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# Pharmaceutical Inorganic and Analytical Chemistry

BP106T — B.Pharm Semester I

## Exam Success Notes

Theory-exam mastery: complete answers, the way examiners want them

As per PCI B.Pharm (NEP 2020) syllabus

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# Unit I — Pharmaceutical Analysis, Errors and Impurities

## Introduction to pharmaceutical analysis

Pharmaceutical analysis answers two questions about every drug sample: what is in it (qualitative analysis) and how much of it is there (quantitative analysis). It is how you confirm identity, check purity and verify strength — every "Assay" section of an IP monograph is built on these techniques.

### Techniques of analysis

- Titrimetry (volumetric analysis) — measuring the volume of a standard solution needed to react completely with the sample. Fast, cheap and still the workhorse of IP assays.
- Gravimetry — converting the analyte into a pure, weighable precipitate. Slow but very accurate; used as a reference method.
- Instrumental methods — UV-Visible spectroscopy, IR spectroscopy, HPLC, gas chromatography, atomic absorption spectroscopy and electroanalytical methods like pH-metry and potentiometry. You meet these properly in later semesters; here, know what each one measures.

Exam tip: When a question asks you to "classify techniques of analysis", give the three heads above with one line each, and name two instrumental methods. Examiners want the words qualitative and quantitative in your first sentence.

### Methods of expressing strength of solutions

These definitions are direct one- and two-mark questions — learn every one word-perfect:

- Molarity (M) — moles of solute per litre of solution.
- Normality (N) — gram-equivalents of solute per litre of solution. Normality = Molarity  $\times$  n-factor (valency).
- Molality (m) — moles of solute per kg of solvent. It is temperature-independent, unlike molarity.
- % w/v — grams of solute per 100 mL of solution. % v/v — mL of solute per 100 mL. % w/w — grams of solute per 100 g of solution.
- Parts per million (ppm) — mg of solute per litre of solution; used for very dilute solutions such as impurities.
- Ratio strength — e.g. 1:1000 means 1 g of solute in 1000 mL of solution.
- Milliequivalents (mEq) — used for electrolytes:  $\text{mEq} = (\text{mg} \times \text{valency}) \div \text{atomic weight}$ .

## Primary and secondary standards

A primary standard is a high-purity substance that can be weighed directly to prepare a standard solution. A secondary standard is a solution whose exact strength must be found by standardisation against a primary standard.

|            | Primary standard                                                                                                               | Secondary standard                                                                                                                     |
|------------|--------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|
| Definition | Weighed directly to prepare a standard solution                                                                                | Strength found by standardisation against a primary standard                                                                           |
| Properties | Stable, non-hygroscopic, high equivalent weight, available in high purity                                                      | May be unstable, hygroscopic or reactive                                                                                               |
| Examples   | Anhydrous sodium carbonate, potassium hydrogen phthalate (KHP), oxalic acid, zinc oxide, sodium chloride, potassium dichromate | NaOH, HCl, H <sub>2</sub> SO <sub>4</sub> , KMnO <sub>4</sub> , sodium thiosulphate, iodine, AgNO <sub>3</sub> , EDTA, perchloric acid |

Exam tip: "Why can't NaOH be a primary standard?" is a classic. It is hygroscopic and absorbs CO<sub>2</sub> from air, so its weighed mass never corresponds to pure NaOH — it must be standardised against KHP.

## Errors in analysis

### Sources and types of errors

Sources of errors:

- 1 Instrumental errors — uncalibrated burette, faulty balance, impure reagents.
- 2 Personal (operative) errors — wrong endpoint judgement, parallax while reading the burette, faulty technique.
- 3 Method errors — incomplete reaction, co-precipitation, wrong indicator choice.

Gross mistakes, like spilling the sample, are not "errors" in this classification — they invalidate the analysis outright.

Types of errors:

- Determinate (systematic) errors — reproducible and always in the same direction; they can be detected and corrected. Subdivided into constant errors (independent of sample size) and proportional errors (grow with sample size).
- Indeterminate (random) errors — small, unpredictable fluctuations around the true value; reduced by replicates but never fully removed.
- Absolute error = measured value – true value.
- Relative error = (absolute error ÷ true value) × 100.

## Methods of minimising errors

- Calibrate instruments (balance, burettes, pipettes) regularly.
- Run blank determinations to correct for reagent impurities.
- Analyse replicates and take the mean — this shrinks random error.
- Use control or standard samples of known composition.
- Choose a suitable sample size — weighing a larger quantity reduces the relative error.

## Accuracy, precision and significant figures

- Accuracy is closeness of a measurement to the true value.
- Precision is the agreement between repeated measurements of the same thing.

Think of a target: a tight cluster of shots off-centre is precise but not accurate; scattered shots centred on the bullseye average out to accurate but not precise. An uncalibrated burette gives precise-but-wrong results — which is exactly why calibration matters. A good analysis needs both.

Significant figures — a measurement is reported only up to the digit you can reasonably read:

- Zeros between non-zero digits are significant.
- Trailing zeros after a decimal point are significant.
- In multiplication/division, the answer carries the fewest significant figures of the inputs.
- In addition/subtraction, the answer follows the decimal places, not the digit count.

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## Impurities in pharmaceuticals

### Definition, types, sources and regulatory importance

An impurity is any unwanted foreign matter present in a drug substance or formulation.

Types of impurities:

- 1 Organic impurities — starting materials, synthetic by-products, degradation products.
- 2 Inorganic impurities — heavy metals (lead, arsenic, mercury), residual catalysts, reagents.
- 3 Residual solvents — left over from manufacture.

Why regulators care: impurities can be toxic (lead, arsenic), reduce the efficacy of the drug, or destabilise the product. The IP therefore prescribes a limit test for specific impurities in each monograph — a semi-quantitative check that the impurity is below a permitted level.

Sources of impurities in pharmaceuticals:

- 1 Raw materials and starting materials.
- 2 Reagents and solvents used in manufacture.
- 3 The manufacturing process and equipment (metal leaching from reactors).

- 4 Containers and closures (alkali leaching from glass).
- 5 Storage conditions — moisture, light, temperature.
- 6 Decomposition of the drug itself over time.

### Limit tests — principle

A limit test compares the opalescence, turbidity or colour produced by the sample with that produced by a standard solution containing a known amount of the impurity, under identical conditions. If the sample's effect is less than the standard's, the sample passes. A limit test is semi-quantitative — it only tells you whether the impurity is below the limit, not how much is present. That is the key difference from an assay.

Learn each test as: reagent → observation → comparison standard.

Limit test for chloride: To the sample solution add dilute nitric acid and silver nitrate → white opalescence of silver chloride ( $\text{Ag}^+ + \text{Cl}^- \rightarrow \text{AgCl}$ ). Compared against a standard prepared from sodium chloride. The nitric acid keeps the medium acidic so that silver carbonate or phosphate do not precipitate and confuse the result.

Limit test for sulphate: Sample + dilute hydrochloric acid + barium chloride → white turbidity of barium sulphate ( $\text{Ba}^{2+} + \text{SO}_4^{2-} \rightarrow \text{BaSO}_4$ ). Compared against a potassium sulphate standard.

Limit test for iron: Sample + citric acid + thioglycollic acid, made alkaline with ammonia → purple colour of ferrous thioglycollate. Citric acid prevents precipitation of iron by ammonia. Compared against a ferric ammonium sulphate standard.

Limit test for arsenic (Gutzeit test): The sample goes into a Gutzeit generator bottle with zinc and hydrochloric acid. Nascent hydrogen reduces any arsenic to arsine gas ( $\text{AsH}_3$ ), which rises and stains mercuric chloride paper yellow to brown. The stain is compared with a standard stain. Key reaction:  $\text{As}_2\text{O}_3 + 6\text{Zn} + 12\text{HCl} \rightarrow 2\text{AsH}_3\uparrow + 6\text{ZnCl}_2 + 3\text{H}_2\text{O}$ . A lead acetate cotton plug in the tube traps  $\text{H}_2\text{S}$ , which would otherwise give a false stain.

Limit test for lead: The sample is extracted with dithizone (diphenylthiocarbazone) in chloroform at controlled pH → violet-red lead dithizonate in the chloroform layer, compared against a standard lead solution. Dithizone is chosen because it is highly selective for lead at the prescribed pH.

Limit test for heavy metals: Sample solution + hydrogen sulphide (or thioacetamide as the  $\text{H}_2\text{S}$  source) → brown to black precipitate of metallic sulphides ( $\text{PbS}$ ,  $\text{HgS}$  and others), compared against a standard lead solution. This is a group test for metals that precipitate as sulphides.

### Limit Tests of the IP — Reagent, Observation and Comparison Standard

| Limit test        | Key reagent                                        | Observation                                   | Compared against                        |
|-------------------|----------------------------------------------------|-----------------------------------------------|-----------------------------------------|
| Chloride          | AgNO <sub>3</sub> + dil. HNO <sub>3</sub>          | White opalescence (AgCl)                      | NaCl standard                           |
| Sulphate          | BaCl <sub>2</sub> + dil. HCl                       | White turbidity (BaSO <sub>4</sub> )          | K <sub>2</sub> SO <sub>4</sub> standard |
| Iron              | Thioglycollic acid + citric acid + NH <sub>3</sub> | Purple colour (ferrous thioglycollate)        | Ferric ammonium sulphate standard       |
| Arsenic (Gutzeit) | Zn + HCl → AsH <sub>3</sub> gas                    | Yellow-brown stain on HgCl <sub>2</sub> paper | Standard stain                          |
| Lead              | Dithizone in CHCl <sub>3</sub>                     | Violet-red colour in CHCl <sub>3</sub> layer  | Standard lead solution                  |
| Heavy metals      | H <sub>2</sub> S / thioacetamide                   | Brown-black ppt (metal sulphides)             | Standard lead solution                  |

Principle: sample effect must be LESS than the standard effect under identical conditions.

Limit tests of the IP — reagent, observation and comparison standard

### Modified limit test for chloride and sulphate

The normal tests fail when the substance itself interferes — for example a strongly coloured substance (like potassium permanganate) whose colour hides the opalescence or turbidity, or a substance that reacts with silver nitrate or barium chloride. In such cases the IP monograph prescribes a modified procedure — decolourisation, filtration or pH adjustment before adding the reagent. The exact pre-treatment differs from monograph to monograph, so the exam point is why the modification is needed, not one fixed recipe.

Exam tip: Frame your answer as: normal test → what interferes → what the modification does. "Potassium permanganate's own purple colour masks the white opalescence, so it is decolourised first" is the model sentence examiners reward.

### Very short questions (2 marks)

- 1 Define a limit test and state how it differs from an assay in one line.
- 2 Name the reagent and the observation in the limit test for sulphate.
- 3 Why is dilute nitric acid added in the limit test for chloride?
- 4 Give two examples each of primary and secondary standards.
- 5 Define absolute error and relative error.

### Short questions (5 marks)

- 1 Explain determinate and indeterminate errors with one example each, and list three methods of minimising errors.

- 2 Describe the principle and procedure of the Gutzeit limit test for arsenic, including the key reaction.
- 3 Distinguish between accuracy and precision with the target analogy, and state the rules of significant figures.

### Long questions (10 marks)

- 1 Describe the limit tests for chloride, sulphate and iron: principle, reagents, observations and the comparison standard in each case.
- 2 Discuss the sources and types of impurities in pharmaceuticals and explain the regulatory importance of limit tests, with a note on the modified limit tests for chloride and sulphate.

### How to approach these answers

- Very-short Q1: one-line definition of limit test + one-line contrast with assay; stop there.
- Very-short Q2: reagent ( $\text{BaCl}_2 + \text{dil. HCl}$ ) + observation (white turbidity of  $\text{BaSO}_4$ ); one line each.
- Very-short Q3: one sentence — acidic medium prevents  $\text{Ag}_2\text{CO}_3/\text{Ag}_3\text{PO}_4$  precipitation.
- Very-short Q4: two names per column from the standards table; no explanation needed.
- Very-short Q5: write both formulae; one line each.
- Short Q1: open with definitions, one example each, then three minimisation methods as bullets.
- Short Q2: structure — apparatus (Gutzeit bottle), reaction with equation, stain observation, comparison with standard.
- Short Q3: definitions first, then the target analogy, then the four significant-figure rules as bullets.
- Long Q1: structure — common principle paragraph, then one subhead per test (reagent → observation → standard), close with the labelled comparison figure.
- Long Q2: structure — definition and types, six sources as numbered points, regulatory importance paragraph, modified tests paragraph with the interference reason.

## Unit II — Acid-Base Chemistry, Buffer Systems and Electrolytes

### Acids, bases, buffers and pH

#### Definitions of acids and bases

All three definitions are asked as a set — learn them together:

| Theory         | Acid                   | Base                  |
|----------------|------------------------|-----------------------|
| Arrhenius      | Gives $H^+$ in water   | Gives $OH^-$ in water |
| Bronsted-Lowry | Proton donor           | Proton acceptor       |
| Lewis          | Electron-pair acceptor | Electron-pair donor   |

Arrhenius is the simplest but limited to aqueous solutions. Bronsted-Lowry explains conjugate acid-base pairs (e.g.  $CH_3COOH / CH_3COO^-$ ). Lewis is the broadest definition.

## pH scale and its significance

$pH = -\log_{10}[H^+]$ . At 25 °C, pH 7 is neutral; below 7 is acidic, above 7 is alkaline. Each pH unit is a tenfold change in  $[H^+]$ .

Why pH matters in pharmacy:

- Drug solubility — many drugs are weak acids or bases; their ionised form dissolves but the unionised form absorbs.
- Drug stability — many drugs hydrolyse at extreme pH.
- Drug absorption — weak acids are absorbed better from the acidic stomach, weak bases from the alkaline intestine.
- Preservative efficacy — most preservatives work only in their unionised form, so within a pH range.

Exam tip: If asked "significance of pH in pharmacy", give the four points above as bullets with one line each. Never write a paragraph where four points will do.

## Buffers

A buffer is a solution that resists change in pH when small amounts of acid or alkali are added.

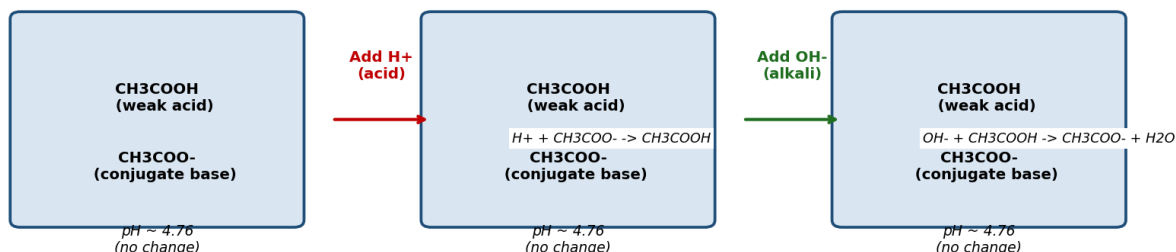
Types of buffers:

- Acidic buffers — a weak acid + its salt, e.g. acetic acid / sodium acetate.
- Basic buffers — a weak base + its salt, e.g. ammonia / ammonium chloride.

Pharmaceutical examples: citrate and phosphate buffers in injections and eye drops.

How a buffer works: it contains a reserve of both the acid and its conjugate base. Added  $H^+$  is mopped up by the base partner; added  $OH^-$  is mopped up by the acid partner — so  $[H^+]$  barely moves.

### How a Buffer Resists pH Change (Acetic Acid / Acetate System)



The added  $\text{H}^+$  or  $\text{OH}^-$  is consumed by the reserve partner, so  $[\text{H}^+]$  barely moves.

How a buffer resists pH change — the added acid or alkali is consumed by the reserve partner

### Buffer equation and calculation of pH

Henderson-Hasselbalch equation:

$$\text{pH} = \text{pK}_a + \log\left(\frac{[\text{salt}]}{[\text{acid}]}\right)$$

For a basic buffer:  $\text{pOH} = \text{pK}_b + \log\left(\frac{[\text{salt}]}{[\text{base}]}\right)$ .

Maximum buffering is at  $\text{pH} = \text{pK}_a$ , when  $[\text{salt}] = [\text{acid}]$  and the log term is zero.

Worked pattern (the numerical examiners repeat): for a buffer of 0.1 M acetic acid and 0.1 M sodium acetate ( $\text{pK}_a$  4.76):

$$\text{pH} = 4.76 + \log(0.1 / 0.1) = 4.76 + \log(1) = 4.76$$

Change the ratio and the log term shifts the pH — practice two or three such sums before the exam, because the numbers change but the pattern never does.

Buffer capacity is the moles of acid or base per litre needed to change the pH by one unit. It is highest when  $\text{pH} = \text{pK}_a$  (ratio 1:1) and increases with total buffer concentration.

### Isotonicity and its applications

An isotonic solution has the same osmotic pressure as body fluids — equivalent to 0.9% w/v NaCl, with a freezing point of  $-0.52^\circ\text{C}$ . A hypertonic solution is more concentrated; a hypotonic solution is less concentrated.

Why it matters:

- IV fluids: a hypotonic injection makes water rush into red blood cells → haemolysis (cells burst); a hypertonic one draws water out → crenation (cells shrink). Large-volume parenterals must be isotonic.
- Ophthalmic solutions: non-isotonic eye drops sting, irritate and trigger tearing, which washes the drug out. Isotonicity adjustment keeps the drop comfortable so the drug stays in contact with the eye.

Methods of adjusting isotonicity:

- 1 Freezing-point depression method — the most often asked. Calculate the freezing-point lowering of the drug solution and add enough NaCl to bring the total depression to 0.52 °C.
- 2 Sodium chloride equivalent method.
- 3 White-Vincent method.
- 4 Sprowls method.

Exam tip: "Haemolysis vs crenation" is the one-line pair that proves you understand isotonicity. Write it exactly: hypotonic → haemolysis, hypertonic → crenation.

## Electrolytes

### Major extra- and intracellular electrolytes

| Location            | Major ions                                                        | Key functions                                           |
|---------------------|-------------------------------------------------------------------|---------------------------------------------------------|
| Extracellular fluid | Na <sup>+</sup> , Cl <sup>-</sup> , HCO <sub>3</sub> <sup>-</sup> | Fluid balance, osmotic pressure, acid-base balance      |
| Intracellular fluid | K <sup>+</sup> , Mg <sup>2+</sup> , phosphate, protein            | Membrane potential, enzyme activity, muscle contraction |

Functions across both: maintaining fluid balance and osmotic pressure, acid-base balance, nerve impulse transmission (Na<sup>+</sup>/K<sup>+</sup>), and muscle contraction (Ca<sup>2+</sup> in excitation-contraction coupling).

### Electrolytes used in replacement therapy

Sodium chloride\* — 0.9% w/v "normal saline" for fluid and electrolyte replacement; also the reference standard for isotonicity and a primary standard in argentometric titrations. (The asterisk marks it as syllabus-priority — expect it as a short note.)

Potassium chloride — treatment of hypokalaemia (low K<sup>+</sup>), e.g. after diuretic therapy or vomiting. Given diluted and slowly — never as a rapid IV bolus, because concentrated KCl can cause cardiac arrest.

Calcium chloride — hypocalcaemia and cardiac resuscitation; supplies Ca<sup>2+</sup> rapidly.

Oral Rehydration Salt (ORS) — for dehydration in diarrhoea. WHO reduced-osmolality formula per litre of water:

| Component                   | Amount |
|-----------------------------|--------|
| Sodium chloride             | 2.6 g  |
| Potassium chloride          | 1.5 g  |
| Anhydrous glucose           | 13.5 g |
| Trisodium citrate dihydrate | 2.9 g  |

Total osmolarity 245 mOsm/L. Glucose is essential — sodium is absorbed in the gut by sodium-glucose co-transport, which is why sugar + salt works far better than salt alone.

### Physiological acid-base balance

Blood pH is held at 7.35–7.45 by:

- The bicarbonate buffer system ( $\text{H}_2\text{CO}_3$  /  $\text{HCO}_3^-$ ) — the main blood buffer.
- Phosphate and protein buffers.
- The lungs (removing  $\text{CO}_2$ ) and kidneys (excreting  $\text{H}^+$ , reabsorbing  $\text{HCO}_3^-$ ) as the long-term regulators.

Acidosis = blood pH below 7.35; alkalosis = blood pH above 7.45.

### Very short questions (2 marks)

- 1 Define a buffer and name its two types with one example each.
- 2 State the Henderson-Hasselbalch equation.
- 3 Define isotonicity and state its reference standard.
- 4 Name the major extracellular and intracellular ions.
- 5 What is buffer capacity?

### Short questions (5 marks)

- 1 Compare the Arrhenius, Bronsted-Lowry and Lewis definitions of acids and bases.
- 2 Explain why IV fluids must be isotonic, using the terms haemolysis and crenation, and list the methods of adjusting isotonicity.
- 3 Give the WHO ORS composition and explain the role of glucose in it.

### Long questions (10 marks)

- 1 Derive the Henderson-Hasselbalch equation, explain how to calculate the pH of a buffer solution, and discuss buffer capacity and the significance of pH in pharmacy.
- 2 Describe the electrolytes used in replacement therapy — sodium chloride\*, potassium chloride, calcium chloride and ORS — with the physiological acid-base balance of blood.

### How to approach these answers

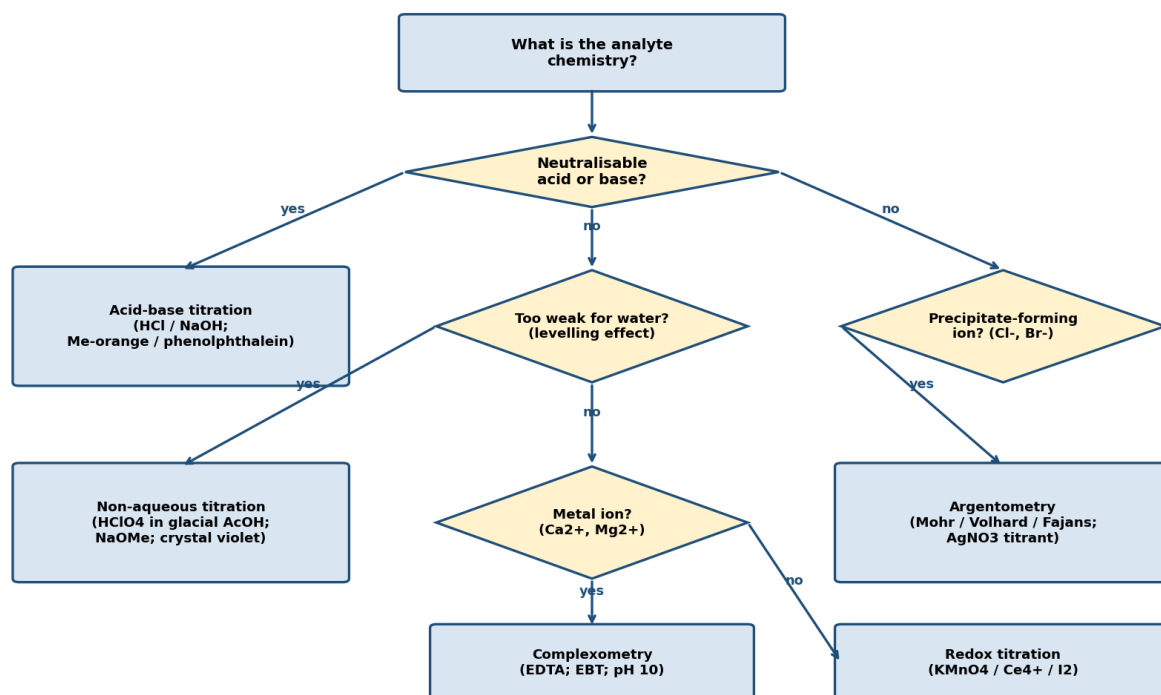
- Very-short Q1: one-line definition + two types with one example each; four short lines total.
- Very-short Q2: write the equation exactly; add the basic-buffer form only if space allows.
- Very-short Q3: definition + "0.9% w/v NaCl, freezing point  $-0.52^\circ\text{C}$ ".
- Very-short Q4: extracellular ( $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{HCO}_3^-$ ) and intracellular ( $\text{K}^+$ ,  $\text{Mg}^{2+}$ , phosphate) as two lines.
- Very-short Q5: one-line definition + the two conditions for maximum capacity.

- Short Q1: open with a three-row table (theory | acid | base), then one limitation line for Arrhenius.
- Short Q2: start with hypotonic → haemolysis / hypertonic → crenation, then list the four adjustment methods with one line on the freezing-point method.
- Short Q3: table of the four ORS components with amounts, then the sodium-glucose co-transport explanation.
- Long Q1: structure — buffer definition and types, derivation of the equation, worked pH calculation, buffer capacity, significance of pH in pharmacy.
- Long Q2: structure — ion table (extra vs intracellular), one subhead per replacement electrolyte with its use, then the acid-base balance paragraph (buffers, lungs, kidneys, pH range).

## Unit III — Titrimetric Analysis

This is the largest unit (14 hours) and the most scoring one — almost every technique here doubles as a BP111P practical. Learn each titration as: principle → titrant → indicator → endpoint observation → example assay.

Which Titration? — Decision Flowchart



Which titration to use — decision flowchart

## Acid-base titrations

### Theories of acid-base indicators

- Ostwald's (ionisation) theory: the indicator is a weak acid or weak base whose ionised and unionised forms have different colours. The colour change follows the shift in ionisation with pH.
- Quinonoid theory: the indicator exists in two tautomeric forms — benzenoid and quinonoid — with different colours, and pH shifts the equilibrium between them. Phenolphthalein is the classic example: colourless benzenoid form in acid, pink quinonoid form in alkali.

## Classification of acid-base titrations

| Type                       | Example                                    | Equivalence pH    | Suitable indicator               |
|----------------------------|--------------------------------------------|-------------------|----------------------------------|
| Strong acid vs strong base | HCl vs NaOH                                | pH 7 — sharp jump | Methyl orange or phenolphthalein |
| Strong acid vs weak base   | HCl vs NH <sub>4</sub> OH                  | Below pH 7        | Methyl orange / methyl red       |
| Weak acid vs strong base   | CH <sub>3</sub> COOH vs NaOH               | Above pH 7        | Phenolphthalein                  |
| Weak acid vs weak base     | CH <sub>3</sub> COOH vs NH <sub>4</sub> OH | No sharp jump     | No direct visual titration       |

The weak acid-weak base pair gives no sharp pH jump at equivalence, so it cannot be titrated directly with a visual indicator — it needs other methods.

Exam tip: Always link the indicator to the equivalence pH in one sentence: "Methyl orange (3.1–4.4) suits strong acid-weak base because the equivalence lies below pH 7." That single linking sentence is what separates a full-marks answer from a list.

## Preparation and standardisation of titrants

Hydrochloric acid — standardised against weighed anhydrous sodium carbonate (primary standard) using methyl orange indicator:

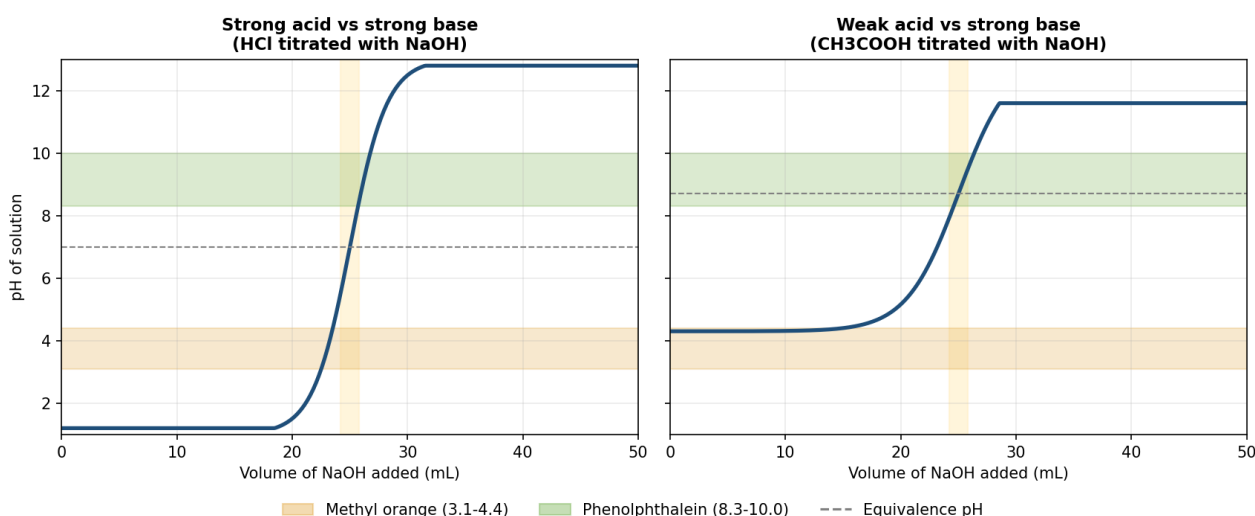


Sodium hydroxide — standardised against potassium hydrogen phthalate (KHP) using phenolphthalein. Prepare it with carbon-dioxide-free water and protect it from air — NaOH absorbs CO<sub>2</sub> forming carbonate, which causes titration errors. (This is also why NaOH can never be a primary standard.)

## Neutralisation curves

A neutralisation (titration) curve plots pH against volume of titrant. The steep vertical portion marks the equivalence point. An indicator is suitable only if its colour-change pH range falls on that steep part — which is exactly why indicator choice depends on the titration type in the table above.

### Neutralisation Curves — the indicator's range must fall on the steep part



Neutralisation curves — the indicator's range must fall on the steep part

## Assay of ammonium hydroxide

Ammonia solution is assayed by titration with standard acid using methyl red indicator. Because ammonia is volatile, the assay is done quickly in a cooled, stoppered flask — a small detail examiners like to ask.

## Non-aqueous titrations

### Why non-aqueous?

Water has a levelling effect — it is too good a proton donor and acceptor, so very weak acids and bases (many drugs are) give no sharp endpoint in water. Titrating in a non-aqueous solvent sharpens the endpoint.

### Types of solvents used

| Solvent type | Behaviour                                                            | Examples                                    |
|--------------|----------------------------------------------------------------------|---------------------------------------------|
| Aprotic      | Inert — neither donates nor accepts protons                          | Benzene, chloroform, toluene                |
| Protophilic  | Basic — accepts protons; enhances acidic strength of dissolved acids | Dimethylformamide, pyridine, liquid ammonia |
| Protogenic   | Acidic — donates protons; enhances basic strength of dissolved bases | Glacial acetic acid (the most used solvent) |
| Amphiprotic  | Can both donate and accept protons                                   | Glacial acetic acid, alcohols               |

## Acidimetric and alkalimetric titrations

Acidimetry (titration of bases): the titrant is perchloric acid in glacial acetic acid, standardised against potassium hydrogen phthalate; the indicator is crystal violet (violet → green endpoint). Used for weakly basic drugs.

Alkalimetry (titration of acids): the titrant is sodium or lithium methoxide in methanol-benzene (or toluene-methanol), standardised against benzoic acid; the indicator is thymol blue. Used for weakly acidic drugs.

Estimation of sodium benzoate — the classic example. Dissolve sodium benzoate in glacial acetic acid and titrate with perchloric acid (crystal violet indicator). Sodium benzoate is too weak a base to titrate in water, which is precisely why the non-aqueous route is needed.

Exam tip: "Why glacial acetic acid?" has a two-part answer: it is protogenic (donates protons, so it boosts the basic strength of weak bases) and it dissolves the perchloric acid titrant. Write both.

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## Precipitation titrations and gravimetry

### Gravimetric analysis — principle and steps

The analyte is converted into a pure compound of known composition that is precipitated, filtered, washed, dried or ignited, and weighed.

- 1 Precipitation — with digestion (heating in the mother liquor) to grow large, filterable crystals that adsorb fewer impurities.
- 2 Filtration.
- 3 Washing — to remove adsorbed impurities.
- 4 Drying or ignition to constant weight.
- 5 Weighing and calculation via the gravimetric factor.

A good gravimetric precipitate must be highly insoluble, pure, easily filterable, and of definite composition after drying or ignition.

Estimation of barium sulphate by gravimetry:  $\text{Ba}^{2+}$  is precipitated with dilute sulphuric acid as  $\text{BaSO}_4$ , digested, filtered through ashless filter paper, ignited and weighed as  $\text{BaSO}_4$ . The result is calculated using the gravimetric factor ( $\text{Ba} / \text{BaSO}_4$ ).

### Precipitation (argentometric) titrations

The titrant is silver nitrate. Learn the four named methods as a comparison table:

| Method             | Type                                                                         | Indicator                                 | Endpoint                                                                                                | Medium / key note                                                                                                        |
|--------------------|------------------------------------------------------------------------------|-------------------------------------------|---------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| Mohr's             | Direct titration of $\text{Cl}^-$ / $\text{Br}^-$ with $\text{AgNO}_3$       | Potassium chromate                        | Red silver chromate ( $\text{Ag}_2\text{CrO}_4$ ) after all $\text{Cl}^-$ precipitates as $\text{AgCl}$ | Neutral pH — in acid the chromate dissolves; in alkali $\text{AgOH}$ precipitates                                        |
| Volhard's          | Back titration: excess $\text{AgNO}_3$ added, back-titrated with thiocyanate | Ferric alum                               | Red $\text{Fe}(\text{SCN})^{2+}$ complex                                                                | Acidic medium (nitric acid); suits $\text{Cl}^-$ , $\text{Br}^-$ , $\text{I}^-$                                          |
| Modified Volhard's | For chloride specifically                                                    | Same as Volhard's                         | Same                                                                                                    | $\text{AgCl}$ is filtered off before back-titration — $\text{AgCl}$ reacts with thiocyanate and would spoil the endpoint |
| Fajans             | Direct titration                                                             | Adsorption indicator (fluorescein, eosin) | Indicator adsorbs onto the precipitate surface at the endpoint with a colour change                     | Dextrin may be added to keep the precipitate colloidal                                                                   |

Key reactions —  $\text{Ag}^+ + \text{Cl}^- \rightarrow \text{AgCl} \downarrow$  (white); at Mohr's endpoint,  $2\text{Ag}^+ + \text{CrO}_4^{2-} \rightarrow \text{Ag}_2\text{CrO}_4 \downarrow$  (red). Volhard's:  $\text{Ag}^+ + \text{SCN}^- \rightarrow \text{AgSCN} \downarrow$ ; endpoint,  $\text{Fe}^{3+} + \text{SCN}^- \rightarrow [\text{Fe}(\text{SCN})]^{2+}$  (red).

## Complexometric titrations

Classification: EDTA (used as disodium EDTA) forms stable 1:1 complexes with metal ions regardless of the metal's valency — this is the basis of complexometry. Types include direct titration, back titration, replacement (substitution) titration and indirect titration.

### Metal ion indicators

Eriochrome Black T (EBT) and murexide are the syllabus indicators. EBT forms a wine-red complex with the metal ion; at the endpoint EDTA strips the metal from the indicator, freeing it — the colour changes wine red  $\rightarrow$  blue (at pH 10).

### Masking and demasking reagents

- Masking agents tie up interfering ions so they do not react with EDTA — e.g. cyanide masks heavy metals, fluoride masks aluminium, triethanolamine masks iron.
- Demasking selectively releases one masked ion afterwards so it can be titrated.

## Preparation and standardisation of disodium EDTA

Standardised against a primary standard such as zinc oxide or calcium carbonate (dissolved in acid, buffered to pH 10, EBT indicator).

## Estimations

Estimation of magnesium sulphate: direct titration with EDTA at pH 10 (ammonia buffer), EBT indicator, wine red → blue endpoint.

Estimation of calcium gluconate\*: same principle —  $\text{Ca}^{2+}$  titrated with EDTA (murexide or Patton-Reeder indicator is typical for calcium). The asterisk marks it as syllabus-priority.

Exam tip: Three facts about EDTA always score: 1:1 complexes irrespective of valency, pH 10 ammonia buffer for the  $\text{Mg}^{2+}$ /EBT system, and the wine red → blue endpoint. Write them as a numbered trio.

## Very short questions (2 marks)

- 1 State Ostwald's theory of acid-base indicators in one line.
- 2 Why can't a weak acid-weak base pair be titrated directly with a visual indicator?
- 3 Name the titrant and indicator used in the acidimetric non-aqueous titration of bases.
- 4 What is the endpoint colour change with Eriochrome Black T?
- 5 State the two reactions involved in Mohr's method.

## Short questions (5 marks)

- 1 Compare Mohr's, Volhard's, modified Volhard's and Fajans methods in a table.
- 2 Explain the types of non-aqueous solvents with one example each, and state why glacial acetic acid is the solvent of choice in acidimetry.
- 3 Describe masking and demasking in complexometry with one example each.

## Long questions (10 marks)

- 1 Discuss the preparation and standardisation of hydrochloric acid and sodium hydroxide, the classification of acid-base titrations with suitable indicators, and the assay of ammonium hydroxide.
- 2 Describe the principle and steps of gravimetric analysis with the estimation of barium sulphate, and explain complexometric titrations including metal ion indicators, masking-demasking, and the estimation of magnesium sulphate and calcium gluconate\*.

## How to approach these answers

- Very-short Q1: one line — indicator as weak acid/base, ionised vs unionised forms differ in colour.
- Very-short Q2: one line — no sharp pH jump at equivalence, so no indicator changes sharply.

- Very-short Q3: perchloric acid in glacial acetic acid + crystal violet (violet → green); one line.
- Very-short Q4: wine red → blue at pH 10; one line.
- Very-short Q5: write both equations (AgCl white; Ag<sub>2</sub>CrO<sub>4</sub> red); no extra text.
- Short Q1: draw the four-column comparison table (method | type | indicator | key note); that is the whole answer.
- Short Q2: four-row solvent table first, then the two-part glacial acetic acid justification.
- Short Q3: define each term, then one masked example (cyanide/heavy metals) and the demasking idea.
- Long Q1: structure — standardisation reactions with equations, classification table with indicators, assay of ammonium hydroxide with the volatility precaution.
- Long Q2: structure — gravimetric steps as numbered points, BaSO<sub>4</sub> estimation paragraph, then complexometry subheads (EDTA 1:1, EBT endpoint, masking, the two estimations).

## Unit IV — Redox Titrations, Gastrointestinal Agents and Radiopharmaceuticals

### Redox titrations

#### Concepts of oxidation and reduction

Oxidation is loss of electrons, reduction is gain of electrons — they always occur together. The oxidising agent gets reduced; the reducing agent gets oxidised. A redox titration needs a visible endpoint: some titrants are self-indicators (KMnO<sub>4</sub>), others need specific indicators (starch for iodine, ferroin or diphenylamine for cerimetry).

#### Types of redox titrations

Permanganometry: the titrant is KMnO<sub>4</sub>, a self-indicator — its purple colour persists at the endpoint. The titration is done in acidic medium with sulphuric acid — never HCl, because HCl is itself oxidised by permanganate to chlorine gas, consuming extra KMnO<sub>4</sub> and giving a wrong, high result. Key half-reaction:



KMnO<sub>4</sub> is standardised against oxalic acid or sodium oxalate (heated to about 70 °C). It is used to estimate Fe<sup>2+</sup>, hydrogen peroxide and oxalates.

Cerimetry: the titrant is ceric sulphate — Ce<sup>4+</sup> → Ce<sup>3+</sup> is a single-electron change, so calculations are simple and the solution is very stable. Indicator: ferroin or diphenylamine. Used for Fe<sup>2+</sup> estimations where permanganate's side reactions are a problem.

Iodimetry vs iodometry — the pair examiners love to confuse:

|                 | Iodimetry                                          | Iodometry                                                                   |
|-----------------|----------------------------------------------------|-----------------------------------------------------------------------------|
| Type            | Direct titration with standard iodine solution     | Indirect — analyte liberates I <sub>2</sub> from KI, which is then titrated |
| Analyte is a... | Reducing agent                                     | Oxidising agent                                                             |
| Titration       | Standard iodine                                    | Standard sodium thiosulphate                                                |
| Example         | Estimation of arsenious oxide, sodium thiosulphate | Assay of copper sulphate, potassium permanganate                            |

Starch indicator is added near the endpoint (the deep blue starch-iodine complex disappears).  
Key reaction:  $I_2 + 2S_2O_3^{2-} \rightarrow 2I^- + S_4O_6^{2-}$ .

Titration with potassium iodate: KIO<sub>3</sub> is a stable, primary-standard-grade oxidant (Andrews titration — iodine monochloride endpoint in strong HCl), used where iodine titrations are unsuitable.

Exam tip: For iodimetry vs iodometry, memorise the one-line logic: "Iodimetry — measure directly with iodine; iodometry — the oxidant liberates iodine first." Then attach one example to each.

## Gastrointestinal agents

### Acidifiers

Given when stomach acid is deficient (achlorhydria):

- Dilute hydrochloric acid — supplements gastric HCl to aid digestion.
- Sodium acid phosphate — also used as a urinary acidifier.

### Antacids

Antacids are bases that neutralise excess gastric acid in hyperacidity.

Ideal properties of antacids:

- 1 Rapid onset of action, with reasonably sustained effect.
- 2 Should not cause systemic alkalosis.
- 3 Should be neither constipating nor laxative on its own.
- 4 Palatable and cheap.

Combinations of antacids — why combine? Aluminium salts constipate while magnesium salts are laxative. Combining them (e.g. aluminium hydroxide + magnesium hydroxide/trisilicate) balances the bowel effect and broadens the action — a favourite short question, so learn the one-line reason.

Sodium bicarbonate\* — a systemic antacid: very rapid, but it releases CO<sub>2</sub> (belching, flatulence) and the absorbed sodium can cause systemic alkalosis — caution in hypertension and cardiac

patients.

Aluminium hydroxide gel\* — non-systemic, slow-acting and constipating; it also adsorbs phosphate, which is why it is used in chronic kidney disease to control phosphate levels.

### Agents that promote bowel movement

- Magnesium hydroxide (milk of magnesia) — osmotic laxative that also acts as an antacid.
- Sodium orthophosphate — saline purgative; draws water into the bowel osmotically.
- Sodium potassium tartrate (Rochelle salt) — saline purgative.
- Magnesium trisilicate — antacid with adsorbent action; mildly laxative, which is why it pairs well with aluminium hydroxide.

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## Antimicrobials (inorganic)

Inorganic antimicrobials act by oxidation, protein precipitation or halogenation — a broader, less selective attack than organic antibiotics, which is why most are for external or antiseptic use.

- Potassium permanganate — strong oxidising agent; used as a gargle/mouthwash and wound wash in very dilute solution (about 1:10000). Stains skin brown — a practical point worth remembering.
- Boric acid — weak antiseptic; used in eye washes and dusting powders. Toxic if absorbed in large amounts, especially in infants.
- Hydrogen peroxide\* — the 3% solution releases nascent oxygen with effervescence ( $2\text{H}_2\text{O}_2 \rightarrow 2\text{H}_2\text{O} + \text{O}_2 \uparrow$ ), which mechanically cleans wounds. It decomposes on storage, so it is kept in light-resistant, cool containers.
- Chlorinated lime\* (bleaching powder) — releases chlorine on exposure to air and moisture; used as a disinfectant for water and surfaces.
- Iodine and its preparations — tincture of iodine, povidone-iodine (less staining, sustained release), Lugol's solution. Broad-spectrum antiseptic; the brown colour itself shows where it has been applied.

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## Radiopharmaceuticals

### Basics of radioactivity

Unstable nuclei decay by emitting alpha, beta or gamma radiation. The half-life ( $t_{1/2}$ ) is the time for half the atoms to decay — it decides whether an isotope suits diagnosis (short  $t_{1/2}$ , hours) or therapy. Activity is measured in becquerel (Bq) and curie (Ci).

### Applications of radioisotopes

| Isotope             | Half-life   | Use                                                                                                                                              |
|---------------------|-------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| Sodium iodide I-131 | ~8 days     | Thyroid diagnosis and therapy (thyroid cancer, hyperthyroidism) — the thyroid selectively takes up iodine                                        |
| Technetium-99m      | ~6 hours    | The workhorse of diagnostic imaging (bone, heart, kidney scans); obtained from a molybdenum-99 generator; short half-life keeps patient dose low |
| Cobalt-60           | ~5.27 years | External beam radiotherapy for cancer (gamma rays)                                                                                               |
| Phosphorus-32       | ~14.3 days  | Therapy of polycythaemia vera and some bone conditions (beta emitter)                                                                            |

### Safe handling, storage and disposal

Follow the ALARA principle — As Low As Reasonably Achievable: minimise time near the source, maximise distance, use shielding (lead containers). Store in labelled, shielded areas; dispose only through authorised radioactive-waste channels. In India this is regulated under AERB (Atomic Energy Regulatory Board) guidelines — the exam expects you to name the safe-handling principles and the regulatory adherence, not the full rulebook.

Exam tip: The isotope table (name → half-life → one use) is a ready-made 5-mark answer. ALARA spelled out plus "lead shielding, labelled storage, AERB-regulated disposal" completes it.

### Very short questions (2 marks)

- 1 Why is sulphuric acid, and not hydrochloric acid, used in permanganometry?
- 2 Distinguish between iodimetry and iodometry in one line each.
- 3 State two ideal properties of antacids.
- 4 Why are antacids combined instead of given singly?
- 5 Expand ALARA and state what it means.

### Short questions (5 marks)

- 1 Explain permanganometry with the half-reaction, the role of sulphuric acid, and the standardisation of  $\text{KMnO}_4$ .
- 2 Write short notes on sodium bicarbonate and aluminium hydroxide gel as antacids.
- 3 Give the half-life and one use each of I-131, Tc-99m, Co-60 and P-32, with a note on safe handling of radiopharmaceuticals.

## Long questions (10 marks)

- 1 Describe the types of redox titrations — permanganometry, cerimetry, iodimetry, iodometry and titrations with potassium iodate — with one example estimation each.
- 2 Classify inorganic antimicrobials by mechanism and write notes on potassium permanganate, boric acid, hydrogen peroxide, chlorinated lime and iodine preparations.

## How to approach these answers

- Very-short Q1: one line — HCl is oxidised to  $\text{Cl}_2$  by  $\text{KMnO}_4$ , giving falsely high results.
- Very-short Q2: iodimetry = direct titration with iodine (analyte reduces); iodometry = liberated iodine titrated with thiosulphate (analyte oxidises).
- Very-short Q3: any two of the four ideal properties; one line each.
- Very-short Q4: one line — aluminium constipates, magnesium loosens; the combination balances bowel effect.
- Very-short Q5: "As Low As Reasonably Achievable" + one line on minimising exposure.
- Short Q1: structure — half-reaction, self-indicator point,  $\text{H}_2\text{SO}_4$  vs HCl reason, standardisation detail.
- Short Q2: two subheads; per compound — systemic/non-systemic, speed, one caution.
- Short Q3: four-row table (isotope | half-life | use), then ALARA + shielding + AERB as bullets.
- Long Q1: structure — oxidation/reduction concept line, then one subhead per titration type with indicator and one example estimation.
- Long Q2: structure — mechanism classification line, then one subhead per antimicrobial with use and one key property.

## Unit V — Miscellaneous Compounds

Short unit, but every compound here is a direct "write a short note" question. Learn each as: use → key property → one caution.

### Expectorants

Expectorants increase bronchial secretion or make sputum less viscous so it can be coughed out.

Potassium iodide — stimulates the bronchial glands to increase respiratory-tract fluid, thinning mucus. It is also the classic reagent for liberating iodine in iodometry — a Unit IV crossover examiners like to link.

Ammonium chloride\* — a reflex expectorant: it irritates the gastric mucosa, triggering a vagal reflex that increases bronchial secretion. It is also a systemic acidifier and diuretic — large doses can cause systemic acidosis, the caution to quote.

## Emetics

Emetics induce vomiting; they were used in certain poisonings to empty the stomach before safer methods like gastric lavage took over.

Copper sulphate\* — a prompt emetic; also an astringent and fungicide. Excess is toxic (copper poisoning), so the dose window matters.

Sodium potassium tartrate (Rochelle salt) — listed here as an emetic; it is better known as a saline purgative (you also met it in Unit IV). Know both roles — examiners test the double listing.

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## Haematinics

Haematinics supply iron for haemoglobin synthesis in iron-deficiency anaemia.

Ferrous sulphate\* — the standard oral iron salt. Ferrous ( $\text{Fe}^{2+}$ ) iron is absorbed far better than ferric ( $\text{Fe}^{3+}$ ) — iron is absorbed in the ferrous state in the duodenum, and ferric iron must first be reduced. Given with vitamin C to keep iron reduced and improve absorption. Common side effects: constipation and black stools — warn the patient so they don't panic.

Ferrous gluconate — milder on the stomach than ferrous sulphate, often preferred when the sulphate causes gastric irritation; slightly lower elemental iron content.

Exam tip: "Why ferrous and not ferric?" is the whole haematinics question in one line: iron is absorbed as  $\text{Fe}^{2+}$  in the duodenum. Attach the vitamin C point and the black-stools counselling point for full marks.

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## Poison and antidote

Poison — any substance that causes injury, illness or death on entering the body in relatively small amounts.

Antidote — a substance that counteracts a poison. Classification:

- 1 Physiological (pharmacological) antidotes — oppose the poison's action on the body, e.g. physostigmine for atropine poisoning.
- 2 Chemical antidotes — react with the poison to form a harmless compound, e.g. sodium thiosulphate for cyanide.
- 3 Mechanical antidotes — prevent absorption of the poison, e.g. activated charcoal adsorbing the poison, demulcents coating the gut.

Sodium thiosulphate — the syllabus antidote. In cyanide poisoning (given with sodium nitrite) it donates sulphur to convert toxic cyanide into thiocyanate, which the kidneys excrete. It also neutralises excess iodine and chlorine. The reaction to remember is the same chemistry as the iodometric endpoint:  $\text{I}_2 + 2\text{S}_2\text{O}_3^{2-} \rightarrow 2\text{I}^- + \text{S}_4\text{O}_6^{2-}$  — iodine reduced to harmless iodide.

## Very short questions (2 marks)

- 1 Define an expectorant and name the two expectorants in the syllabus.
- 2 Why are ferrous salts preferred over ferric salts as haematinics?
- 3 Define poison and antidote.
- 4 Name the three classes of antidotes with one example each.
- 5 State the role of sodium thiosulphate in cyanide poisoning.

### Short questions (5 marks)

- 1 Write short notes on potassium iodide and ammonium chloride\* as expectorants.
- 2 Write short notes on copper sulphate\* and sodium potassium tartrate, covering both their emetic and purgative roles.
- 3 Classify antidotes with examples and explain the antidotal action of sodium thiosulphate.

### Long questions (10 marks)

- 1 Describe the haematinics ferrous sulphate\* and ferrous gluconate — why iron is given as  $\text{Fe}^{2+}$ , how absorption is improved, side effects and patient counselling points.
- 2 Define poison and antidote, classify antidotes with one example each, and discuss sodium thiosulphate as an antidote including its use in cyanide poisoning.

### How to approach these answers

- Very-short Q1: one-line definition + the two names; nothing more.
- Very-short Q2: one line — iron is absorbed as  $\text{Fe}^{2+}$  in the duodenum; ferric must be reduced first.
- Very-short Q3: one line per definition; keep both tight.
- Very-short Q4: three classes with one example each as a numbered list.
- Very-short Q5: one line — donates sulphur, converting cyanide to excretable thiocyanate.
- Short Q1: two subheads; per drug — mechanism (KI: bronchial secretion;  $\text{NH}_4\text{Cl}$ : reflex), one extra use, one caution.
- Short Q2: two subheads; state both roles of sodium potassium tartrate explicitly.
- Short Q3: classification table first (class | example), then the thiosulphate mechanism with the iodine reaction.
- Long Q1: structure — iron absorption ( $\text{Fe}^{2+}$  vs  $\text{Fe}^{3+}$ ), ferrous sulphate subhead (vitamin C, side effects, counselling), ferrous gluconate subhead (gentler, lower elemental iron).
- Long Q2: structure — definitions, classification with examples, sodium thiosulphate (cyanide → thiocyanate; halogens), closing line on why chemical antidotes matter.