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B.PHARM SEMESTER I

Pharmaceutical Inorganic and Analytical Chemistry

(Course Code: BP106T)

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UNIT III

Titrimetric Analysis

SHORT NOTES

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

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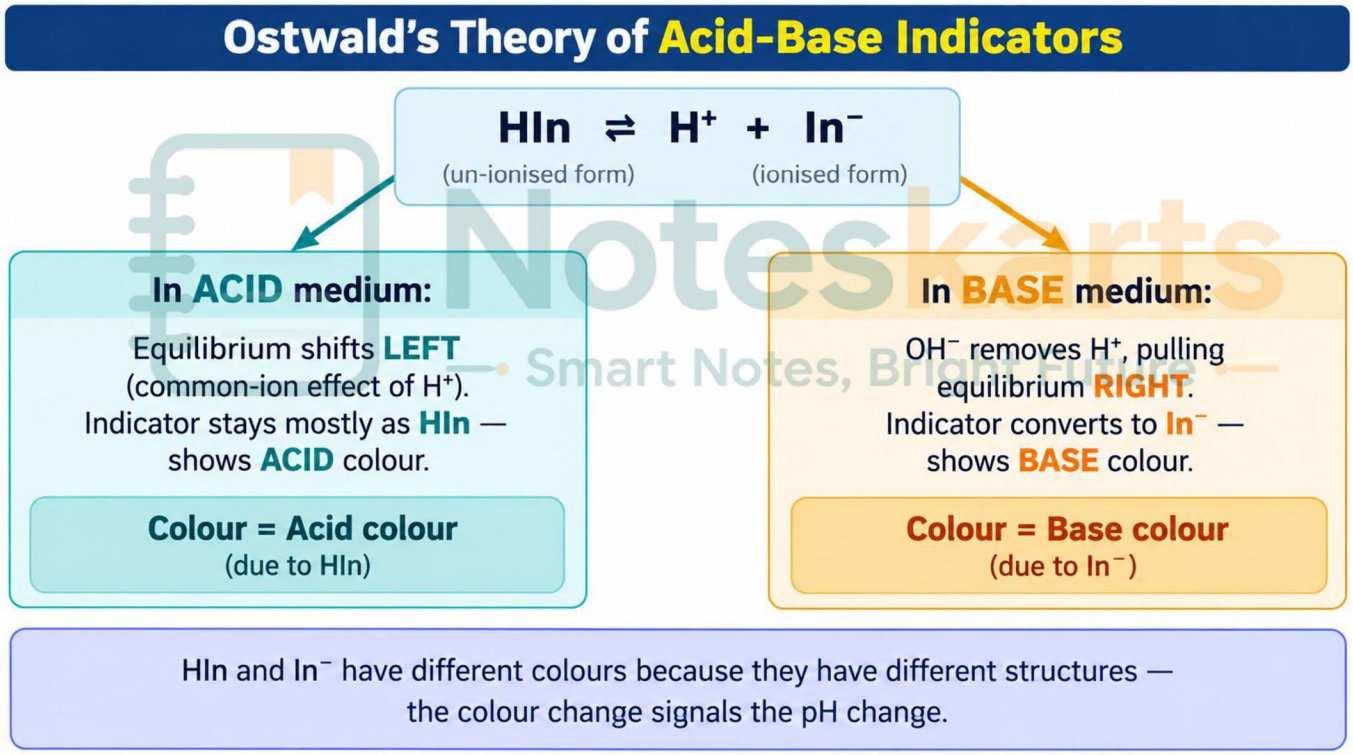
Short notes for Unit III, covering all five types of titrimetric analysis. Condensed bullets, tables and key diagrams for fast revision.

3.1 Acid-Base Titrations

- **Ostwald's Theory of Indicators:**
  An acid–base indicator is a **weak organic acid or weak base** that shows different colours in its ionised and unionised forms.
- For an acidic indicator:

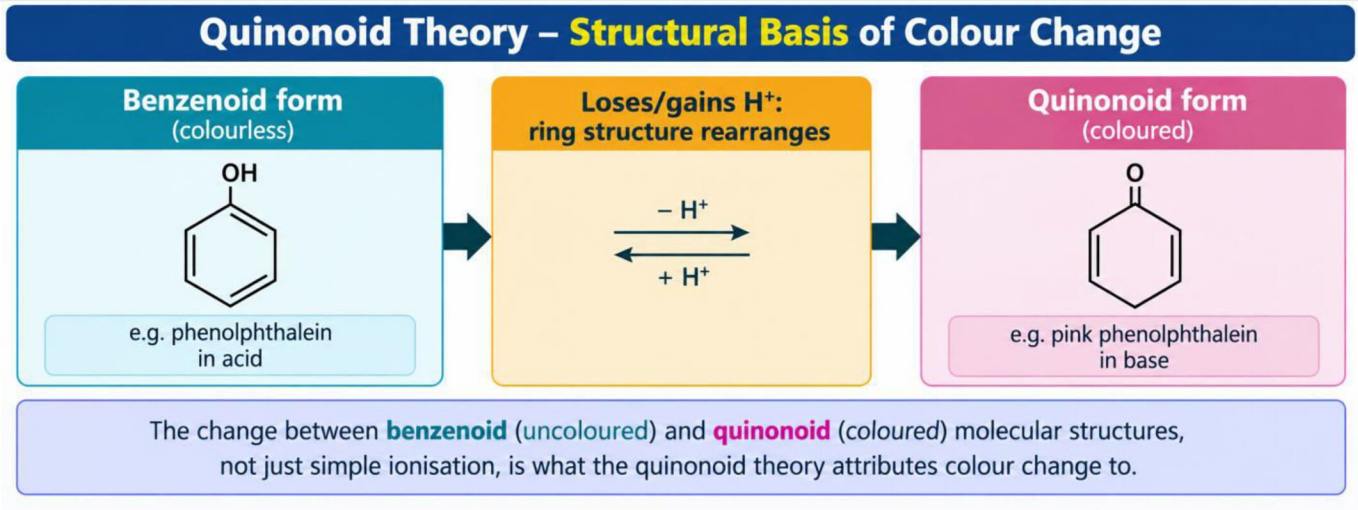
  $HIn \rightleftharpoons H^+ + In^-$

  - **HIn** → unionised form → **acid colour**
  - **In^-** → ionised form → **base colour**
- The colour of the indicator changes depending on the **pH of the solution**.
- The indicator changes colour over a specific **pH transition range**, which should ideally include the **equivalence point** of the titration.

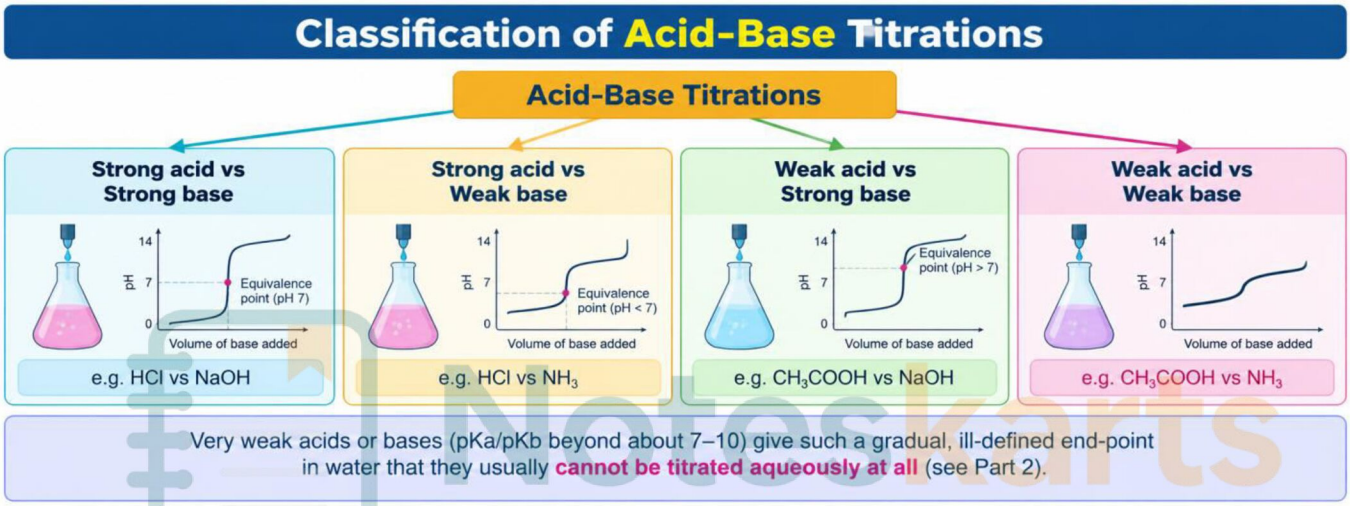


Ostwald's ionisation theory

- Quinonoid theory: colour change = benzenoid (uncoloured) ↔ quinonoid (coloured) structural change.

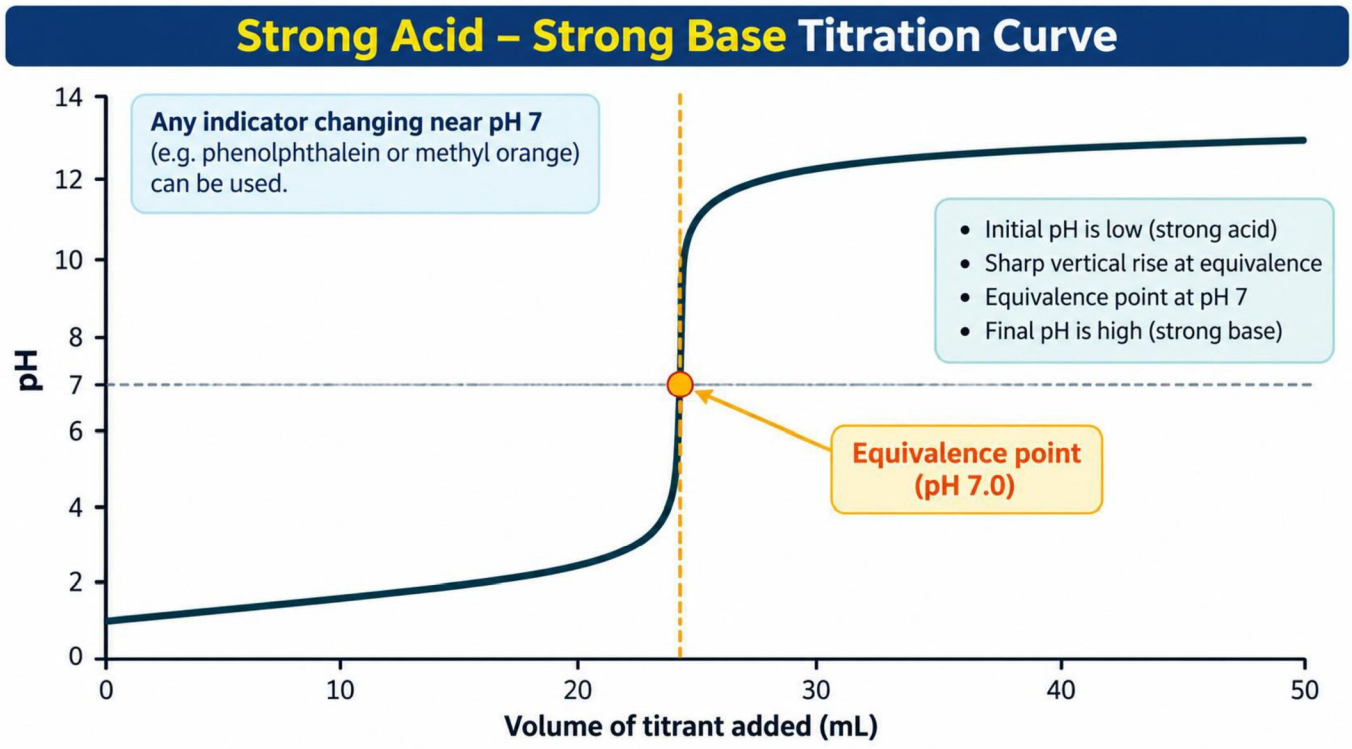


Quinonoid structural change

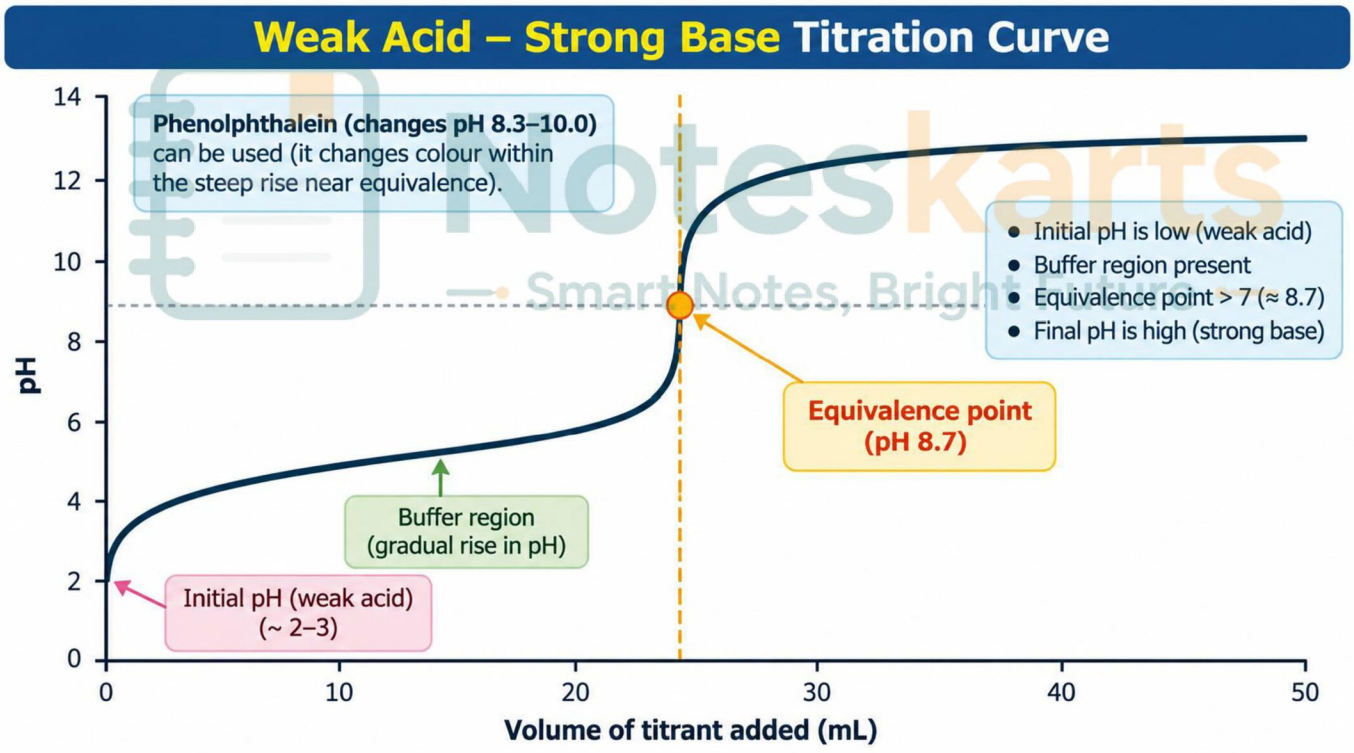


Classification of acid-base titrations

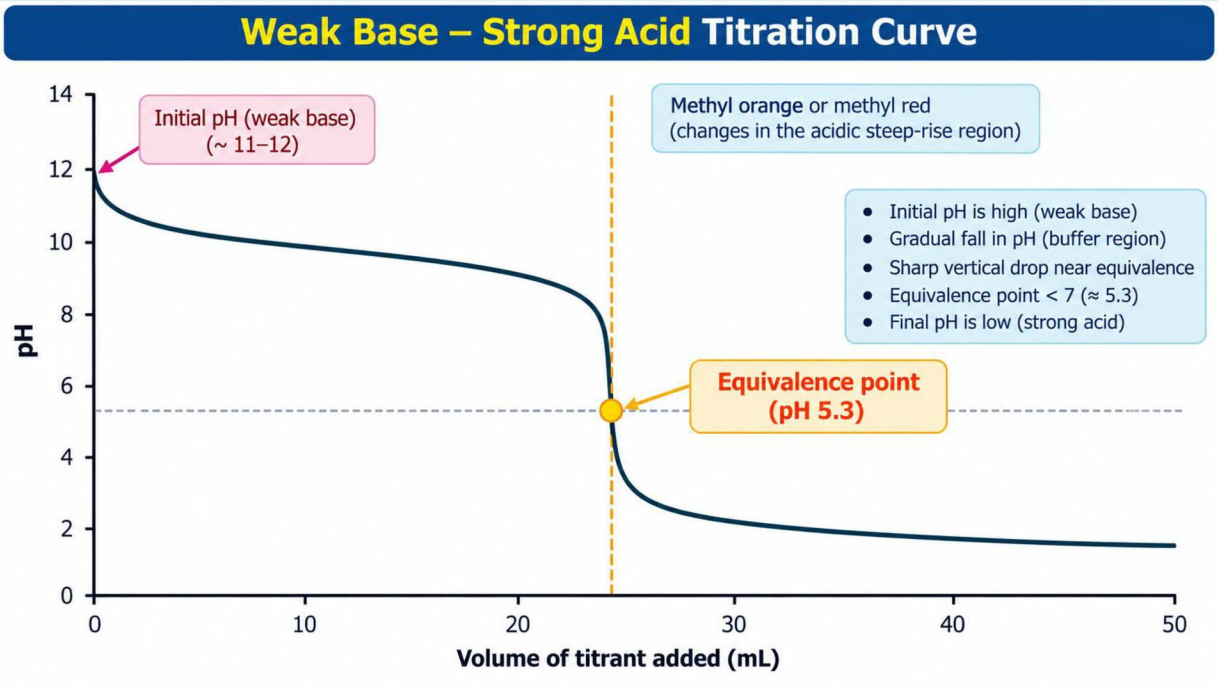
Combination	Equivalence pH	Indicator
Strong acid / Strong base	7	Phenolphthalein or methyl orange
Strong acid / Weak base	< 7	Methyl orange / methyl red
Weak acid / Strong base	> 7	Phenolphthalein
Weak acid / Weak base	No sharp break	None reliable



Strong acid–strong base titration curve



Weak acid–strong base titration curve



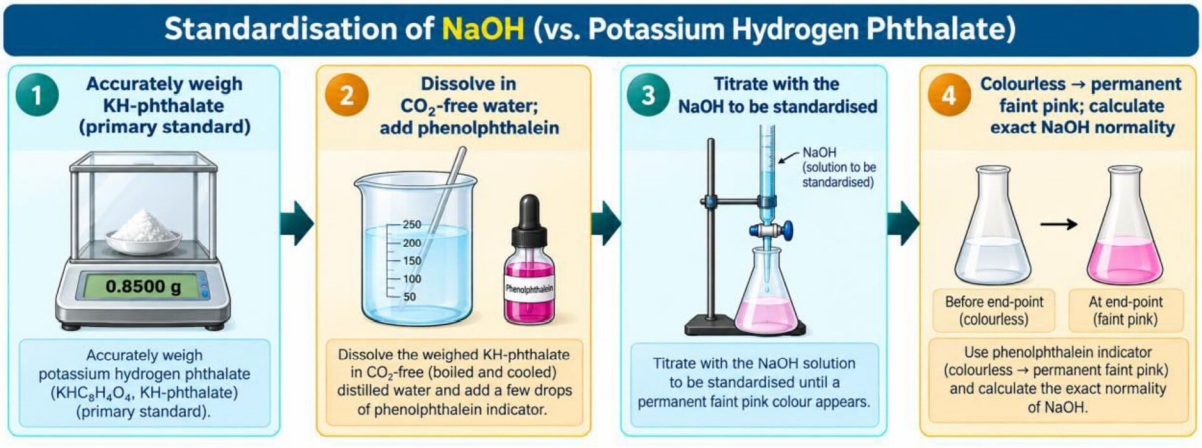
Weak base–strong acid titration curve

Standardising HCl against sodium carbonate

WORKED EXAMPLE — STANDARDISING HCL

0.265 g anhydrous Na_2CO_3 (eq. wt. 53) needs 19.8 mL HCl (methyl orange).

Normality of HCl = (0.265/53) / 0.0198 = 0.253 N



Standardising NaOH against KH-phthalate

WORKED EXAMPLE — STANDARDISING NAOH

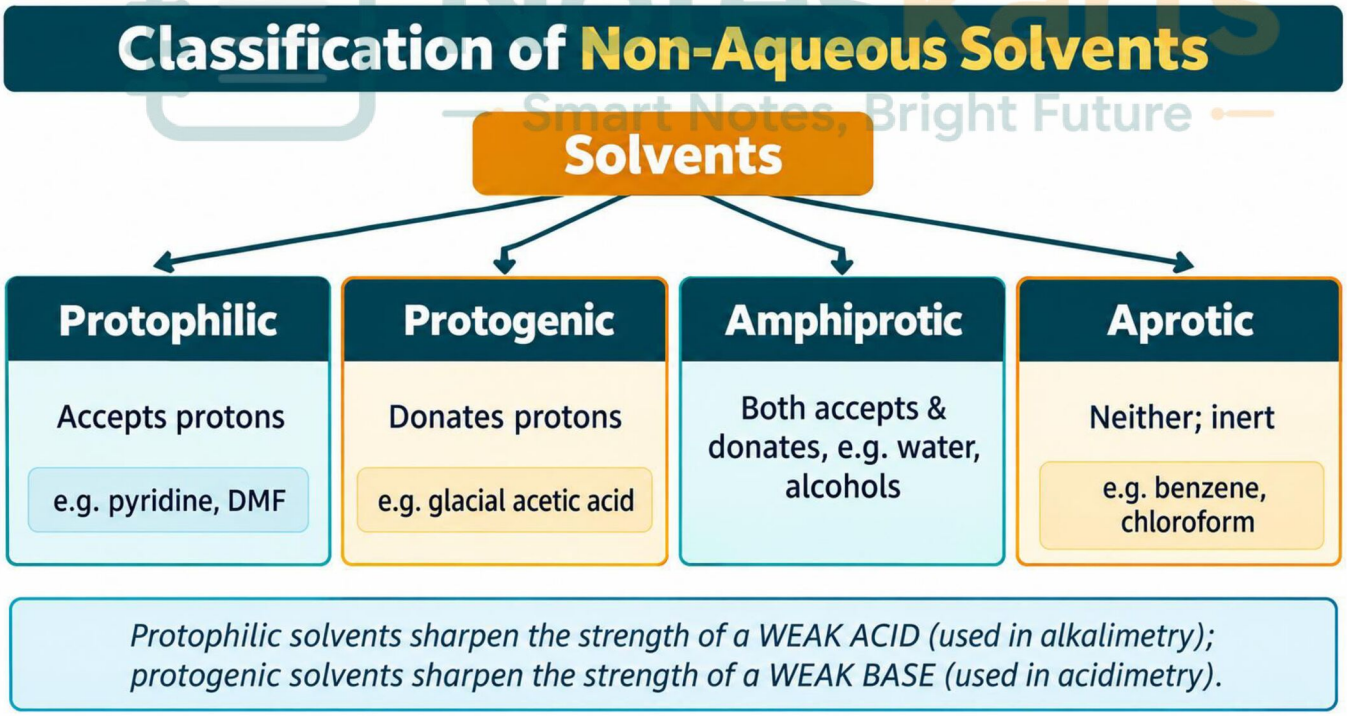
0.408 g KH-phthalate (eq. wt. 204.2) needs 20.0 mL NaOH (phenolphthalein).

Normality of NaOH = (0.408/204.2) / 0.020 = 0.100 N

- **Ammonium hydroxide assay**: direct titration vs standard acid, methyl red indicator (equivalence point is acidic; never phenolphthalein).
- **Double indicator method (Na_2CO_3/$NaHCO_3$ mixture):** titrate to phenolphthalein end-point (V_1), then continue with methyl orange (V_2); V_1 → carbonate, (V_2−V_1) → bicarbonate.

3.2 Non-Aqueous Titrations

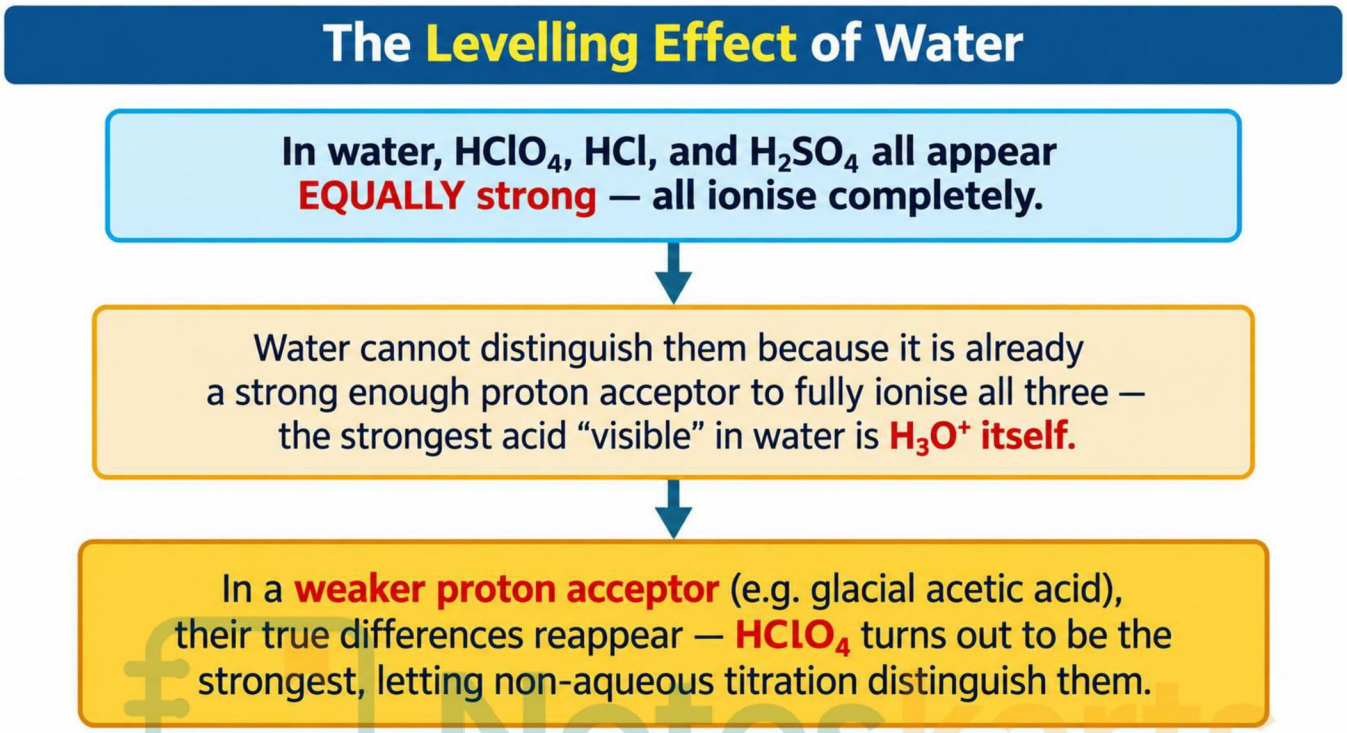
- **Non-aqueous titration** is a titration carried out in a **solvent other than water**.
- It is mainly used for the assay of **very weak acids or weak bases** that do not give a sharp end-point in aqueous solution.
- In water, the **levelling effect** can make weak acids or bases behave similarly, resulting in a **poor or indistinct end-point**.
- Using a suitable non-aqueous solvent increases the apparent strength of the analyte and produces a **sharper, more distinct end-point**.
- **Pharmaceutical importance:** Commonly used for the assay of **weakly acidic or basic drug substances**.



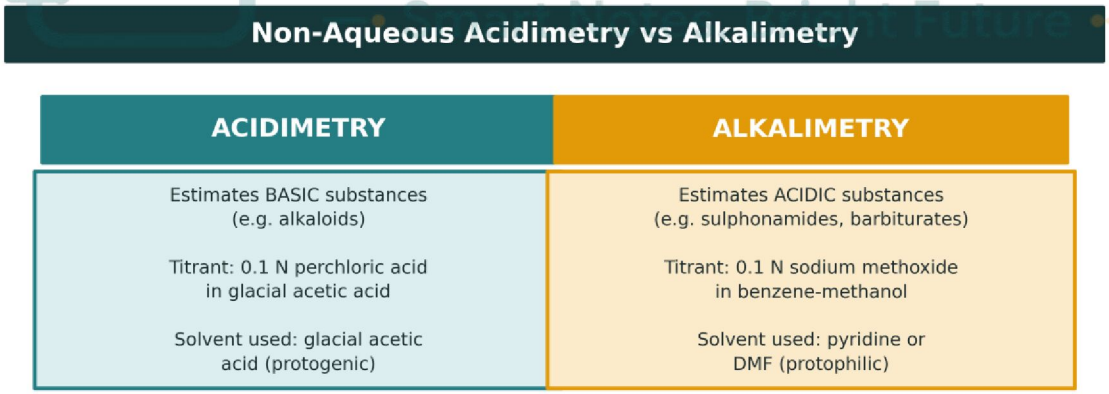
Classification of non-aqueous solvents

Solvent Type	Behaviour	Example	Used For
Protophilic	Accepts protons	Pyridine, DMF	Alkalimetry (weak acids)

Solvent Type	Behaviour	Example	Used For
Protogenic	Donates protons	Glacial acetic acid	Acidimetry (weak bases)
Amphiprotic	Both	Water, methanol	Co-solvent
Aprotic	Neither	Benzene, chloroform	Lowers dielectric constant



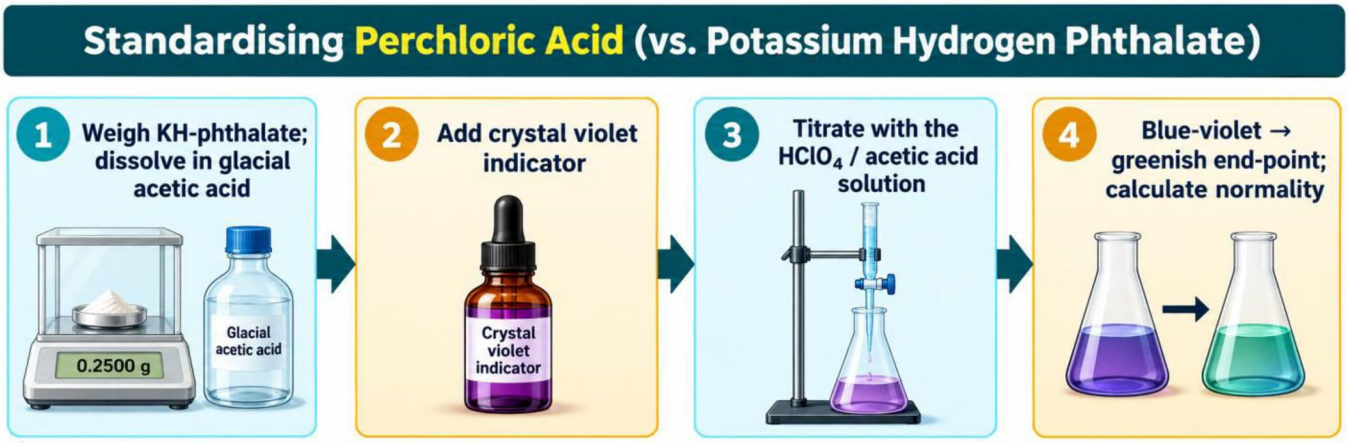
The levelling effect of water



Acidimetry vs alkalimetry

	Acidimetry	Alkalimetry
Estimates	Basic substances (alkaloids)	Acidic substances (sulphonamides, barbiturates)
Titrant	0.1 N $HClO_4$ in glacial acetic acid	0.1 N sodium methoxide in benzene-methanol
Indicator	Crystal violet	Thymol blue

- Mercuric acetate is added when the sample is a hydrochloride salt, masking Cl^- so it does not consume titrant.

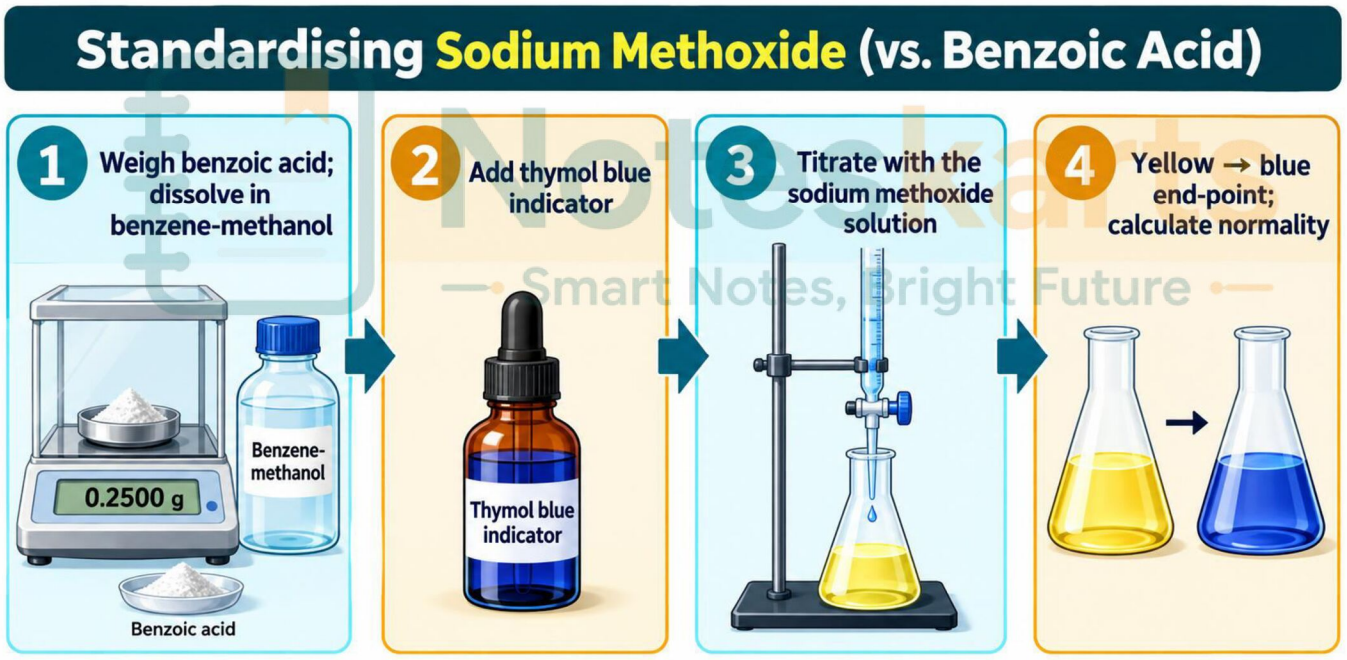


Standardising $HClO_4$

WORKED EXAMPLE — STANDARDISING PERCHLORIC ACID

0.204 g KH-phthalate (204.2) needs 10.0 mL $HClO_4$ (crystal violet).

Normality = (0.204/204.2)/0.010 = 0.100 N

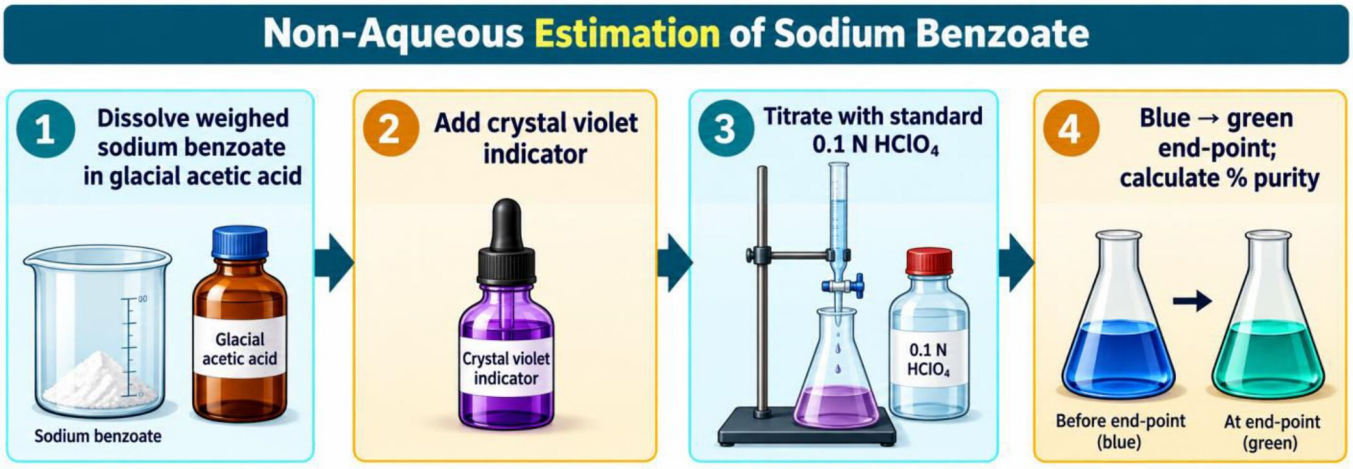


Standardising sodium methoxide

WORKED EXAMPLE — STANDARDISING SODIUM METHOXIDE

0.122 g benzoic acid (122.1) needs 10.0 mL sodium methoxide (thymol blue).

Normality = (0.122/122.1)/0.010 = 0.100 N

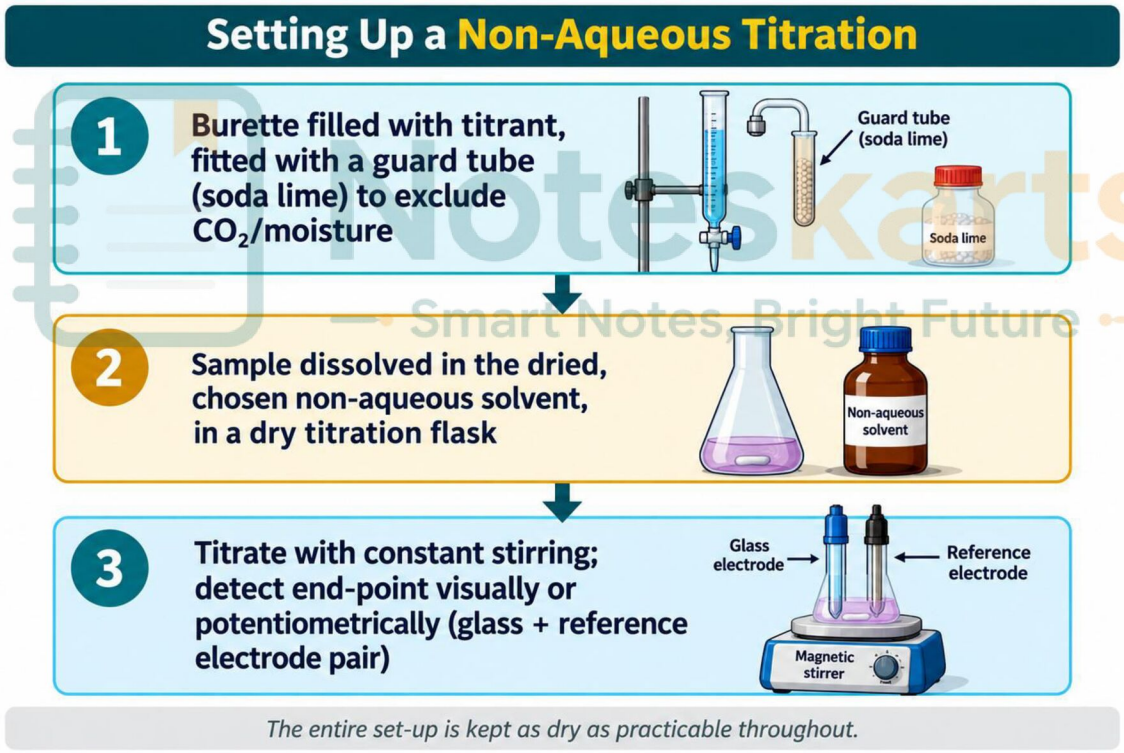


Non-aqueous estimation of sodium benzoate

WORKED EXAMPLE — ESTIMATION OF SODIUM BENZOATE

0.144 g sodium benzoate (144.1) needs 9.8 mL of 0.1 N $HClO_4$.

Weight reacting = 0.1×0.0098×144.1 = 0.1412 g; % purity = 98.1%



General set-up for a non-aqueous titration

3.3 Precipitation Titrations and Gravimetry

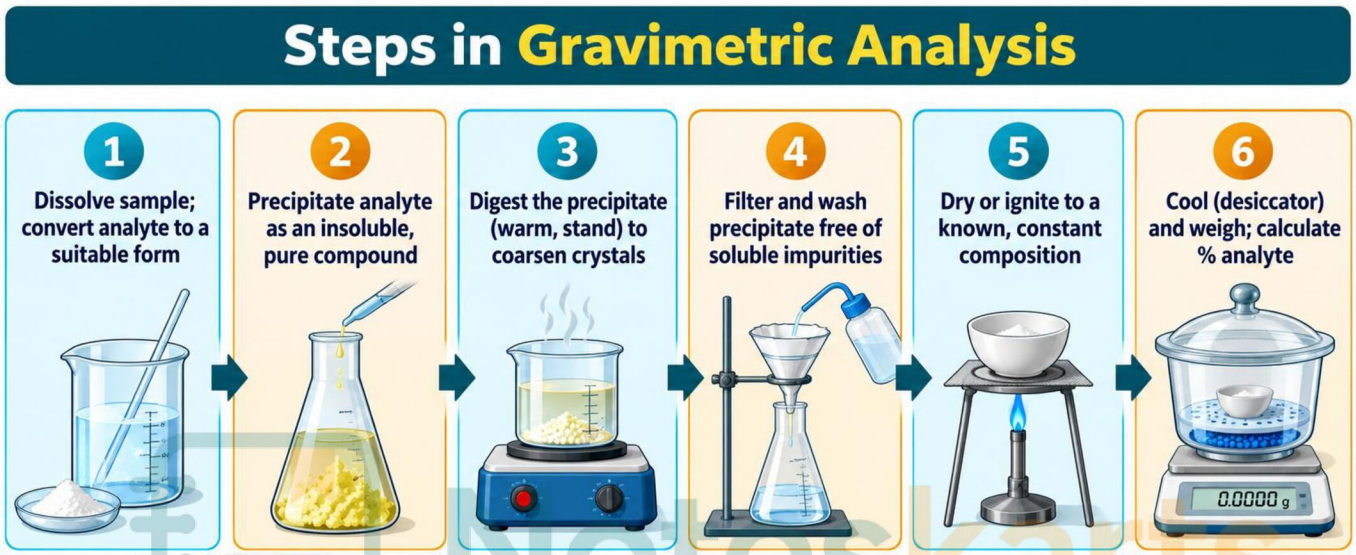
Gravimetric Analysis

- **Dissolve** – dissolve the sample and convert the analyte into a suitable soluble form.
- **Precipitate** – convert the analyte into an **insoluble precipitate**.
- **Digest** – warm and allow the precipitate to stand so that the particles become larger and purer.

- **Filter & Wash** – separate the precipitate and wash it to remove soluble impurities.
- **Dry or Ignite** – dry or heat the precipitate to obtain a **known, constant composition**.
- **Cool & Weigh** – cool the precipitate in a **desiccator**, then weigh it accurately.
- **Calculate** – determine the amount or **percentage of analyte** from the mass of the precipitate.

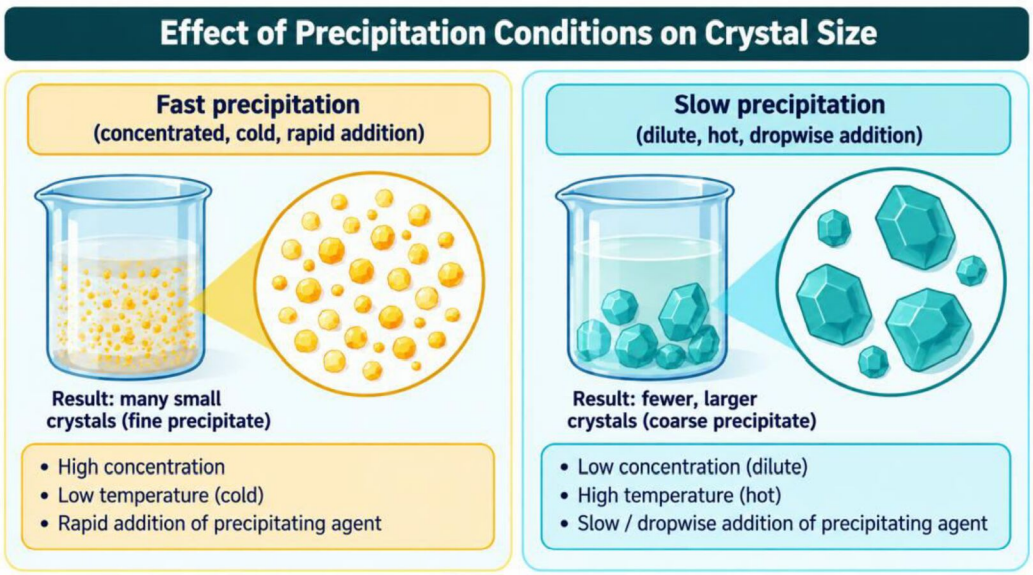
Sequence

Dissolve → Precipitate → Digest → Filter & Wash → Dry/Ignite → Cool & Weigh → Calculate % Analyte



The six steps of gravimetric analysis

- A good precipitate: low solubility, easily filterable (large crystals, not colloidal), high purity, known fixed composition after drying/igniting.

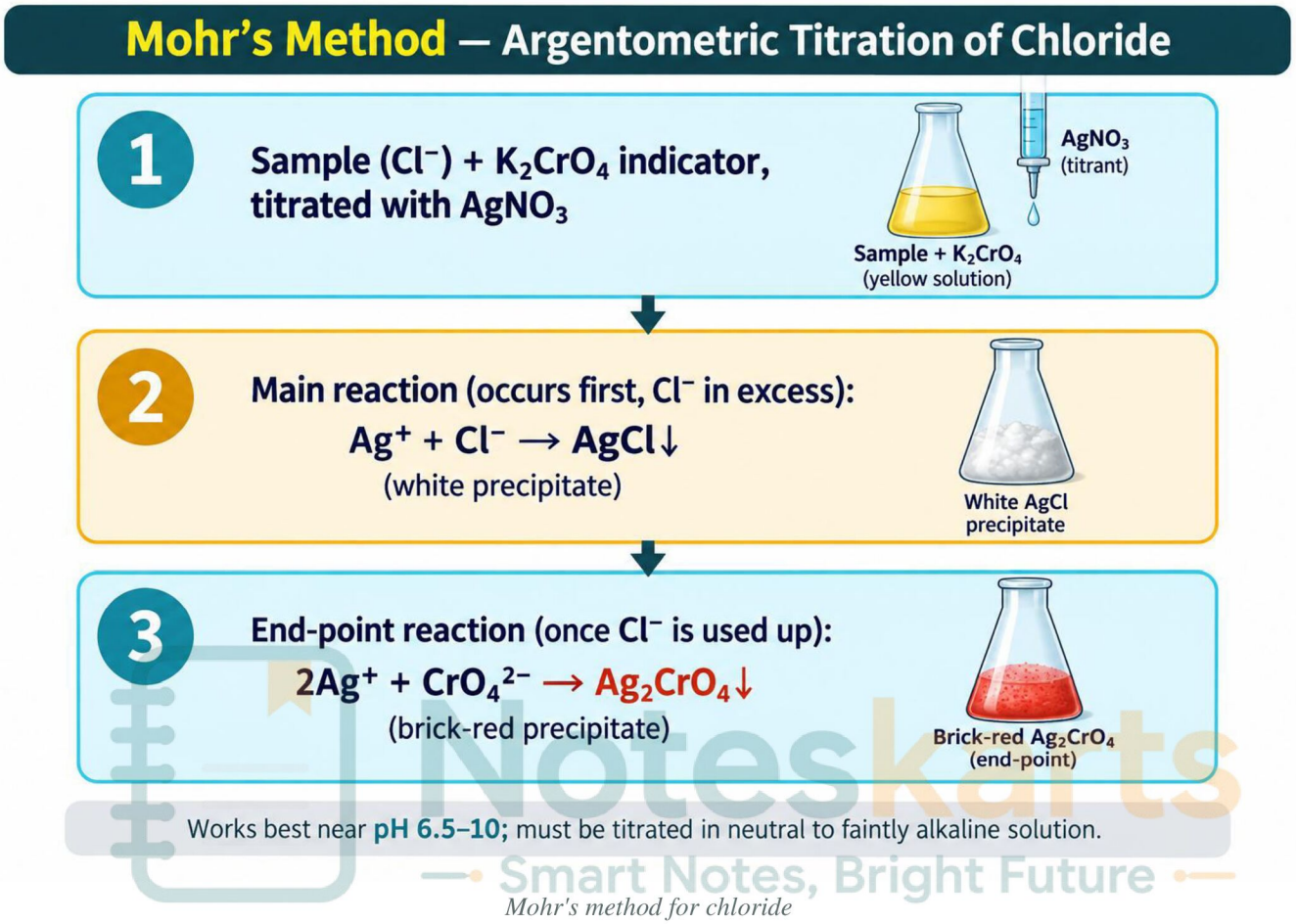


Effect of precipitation conditions on crystal size

WORKED EXAMPLE — GRAVIMETRIC FACTOR

0.4200 g $BaSO_4$ (233.4) obtained. Weight of Ba (137.3) present?

Gravimetric factor = 137.3/233.4 = 0.588; Weight of Ba = 0.4200×0.588 = 0.247 g



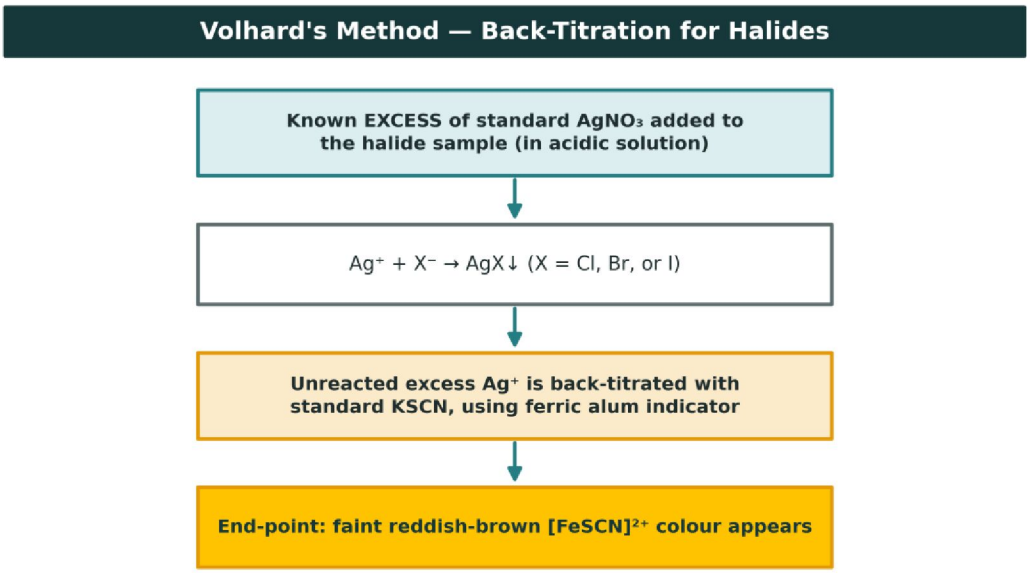
Mohr's method for chloride

- Mohr's method: Cl^- + $AgNO_3$, K_2CrO_4 indicator (brick-red Ag_2CrO_4 end-point); needs pH 6.5–10.5.

WORKED EXAMPLE — MOHR'S METHOD

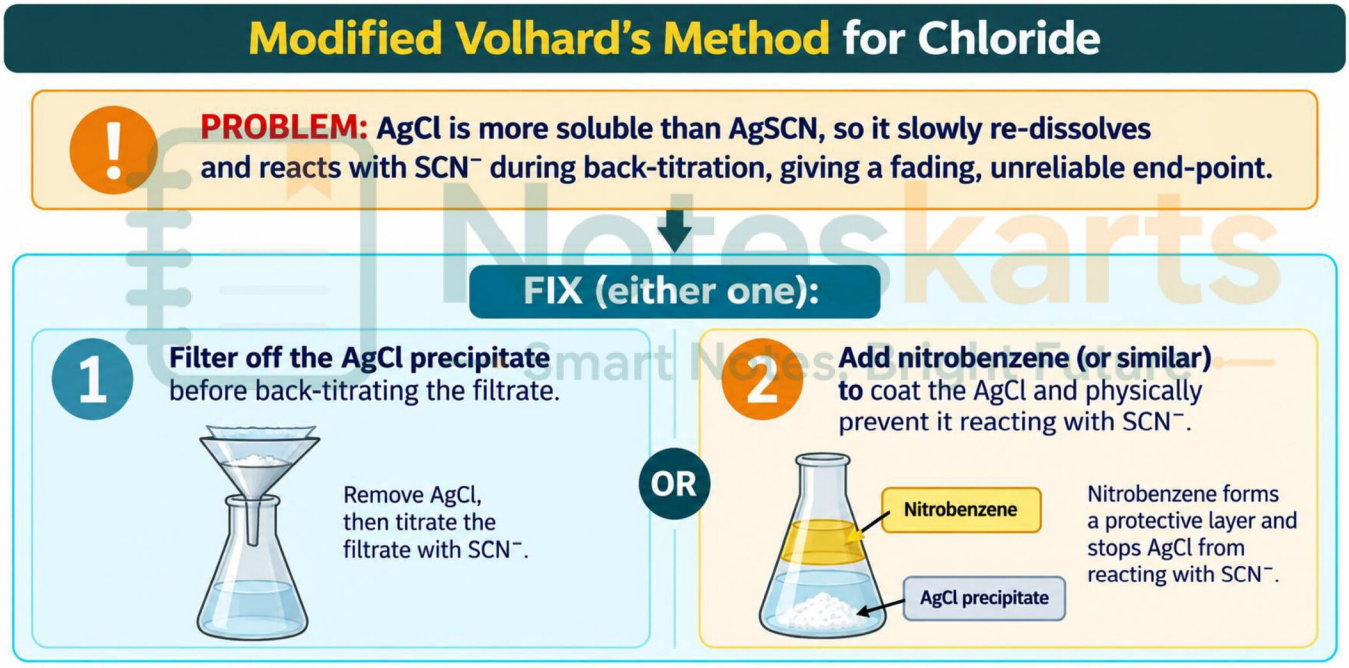
0.500 g NaCl titrated with 0.100 M $AgNO_3$, requiring 82.4 mL.

Moles $AgNO_3$ = 0.00824 mol = moles NaCl; Weight = 0.4816 g; % purity = 96.3%



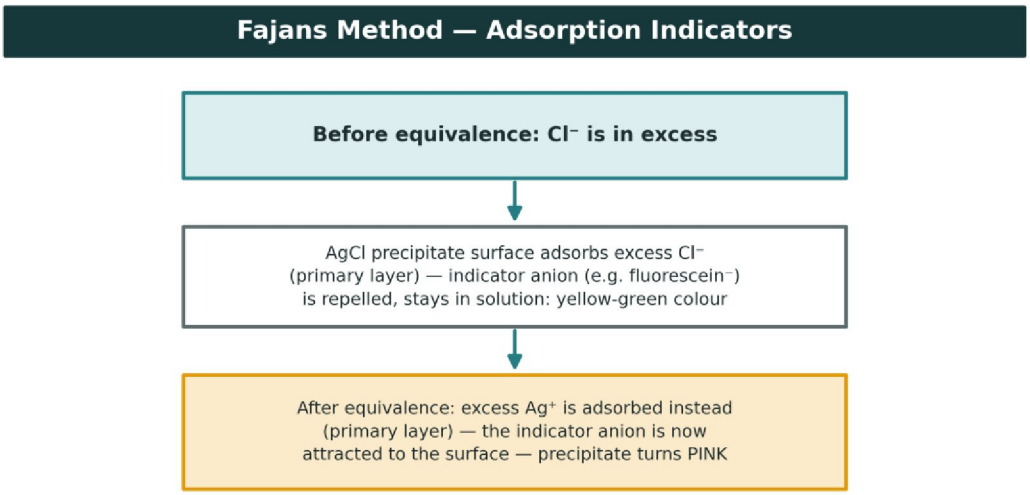
Volhard's back-titration

- Volhard's method: excess $AgNO_3$ added, back-titrated with KSCN, ferric alum indicator (red $[FeSCN]^{2+}$); works in acid.



The AgCl solubility problem and its fix

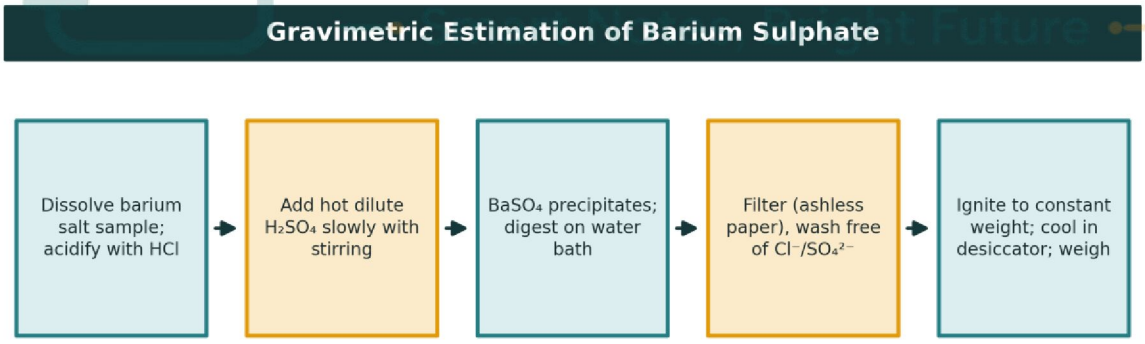
- Modified Volhard's: for Cl^- specifically, AgCl is more soluble than AgSCN — filter AgCl first or add nitrobenzene to isolate it. Not needed for Br^-/I^-.



Adsorption indicator mechanism

- Fajans' method: direct titration using an adsorption indicator (fluorescein) — precipitate turns pink at the end-point; wider pH range, no back-titration needed.

Method	Type	Indicator/Detection	Key Limitation
Mohr's	Direct	K_2CrO_4	Narrow pH range; not for I^-/SCN^-
Volhard's	Back-titration	Ferric alum	Chloride needs modification
Modified Volhard's	Back-titration	Ferric alum	Extra filtration/nitrobenzene step
Fajans'	Direct	Adsorption indicator	Precipitate must stay colloidal



Gravimetric estimation of barium sulphate

WORKED EXAMPLE — GRAVIMETRIC ESTIMATION OF BARIUM

1.000 g $BaCl_2 \cdot 2H_2O$ (244.3) yields 0.9515 g pure $BaSO_4$ (233.4).

Gravimetric factor = 244.3/233.4 = 1.047; Weight = 0.996 g; % purity = 99.6%

Choosing a Filtration Medium for Gravimetry

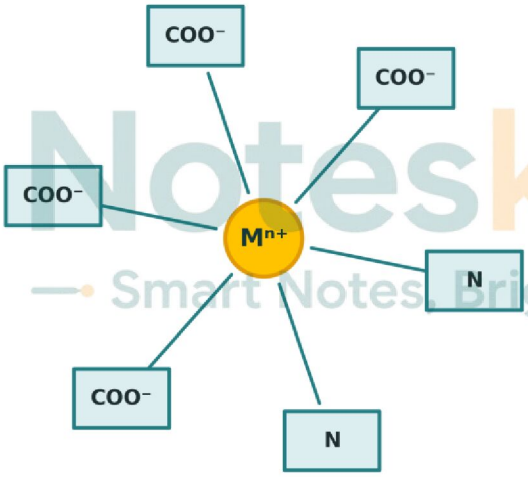
Ashless filter paper	Sintered-glass crucible	Gooch crucible (asbestos/glass mat)
For precipitates that will be IGNITED — paper burns away leaving negligible ash	For precipitates dried (not ignited) at moderate temperature; paper not needed	Older technique for precipitates needing filtration under suction

Choosing a filtration medium for gravimetry

3.4 Complexometric Titrations

- EDTA: hexadentate ligand (2 N + 4 COO^-), forms stable 1:1 chelate with metal ions regardless of the metal's valency.

EDTA — A Hexadentate Chelating Ligand



EDTA binds a metal ion through 2 nitrogen atoms and 4 carboxylate oxygen atoms, forming a very stable 1:1 ring complex (chelate) regardless of the metal's normal valency.

EDTA's hexadentate chelation of a metal ion

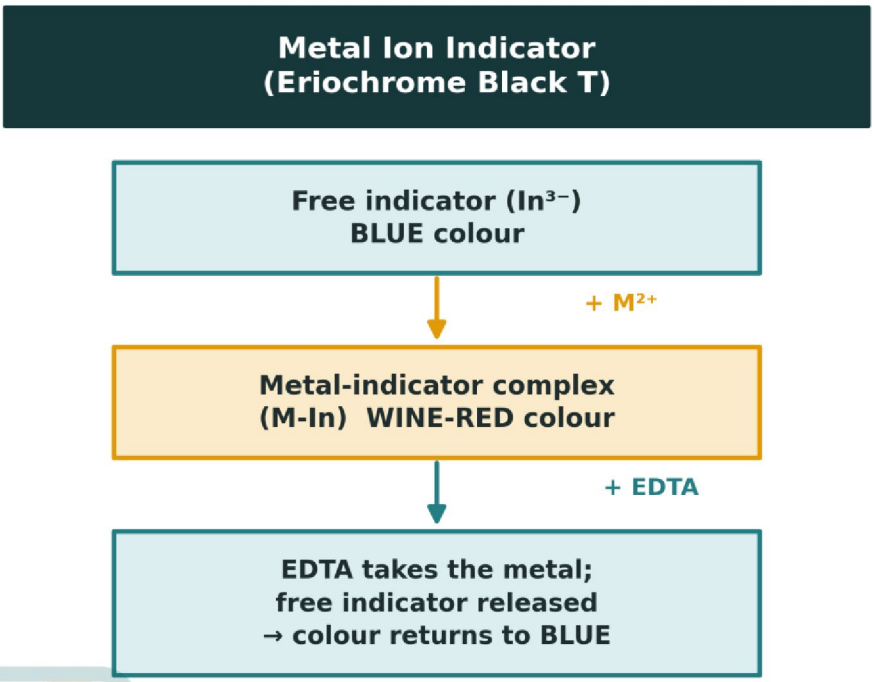
Classification of Complexometric Titrations

Complexometric Titrations

Direct titration	Back titration	Replacement (substitution)	Alkalimetric titration
Metal ion titrated directly with EDTA	Excess EDTA added, back-titrated with a second metal solution	Analyte displaces a weakly-bound metal from its EDTA complex	H^+ released when EDTA binds metal is titrated with NaOH

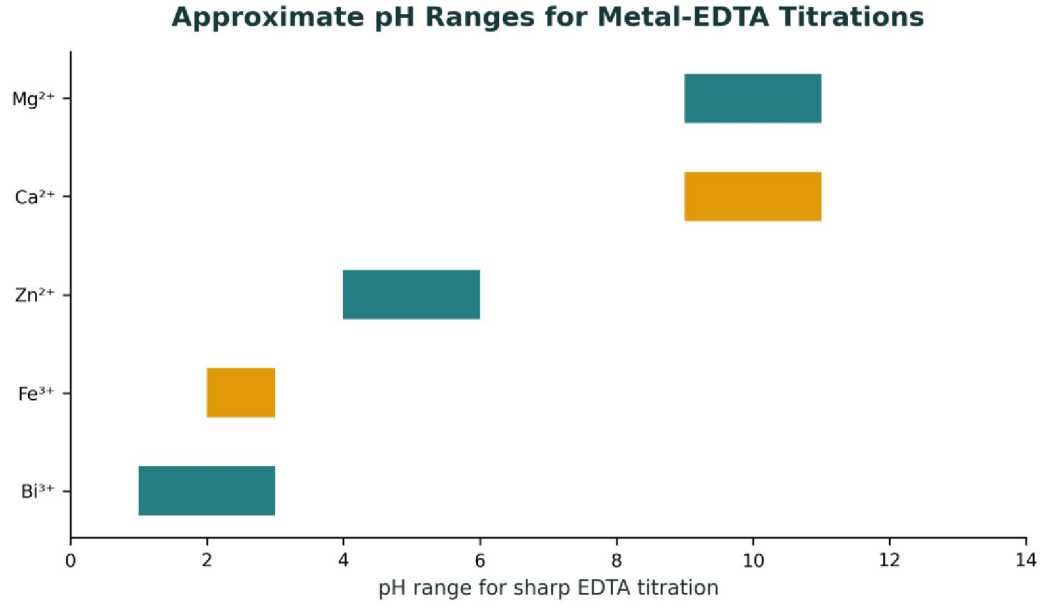
The four types of complexometric titration

- Direct: metal titrated straight with EDTA. Back-titration: excess EDTA added, unreacted titrated with a second metal (used when no indicator exists or reaction is slow — e.g. Al^{3+}).
- Replacement: analyte displaces a weakly-bound metal (e.g. Mg^{2+}) from its EDTA complex, then the liberated metal is titrated. Alkalimetric: H^{+} released is titrated with NaOH.



Metal ion indicator mechanism

Indicator	Metal-Indicator Colour	Free Colour	Typical Use
Eriochrome Black T	Wine-red	Blue	Ca^{2+}, Mg^{2+} at pH ~10
Murexide	Pink/red	Violet	Ca^{2+} alone at pH ~12–13



pH ranges needed for a sharp EDTA titration by metal

Masking and Demasking in Complexometric Titrations

MASKING	DEMASKING
An interfering metal ion is converted to a stable complex that will NOT react with EDTA (e.g. CN^- masks Zn^{2+}, Cd^{2+})	The masked metal is released back into solution, freed to react with EDTA again (e.g. formaldehyde demasks CN^--masked Zn^{2+})

Purpose: allows one metal ion to be titrated selectively while others present in the same solution are temporarily "hidden".

Masking and demasking

- Masking agents (e.g. KCN, triethanolamine) block interfering metals from reacting with EDTA. Demasking (e.g. formaldehyde) reverses this.

Standardising Disodium EDTA (vs. Calcium Carbonate)

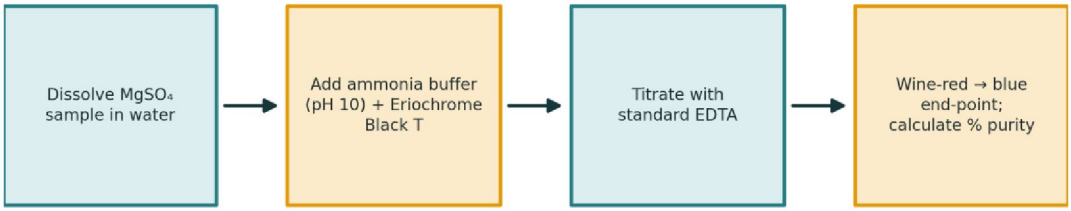
Standardising EDTA against $CaCO_3$

WORKED EXAMPLE — STANDARDISING EDTA

0.1001 g $CaCO_3$ (100.1) needs 20.0 mL EDTA (Eriochrome Black T, pH 10).

Moles $CaCO_3$ = 0.0010 mol = moles EDTA; Molarity of EDTA = 0.0010/0.020 = 0.0500 M

Complexometric Estimation of Magnesium Sulphate



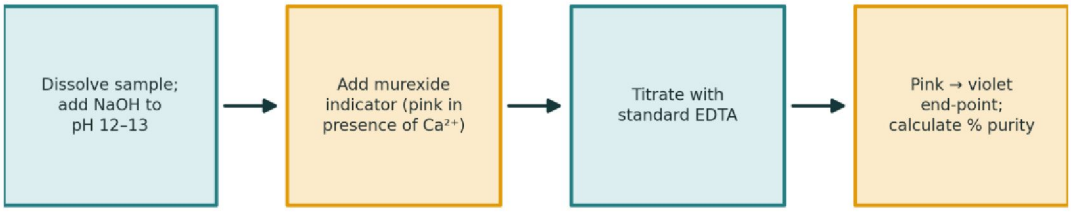
Complexometric estimation of $MgSO_4$

WORKED EXAMPLE — ESTIMATION OF MAGNESIUM SULPHATE

0.246 g $MgSO_4 \cdot 7H_2O$ (246.5) titrated with 0.05 M EDTA (Eriochrome Black T, pH 10), 19.8 mL.

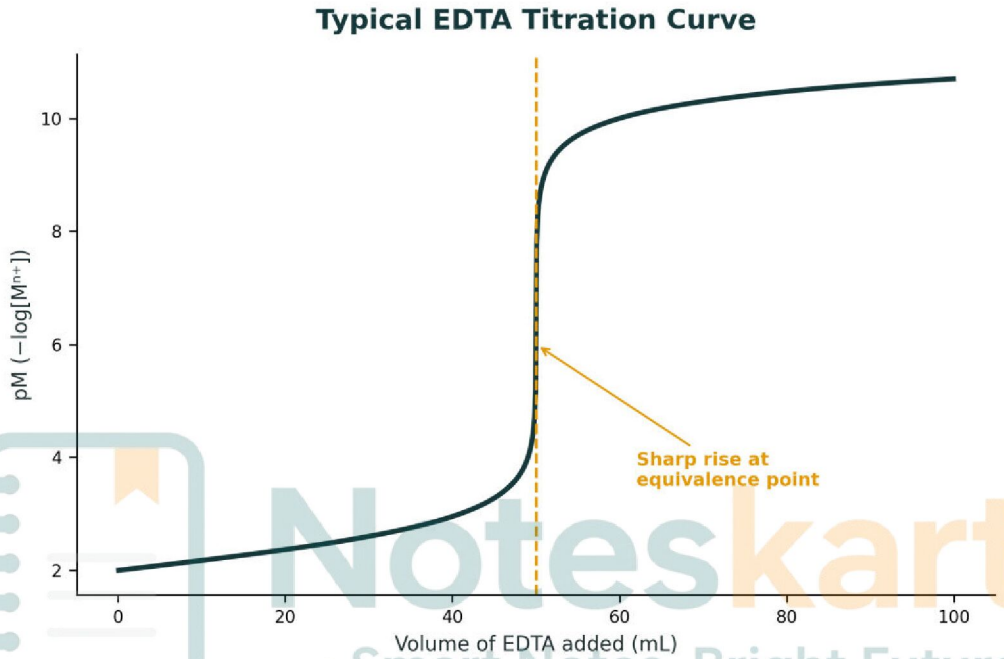
Moles EDTA = 0.00099 mol = moles Mg^{2+}; Weight = 0.244 g; % purity = 99.2%

Complexometric Estimation of Calcium Gluconate



Complexometric estimation of calcium gluconate

- Calcium alone needs murexide at pH 12–13 (Mg^{2+} present precipitates as hydroxide at this pH).



A typical EDTA (pM vs volume) titration curve

3.5 Redox Titrations

- Oxidation = loss of electrons (↑ oxidation number); Reduction = gain of electrons (↓ oxidation number) — always occur together.

Oxidation and Reduction — Always Together

OXIDATION	REDUCTION
Loss of electrons Increase in oxidation number (the reducing agent is oxidised)	Gain of electrons Decrease in oxidation number (the oxidising agent is reduced)

electrons transferred

Example: $Fe^{2+} \rightarrow Fe^{3+} + e^-$ (oxidation)
$MnO_4^- + 8H^+ + 5e^- \rightarrow Mn^{2+} + 4H_2O$ (reduction)

Both reactions always occur together — there is no oxidation without a corresponding reduction.

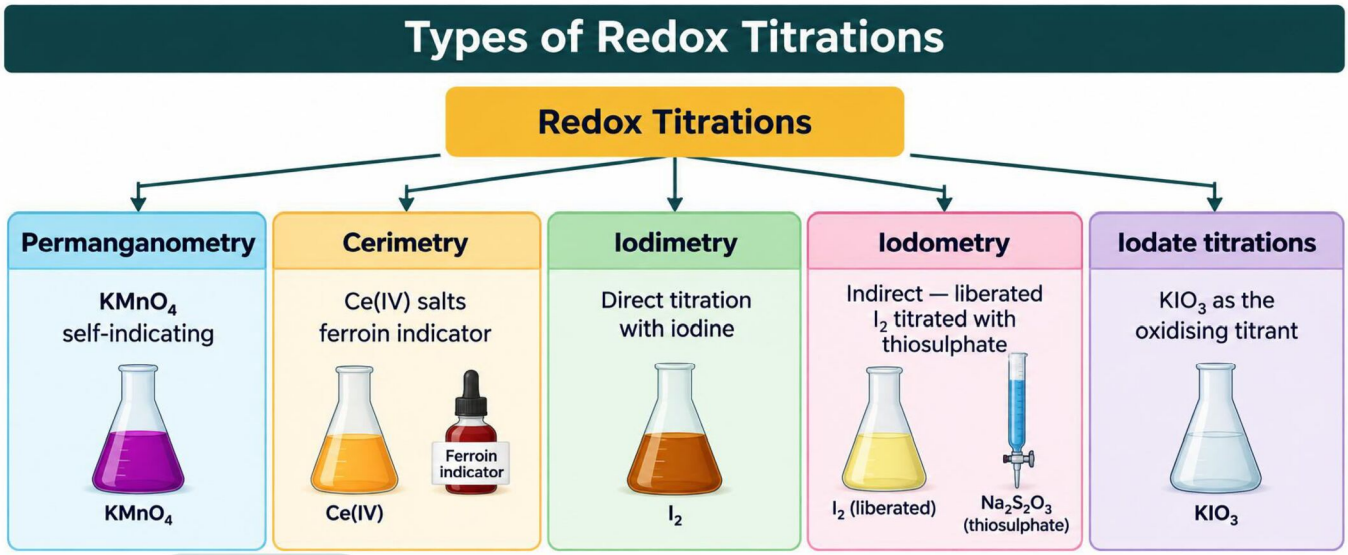
Oxidation and reduction always occur together

WORKED EXAMPLE — BALANCING A REDOX EQUATION

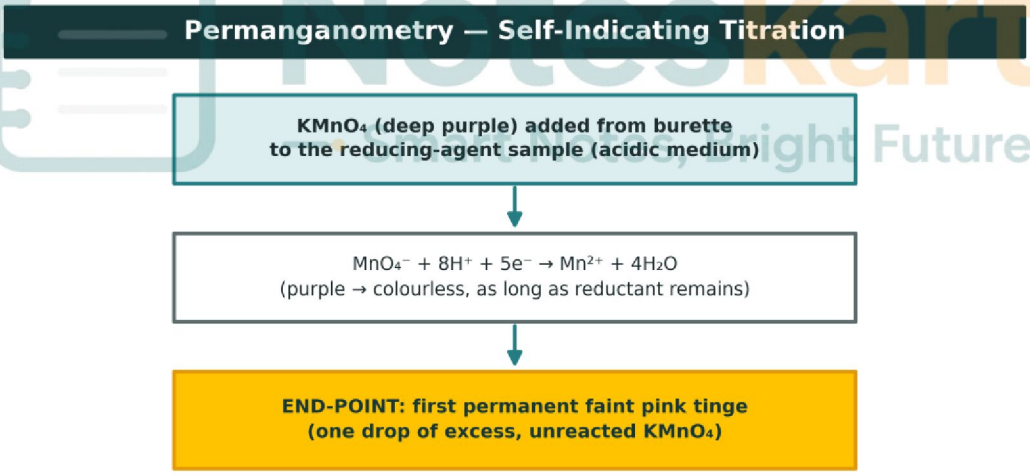
MnO_4^- + Fe^{2+} → Mn^{2+} + Fe^{3+} (acidic).

Oxidation: $Fe^{2+} \rightarrow Fe^{3+} + e^-$ (×5). Reduction: $MnO_4^- + 8H^+ + 5e^- \rightarrow Mn^{2+} + 4H_2O$.

Balanced: $MnO_4^- + 8H^+ + 5Fe^{2+} \rightarrow Mn^{2+} + 4H_2O + 5Fe^{3+}$



The five classes of redox titration



Permanganometry is self-indicating

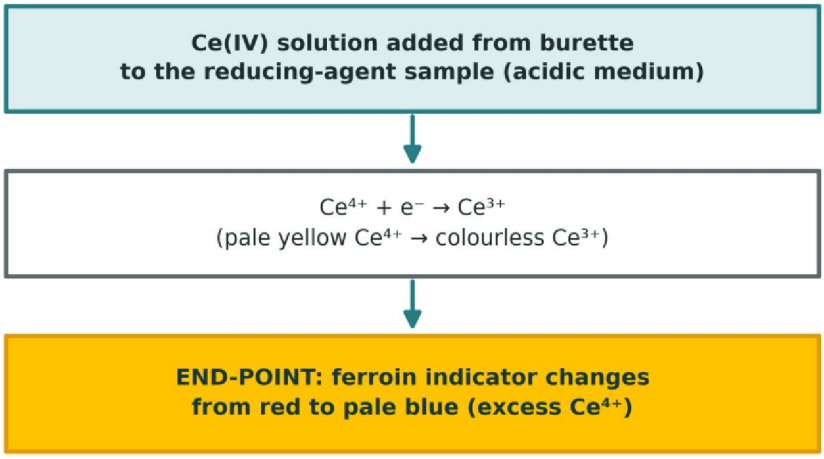
- Permanganometry: $MnO_4^- + 8H^+ + 5e^- \rightarrow Mn^{2+} + 4H_2O$. Self-indicating (pink end-point). Must use dilute H_2SO_4, never HCl.

WORKED EXAMPLE — STANDARDISING $KMnO_4$

0.134 g sodium oxalate (eq. wt. 67), warmed ~60°C, needs 20.0 mL $KMnO_4$.

Normality of $KMnO_4$ = (0.134/67)/0.020 = 0.100 N

Cerimetry — Ceric Ammonium Sulphate Titration



Cerimetry using ferroin

- Cerimetry: $Ce^{4+}+e^{-}\rightarrow Ce^{3+}$. Ferroin indicator (red→pale blue). More stable than $KMnO_4$, usable in HCl medium.

Iodimetry vs Iodometry

IODIMETRY (direct)	IODOMETRY (indirect)
Sample is a REDUCING agent	Sample is an OXIDISING agent
Titrated DIRECTLY with a standard iodine solution	Liberates I_2 from excess KI; the liberated I_2 is titrated with standard sodium thiosulphate
$I_2 + 2e^- \rightarrow 2I^-$	
Starch indicator: blue-black colour appears at end-point	Starch indicator: blue-black colour disappears at end-point

Iodimetry vs iodometry

	Iodimetry (Direct)	Iodometry (Indirect)
Sample is	A reducing agent	An oxidising agent
Method	Titrated directly with I_2	Liberates I_2 from excess KI; titrated with $Na_2S_2O_3$
Starch	Blue-black appears at end-point	Blue-black disappears at end-point
Typical use	Ascorbic acid, sulphites	Copper salts, oxidising agents

WORKED EXAMPLE — IODOMETRIC ASSAY OF COPPER

$2Cu^{2+}+4I^{-}\rightarrow 2CuI\downarrow+I_2$. Liberated I_2 titrated with 0.100 M $Na_2S_2O_3$, requiring 20.0 mL.

Moles thiosulphate = 0.00200 mol → moles I_2 = 0.00100 mol → moles Cu^{2+} = 0.00200 mol; Weight Cu = 0.127 g

Titration with Potassium Iodate

Titration with potassium iodate

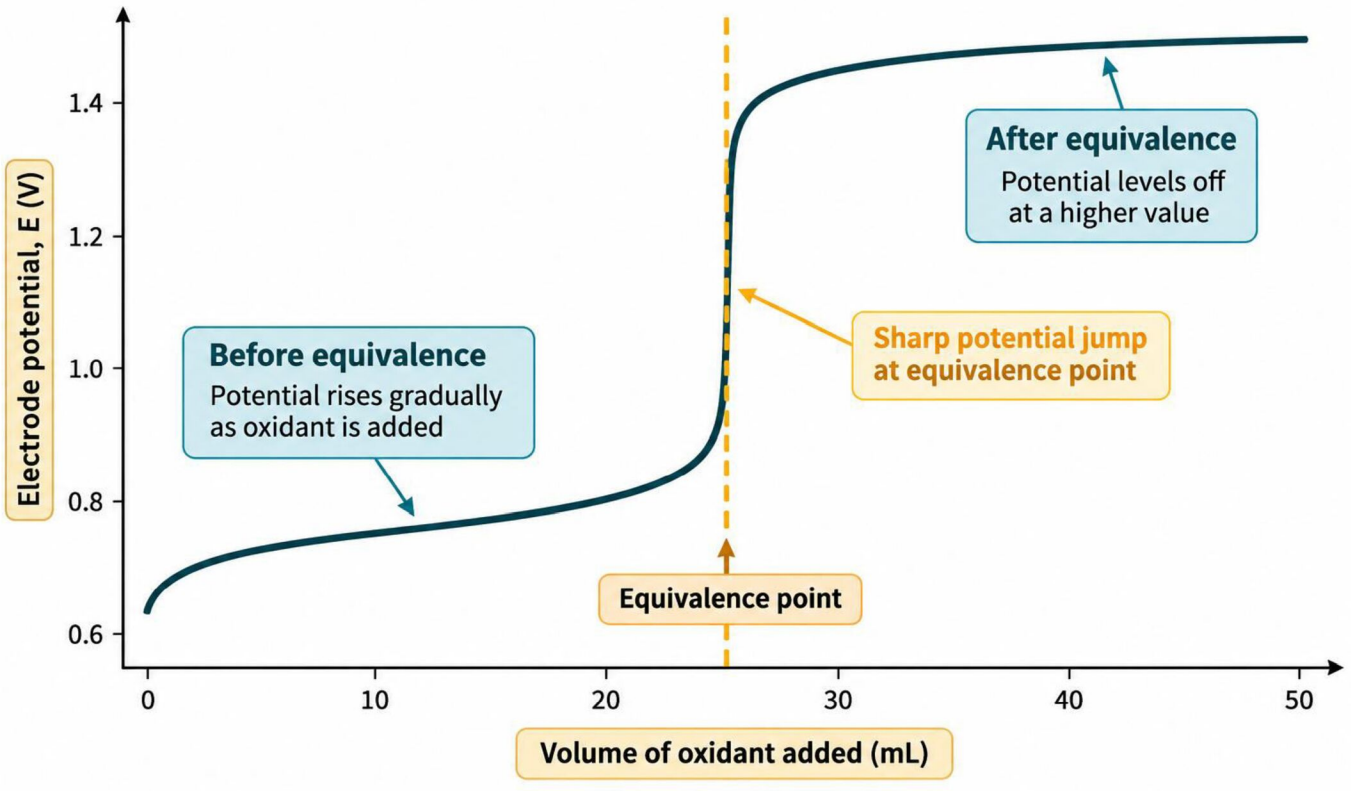
- $IO_3^- + 5I^- + 6H^+ \rightarrow 3I_2 + 3H_2O$. Potassium iodate: high-purity, stable primary standard, used to standardise $Na_2S_2O_3$.

Determination of Iodine Value (Degree of Unsaturation)

Determination of iodine value

- Iodine value (fats/oils): excess Wij's/Hanus reagent (ICl/IBr) reacts with double bonds; unreacted halogen liberates I_2 from KI, titrated with $Na_2S_2O_3$, compared with a blank.

Typical Redox Titration Curve



A typical redox titration curve

▸ Key Half-Reactions

System	Half-Reaction
Permanganate (acidic)	$MnO_4^- + 8H^+ + 5e^- \rightarrow Mn^{2+} + 4H_2O$
Ceric/cerous	$Ce^{4+} + e^- \rightarrow Ce^{3+}$
Iodine/iodide	$I_2 + 2e^- \rightarrow 2I^-$
Thiosulphate/tetrathionate	$2S_2O_3^{2-} \rightarrow S_4O_6^{2-} + 2e^-$
Iodate (acidic, with iodide)	$IO_3^- + 5I^- + 6H^+ \rightarrow 3I_2 + 3H_2O$