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Pharmaceutical Inorganic and Analytical Chemistry

BP106T — B.Pharm Semester I

Concept Mastery Notes

Deep concepts for GPAT & competitive exams — nothing missed

As per PCI B.Pharm (NEP 2020) syllabus

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Unit I — Pharmaceutical analysis, errors, impurities

1.1 What pharmaceutical analysis actually does

Every drug you will ever dispense has passed through analytical chemistry first. Pharmaceutical analysis answers two questions about any sample: what is in it (qualitative analysis) and how much of it is there (quantitative analysis). In practice this splits into three jobs — confirming identity (is this really the drug on the label?), checking purity (how much unwanted stuff is in it?), and verifying strength (does it contain the claimed amount of active ingredient?).

Open any IP monograph and you will see this logic printed in order: Identification tests, then Limit tests for impurities, then the Assay. Units I and III of this subject teach you the chemistry behind those three sections, and Unit III's titrations are the same ones you will perform in your BP111P practicals. Learn the theory and the practical together — examiners love asking "why" about steps you performed with your own hands.

Techniques of analysis

Technique	What you do	What it tells you	Pharmacy example
Titrimetry (volumetric analysis)	Measure the volume of a standard solution that reacts completely with the sample	Exact strength of the drug	Assay of sodium bicarbonate, ammonium hydroxide
Gravimetry	Convert the analyte into a pure, weighable precipitate; weigh it	Very accurate quantity, used as a reference method	Estimation of barium sulphate
Instrumental methods	Measure a physical property with an instrument	Identity and quantity, often at trace levels	UV-Visible (concentration from absorbance), IR (functional groups), HPLC/GC (separation + quantity), atomic absorption (trace metals), pH-metry and potentiometry (endpoints)

Titrimetry is fast and cheap, which is why the IP still builds most assays on it. Gravimetry is slower but more accurate, so it is kept as the referee method. The instrumental methods you meet properly in later semesters — for now, know what each one measures.

Methods of expressing strength of solutions

Examiners lift one-mark definitions straight from this list. Learn each one with its formula:

Expression	Definition	Formula / note
Molarity (M)	Moles of solute per litre of solution	$M = \text{moles} / V(L)$
Normality (N)	Gram-equivalents of solute per litre of solution	$N = M \times \text{n-factor (valency)}$
Molality (m)	Moles of solute per kg of solvent	Temperature-independent (no volume involved)
% w/v	Grams of solute per 100 mL of solution	e.g. 0.9% w/v NaCl = 0.9 g in 100 mL
% v/v	mL of solute per 100 mL of solution	Used for liquids in liquids
% w/w	Grams of solute per 100 g of preparation	Used for ointments, creams
Parts per million (ppm)	mg of solute per litre of solution	For trace impurities
Ratio strength	1:X means 1 g in X mL	$1:1000 = 1 \text{ g in } 1000 \text{ mL} = 0.1\% \text{ w/v}$
Milliequivalents (mEq)	The currency of electrolytes	$\text{mEq} = (\text{mg} \times \text{valency}) / \text{atomic weight}$

Worked example 1 — normality from molarity. What is the normality of 0.5 M H_2SO_4 ? Sulphuric acid gives 2 H^+ per molecule, so its n-factor is 2. $N = 0.5 \times 2 = 1 \text{ N}$. For NaOH (n-factor 1), $0.5 \text{ M} = 0.5 \text{ N}$. The n-factor is simply the number of reacting units — H^+ for acids, OH^- for bases, electrons for redox agents, and the charge for ions.

Worked example 2 — milliequivalents. How many mEq of Na^+ are in 500 mL of normal saline (0.9% w/v NaCl)? 500 mL contains 4.5 g NaCl. Moles = $4.5 / 58.5 = 0.0769 \text{ mol} = 76.9 \text{ mmol}$. Na^+ has valency 1, so $\text{mEq} = 76.9 \times 1 = 76.9 \text{ mEq}$. This is why IV fluid labels talk in mEq — it tells the clinician the actual ionic load, which is what the body cares about.

GPAT angle: Normality = Molarity $\times$ n-factor is asked constantly. Also remember: molality (not molarity) is temperature-independent, because it uses kg of solvent instead of litres of solution — volumes expand with heat, masses don't.

Primary and secondary standards

A standard solution is a solution of exactly known strength, and every titration stands or falls on it. There are two ways to get one:

	Primary standard	Secondary standard
Definition	A high-purity substance you weigh directly to prepare the standard solution	A solution whose exact strength you find by standardising it against a primary standard

	Primary standard	Secondary standard
Must be	Stable, non-hygroscopic, available in high purity, high equivalent weight, not expensive	May be unstable, hygroscopic, or reactive — that's why you can't trust its weighed mass
Examples	Anhydrous sodium carbonate, potassium hydrogen phthalate (KHP), oxalic acid, zinc oxide, sodium chloride, potassium dichromate	NaOH, HCl, H ₂ SO ₄ , KMnO ₄ , sodium thiosulphate, iodine, AgNO ₃ , EDTA, perchloric acid

Why does "high equivalent weight" matter? Suppose your balance reads to ± 0.1 mg. If you weigh 0.1 g of a standard, that 0.1 mg is a 0.1% relative error; if the equivalent weight lets you weigh 1.0 g for the same titration, the relative error drops to 0.01%. A heavier equivalent weight means a bigger weighable mass for the same number of equivalents — the weighing error shrinks. This is the same logic as "use a larger sample size" in the errors section below.

Trap alert: Students write "NaOH is a primary standard because it's a strong base." Wrong — NaOH is the textbook example of what a primary standard is not. It is hygroscopic (absorbs water from air) and absorbs CO₂, forming sodium carbonate. So the mass you weigh is never pure NaOH. It must be standardised, typically against potassium hydrogen phthalate. Similarly, KMnO₄ can't be primary (it decomposes slowly and contains MnO₂ impurities), and HCl can't be primary (it's a volatile liquid — you can't weigh it accurately).

1.2 Errors in analysis

No measurement is perfect. The honest analyst doesn't pretend otherwise — she names the error, finds its source, and shrinks it.

Sources of errors

- Instrumental errors — uncalibrated burette, a balance that drifts, impure reagents. The equipment lies to you.
- Personal (operative) errors — judging the endpoint colour wrong, parallax while reading the burette, faulty technique. The analyst slips.
- Method errors — the chemistry itself is imperfect: incomplete reaction, co-precipitation dragging impurities into a gravimetric precipitate, indicator error. The method has a bias built in.
- Gross mistakes (spilling the sample, using the wrong reagent) are not classified as errors — they invalidate the analysis outright. You repeat the work; you don't "correct" a spill.

Types of errors

	Determinate (systematic) errors	Indeterminate (random) errors
Nature	Reproducible — same direction, same size every time	Small, unpredictable fluctuations around the mean
Cause	A definite, findable cause (uncalibrated instrument, faulty method)	The sum of many tiny uncontrollable variations
Can you remove it?	Yes — find the cause and correct for it	Never fully — only shrink it by taking replicates
Subtypes	Constant errors (same absolute size whatever the sample) and proportional errors (grow with sample size)	—

Two more definitions that get asked as a pair:

- Absolute error = measured value – true value (carries units).
- Relative error = (absolute error / true value) × 100 (a percentage).

Worked example. A sample truly contains 50.00 mg of drug. Your titration gives 49.60 mg. Absolute error = 49.60 – 50.00 = –0.40 mg. Relative error = (–0.40 / 50.00) × 100 = –0.8%. The sign tells you the direction (low reading); determinate errors keep the same sign, random ones scatter around zero.

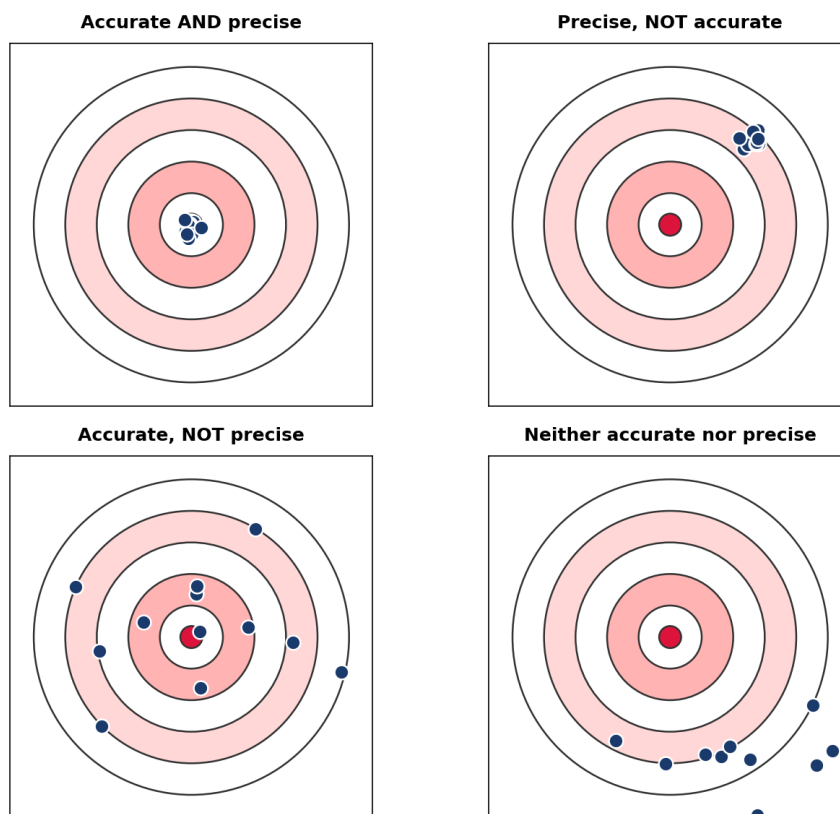
Minimising errors

- 1 Calibrate instruments — the burette, pipette and balance are checked against standards.
- 2 Run a blank determination — titrate everything except the sample; subtract the blank reading so reagent and indicator consumption don't inflate your result.
- 3 Analyse replicates and take the mean — random errors cancel out across repeats.
- 4 Use control / standard samples — a known sample tells you whether your method is biased.
- 5 Choose the right sample size — weighing 1.000 g instead of 0.100 g on a ±0.1 mg balance cuts the relative weighing error tenfold.

Accuracy vs precision

Accuracy is closeness to the true value. Precision is agreement between repeats — reproducibility. They are independent: you can be precise without being accurate (every reading wrong by the same amount, e.g. an uncalibrated burette giving tight but biased titres — that's a determinate error), and you can be accurate on average without being precise (scattered readings centred on the true value). A good analysis needs both.

Accuracy vs precision: the target analogy



Accuracy = closeness to the true value (bullseye). Precision = agreement between repeats (tight cluster).
A good analysis needs both: a tight cluster on the bullseye.

Accuracy vs precision shown with targets

Trap alert: "The results were precise, so they must be correct." No. Precision only means the repeats agree with each other. If a determinate error is shifting every reading the same way, your tight cluster sits neatly off the bullseye. Calibration buys accuracy; replication buys precision.

Significant figures

Report a measurement only up to the digit you can genuinely read — extra digits are fiction. The rules examiners test:

- All non-zero digits are significant. Zeros between non-zero digits are significant (1.008 has 4).
- Trailing zeros after a decimal point are significant (25.00 mL has 4 — the burette was read to 0.01 mL).
- In multiplication/division, the answer carries the fewest significant figures of the inputs.
- In addition/subtraction, the answer follows decimal places, not digit count — it's limited by the least precise decimal position.

Worked example. Titre 24.35 mL (4 sf) $\times$ 0.1024 N (4 sf) $\times$ 40.00 (4 sf) $\rightarrow$ report 4 significant figures. But 25.0 mL $-$ 24.35 mL = 0.65 mL — wait, 25.0 has one decimal place, so the answer

keeps one decimal place: 0.7 mL, even though it looks like two significant figures. Addition follows decimal places. This trips students every year.

1.3 Impurities in pharmaceuticals

Definition: an impurity is any unwanted foreign matter present in a drug substance or formulation. Three types:

Type	What it is	Examples
Organic impurities	Carbon-containing leftovers of synthesis	Starting materials, by-products, intermediates, degradation products
Inorganic impurities	Non-carbon contaminants	Heavy metals (lead, arsenic), residual catalysts, reagents
Residual solvents	Traces of solvents from manufacture	Methanol, acetone, toluene left after crystallisation

Contents means the permitted amount — the IP doesn't demand zero impurity (that's impossible), it sets a limit: the maximum tolerable quantity. Regulatory importance: impurities can be toxic (lead and arsenic are cumulative poisons — the body can't excrete them efficiently, so even small daily doses build up over years), can reduce the drug's efficacy, and can destabilise the formulation. The IP therefore writes a limit test for specific impurities into each monograph — a routine, semi-quantitative check that every batch must pass.

Why a comparison instead of an exact measurement? Because a limit test is a gate, not a scale. Measuring the exact ppm of lead in every batch would need atomic absorption spectroscopy — expensive, slow, overkill for a yes/no decision. A Nessler-cylinder comparison takes minutes, costs almost nothing, and answers the only question the regulator asks: is it below the limit?

Sources of impurities in pharmaceuticals

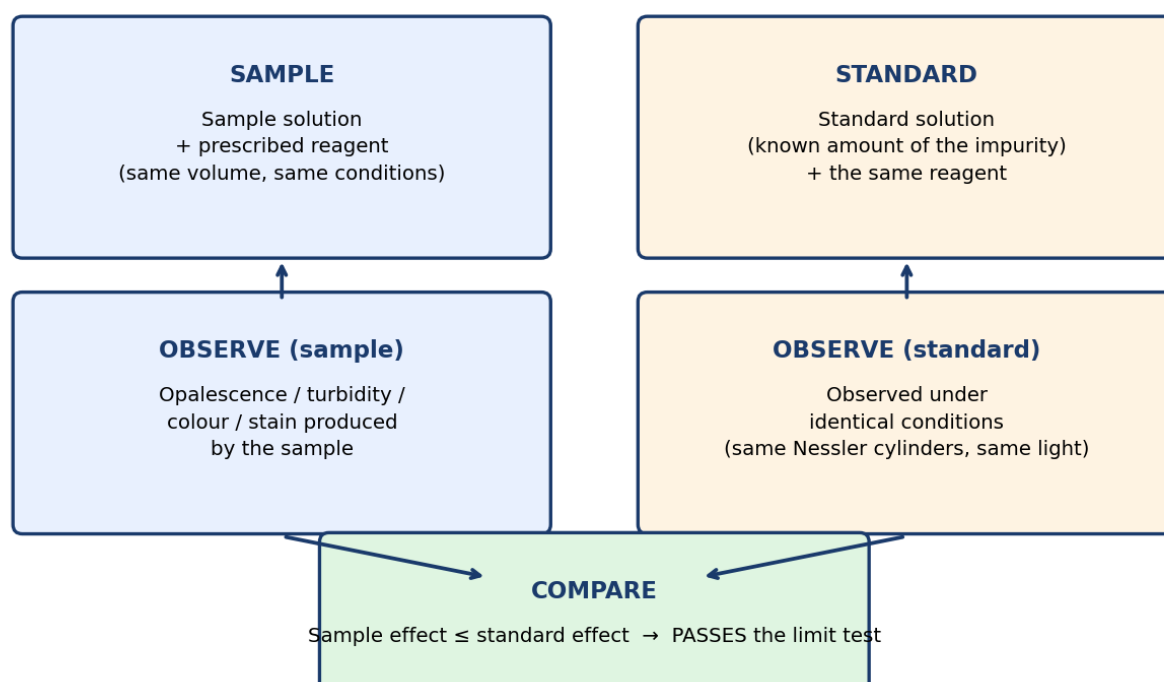
- 1 Raw materials and starting materials — impurities ride in with the ingredients.
- 2 Reagents and solvents used in manufacture.
- 3 The manufacturing process and equipment — metals leaching from reactors and pipes.
- 4 Containers and closures — alkali leaching from glass, extractables from rubber stoppers.
- 5 Storage conditions — moisture, light and heat driving degradation.
- 6 Decomposition of the drug itself over time.

Limit tests — principle and procedures

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 or equal to the standard's, the batch passes. It is a comparison, not a measurement — it never tells you the exact amount, only whether you're below the permitted limit.

Principle of a limit test: a comparison, not a measurement

It only tells you whether the impurity is BELOW a permitted limit — it never tells you the exact amount.



Principle of a limit test: sample vs standard comparison

Learn each test as reagent → observation → comparison standard → the WHY:

Impurity	Reagent(s) added	Observation	Standard prepared from	Why it works this way
Chloride	Dilute nitric acid + silver nitrate	White opalescence of AgCl	Sodium chloride	Nitric acid keeps the solution acidic so silver carbonate or phosphate can't precipitate and fake the result. $\text{Ag}^+ + \text{Cl}^- \rightarrow \text{AgCl} \downarrow$
Sulphate	Dilute hydrochloric acid + barium chloride	White turbidity of BaSO ₄	Potassium sulphate	$\text{Ba}^{2+} + \text{SO}_4^{2-} \rightarrow \text{BaSO}_4 \downarrow$, one of the most insoluble salts known — even traces show up

Impurity	Reagent(s) added	Observation	Standard prepared from	Why it works this way
Iron	Citric acid + thioglycollic acid, then ammonia to make alkaline	Purple colour of ferrous thioglycollate	Ferric ammonium sulphate	Citric acid complexes the iron so ammonia can't precipitate it as $\text{Fe}(\text{OH})_3$; thioglycollic acid reduces Fe^{3+} to Fe^{2+} and forms the purple complex
Arsenic (Gutzeit test)	Zinc + hydrochloric acid in a Gutzeit generator bottle; mercuric chloride paper at the top	Yellow to brown stain on the paper	Standard arsenic solution (matching stain)	Nascent hydrogen reduces arsenic to arsine gas (AsH_3), which rises and stains the paper
Lead	Dithizone (diphenylthiocarbazone) in chloroform, at controlled pH	Violet-red lead dithizonate in the chloroform layer	Standard lead solution	Dithizone is highly selective for lead at the prescribed pH; the colour extracts into chloroform, separating it from the sample matrix
Heavy metals	Hydrogen sulphide (or thioacetamide as the H_2S source)	Brown to black precipitate of metallic sulphides	Standard lead solution	A group test — PbS , HgS and friends all precipitate as dark sulphides together

The chemistry behind the famous ones

Chloride — why nitric acid? Silver nitrate would also precipitate carbonate and phosphate as silver salts. Adding dilute nitric acid first keeps carbonates dissolved (as CO_2 escapes) and phosphates in solution, so the only white opalescence you see is AgCl . Opalescence (a faint milky shimmer) rather than a heavy precipitate is what you compare, because we're dealing with traces.

Iron — why citric acid? The test needs alkaline conditions (ammonia) to develop the purple ferrous thioglycollate colour — but ammonia alone would precipitate iron as brown $\text{Fe}(\text{OH})_3$ and ruin the test. Citric acid is added first: it complexes the iron and holds it in solution. Thioglycollic acid then reduces any Fe^{3+} to Fe^{2+} and forms the purple complex you actually compare.

Arsenic — the Gutzeit mechanism, step by step. Zinc + HCl generates nascent hydrogen (freshly born, highly reactive H). It reduces any arsenic present: $\text{As}_2\text{O}_3 + 6\text{Zn} + 12\text{HCl} \rightarrow 2\text{AsH}_3 \uparrow + 6\text{ZnCl}_2 + 3\text{H}_2\text{O}$. Arsine gas rises through the tube and reacts with mercuric chloride paper, staining it yellow to brown. A plug of lead acetate cotton sits in the tube to trap any H_2S (which would give a false black stain with the paper). The length/intensity of the stain is compared with a standard stain. GPAT loves this: name the gas (arsine, AsH_3) and the stain colour.

Lead — why dithizone? At the prescribed pH, dithizone binds lead far more strongly than other metals present, and the violet-red lead dithizonate complex extracts into the chloroform layer — so you compare a clean coloured organic layer instead of a murky aqueous one. pH control is the whole trick: change the pH and other metals start coming along.

GPAT angle: Gutzeit test = arsenic = arsine gas = yellow-brown stain on mercuric chloride paper. Limit test for lead = dithizone = violet-red complex in chloroform. Limit test for iron = thioglycollic acid = purple colour (and citric acid is there to stop $\text{Fe}(\text{OH})_3$ precipitation). These three "reagent → colour" pairs are asked almost every year.

Trap alert: A limit test is not an assay. A limit test is semi-quantitative — it only checks whether an impurity is below a permitted limit by comparison with a standard. An assay quantitatively determines how much of the drug is present. Limit tests police impurities; assays confirm strength. If a question asks for "the principle of the limit test for chlorides" and you describe a full titration, you've answered the wrong question.

Modified limit tests for chloride and sulphate

The normal tests assume the sample is a well-behaved, colourless solution that doesn't react with the reagent. Real drugs misbehave: a strongly coloured substance (like potassium permanganate) hides the opalescence behind its own colour; some substances react with silver nitrate or barium chloride themselves. For these, the IP monograph prescribes a modified procedure — decolourise, filter, or adjust pH before adding the reagent.

The exam point is the reason, not a memorised recipe: the modification exists to remove the interference so the comparison is valid. The exact pre-treatment differs from monograph to monograph.

Very short questions (2 marks)

- 1 Define a primary standard and give two examples.
- 2 What is the difference between accuracy and precision?
- 3 Name the gas liberated in the Gutzeit test for arsenic.
- 4 Why is dilute nitric acid added in the limit test for chlorides?
- 5 Define ppm and give its pharmaceutical use.

Short questions (5 marks)

- 1 Explain determinate and indeterminate errors with two examples each, and list four ways of minimising errors.
- 2 Describe the principle of a limit test. How does it differ from an assay?
- 3 Give the sources of impurities in pharmaceuticals and explain their regulatory importance.

Long questions (10 marks)

- 1 Describe the limit tests for chloride, sulphate, iron and arsenic, giving the reagent, observation and the chemistry behind each test.
- 2 Define primary and secondary standards. Explain the properties of a good primary standard and why NaOH and KMnO_4 cannot be primary standards.

How to approach these answers

- Very-short Q1: one-line definition + two examples (Na_2CO_3 , KHP); don't write a paragraph.
- Very-short Q2: one line each — accuracy = closeness to true value, precision = agreement between repeats.
- Very-short Q3: arsine gas (AsH_3) — one line, plus the yellow-brown stain if you want the extra half mark.
- Very-short Q4: one line — keeps carbonates/phosphates from precipitating as silver salts.
- Very-short Q5: definition (mg per litre) + one use (trace impurities).
- Short Q1: open with the two definitions, then a two-column comparison, then the four minimisation methods as numbered points.
- Short Q2: open with the comparison principle, then the diagram logic in words, then a small table contrasting limit test vs assay.
- Short Q3: list the six sources numbered, then one paragraph on regulatory importance (toxicity, efficacy, stability, IP limits).
- Long Q1: structure — intro (principle of limit tests), then one subhead per test with reagent, observation and the WHY chemistry, close with the modified-test note.
- Long Q2: structure — intro, comparison table, properties of a primary standard with the reasoning for each, then NaOH and KMnO_4 as counter-examples, conclusion.

Unit II — Acid-Base Chemistry and Buffer Systems; electrolytes

2.1 Acids, bases, buffers and pH

Three definitions of acids and bases are asked as a set — learn all three, because the examiner wants to see you know the story got broader over time:

Theory	Acid	Base	Limitation
Arrhenius	Gives H^+ in water	Gives OH^- in water	Only works in water; can't explain NH_3 as a base

Theory	Acid	Base	Limitation
Bronsted-Lowry	Proton donor	Proton acceptor	The workhorse of pharmacy — gives us conjugate acid-base pairs ($\text{CH}_3\text{COOH} / \text{CH}_3\text{COO}^-$, $\text{NH}_4^+ / \text{NH}_3$)
Lewis	Electron-pair acceptor	Electron-pair donor	Broadest; covers reactions with no protons at all (e.g. $\text{BF}_3 + \text{NH}_3$)

In pharmacy you will live inside the Bronsted-Lowry world: every buffer, every titration curve and every drug-ionisation problem is a proton being donated and accepted.

The pH scale — and why a log scale

$\text{pH} = -\log_{10}[\text{H}^+]$. The logarithm exists because hydrogen ion concentrations span an absurd range — from 10^0 M in concentrated acid to 10^{-14} M in concentrated alkali. A log scale squeezes that into 0–14. Each single pH unit is a tenfold change in $[\text{H}^+]$: pH 3 has ten times the H^+ of pH 4. At 25°C , pH 7 is neutral, below 7 acidic, above 7 alkaline.

Why pH matters in pharmacy — four places you will meet it again and again:

- 1 Drug solubility — most drugs are weak acids or bases; their ionised form dissolves in water while the unionised form doesn't. pH decides the ratio.
- 2 Drug stability — many drugs hydrolyse at extreme pH (aspirin, penicillins), so formulations are pH-adjusted to the stability sweet spot.
- 3 Drug absorption — weak acids absorb better from the acidic stomach, weak bases from the more alkaline intestine (pH-partition idea you'll meet in biopharmaceutics).
- 4 Preservative efficacy — preservatives like benzoic acid work only in their unionised form, which exists at acidic pH.

Buffers — how they actually resist pH change

Definition: a buffer is a solution that resists change in pH when small amounts of acid or alkali are added. Two types: acidic buffers (a weak acid + its salt, e.g. acetic acid / sodium acetate) and alkaline buffers (a weak base + its salt, e.g. ammonia / ammonium chloride). Pharmaceutical examples: citrate, phosphate and acetate buffers in injections, eye drops and syrups.

Now the WHY, because "it resists pH change" is a slogan, not an understanding. Take the acetate buffer: $\text{CH}_3\text{COOH} \rightleftharpoons \text{CH}_3\text{COO}^- + \text{H}^+$. The solution holds a large reservoir of both the weak acid and its conjugate base. Add a little strong acid (H^+): the conjugate base mops it up — $\text{CH}_3\text{COO}^- + \text{H}^+ \rightarrow \text{CH}_3\text{COOH}$ — so free H^+ barely rises. Add a little strong alkali (OH^-): the weak acid neutralises it — $\text{CH}_3\text{COOH} + \text{OH}^- \rightarrow \text{CH}_3\text{COO}^- + \text{H}_2\text{O}$ — so free OH^- barely rises. The pH stays put because every invader gets converted into a weak, barely-dissociated species. A buffer is essentially a chemical shock absorber with two reservoirs.

The buffer equation (Henderson-Hasselbalch)

For a weak acid $\text{HA} \rightleftharpoons \text{H}^+ + \text{A}^-$, the dissociation constant is $K_a = [\text{H}^+][\text{A}^-] / [\text{HA}]$. Take $-\log$ of both sides and rearrange:

$$\text{pH} = \text{pK}_a + \log([\text{salt}] / [\text{acid}]) \text{ — more precisely, } \log([\text{conjugate base}] / [\text{weak acid}]).$$

For an alkaline buffer: $\text{pOH} = \text{pK}_b + \log([\text{salt}] / [\text{base}])$, then $\text{pH} = 14 - \text{pOH}$.

Two intuitions that make this equation yours rather than a formula you parrot:

- 1 When $[\text{salt}] = [\text{acid}]$, the log term is $\log(1) = 0$, so $\text{pH} = \text{pK}_a$. The buffer sits exactly at the acid's pK_a — its point of maximum resistance.
- 2 The pH depends on the ratio, not the absolute concentrations. Double both and the pH doesn't move — but the buffer gets stronger (see buffer capacity below).

Buffer capacity is the moles of strong acid or base per litre needed to change the pH by one unit. It is maximum when $\text{pH} = \text{pK}_a$ (the 1:1 ratio, where both reservoirs are equally full) and it increases with total buffer concentration (bigger reservoirs absorb bigger shocks). A dilute buffer at the right pH beats a concentrated buffer far from its pK_a — another favourite trap.

Worked example 1 — direct pH. A buffer contains 0.10 M acetic acid and 0.15 M sodium acetate. $K_a = 1.8 \times 10^{-5}$, so $\text{pK}_a = -\log(1.8 \times 10^{-5}) = 4.74$. $\text{pH} = 4.74 + \log(0.15 / 0.10) = 4.74 + \log(1.5) = 4.74 + 0.176 = 4.92$. Notice: more salt than acid pushes the pH above the pK_a — the log term is the nudge.

Worked example 2 — proving the shock absorber. Take 1 L of a 0.10 M / 0.10 M acetate buffer ($\text{pH} = 4.74$). Add 0.01 mol of HCl. The H^+ converts 0.01 mol of acetate into acetic acid: $[\text{salt}] = 0.09$, $[\text{acid}] = 0.11$. New $\text{pH} = 4.74 + \log(0.09 / 0.11) = 4.74 - 0.087 = 4.65$. Adding that much strong acid to pure water would have crashed the pH to 2 — the buffer moved only 0.09 units. That is buffer action, in numbers.

Worked example 3 — alkaline buffer. An ammonia buffer has 0.20 M NH_3 and 0.10 M NH_4Cl . K_b for $\text{NH}_3 = 1.8 \times 10^{-5}$, $\text{pK}_b = 4.74$. $\text{pOH} = 4.74 + \log(0.10 / 0.20) = 4.74 - 0.30 = 4.44$. $\text{pH} = 14 - 4.44 = 9.56$.

GPAT angle: $\text{pH} = \text{pK}_a + \log([\text{salt}]/[\text{acid}])$ — know it cold, including the alkaline-buffer version. Maximum buffer capacity at $\text{pH} = \text{pK}_a$ is asked as a one-liner almost every year.

2.2 Isotonicity

An isotonic solution has the same osmotic pressure as body fluids — equivalent to 0.9% w/v NaCl, which freezes at -0.52°C . Hypertonic = more concentrated than body fluids; hypotonic = less.

Why it matters — the cell as a water balloon. A red blood cell's membrane lets water through but not salts. Put the cell in a hypotonic injection and water rushes in to equalise the concentration — the cell swells and bursts (haemolysis). Put it in a hypertonic solution and water rushes out — the cell shrivels (crenation). Either way the patient is harmed, which is why

large-volume IV fluids must be isotonic. Ophthalmic solutions are adjusted to isotonicity for a different reason — comfort: a non-isotonic eye drop stings, triggers tearing, and the tears wash the drug straight out, so the dose is lost.

Methods of adjusting isotonicity

Method	Idea
Freezing-point depression method	Calculate the freezing-point lowering caused by the drug; add enough NaCl to bring the total depression to 0.52 °C (the value for body fluids)
Sodium chloride equivalent method	Convert the drug quantity into its NaCl equivalent (the amount of NaCl with the same osmotic effect), then make up the difference to 0.9%
White-Vincent method	Calculates the volume of isotonic vehicle needed for a given drug weight
Sprowls method	A simplified tabular version of the White-Vincent calculation

The freezing-point method is the one most often asked: body fluids freeze at $-0.52\text{ }^{\circ}\text{C}$, so any solution freezing at $-0.52\text{ }^{\circ}\text{C}$ is isotonic with them. Find how much your drug depresses the freezing point, and add NaCl to cover the shortfall.

Worked example — freezing-point method. A 1% w/v solution of a drug depresses the freezing point by $0.12\text{ }^{\circ}\text{C}$. How much NaCl must be added to 100 mL to make it isotonic? Needed total depression = $0.52\text{ }^{\circ}\text{C}$; shortfall = $0.52 - 0.12 = 0.40\text{ }^{\circ}\text{C}$. Since 0.9% w/v NaCl gives the full $0.52\text{ }^{\circ}\text{C}$ depression, the NaCl needed = $(0.40 / 0.52) \times 0.9 = 0.69\%$ w/v, i.e. 0.69 g per 100 mL. Simple proportion — but it only works because freezing-point depression is additive and linear at these concentrations.

Trap alert: Isotonic $\neq$ iso-osmotic in the strict physical-chemistry sense examiners sometimes probe, but for this syllabus treat them as the working definition — same osmotic pressure as 0.9% NaCl. And remember the direction: hypotonic $\rightarrow$ water enters the cell $\rightarrow$ haemolysis; hypertonic $\rightarrow$ water leaves $\rightarrow$ crenation. Students flip this under pressure.

2.3 Electrolytes

Compartment	Major ions	Key functions
Extracellular (blood plasma, interstitial fluid)	Na^+ , Cl^- , HCO_3^-	Fluid balance and osmotic pressure (Na^+), acid-base balance (HCO_3^-)

Compartment	Major ions	Key functions
Intracellular (inside cells)	K ⁺ , Mg ²⁺ , phosphate, protein	Membrane potential and nerve impulses (Na ⁺ /K ⁺ pump), muscle contraction (Ca ²⁺ in excitation-contraction coupling), enzyme cofactor (Mg ²⁺)

Electrolytes used in replacement therapy

- Sodium chloride* (NaCl) — 0.9% w/v "normal saline" for fluid and electrolyte replacement; also the reference standard for isotonicity and (in Unit III) a primary standard for argentometric titrations. One compound, three syllabi roles — that's why it carries the asterisk.
- Potassium chloride (KCl) — treats hypokalaemia (low K⁺), common after diuretic therapy or prolonged vomiting. Given diluted, never as a rapid IV bolus — a fast concentrated dose can stop the heart, because extracellular K⁺ sets the cardiac resting membrane potential.
- Calcium chloride (CaCl₂) — treats hypocalcaemia and is used in cardiac resuscitation; supplies Ca²⁺ rapidly into the blood.
- Oral Rehydration Salt (ORS) — for dehydration in diarrhoea. WHO reduced-osmolality formula per litre of clean water: sodium chloride 2.6 g, potassium chloride 1.5 g, anhydrous glucose 13.5 g, trisodium citrate dihydrate 2.9 g (total osmolality 245 mOsm/L). The glucose is not there for energy — the gut absorbs sodium together with glucose through the sodium-glucose co-transporter, so sugar + salt pulls far more water into the body than salt alone. That one line of physiology is the entire reason ORS works, and examiners ask for it directly.

Physiological acid-base balance

Blood pH is held at 7.35–7.45 — a window so tight that drifting outside it is a medical emergency. Three lines of defence:

- 1 Chemical buffers (seconds) — the bicarbonate system (H₂CO₃ / HCO₃⁻) does most of the work, backed by phosphate and protein buffers. The Henderson-Hasselbalch equation for blood is usually written $\text{pH} = 6.1 + \log([\text{HCO}_3^-] / [\text{CO}_2])$.
- 2 The lungs (minutes) — blow off CO₂ to raise pH, retain it to lower pH.
- 3 The kidneys (hours to days) — excrete H⁺ and reabsorb HCO₃⁻ for the long-term correction.

Acidosis = blood pH below 7.35; alkalosis = above 7.45. Each splits into respiratory (a CO₂ problem — lungs) and metabolic (a HCO₃⁻ problem — kidneys/metabolism).

GPAT angle: Blood pH 7.35–7.45; the bicarbonate buffer is the chief blood buffer; ORS composition with the glucose co-transport point; extracellular Na⁺/Cl⁻/HCO₃⁻ vs intracellular K⁺/Mg²⁺/phosphate. This set is pure one-mark territory.

Very short questions (2 marks)

- 1 Write the Henderson-Hasselbalch equation and define each term.
- 2 What is buffer capacity? When is it maximum?
- 3 Define an isotonic solution with an example.
- 4 Name the major extracellular and intracellular ions.
- 5 Give the WHO formula of ORS (per litre).

Short questions (5 marks)

- 1 Explain how a buffer resists pH change when a small amount of strong acid is added, using the acetate buffer as an example.
- 2 Why must large-volume IV fluids be isotonic? Explain haemolysis and crenation.
- 3 Describe the role of lungs and kidneys in maintaining physiological acid-base balance.

Long questions (10 marks)

- 1 Derive the Henderson-Hasselbalch equation. Calculate the pH of a buffer containing 0.10 M acetic acid and 0.15 M sodium acetate ($K_a = 1.8 \times 10^{-5}$), showing every step.
- 2 Discuss the electrolytes used in replacement therapy: sodium chloride, potassium chloride, calcium chloride and ORS — with the composition of ORS and the physiological reason glucose is included.

How to approach these answers

- Very-short Q1: write the equation, then one phrase per term ([salt] = conjugate base, [acid] = weak acid).
- Very-short Q2: definition in one line + "maximum at $\text{pH} = \text{pK}_a$ " — that's the whole answer.
- Very-short Q3: definition + "0.9% w/v NaCl" as the example.
- Very-short Q4: two short lists — extracellular (Na^+ , Cl^- , HCO_3^-), intracellular (K^+ , Mg^{2+} , phosphate).
- Very-short Q5: the four quantities per litre — write them as a clean list.
- Short Q1: open with the buffer definition, then the acetate equilibrium, then trace what happens to added H^+ step by step.
- Short Q2: open with the water-movement logic, then hypotonic → haemolysis and hypertonic → crenation as two contrasting points, close with the IV conclusion.
- Short Q3: one paragraph each for lungs (CO_2 , fast) and kidneys ($\text{H}^+/\text{HCO}_3^-$, slow), plus the buffer first line.
- Long Q1: structure — intro, derivation from K_a step by step, then the numerical with every step shown, conclusion on what the ratio means.
- Long Q2: structure — intro (why replacement therapy), one subhead per electrolyte with use + caution, ORS composition table + the glucose co-transport explanation, conclusion.

Unit III — Titrimetric analysis

This is the heaviest 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. And read the next section with the curves diagram beside you.

3.1 Acid-base titrations

Theories of acid-base indicators — why the colour changes

An indicator doesn't "know" the equivalence point. It is a molecule whose colour depends on pH, and you choose one whose colour-change window sits on the steep part of your titration curve. Two theories explain the colour change:

1. Ostwald's (ionisation) theory. The indicator is itself a weak acid (HIn) or weak base, and its ionised and unionised forms have different colours: $\text{HIn} \rightleftharpoons \text{H}^+ + \text{In}^-$ (say, colour A $\rightleftharpoons$ colour B). By Le Chatelier's principle, adding H^+ (acidic solution) pushes the equilibrium left — you see colour A; removing H^+ (alkaline solution) pulls it right — you see colour B. The colour you observe at any moment is decided by the ratio $[\text{In}^-]/[\text{HIn}]$, which is decided by the pH. The change isn't instantaneous at one pH — it spreads over roughly 2 pH units, which is exactly why every indicator has a range, not a point.

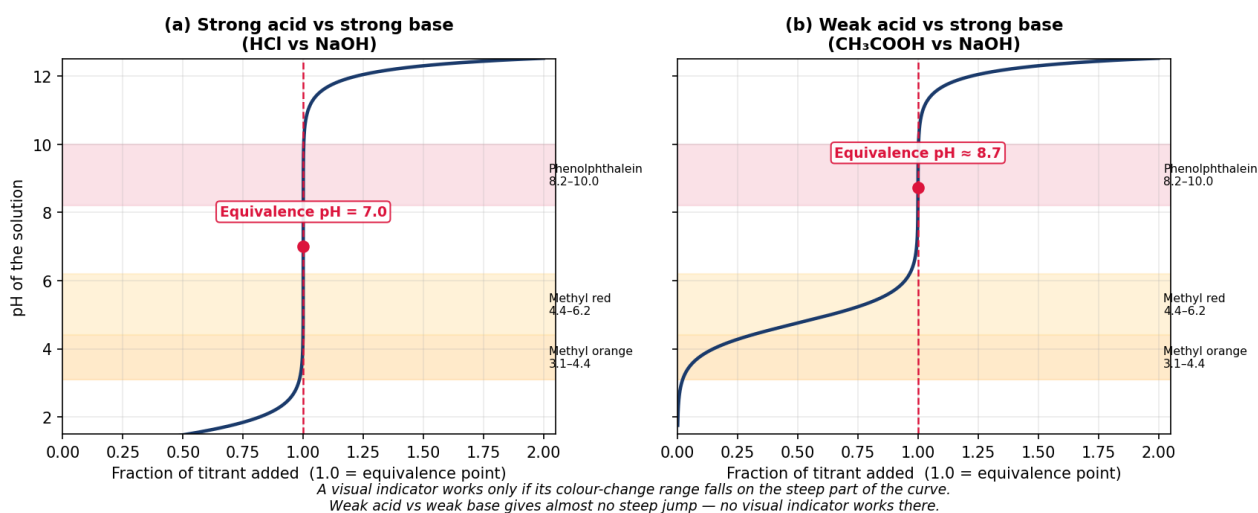
2. Quinonoid theory. The indicator exists in two tautomeric (interconvertible) forms — benzenoid and quinonoid — with different colours, and pH shifts the equilibrium between them. The classic case is phenolphthalein: in acid it sits as the colourless benzenoid lactone (ring closed); in alkali the ring opens to the pink quinonoid form. Methyl orange is the mirror image: red quinonoid in acid, yellow benzenoid in alkali. Ostwald tells you that the ionisation ratio follows pH; quinonoid theory tells you what structural change makes the colour.

Classification of acid-base titrations

Titration	Equivalence pH	Curve shape	Suitable indicator (range)	Why
Strong acid vs strong base (HCl vs NaOH)	7.0	Huge steep jump (pH ~4→10)	Methyl orange (3.1-4.4) or phenolphthalein (8.2-10.0) — both work	The jump is so wide that any indicator changing between pH 4 and 10 lands on it
Strong acid vs weak base (HCl vs NH_4OH)	Below 7 (~5)	Steep jump only on the acidic side	Methyl orange / methyl red (4.4-6.2)	Phenolphthalein changes too late (pH 8+) — past the real equivalence, giving a wrong high titre

Titration	Equivalence pH	Curve shape	Suitable indicator (range)	Why
Weak acid vs strong base (CH_3COOH vs NaOH)	Above 7 (~ 8.7)	Steep jump only on the alkaline side	Phenolphthalein	Methyl orange changes too early (pH ~ 4) — before the real equivalence, giving a wrong low titre
Weak acid vs weak base	~ 7 , but no sharp jump	Nearly flat curve	No visual indicator works	The pH creeps instead of jumping, so no indicator range fits the "steep part" — done by potentiometry or other methods instead

Neutralisation curves: why the indicator must match the titration



Neutralisation curves with indicator ranges marked

Read the diagram carefully: in curve (a) the vertical jump spans the ranges of both methyl orange and phenolphthalein, so both are valid. In curve (b) the jump sits up at pH ~ 8.7 — only phenolphthalein's range touches it. Methyl orange would change colour down at pH 4, while the titration is still far from done. The indicator must match the titration, not the other way round. And the footnote on the diagram is a direct exam statement: weak acid vs weak base has almost no steep portion, so direct visual titration is impossible.

GPAT angle: Indicator pH ranges are pure recall marks — methyl orange 3.1–4.4, methyl red 4.4–6.2, phenolphthalein 8.2–10.0. Pair each with its titration: methyl orange $\rightarrow$ strong acid vs weak base; phenolphthalein $\rightarrow$ weak acid vs strong base; either $\rightarrow$ strong vs strong.

Very weak acids and bases — where water gives up

Between "weak" and "untitratable" lies a class of analytes — very weak acids and bases (many alkaloids, barbiturates, antihistamines) — whose titration curves in water are so flat that no indicator, however well chosen, can find the endpoint. Water's levelling effect caps how acidic or alkaline anything can appear in it. These substances aren't titrated in water at all; they're handed over to non-aqueous titrations (section 3.2), where a protogenic or protophilic solvent boosts the analyte's effective strength until the endpoint snaps into focus. When a question asks "why is this drug assayed non-aqueously?", the answer is always some version of this sentence.

Preparation and standardisation of titrants

Hydrochloric acid is standardised against weighed anhydrous sodium carbonate (primary standard), with methyl orange as indicator: $\text{Na}_2\text{CO}_3 + 2\text{HCl} \rightarrow 2\text{NaCl} + \text{CO}_2 + \text{H}_2\text{O}$. Why methyl orange specifically? Carbonate neutralises in two stages — first to bicarbonate (phenolphthalein endpoint), then to $\text{CO}_2 + \text{water}$ (methyl orange endpoint). Only the methyl orange endpoint captures both protons, so the equivalent weight of Na_2CO_3 is $106/2 = 53$. Using phenolphthalein would give you half the titre and a wrong normality.

Sodium hydroxide is standardised against potassium hydrogen phthalate (KHP) with phenolphthalein. Two precautions, both with the same enemy — carbon dioxide. NaOH solution is prepared with CO_2 -free water (boiled and cooled distilled water) and protected from air, because NaOH absorbs CO_2 to form sodium carbonate — and carbonate titrates differently from hydroxide, silently corrupting every assay you run with that bottle. This is also why NaOH can never be a primary standard (Unit I logic, applied).

Assay of ammonium hydroxide

Ammonia solution (NH_4OH) is assayed by direct titration with standard HCl using methyl red indicator (strong acid vs weak base — the table above tells you why methyl orange/methyl red, not phenolphthalein): $\text{NH}_4\text{OH} + \text{HCl} \rightarrow \text{NH}_4\text{Cl} + \text{H}_2\text{O}$. The practical catch examiners love: ammonia is volatile. The assay is done quickly, in a cooled, stoppered flask, weighing the sample by difference — otherwise ammonia escapes into the air and your assay reads low.

Worked example. 10 mL of ammonia solution is diluted to 100 mL; 25 mL of the dilution needs 18.2 mL of 0.5 M HCl (methyl red endpoint). Moles HCl = $0.5 \times 0.0182 = 0.0091 \text{ mol}$ = moles NH_3 in the 25 mL aliquot. So the 100 mL dilution contains 0.0364 mol, which came from the original 10 mL. Mass $\text{NH}_3 = 0.0364 \times 17.03 = 0.620 \text{ g}$ in 10 mL $\rightarrow 6.20\% \text{ w/v } \text{NH}_3$. Every step is mole bookkeeping — dilution factor first, then the 1:1 reaction.

3.2 Non-aqueous titrations

Why leave water? The levelling effect

Water is an excellent proton donor and acceptor — so good, in fact, that it levels all strong acids to the same strength (H_3O^+) and all strong bases to OH^- . For very weak acids and very weak bases — which many drugs are — water gives a hopelessly flat titration curve with no sharp endpoint. The fix: titrate in a non-aqueous solvent chosen to enhance the acid or base strength of the analyte, sharpening the endpoint.

Types of solvents

Type	Behaviour toward protons	Examples	Used for
Aprotic	Neither donate nor accept — chemically inert, just dissolve	Benzene, chloroform, toluene	Diluent alongside active solvents
Protophilic	Accept protons (proton-accepting solvents) — enhance the strength of dissolved acids	Dimethylformamide (DMF), pyridine, liquid ammonia	Alkalimetry (titration of weak acids)
Protogenic	Donate protons (acidic solvents) — enhance the strength of dissolved bases	Glacial acetic acid	Acidimetry (titration of weak bases)
Amphiprotic	Can both donate and accept	Glacial acetic acid, alcohols	Versatile; acetic acid is the workhorse

Acidimetry (titration of bases): the titrant is perchloric acid in glacial acetic acid, standardised against potassium hydrogen phthalate, with crystal violet indicator (violet → blue → green; the endpoint is taken at the blue-green). Why perchloric acid? In glacial acetic acid it is the strongest available acid — the actual titrating species is protonated acetic acid ($\text{CH}_3\text{COOH}_2^+$), which hands its proton to the weak base sharply. Used for weak-base drugs that water can't handle.

Alkalimetry (titration of acids): the titrant is sodium or lithium methoxide in methanol-benzene (or toluene-methanol), standardised against benzoic acid, with thymol blue indicator. Used for weakly acidic drugs. The solvent mixture must be kept free of water and CO_2 (both are acidic enough here to interfere), and volumes need temperature correction because organic solvents expand much more than water.

Estimation of sodium benzoate — the textbook example. Sodium benzoate is too weak a base to titrate in water, so it's dissolved in glacial acetic acid and titrated with perchloric acid (crystal violet): $\text{C}_6\text{H}_5\text{COONa} + \text{HClO}_4 \rightarrow \text{C}_6\text{H}_5\text{COOH} + \text{NaClO}_4$. Equivalent weight = molecular weight (144.11), so 1 mL of 0.1 M $\text{HClO}_4 \equiv 14.41$ mg of sodium benzoate.

Worked example. A 0.300 g sample of sodium benzoate needed 21.3 mL of 0.1 M HClO_4 . Mass found = 21.3×14.41 mg = 307 mg = 0.307 g. Assay = $(0.307 / 0.300) \times 100 = 102.3\%$ —

slightly over, which in a real lab would trigger a repeat (or an investigation), not a celebration.

Trap alert: "Protogenic" and "protophilic" get swapped constantly. Anchor them: protogenic generates protons (acidic — glacial acetic acid, used to titrate bases); protophilic is proton-philic, proton-loving (proton-accepting — DMF, used to titrate acids). The solvent does the opposite job of what its name suggests — it boosts the analyte, not itself.

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

- 1 Precipitation (with digestion) — the precipitate is heated in its mother liquor ("digested"). Digestion grows larger crystals, which filter easily and adsorb fewer impurities. Skip it and you get a colloidal mess that clogs the filter and drags contaminants along.
- 2 Filtration — through ashless filter paper (ashless, so the paper's own ash doesn't add weight after ignition).
- 3 Washing — removes adsorbed impurities from the crystal surfaces. Washed with a dilute electrolyte solution, not pure water — pure water can peptise the precipitate (break it back into colloidal particles that slip through the filter).
- 4 Drying or ignition to constant weight — "constant weight" means two successive weighings agree: all volatile matter is gone and the composition is fixed.
- 5 Weighing and calculation via the gravimetric factor = (formula weight of analyte / formula weight of precipitate) × (stoichiometric ratio).

Estimation of barium sulphate by gravimetry: Ba^{2+} is precipitated with dilute sulphuric acid as BaSO_4 , digested, filtered, washed, ignited and weighed as BaSO_4 .

Worked example. 1.000 g of a sample gave 0.850 g of BaSO_4 . Gravimetric factor for Ba = $137.3 / 233.4 = 0.5885$. Mass of Ba = $0.850 \times 0.5885 = 0.500 \text{ g} \rightarrow 50.0\% \text{ Ba}$ in the sample. To find sulphate instead, the factor would be $96.1/233.4$ — the factor always points from what you weighed to what you want.

Precipitation (argentometric) titrations — Mohr vs Volhard vs Fajans

The titrant is silver nitrate throughout. Learn the four named methods as one comparison — this table is asked as a 5-marker almost verbatim:

Method	Style	Titrant / indicator	Endpoint observation	Conditions — and WHY
Mohr's	Direct titration of Cl^-/Br^- with AgNO_3	Potassium chromate (K_2CrO_4)	Brick-red Ag_2CrO_4 appears — but only after all Cl^- has precipitated as white AgCl	Neutral solution. In acid, chromate converts to dichromate and the red endpoint never forms properly; in alkali, brown $\text{Ag}_2\text{O}/\text{AgOH}$ precipitates and masks everything
Volhard's	Back titration: excess AgNO_3 added first, the leftover titrated with thiocyanate	Ferric alum (ferric ammonium sulphate)	Red $\text{Fe}(\text{SCN})^{2+}$ complex	Acidic (nitric acid) conditions — acid stops Fe^{3+} hydrolysing to brown $\text{Fe}(\text{OH})_3$, which would hide the endpoint. Suits coloured or acidic samples where Mohr's fails
Modified Volhard's	Volhard's, for chloride specifically	Same as Volhard's	Same red complex	AgCl is filtered off before back-titration, because AgCl reacts with thiocyanate ($\text{AgCl} + \text{SCN}^- \rightarrow \text{AgSCN} \downarrow + \text{Cl}^-$; AgSCN is less soluble). Left in place, it would consume extra thiocyanate and spoil the endpoint

Method	Style	Titrant / indicator	Endpoint observation	Conditions — and WHY
Fajans	Direct titration	Adsorption indicator (fluorescein, eosin)	Colour change on the precipitate surface	Before the endpoint, AgCl particles adsorb Cl^- (negative surface, repels the anionic dye). Just past the endpoint, excess Ag^+ adsorbs instead (positive surface, attracts the dye anion) — the dye adsorbs and changes colour. Dextrin may be added to keep the precipitate colloidal with maximum surface area

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 back-titration $\text{Ag}^+ + \text{SCN}^- \rightarrow \text{AgSCN} \downarrow$, then $\text{Fe}^{3+} + \text{SCN}^- \rightarrow [\text{Fe}(\text{SCN})]^{2+}$ (red).

Trap alert: Three classic confusions in one table. (1) Mohr's is direct, Volhard's is a back titration — if the question says "excess silver nitrate is added first," that's Volhard's, not Mohr's. (2) Mohr's needs neutral solution; Volhard's needs acidic. Swap them and the method fails. (3) Modified Volhard's exists only because of the AgCl-thiocyanate reaction — it's not a different indicator, it's Volhard's plus a filtration step, used for chlorides.

3.4 Complexometric titrations

EDTA (used as disodium EDTA) is a hexadentate ligand — one EDTA molecule wraps a metal ion at six points, forming a stable 1:1 complex regardless of the metal's valency. That 1:1 stoichiometry is the whole basis of complexometry: moles of EDTA used = moles of metal ion present. No valency arithmetic, ever.

Classification

- Direct titration — the metal ion solution is titrated directly with EDTA (e.g. Mg^{2+} , Ca^{2+}).
- Back titration — excess EDTA is added, then the leftover is back-titrated with a standard metal ion solution (for metals that react slowly or precipitate at the titration pH, e.g. aluminium).
- Replacement (substitution) titration — the analyte metal displaces another metal from its EDTA complex, and the freed metal is titrated (for metals without a good indicator of their own).

- Indirect (alkalimetric) titration — used for anions: the anion precipitates a metal, and the leftover metal is titrated with EDTA.

Metal ion indicators — the Eriochrome Black T story

A metal ion indicator is a dye that forms a coloured complex with the metal ion, with a different colour from the free dye. Eriochrome Black T (EBT) at pH 10: the Mg-EBT complex is wine red, free EBT is blue. During the titration, EDTA (which binds the metal far more strongly) strips the metal from the indicator — at the endpoint the last of the wine-red complex breaks and the solution turns blue. So the colour change is wine red → blue, and it happens because EDTA out-competes the indicator for the metal.

Why pH 10? Two reasons: EDTA binds metals effectively only when sufficiently ionised (it needs alkaline conditions to exist as the active Y^{4-} species), and EBT itself shows its proper colours in the pH ~7–11 window. An ammonia-ammonium chloride buffer holds pH 10 through the titration. For calcium specifically, murexide (or Patton-Reeder indicator) is the usual choice.

Masking and demasking agents

Real samples contain interfering metal ions that would also consume EDTA. A masking agent ties up the interferent so it can't react; demasking selectively releases one masked ion later when you want to titrate it.

Agent	What it masks	Note
Potassium cyanide	Heavy metals (Cu^{2+} , Co^{2+} , Ni^{2+} , Zn^{2+})	Forms very stable cyanide complexes; classic but toxic — handled carefully
Sodium fluoride	Al^{3+}	Forms $[AlF_6]^{3-}$
Triethanolamine	Fe^{3+} , Al^{3+}	Complexes them out of the way
Demasking example	Formaldehyde demasks Zn^{2+} from its cyanide complex	Lets you titrate zinc after the rest

Preparation and standardisation of disodium EDTA

EDTA is standardised against a primary standard such as zinc oxide or calcium carbonate (dissolved in a little acid, then buffered to pH 10 and titrated with EBT indicator). EDTA itself can't be primary — the disodium salt's water of crystallisation varies.

Estimation of magnesium sulphate: direct titration with standard EDTA at pH 10 (ammonia buffer), EBT indicator, wine red → blue endpoint. 1 mL of 0.01 M EDTA $\equiv$ 2.465 mg of $MgSO_4 \cdot 7H_2O$.

Worked example. 20.0 mL of a magnesium sulphate solution required 18.5 mL of 0.01 M EDTA. Mass of $MgSO_4 \cdot 7H_2O$ in the 20 mL = 18.5×2.465 mg = 45.6 mg. The 1:1 stoichiometry makes this a single multiplication — that's the beauty of complexometry.

Estimation of Calcium gluconate* — the same principle applied to Ca^{2+} : the sample is dissolved, buffered, and titrated with standard EDTA (murexide or Patton-Reeder indicator for the sharper

calcium endpoint). Moles EDTA = moles Ca^{2+} = moles Calcium gluconate, and the assay follows.

GPAT angle: EDTA forms 1:1 complexes with metal ions irrespective of valency; EBT changes wine red → blue at pH 10; cyanide masks heavy metals, fluoride masks aluminium. These four facts are asked in some form nearly every year.

Very short questions (2 marks)

- 1 State Ostwald's theory of acid-base indicators.
- 2 Why can't a weak acid vs weak base titration be done with a visual indicator?
- 3 Name the titrant, solvent and indicator used in the acidimetric non-aqueous titration of weak bases.
- 4 Why is AgCl filtered off in the modified Volhard's method?
- 5 What colour change does Eriochrome Black T show at the endpoint, and at what pH?

Short questions (5 marks)

- 1 Explain the classification of acid-base titrations with the suitable indicator for each type and the reason for the choice.
- 2 Describe the four types of solvents used in non-aqueous titrations with one example each.
- 3 Compare Mohr's, Volhard's and Fajans methods of precipitation titration.

Long questions (10 marks)

- 1 Describe the principle and steps of gravimetric analysis. Explain the estimation of barium sulphate by gravimetry with a calculation using the gravimetric factor.
- 2 Explain masking and demasking in complexometric titrations with examples. Describe the estimation of magnesium sulphate using EDTA, including the role of Eriochrome Black T and the pH 10 buffer.

How to approach these answers

- Very-short Q1: "indicator is a weak acid/base; ionised and unionised forms have different colours; pH shifts the ionisation" — three phrases, done.
- Very-short Q2: one line — no steep pH jump at equivalence, so no indicator range fits.
- Very-short Q3: three names — perchloric acid in glacial acetic acid, crystal violet. One line.
- Very-short Q4: one line — AgCl reacts with thiocyanate (forming AgSCN), consuming extra titrant.
- Very-short Q5: "wine red to blue, at pH 10" — the whole answer in six words.
- Short Q1: draw the four-row table (titration, equivalence pH, indicator, why) — the table IS the answer.

- Short Q2: four solvent types, one line of behaviour + one example each; close with which type suits acids vs bases.
- Short Q3: the comparison table (style, indicator, endpoint, conditions) — add one WHY per method.
- Long Q1: structure — intro (principle), the five steps with the reason for digestion/washing/constant weight, BaSO_4 procedure, then the worked calculation step by step.
- Long Q2: structure — intro (why interferences matter), masking vs demasking with the agent table, then MgSO_4 estimation: conditions, EBT colour-change mechanism, the pH 10 reasoning, calculation pattern.

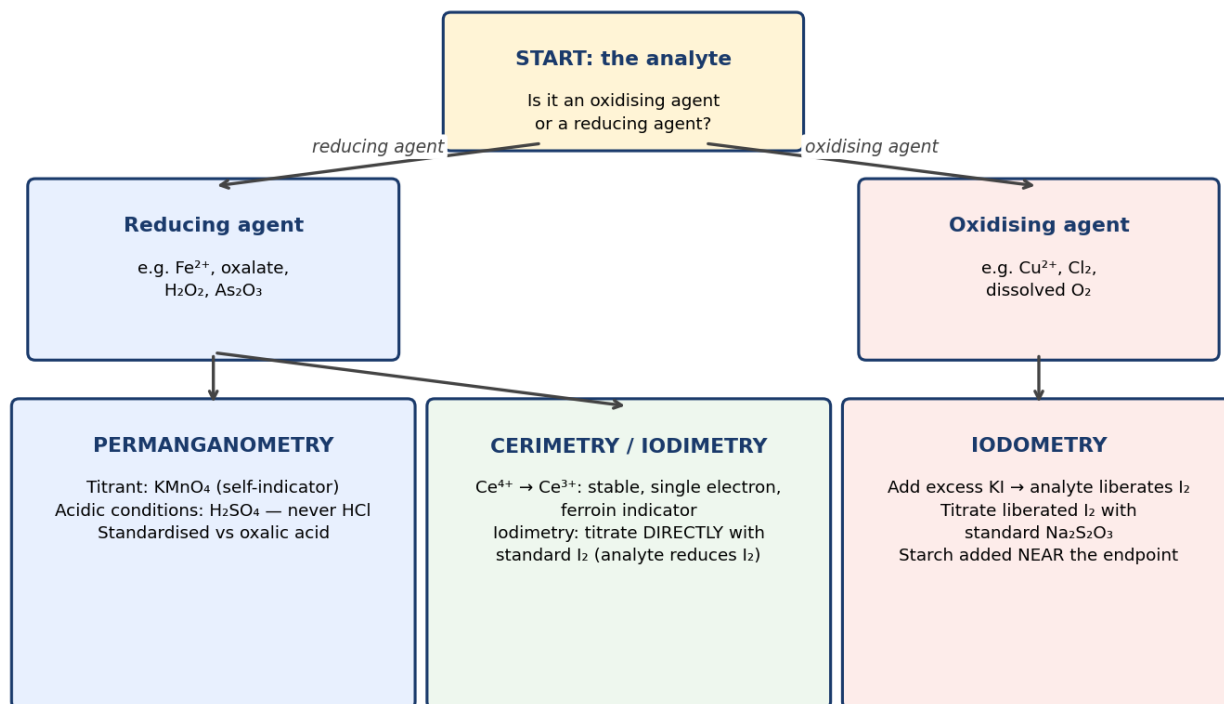
Unit IV — Redox titrations; gastrointestinal agents; radiopharmaceuticals

4.1 Redox titrations

Concepts first. Oxidation is loss of electrons, reduction is gain — they always happen together, because an electron given up must be taken up somewhere. The oxidising agent is the one that gets reduced (it steals electrons); the reducing agent gets oxidised (it donates them). A redox titration needs a visible endpoint: some titrants are self-indicators (KMnO_4 — its own purple colour marks the endpoint), some need a specific indicator (starch for iodine), and some use a redox indicator (ferroin, diphenylamine) that changes colour at a particular electrode potential.

Which redox titration? Follow the analyte

Potassium iodate titrations: a primary-standard-grade oxidant for strongly acidic conditions (Andrews titration).



Which redox titration? Follow the analyte

Permanganometry

Titrant: KMnO₄, a self-indicator — the first drop in excess leaves a permanent pale pink that doesn't fade on shaking. The reaction runs in acidic conditions: $\text{MnO}_4^- + 8\text{H}^+ + 5\text{e}^- \rightarrow \text{Mn}^{2+} + 4\text{H}_2\text{O}$ (purple → colourless). The acid is not optional decoration: without H⁺, permanganate reduces only to brown MnO₂ precipitate instead, and you get no sharp endpoint.

Why sulphuric acid — never hydrochloric acid. HCl is itself oxidised by permanganate to chlorine gas ($2\text{Cl}^- \rightarrow \text{Cl}_2 + 2\text{e}^-$), which consumes extra KMnO₄ and gives a wrong, high titre. Nitric acid is no good either — it's an oxidising agent in its own right and would join the reaction. Dilute H₂SO₄ is the spectator that stays out of the fight.

KMnO₄ is standardised against oxalic acid or sodium oxalate, heated to about 70 °C. Why hot? The permanganate-oxalate reaction is sluggish at room temperature — the first drops decolourise slowly, then the reaction speeds up (the Mn²⁺ formed catalyses it further). Heating gets you past that slow start so the endpoint is trustworthy. Uses: estimation of Fe²⁺, hydrogen peroxide, oxalates.

Cerimetry

Titrant: ceric sulphate (Ce⁴⁺ → Ce³⁺). Two virtues: it's a single-electron change, so the stoichiometry is beautifully simple (1 mole Ce⁴⁺ = 1 mole of electrons = 1 equivalent), and ceric solutions are far more stable than permanganate — they don't decompose on standing or demand the same acidic gymnastics. Indicator: ferroin or diphenylamine. Used for Fe²⁺ estimations where permanganate's side reactions (like the HCl problem) would interfere.

Iodimetry vs iodometry — the pair examiners love to confuse

	Iodimetry	Iodometry
Style	Direct titration with standard iodine solution	Indirect — the analyte liberates iodine first, then you titrate that iodine
The analyte is a...	Reducing agent (it reduces I_2)	Oxidising agent (it oxidises I^- to I_2)
What's in the burette	Standard iodine	Standard sodium thiosulphate
Example	Estimation of arsenious oxide, sodium thiosulphate	Assay of copper sulphate, potassium permanganate — the analyte oxidises added KI, liberating I_2 , which you titrate

The thiosulphate reaction to memorise: $I_2 + 2S_2O_3^{2-} \rightarrow 2I^- + S_4O_6^{2-}$ (iodine $\rightarrow$ iodide; thiosulphate $\rightarrow$ tetrathionate). Starch is the indicator — deep blue starch-iodine complex that vanishes at the endpoint — and it is added near the endpoint, not at the start. Why? At high iodine concentrations the starch-iodine complex binds so tightly that it releases iodine sluggishly, dragging the endpoint and overshooting the titre. Near the endpoint, when most iodine is already gone, the blue appears and disappears crisply.

Trap alert: "Iodimetry" and "iodometry" differ by one letter and everything else. Anchor: iodimetry = I directly (direct titration with iodine; analyte is a reducing agent). Iodometry = I liberated, then measured (analyte is an oxidising agent; KI added; liberated I_2 titrated with thiosulphate; starch near the end). If the burette holds thiosulphate, you're doing iodometry — always.

Titration with potassium iodate

KIO_3 is a stable, high-purity solid — close to primary-standard grade, a relief after temperamental $KMnO_4$. In the Andrews titration (strongly HCl-acidic conditions), iodate oxidises the analyte and the endpoint is marked by iodine monochloride (ICl). Used where iodine titrations are unsuitable — e.g. estimation of arsenious oxide and other reducing agents in strongly acidic solution.

GPAT angle: $KMnO_4$ is self-indicating; H_2SO_4 (not HCl) is the acid in permanganometry — with the chlorine-evolution reason; iodimetry (direct, reducing analyte) vs iodometry (indirect, oxidising analyte, thiosulphate in burette, starch near endpoint). This cluster is among the most repeated in competitive exams.

4.2 Gastrointestinal agents

Acidifiers

Given when stomach acid is deficient (achlorhydria) — without HCl, protein digestion and iron absorption suffer.

- Dilute hydrochloric acid — supplements gastric HCl directly to aid digestion.
- Sodium acid phosphate (NaH_2PO_4) — also used as a urinary acidifier.

Antacids — bases that neutralise excess gastric acid

Ideal properties of an antacid: rapid onset yet reasonably sustained action; should not cause systemic alkalosis; should be bowel-neutral (neither constipating nor laxative on its own); palatable; cheap; and should not evolve large volumes of gas.

Why antacids are combined — the favourite short question in this section. No single antacid is ideal: aluminium salts constipate while magnesium salts are laxative, so combining them (aluminium hydroxide + magnesium hydroxide/trisilicate) balances the bowel effect. Combinations also marry fast onset (e.g. magnesium hydroxide) with slow, sustained action (aluminium hydroxide) and broaden the neutralising capacity. The mixture behaves better than either partner alone.

Antacid	Formula	Key points
Sodium bicarbonate*	NaHCO_3	Systemic antacid — very rapid, but releases CO_2 (belching, flatulence, and in theory rebound distension) and the absorbed sodium can cause systemic alkalosis. Caution in hypertension, cardiac and renal patients (sodium load). Also used in metabolic acidosis and to alkalinise urine
Aluminium hydroxide gel*	$\text{Al}(\text{OH})_3$	Non-systemic, slow-acting, constipating. The gel form gives a huge surface area for acid neutralisation. Also adsorbs phosphate in the gut — used in chronic kidney disease to control high blood phosphate

Agents that promote bowel movement

Mostly osmotic (saline) agents: poorly absorbed ions hold water in the intestinal lumen, the increased volume stimulates peristalsis, and the bowel moves.

Agent	Formula	Action
Magnesium hydroxide	$\text{Mg}(\text{OH})_2$	Osmotic laxative ("milk of magnesia"); doubles as an antacid — the fast-onset partner in antacid combinations
Sodium orthophosphate	Na_3PO_4	Saline purgative; draws water into the bowel osmotically
Sodium potassium tartrate	$\text{KNaC}_4\text{H}_4\text{O}_6$ (Rochelle salt)	Saline purgative; you will meet it again in Unit V as an emetic
Magnesium trisilicate	$\text{Mg}_2\text{Si}_3\text{O}_8$	Antacid with adsorbent action; mildly laxative — which is exactly why it pairs so well with constipating aluminium hydroxide

4.3 Antimicrobials (inorganic)

Inorganic antimicrobials kill microbes by oxidation, protein precipitation, or halogenation — a broad, non-selective chemical attack, unlike the targeted action of organic antibiotics. That lack of selectivity is why most are for external/antiseptic use rather than systemic therapy.

Classification: (1) Oxidising agents — potassium permanganate, hydrogen peroxide; (2) Halogen compounds — chlorinated lime, iodine and its preparations; (3) Others — boric acid (a weak antiseptic).

Antimicrobial	Formula	Use and key points
Potassium permanganate	KMnO_4	Strong oxidising agent; gargle/mouthwash and wound wash in very dilute solution (~1:10000). Stains skin and fabric brown (MnO_2) — the practical point everyone remembers
Boric acid	H_3BO_3	Weak antiseptic; eye washes and dusting powders. Toxic if absorbed in large amounts, especially in infants — never used casually
Hydrogen peroxide*	H_2O_2	3% solution releases nascent oxygen with effervescence ($2\text{H}_2\text{O}_2 \rightarrow 2\text{H}_2\text{O} + \text{O}_2$), which mechanically cleans wounds. It fizzes on wounds because blood and tissue contain catalase, which decomposes it rapidly. Decomposes on storage — kept in light-resistant, cool containers

Antimicrobial	Formula	Use and key points
Chlorinated lime*	Ca(OCl)Cl (bleaching powder)	Releases chlorine on exposure to air and moisture; disinfectant for water and surfaces
Iodine and its preparations	I ₂	Tincture of iodine, povidone-iodine (iodine complexed with a polymer — sustained release, less staining and irritation), Lugol's solution. Broad-spectrum antiseptic; the brown colour itself shows where it has been applied

4.4 Radiopharmaceuticals

Fundamentals of radioactivity

Unstable nuclei decay by emitting alpha, beta or gamma radiation. Half-life ($t_{1/2}$) is the time for half the radioactive atoms to decay — and it decides the isotope's job: short half-life (hours) suits diagnosis (the patient gets a low radiation dose), longer half-life suits therapy. Activity is measured in becquerel (Bq) and curie (Ci).

Applications of radioisotopes

Isotope	Half-life	Application — and why this isotope
Sodium iodide I-131	~8 days	Thyroid diagnosis and therapy (hyperthyroidism, thyroid cancer) — the thyroid selectively takes up iodine, so the radiation goes exactly where it's needed
Technetium-99m	~6 hours	The workhorse of diagnostic imaging (bone, heart, kidney scans). Obtained from a molybdenum-99 generator in the hospital itself; the short half-life keeps the patient's radiation dose low while leaving enough time to prepare and complete the scan
Cobalt-60	~5.27 years	External beam radiotherapy for cancer — penetrating gamma rays aimed at the tumour
Phosphorus-32	~14.3 days	Therapy of polycythaemia vera and some bone conditions — a beta emitter that targets rapidly dividing marrow cells

Safe handling, storage and disposal

The guiding principle is ALARA — As Low As Reasonably Achievable: minimise time near the source, maximise distance, and use shielding (lead containers, lead-lined storage). Store in labelled, secure, shielded areas; dispose only through authorised radioactive-waste channels (including decay storage for short-lived isotopes). In India this is regulated under AERB (Atomic Energy Regulatory Board) guidelines — the exam expects you to name the ALARA principle, the time-distance-shielding trio, and regulatory adherence, not the full rulebook.

GPAT angle: Half-lives — Tc-99m ~6 h, I-131 ~8 d, P-32 ~14.3 d, Co-60 ~5.27 y — with one use each; ALARA expanded; Tc-99m comes from a Mo-99 generator. Half-life-to-application logic ("short $t_{1/2}$ → diagnosis") is the deeper question behind the recall.

Very short questions (2 marks)

- 1 Why is sulphuric acid used instead of hydrochloric acid in permanganometry?
- 2 Distinguish iodimetry from iodometry in one line each.
- 3 List any four ideal properties of an antacid.
- 4 Why are antacids combined instead of given singly?
- 5 Expand ALARA and state its three components.

Short questions (5 marks)

- 1 Explain why starch is added near the endpoint in iodometric titrations.
- 2 Write short notes on sodium bicarbonate and aluminium hydroxide gel as antacids, including one caution for each.
- 3 Give the half-life and one application each of I-131, Tc-99m, Co-60 and P-32.

Long questions (10 marks)

- 1 Describe permanganometry, cerimetry, iodimetry and iodometry, giving the titrant, indicator, reaction conditions and one example assay for each.
- 2 Discuss the safe handling, storage and disposal of radiopharmaceuticals, including the ALARA principle and regulatory guidelines.

How to approach these answers

- Very-short Q1: one line — HCl is oxidised to Cl_2 by KMnO_4 , consuming extra titrant and giving high results.
- Very-short Q2: "iodimetry = direct titration with iodine (reducing analyte); iodometry = liberated iodine titrated with thiosulphate (oxidising analyte)."
- Very-short Q3: any four — rapid onset, sustained action, no systemic alkalosis, bowel-neutral, palatable, cheap.
- Very-short Q4: one line — Al constipates, Mg loosens; the combination balances bowel effects (plus fast + slow onset).

- Very-short Q5: "As Low As Reasonably Achievable — time, distance, shielding."
- Short Q1: open with the starch-iodine complex, then the "added early = too tight binding = sluggish endpoint" logic, close with the crisp near-endpoint behaviour.
- Short Q2: one compact paragraph per antacid — formula, systemic vs non-systemic, speed, and the caution (alkalosis/sodium load; constipation/phosphate binding).
- Short Q3: a four-row table — isotope, half-life, application. The table IS the answer.
- Long Q1: structure — intro (redox concepts + endpoint detection), one subhead per titration with titrant/indicator/conditions/example, close with the decision logic.
- Long Q2: structure — intro (why safety matters), ALARA with the trio explained, storage, disposal, AERB/regulatory adherence, conclusion.

Unit V — Miscellaneous Compounds

A short unit, but every compound here is a direct "write a short note" question. Learn each as: use → key property → one caution. Notice how many of them link back to earlier units — examiners enjoy those cross-links.

5.1 Expectorants

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

Expectorant	Formula	How it works	Note
Potassium iodide	KI	Stimulates bronchial glands to increase respiratory tract fluid, thinning the mucus	Unit IV crossover: KI is the classic reagent for liberating iodine in iodometry — the same salt, two syllabi
Ammonium chloride*	NH ₄ Cl	Reflex expectorant — it irritates the gastric mucosa, triggering a vagal reflex that increases bronchial secretion	Also a systemic acidifier and diuretic. Large doses can cause systemic acidosis — the liver converts the ammonium part to urea, releasing acid equivalents into the blood. That's the caution to quote

5.2 Emetics

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

Emetic	Formula	Key points
Copper sulphate*	$\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$	Prompt emetic; also an astringent and fungicide. The dose window matters — excess causes copper poisoning, so it is never dosed casually
Sodium potassium tartrate	$\text{KNaC}_4\text{H}_4\text{O}_6 \cdot 4\text{H}_2\text{O}$ (Rochelle salt)	Listed here as an emetic, but better known as a saline purgative — you met it in Unit IV. Know both roles; the question may come from either side

5.3 Haematinics

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

Why ferrous (Fe^{2+}), not ferric (Fe^{3+})? Iron is absorbed in the ferrous state in the duodenum (through the DMT1 transporter). Ferric iron must first be reduced before it can be absorbed — an extra, unreliable step. So ferrous salts give better, more predictable absorption. This is the same redox logic as Unit IV wearing a clinical coat.

Haematinic	Formula	Key points
Ferrous sulphate*	$\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$	The standard oral iron salt. Given with vitamin C, which keeps iron reduced and improves absorption. Common side effects: constipation and black stools — warn the patient so they don't panic. Absorbed best on an empty stomach, but taken with food if it irritates the gut (absorption vs tolerance trade-off)
Ferrous gluconate	$\text{C}_{12}\text{H}_{22}\text{FeO}_{14}$	Milder on the stomach than the sulphate — preferred when ferrous sulphate causes gastric irritation. Slightly lower elemental iron content, so the dose is adjusted accordingly

GPAT angle: "Why are ferrous salts preferred over ferric salts as haematinics?" — because iron is absorbed as Fe^{2+} in the duodenum. One line, one mark, asked repeatedly.

5.4 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 ($\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$) — the syllabus antidote, with two jobs:

- 1 Cyanide poisoning (given with sodium nitrite): it donates sulphur, converting toxic cyanide into thiocyanate (SCN^-), which the kidneys excrete harmlessly.
- 2 Halogen neutralisation: it reduces excess iodine or chlorine — the very same reaction as the iodometric titration endpoint: $\text{I}_2 + 2\text{S}_2\text{O}_3^{2-} \rightarrow 2\text{I}^- + \text{S}_4\text{O}_6^{2-}$. Unit III's titration chemistry, saving lives in the casualty ward.

Very short questions (2 marks)

- 1 What is a reflex expectorant? Give one example.
- 2 Why are ferrous salts preferred over ferric salts as haematinics?
- 3 Classify antidotes with one example each.
- 4 Give the formula and one use of copper sulphate.
- 5 Why is vitamin C given along with ferrous sulphate?

Short questions (5 marks)

- 1 Write short notes on potassium iodide and ammonium chloride as expectorants.
- 2 Explain the classification of antidotes with one example for each type.
- 3 Describe how sodium thiosulphate acts as an antidote in cyanide poisoning.

Long questions (10 marks)

- 1 Discuss haematinics: why ferrous salts are used, the role of vitamin C, and a comparative note on ferrous sulphate and ferrous gluconate including cautions.
- 2 Define poison and antidote. Classify antidotes with examples, and explain the antidotal actions of sodium thiosulphate in detail.

How to approach these answers

- Very-short Q1: one line — acts via gastric irritation → vagal reflex → bronchial secretion; example ammonium chloride.
- Very-short Q2: one line — iron is absorbed as Fe^{2+} in the duodenum; ferric needs prior reduction.

- Very-short Q3: three types, one example each — keep it to three short lines.
- Very-short Q4: " $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ — prompt emetic" — formula plus use, done.
- Very-short Q5: one line — keeps iron in the reduced (ferrous) state, improving absorption.
- Short Q1: one compact paragraph per drug — mechanism, then the caution for ammonium chloride.
- Short Q2: three numbered types with definitions and one example each; close with one line on how they differ.
- Short Q3: trace the mechanism step by step — sulphur donation → thiocyanate → renal excretion; mention the nitrite partner.
- Long Q1: structure — intro (iron-deficiency anaemia), the Fe^{2+} absorption logic, vitamin C role, then a comparison table of the two salts, cautions, conclusion.
- Long Q2: structure — definitions, classification with examples under three subheads, then sodium thiosulphate's two antidotal actions with the key reaction, conclusion.