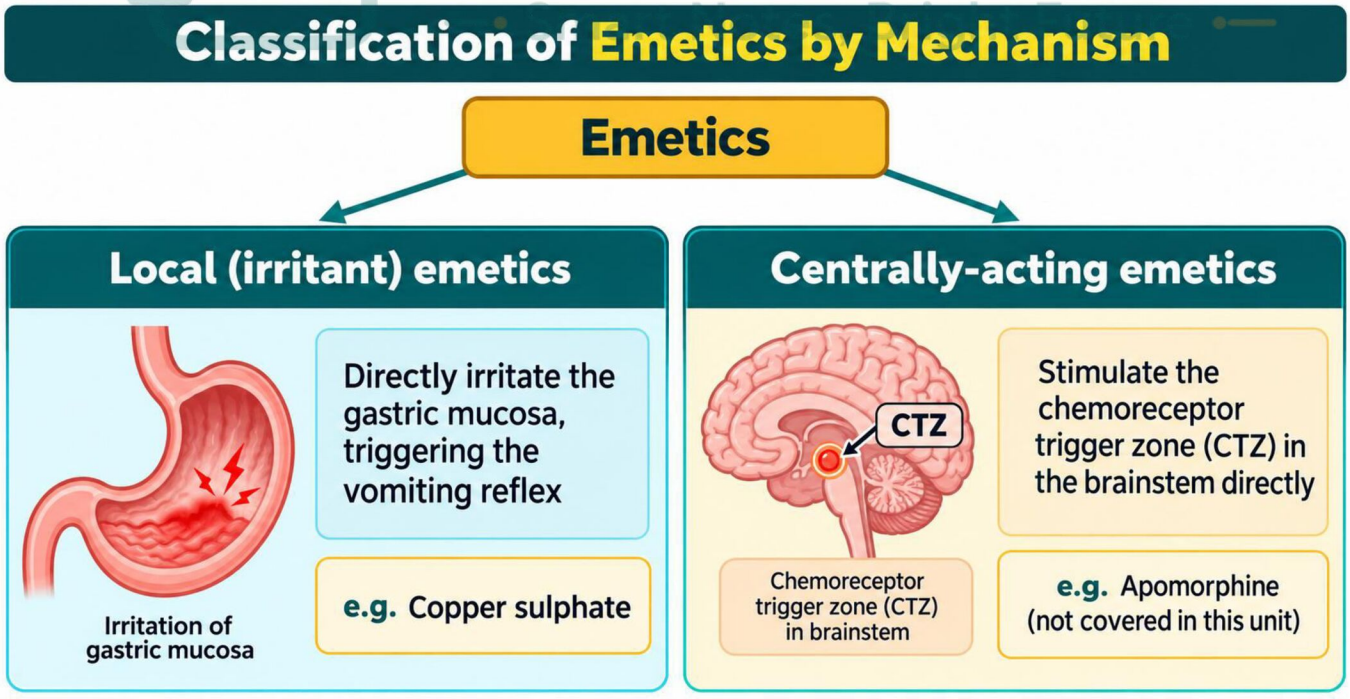
- Additional uses: historically a diagnostic acid-loading test for renal tubular acidosis; sometimes included in urinary antiseptic combinations for the urine-acidifying effect.

## 5.2 Emetics

- **Emetics** are substances or drugs that **induce vomiting**.
- They were historically used to remove **ingested poisons or toxic substances** from the stomach.
- Their action is mainly based on stimulation of the **vomiting centre** either directly or indirectly.

### Classification of Emetics

1. **Local (Irritant) Emetics**
   - Act directly on the **gastric mucosa**.
   - Irritation of the stomach triggers a **reflex pathway** to the vomiting centre.
   - This results in **nausea and vomiting**.
2. **Centrally Acting Emetics**
   - Act directly on the **chemoreceptor trigger zone (CTZ)** in the brainstem.
   - Stimulation of the CTZ activates the **vomiting centre**, producing vomiting.
   - **Example:** Apomorphine.
   - Apomorphine is a **dopamine receptor agonist** that stimulates the CTZ without requiring direct irritation of the gastrointestinal tract.




*Classification of emetics by mechanism*

## Copper Sulphate

- **Copper sulphate** is a **classic local irritant emetic**.
- It acts by **irritating the gastric mucosa**, producing a reflex that induces vomiting.
- It is now **largely obsolete as a therapeutic emetic**.

### Why Copper Sulphate Is Rarely Used Today

- Copper is **toxic in excessive amounts** and may cause copper poisoning if vomiting is delayed.
- Induced vomiting can cause **aspiration** of stomach contents into the lungs.
- With **corrosive poisons**, vomiting may cause repeated exposure of the oesophagus and mouth to the corrosive substance.
- Vomiting usually results in only **partial removal of the ingested poison**.
- Modern poisoning management generally focuses on **supportive care and poison-specific treatment**, with activated charcoal used in selected cases when appropriate.

### Other Historical Emetic — Ipecacuanha

- **Ipecacuanha (ipecac)** is another historical emetic.
- Its active alkaloids include **emetine and cephaeline**.
- It produces vomiting through a combination of:
  - **Local gastric irritation**
  - **Central stimulation of the vomiting pathway**
- It is **no longer recommended for routine home management of poisoning**.

### Present-Day Importance of Copper Sulphate

- Copper sulphate is more important today as:
  - A **laboratory reagent**
  - An **agricultural fungicide**
- It is therefore **not considered a routine therapeutic emetic**.



## Sodium Potassium Tartrate

- **Sodium potassium tartrate** is primarily used as a **saline laxative**.
- At excessive doses, gastrointestinal **irritation and distension** may produce vomiting.
- However, this is an **adverse effect rather than its intended emetic mechanism**.

### Seidlitz Powder

- Sodium potassium tartrate is a key ingredient of the historical **Seidlitz powder**.
- Seidlitz powder contains:
  - **Sodium potassium tartrate**
  - **Sodium bicarbonate**
  - **Tartaric acid**
- It produces an **effervescent preparation** and was historically used as a laxative.

## Gastric Decontamination Methods Compared

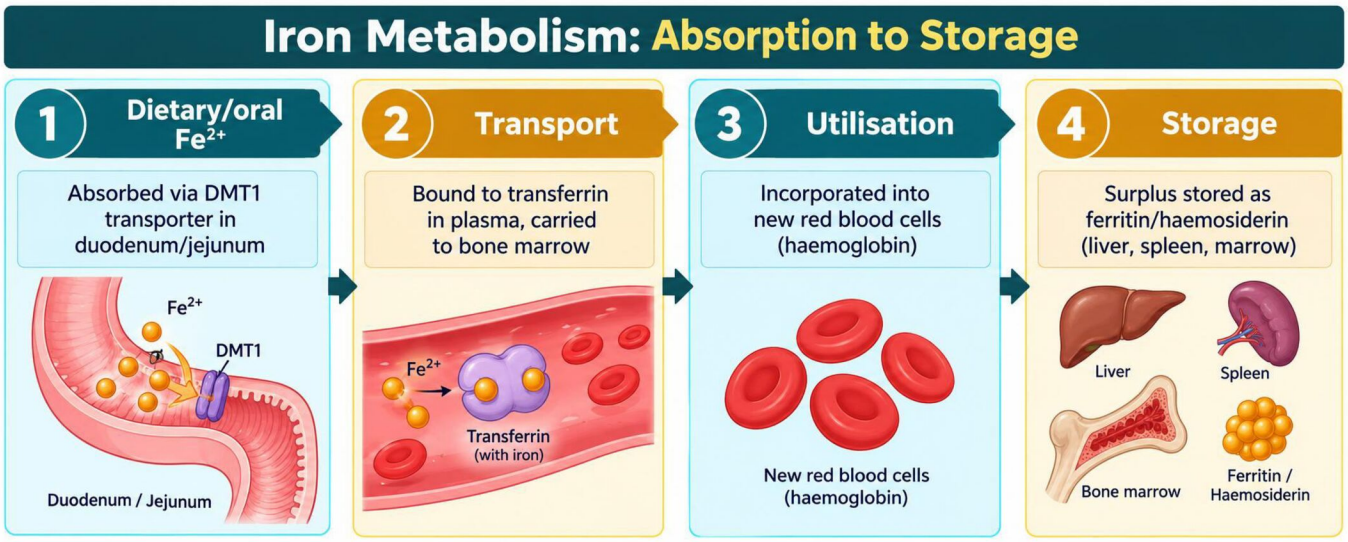
| Method | Principle | Current Status |
|---|---|---|
| Induced emesis | Trigger vomiting to expel stomach contents | Largely abandoned |
| Gastric lavage | Mechanically wash out stomach contents | Reserved for specific, high-risk cases |
| Activated charcoal | Adsorb poison onto charcoal surface in gut | First-line for many oral poisonings |
| Whole bowel irrigation | Flush GI tract with electrolyte solution | Iron, lithium (charcoal-resistant poisons) |

## 5.3 Haematinics

- **Haematinics** are substances that **promote the formation of haemoglobin and red blood cells (RBCs)**.
- They are mainly used in the **prevention and treatment of anaemia**, especially iron-deficiency anaemia.

### Iron Absorption and Metabolism

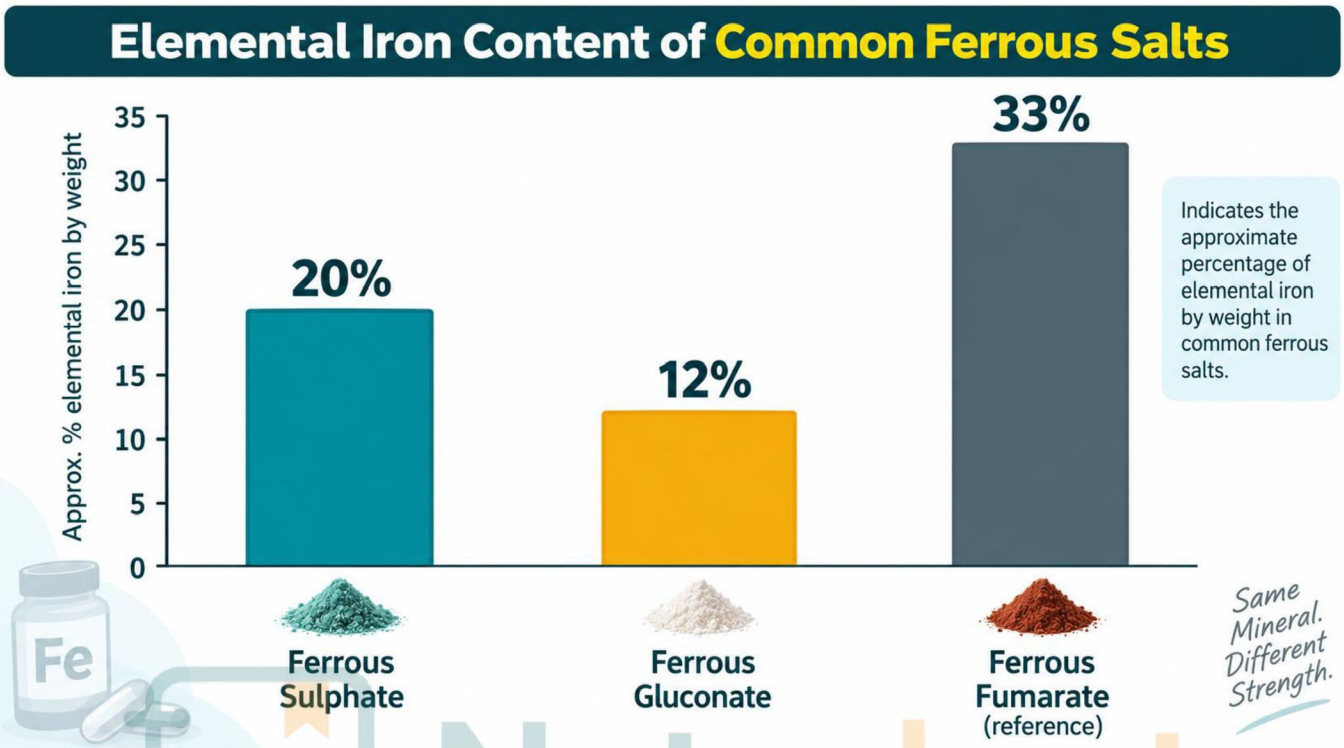
- **Ferrous iron ($Fe^{2+}$)** is absorbed **better than ferric iron ($Fe^{3+}$)**.
- Iron is absorbed mainly from the **duodenum and upper jejunum**.
- Absorption occurs through the **DMT1 (divalent metal transporter 1)**.
- After absorption, iron enters the blood and binds to **transferrin**.
- Transferrin transports iron mainly to the **bone marrow**.
- In the bone marrow, iron is incorporated into **haemoglobin** during RBC formation.
- Excess iron is stored as:
  - **Ferritin** – readily available storage form.
  - **Haemosiderin** – longer-term storage form.
- Major storage sites include the **liver, spleen, and bone marrow**.




*The path of iron from absorption to storage*

- Absorbed iron is carried by transferrin to the bone marrow; surplus stored as ferritin/haemosiderin (liver, spleen, marrow).

## Ferrous Sulphate and Ferrous Gluconate




*Elemental iron content of common ferrous salts*

- **Ferrous sulphate ($FeSO_4$)**
  - Contains approximately **20% elemental iron**.
  - Commonly used as a **standard oral iron supplement**.
  - Relatively **inexpensive**.
  - May cause **gastrointestinal side effects** such as nausea, abdominal discomfort, constipation, or diarrhoea.
  - **Black stools** are common during iron therapy.
- **Ferrous gluconate**
  - Contains approximately **12% elemental iron**.
  - Provides less elemental iron per unit weight than ferrous sulphate.
  - May be **better tolerated gastrointestinally** in some patients.

| Salt | Approx. Elemental Fe | Notes |
|---|---|---|
| Ferrous sulphate | ~20% | Reference standard; cheapest; GI upset common; black stools |
| Ferrous gluconate | ~12% | Often better GI tolerability |

**WORKED EXAMPLE — ELEMENTAL IRON**

325 mg ferrous sulphate tablet (~20% elemental Fe). Elemental iron per tablet?

325 × 0.20 = 65 mg elemental iron

| Salt | Approx. Elemental Fe | Notes |
|---|---|---|

**WORKED EXAMPLE — COMPARING EQUIVALENT DOSES**

Need 130 mg elemental Fe/day. Ferrous sulphate tablets: 325 mg (~65 mg Fe each). Ferrous gluconate tablets: 300 mg (~36 mg Fe each).

Ferrous sulphate: 130/65 = 2 tablets. Ferrous gluconate: 130/36 ≈ 3.6, so 4 tablets needed.

## Counselling and Safety

- **Take on an empty stomach** with water for best absorption.
  - Vitamin C can improve iron absorption.
  - If stomach upset occurs, take it **with food**.
- **Avoid tea and coffee** around the time of iron administration because they can reduce iron absorption.
- **Avoid calcium-containing products** such as milk, dairy products, and calcium-containing antacids near the iron dose.
- **Continue treatment after haemoglobin normalises** to replenish the body's iron stores, as advised by the healthcare professional.
- **Monitor treatment response:**
  - Reticulocyte count may begin to rise within about **1 week**.
  - Haemoglobin should subsequently show a measurable rise.
  - A **repeat blood count after 2–4 weeks** can help assess response.

| Interacting Substance | Effect | Advice |
|---|---|---|
| Tetracycline/quinolones | Iron reduces antibiotic absorption | Separate by ≥2 hours |
| Levothyroxine | Iron reduces absorption | Separate by ≥4 hours |
| Antacids (Al/Mg/Ca) | Reduce iron absorption | Separate by 1–2 hours |
| Vitamin C | Increases absorption | Can take together |

**IRON OVERDOSE — A SERIOUS PAEDIATRIC RISK**

Corrosive to the GI tract; toxic to liver and heart once absorbed.

Can present in deceptively distinct phases: early GI symptoms, an apparent quiet recovery period, then a later, potentially severe shock/acidosis phase.

Iron tablets are a leading cause of accidental fatal poisoning in young children historically — child-resistant packaging is essential.

- Other haematinics for context: Vitamin B12 and folic acid deficiency cause megaloblastic (macrocytic) anaemia, distinct from iron-deficiency (microcytic) anaemia — treating the wrong deficiency doesn't correct the underlying problem.
- Parenteral (IV) iron is used when oral iron is not tolerated, not absorbed adequately, or replenishment is needed faster than oral therapy allows.

| Compound | Typical Regulatory Status |
|---|---|
| Potassium iodide | Generally available; special stockpiling regulations for emergency use |

| Compound | Typical Regulatory Status |
|---|---|
| Ferrous sulphate/gluconate | Generally available; child-resistant packaging (paediatric poisoning risk) |
| Sodium thiosulphate | Available as reagent and hospital antidote kit stock item |

# 5.4 Poison and Antidote

## Definition

- **Poison:** Any substance that can cause **harm, illness, or death** when absorbed or introduced into the body in a sufficient amount.
- **Antidote:** A substance that **counteracts the toxic effects of a poison** by neutralising it, reducing its absorption, increasing its elimination, or opposing its physiological effects.

**Imp principle: "The dose makes the poison."** Almost any substance can become harmful at a sufficiently high dose.

## Basic Toxicology Principles

- **$LD_{50}$ (Median Lethal Dose):**
  - The dose of a substance expected to cause death in **50% of a test population**.
  - Used as a measure of **acute toxicity**.
- **Therapeutic Index (TI):**
  - Indicates the safety margin between an effective dose and a toxic dose.
  - **Narrow therapeutic index → greater risk of toxicity or overdose.**
- **Acute Toxicity:**
  - Results from a **single or short-term exposure**, usually involving a relatively large dose.
- **Chronic Toxicity:**
  - Results from **repeated or prolonged exposure** to smaller amounts of a substance.

1. **Resuscitation and stabilisation (ABC)**
   - **A – Airway**
   - **B – Breathing**
   - **C – Circulation**
2. **Decontamination**
   - Prevent further absorption where appropriate.
   - Example: **activated charcoal** for selected oral poisonings.
3. **Enhanced elimination**
   - Used only for selected poisons.
   - Examples include **urinary alkalinisation** and **haemodialysis**.
4. **Specific antidote**
   - Administered when an appropriate antidote is available.
5. **Supportive care**
   - Maintain vital functions and manage complications until the poison is eliminated.

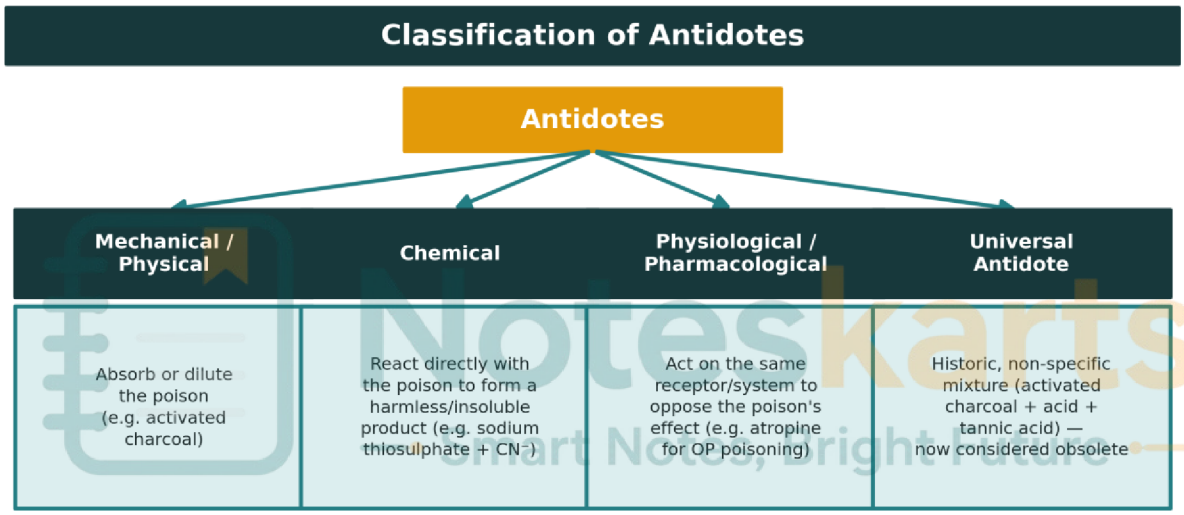
## Enhanced Elimination

- **Urinary alkalinisation:** Increases renal excretion of certain weakly acidic poisons through **ion trapping**.

- **Dialysis:** Can directly remove certain toxins from the blood when the poison has suitable physicochemical properties.

| Route | Example | Key Management Consideration |
|---|---|---|
| Ingestion (oral) | Most drug overdoses | Activated charcoal may still help if given promptly |
| Inhalation | Carbon monoxide, cyanide | Remove from exposure; oxygen; supportive care |
| Dermal (skin contact) | Organophosphate pesticides | Decontaminate skin (remove clothing, irrigate) promptly |
| Parenteral (injection) | Drug overdose by injection | No decontamination possible; supportive care/antidote only |

## Classification of Antidotes




*Classification of antidotes*

| Antidote Class | Mechanism | Example |
|---|---|---|
| Mechanical/Physical | Adsorbs/dilutes poison | Activated charcoal |
| Chemical | Reacts to form harmless product | Sodium thiosulphate + $CN^-$ |
| Physiological | Opposes effect via same receptor/system | Atropine (organophosphate poisoning) |
| Universal (obsolete) | Non-specific historic mixture | Charcoal + MgO + tannic acid |

- Activated charcoal works best within ~1 hour of ingestion; poor for small water-soluble ions (iron, lithium, cyanide) and alcohols.
- A chemical antidote's effectiveness follows the same reaction stoichiometry principle as a titration calculation (Unit III) — the same quantitative reasoning applies whether measuring an analyte or detoxifying a poison.
- Physiological antidotes don't remove the poison — atropine may need continued/repeated dosing until the organophosphate is metabolised, sometimes with pralidoxime (reactivates the inhibited enzyme).

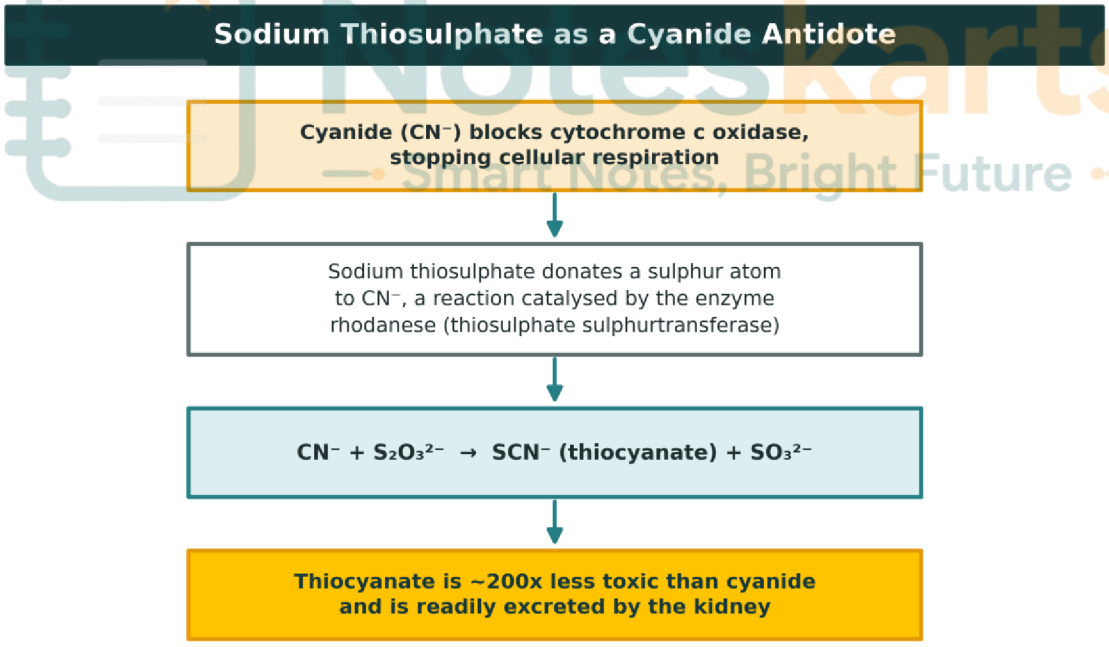
**COMMON MISTAKE**

Assuming any "antidote" works by neutralising the poison chemically overlooks the physiological antidote category entirely — atropine does not react with organophosphate molecules at all.

## Common Poison–Antidote Pairs

| Poison | Antidote | Class |
|---|---|---|
| Paracetamol overdose | N-acetylcysteine | Chemical |
| Opioid overdose | Naloxone | Physiological |
| Benzodiazepine overdose | Flumazenil | Physiological |
| Organophosphate/pesticide | Atropine + pralidoxime | Physiological + chemical |
| Iron overdose | Desferrioxamine | Chemical (chelating agent) |
| Heavy metal poisoning | Dimercaprol / EDTA | Chemical (chelating agents) |
| Cyanide | Sodium thiosulphate ± nitrite/hydroxocobalamin | Chemical |

## Sodium Thiosulphate — Cyanide Antidote




*How sodium thiosulphate detoxifies cyanide*

- $CN^-$ blocks cytochrome c oxidase, halting cellular respiration.
- $CN^- + S_2O_3^{2-} \rightarrow SCN^-$ (thiocyanate) + $SO_3^{2-}$, catalysed by rhodanese (thiosulphate sulphurtransferase).
- Thiocyanate is ~200× less toxic than cyanide and is renally excreted.
- Often combined with sodium nitrite (induces methaemoglobinaemia, pulling $CN^-$ off cytochrome oxidase) or newer hydroxocobalamin (binds $CN^-$ directly → vitamin B12).

**WORKED EXAMPLE — REACTION STOICHIOMETRY**

How many grams of $Na_2S_2O_3$ (158) are needed to detoxify 0.5 g $CN^-$ (26), 1:1 reaction?

Moles $CN^-$ = 0.5/26 = 0.0192 mol; Weight $Na_2S_2O_3$ = 0.0192 × 158 = 3.04 g (theoretical minimum; clinical doses are given in excess).

- Cyanide exposure sources beyond deliberate poisoning: smoke inhalation (burning synthetic materials), sodium nitroprusside infusion (releases $CN^-$ as a by-product), amygdalin in apricot kernels/bitter almonds/cassava.

### ▸ Recognising Common Poisoning Syndromes

| Toxidrome | Key Signs | Likely Poison |
|---|---|---|
| Cholinergic | Salivation, small pupils, bradycardia | Organophosphates — atropine |
| Cyanide toxicity | Rapid unconsciousness, cherry-red skin | Cyanide — thiosulphate |
| Iron overdose (early) | Vomiting, diarrhoea, abdominal pain | Iron salts |
| Opioid | Small pupils, slow breathing | Opioids — naloxone |

### ▸ Key Terms — Unit V

| Term | Meaning |
|---|---|
| Expectorant | Agent that increases/thins respiratory secretions |
| Haematinic | Agent promoting haemoglobin/RBC formation |
| Chemical antidote | Reacts directly with the poison to form a less toxic product |
| Physiological antidote | Opposes a poison's effect without reacting with it chemically |
| Toxidrome | Recognisable cluster of signs/symptoms pointing to a poison class |