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B.PHARM SEMESTER I

Pharmaceutical Inorganic and Analytical Chemistry

(Course Code: BP106T)

UNIT II

Acid-Base Chemistry, Buffers and Electrolytes

SHORT NOTES

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

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Short notes for Unit II, covering acid-base chemistry, buffers, and electrolytes. Condensed bullets and tables for fast revision.

2.1 Acids, Bases and Buffer Theory

1. Arrhenius Theory

- **Acid:** A substance that releases **H^+ ions** in water.
- **Base:** A substance that releases **OH^- ions** in water.
- **Example:**
  - $HCl \rightarrow H^+ + Cl^-$
  - $NaOH \rightarrow Na^+ + OH^-$

2. Brønsted–Lowry Theory

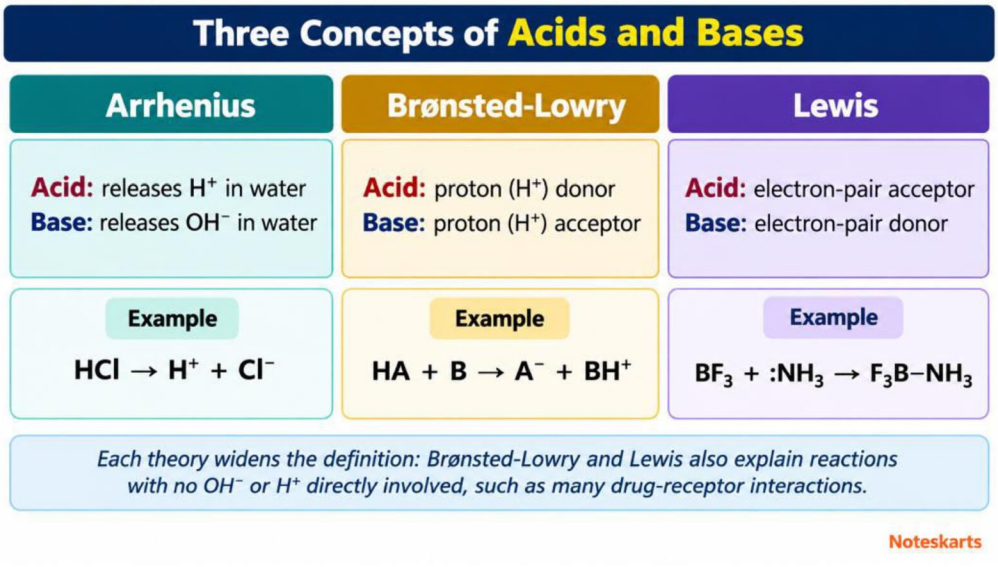
- **Acid:** A **proton (H^+) donor**.
- **Base:** A **proton (H^+) acceptor**.
- This theory explains acid–base reactions through the **transfer of protons**.

3. Lewis Theory

- **Lewis acid:** An **electron-pair acceptor**.
- **Lewis base:** An **electron-pair donor**.
- This is the **broadest** of the three acid–base theories.

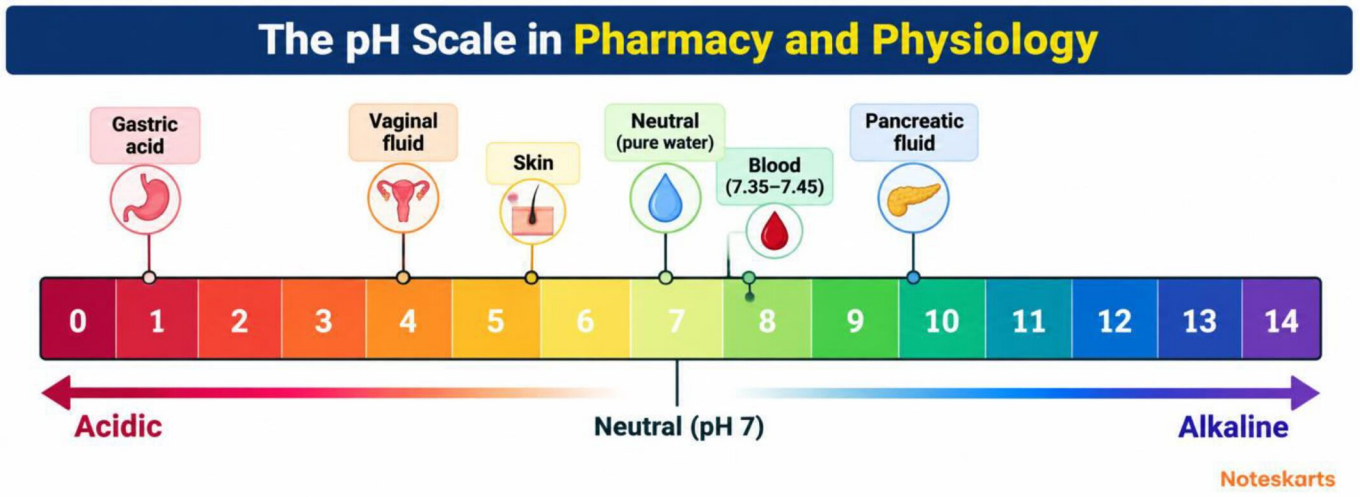
Easy Trick to Remember

- **Arrhenius:** H^+ / OH^-
- **Brønsted–Lowry:** Proton donor / acceptor
- **Lewis:** Electron-pair acceptor / donor



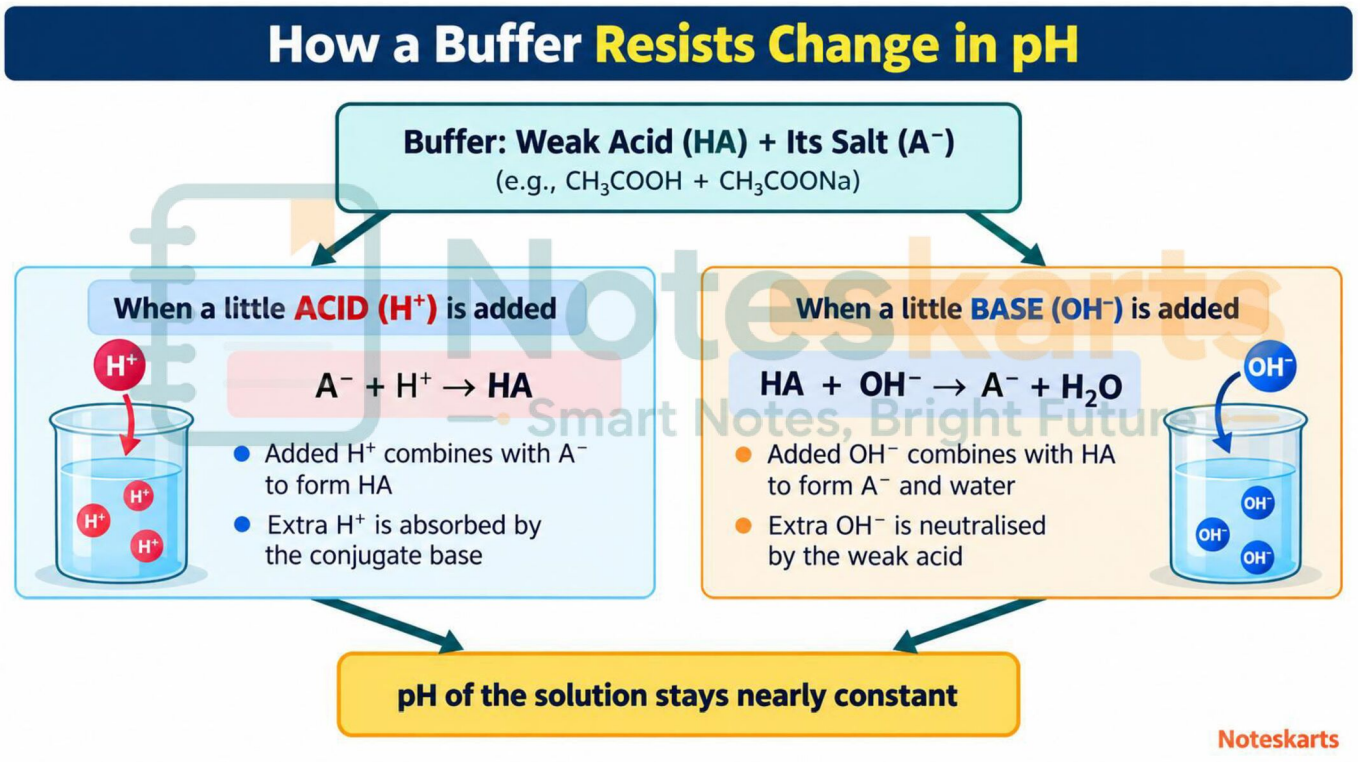
The three acid-base theories compared

- pH = −log[H^+]. pH + pOH = 14 at 25°C (Kw = 1×10^{-14}).



The pH scale with physiological reference points

- A buffer resists pH change on adding small amounts of acid/base — made of a weak acid + its conjugate base (or weak base + conjugate acid).



How buffer action resists pH change

HENDERSON–HASSELBALCH EQUATION

For Acidic Buffer

- **Formula:**
  pH = pKa + log([Salt] / [Acid])
- Used to calculate the **pH of an acidic buffer**.
- **pH = pKa** when **salt : acid = 1 : 1**.

For Basic Buffer

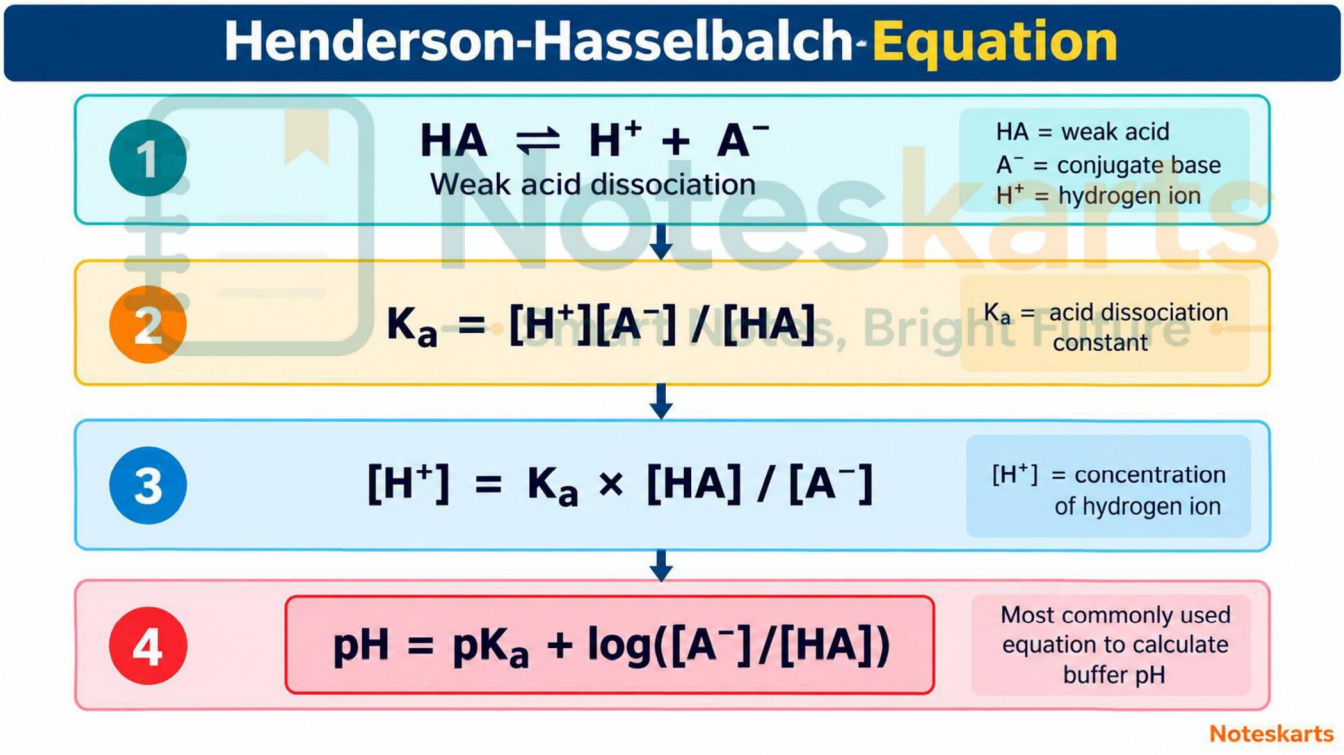
- **Formula:**
  pOH = pKb + log([Salt] / [Base])
- Then:
  pH = 14 − pOH
- Used to calculate the **pH of a basic buffer**.

Buffer Capacity

- Buffer capacity means the **ability of a buffer to resist changes in pH**.
- It is **highest when:**
  pH = pKa
- At this point:
  Salt : Acid = 1 : 1

Easy Point to Remember

pH = pKa → Maximum buffer capacity → Salt = Acid

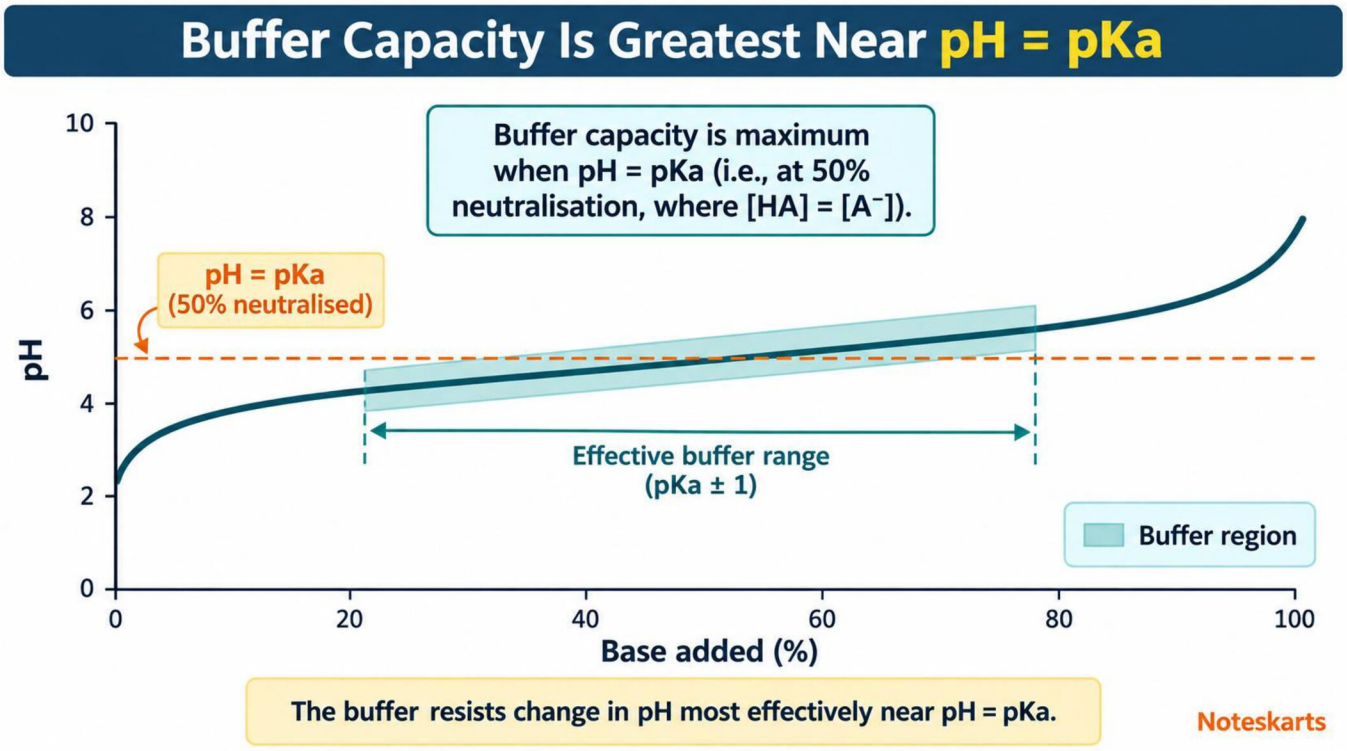


The Henderson–Hasselbalch relationship, visualised

WORKED EXAMPLE — BUFFER PH

Buffer of 0.10 M acetic acid + 0.15 M sodium acetate (pKa 4.76):

pH = 4.76 + log(0.15/0.10) = 4.76 + 0.18 = 4.94



Buffer capacity peaks at pH = pKa

Buffer System	Weak Acid pKa	Useful pH Range
Acetate	4.76	3.8–5.8
Phosphate	7.21	6.2–8.2
Borate	9.24	8.0–10.0
Carbonate	6.35	5.5–7.0

WORKED EXAMPLE — PREPARING A BUFFER

Given:

- Equal-molar **NaH_2PO_4 (acid)** and **Na_2HPO_4 (salt)** stocks are available.
- Required buffer volume = **100 mL**
- Required pH = **7.4**
- **pKa_2 = 7.21**

Step 1: Apply Henderson–Hasselbalch Equation

pH = pKa + log([Salt]/[Acid])

- 7.4 = 7.21 + log([Salt]/[Acid])
- log([Salt]/[Acid]) = **0.19**
- [Salt]/[Acid] = **$10^{0.19}$ = 1.55**

Step 2: Calculate Fractions

- Total ratio = **1 + 1.55 = 2.55**
- Salt fraction = **1.55 / 2.55 = 0.608 = 60.8%**

Buffer System	Weak Acid pKa	Useful pH Range

- Acid fraction = **1 / 2.55 = 0.392 = 39.2%**

Step 3: Prepare 100 mL Buffer

Since both stocks have the **same molarity**:

- **Na_2HPO_4 (salt) = 60.8 mL**
- **NaH_2PO_4 (acid) = 39.2 mL**
- **Total = 100 mL**

Final Answer

Mix 60.8 mL of Na_2HPO_4 stock + 39.2 mL of NaH_2PO_4 stock to prepare 100 mL of pH 7.4 buffer.

Key idea: Higher pH than pKa → **more salt (base form) than acid form**.

Buffer Capacity (β)

- **Buffer capacity (β)** is the amount of **strong acid or strong base** required to change the pH of **1 L of buffer by 1 pH unit**.
- It indicates the **ability of a buffer to resist changes in pH**.
- **Higher β → Greater resistance to pH change.**

Buffers in Pharmaceutical Dosage Forms

- **Injections and ophthalmic solutions:**
  - Buffers are often adjusted close to **pH 7.4**.
  - This helps improve **physiological compatibility**.
- **Topical creams:**
  - Buffers may be maintained around **pH 5.5**.
  - This is close to the skin's natural **acid mantle**.

Easy Point to Remember

Higher β = Stronger buffer = Better resistance to pH change

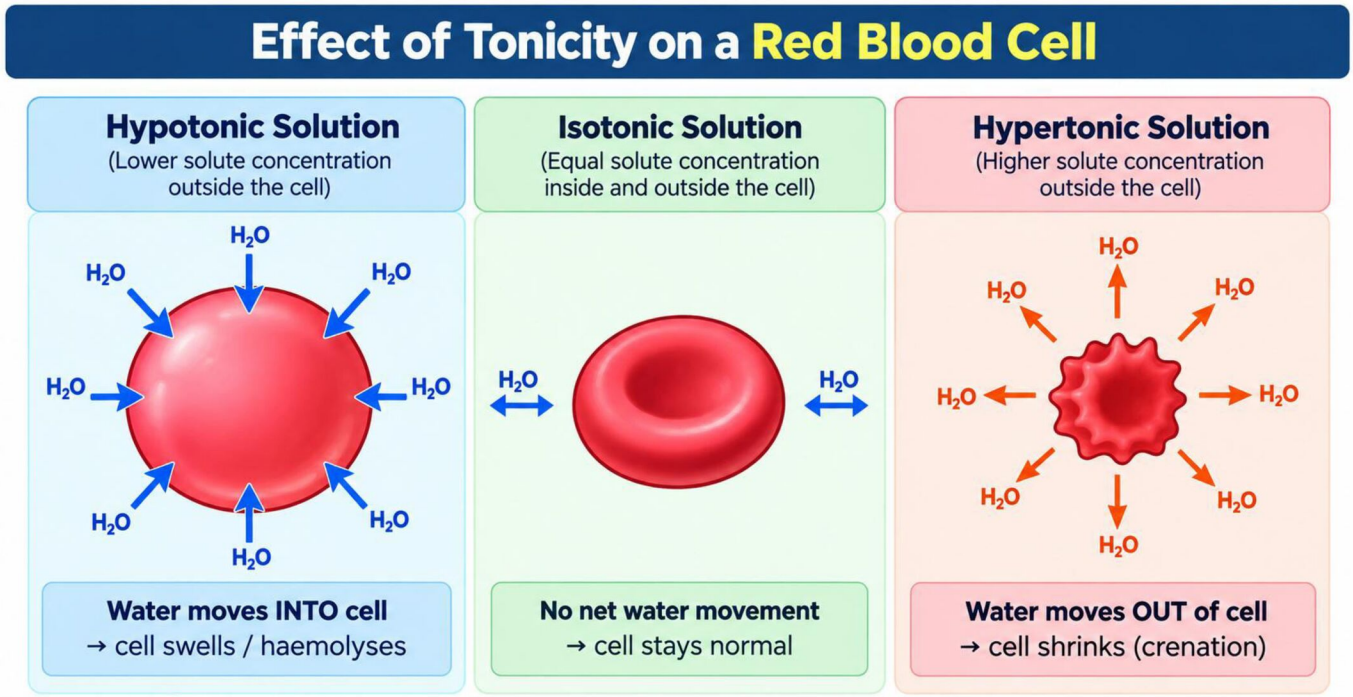
WORKED EXAMPLE — BUFFER FROM WEIGHED QUANTITIES

0.410 g sodium acetate (mol. wt. 82) + 0.300 g acetic acid (mol. wt. 60) in 100 mL water. Find pH. (pKa 4.76)

Moles acetate = 0.410/82 = 0.005 mol; Moles acetic acid = 0.300/60 = 0.005 mol (equal, so pH = pKa)

pH = 4.76 + log(1) = 4.76

2.2 Isotonicity and Its Applications



Effect of tonicity on a red blood cell

- **Isotonic solution:** Has approximately the **same osmotic pressure as body fluids**.
  - Example: **0.9% w/v NaCl** is considered isotonic with body fluids.
- **Hypotonic solution:** Has **lower osmotic pressure** than body fluids.
  - Water moves **into the cells**.
  - Cells may **swell and burst (haemolysis)**.
- **Hypertonic solution:** Has **higher osmotic pressure** than body fluids.
  - Water moves **out of the cells**.
  - Cells **shrink (crenation)**.

Van't Hoff Equation

$\pi = iCRT$

Where:

- **π** = osmotic pressure
- **i** = number of particles produced by the substance
- **C** = concentration
- **R** = gas constant
- **T** = absolute temperature

Example: $NaCl \rightarrow Na^+ + Cl^-$, so **i = 2**.

Methods of Isotonicity Adjustment

1. **Freezing Point Depression Method**
   - The solution is adjusted to have the same freezing point as blood.

- Freezing point of blood is approximately **−0.52°C**.

2. **Sodium Chloride Equivalent (E-value) Method**
   - Uses the **NaCl equivalent value (E-value)** of a drug.
   - Helps calculate the amount of **NaCl needed** to make the solution isotonic.

WORKED EXAMPLE — NACL EQUIVALENT METHOD

1 g of a drug (E = 0.18) made up to 100 mL. Extra NaCl needed for isotonicity?

NaCl already provided = 1 × 0.18 = 0.18 g. NaCl needed = 0.9 g. Extra required = 0.9 − 0.18 = 0.72 g.

Pharmaceutical Importance of Isotonicity

1. Importance of Isotonicity

- **IV fluids:** Proper isotonicity helps prevent:
  - **Haemolysis** – bursting of red blood cells.
  - **Crenation** – shrinking of red blood cells.
- **Ophthalmic solutions:** Appropriate isotonicity helps **reduce eye irritation and discomfort**.
  - The eye can generally tolerate approximately **0.7–1.5% NaCl equivalent**.

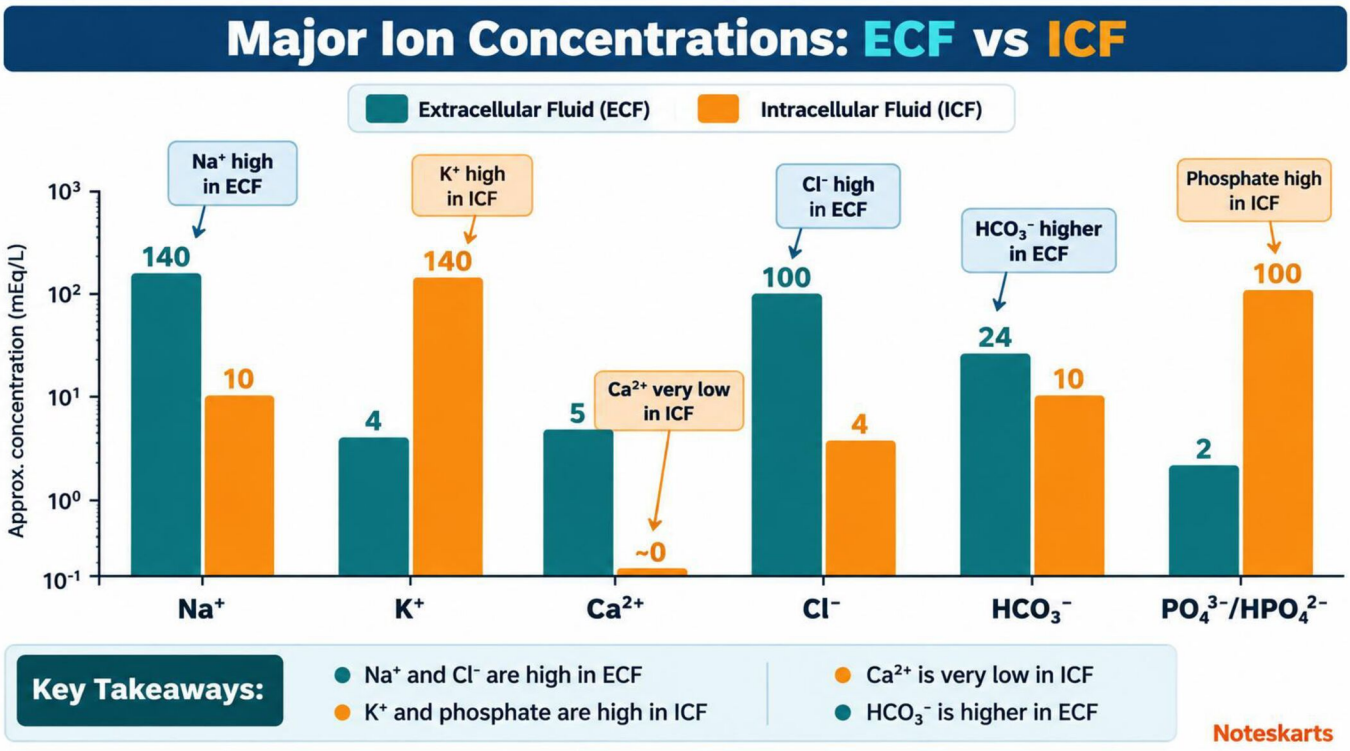
2. Osmolarity and Osmolality

- **Osmolarity:** Number of osmoles per **litre of solution (osmol/L)**.
- **Osmolality:** Number of osmoles per **kilogram of solvent (osmol/kg)**.
- Normal body fluids have an osmolality of approximately **285–295 mOsm/kg**.

3. Effect of Dissociation

- Substances that **dissociate into ions** produce more particles and therefore exert a greater osmotic effect.
- **NaCl:**
  - $NaCl \rightarrow Na^+ + Cl^-$
  - **i ≈ 2**
  - Produces approximately **twice the osmotic effect** of a non-dissociating substance at the same molar concentration.
- **Dextrose:**
  - Does not significantly dissociate in solution.
  - **i ≈ 1**

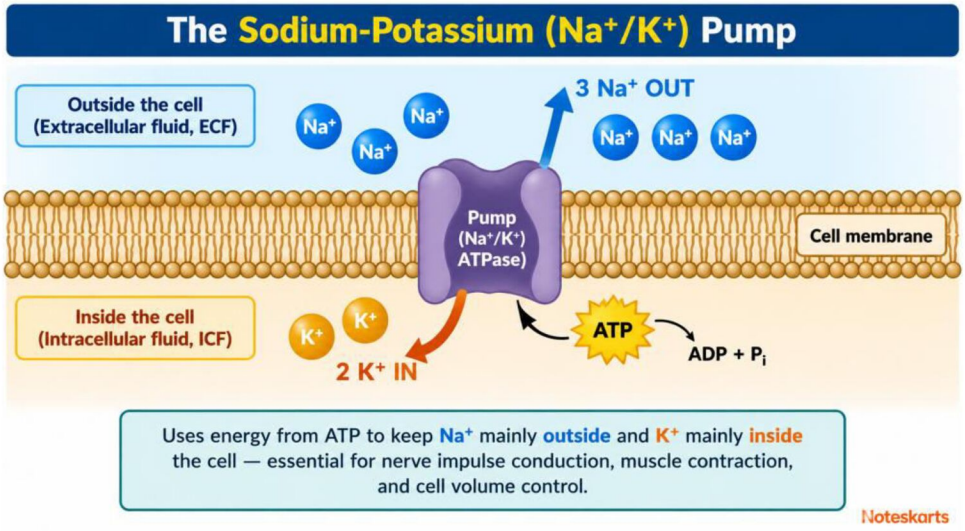
2.3 Body Fluid Compartments and Electrolytes



Extracellular vs intracellular fluid compartments

- Total body water ~60% of body weight: ICF (~2/3) and ECF (~1/3, split into plasma + interstitial fluid).

Ion	Compartment	Key Function	Normal Range
Sodium (Na^+)	ECF (main cation)	Osmolality, nerve conduction	135–145 mEq/L
Potassium (K^+)	ICF (main cation)	Membrane potential, cardiac rhythm	3.5–5.0 mEq/L
Calcium (Ca^{2+})	Bone/ECF	Bone, muscle contraction, clotting	8.5–10.5 mg/dL
Magnesium (Mg^{2+})	ICF	Enzyme cofactor, neuromuscular function	1.5–2.5 mEq/L
Bicarbonate (HCO_3^-)	ECF	Principal acid-base buffer	22–26 mEq/L



The Na^+/K^+ pump maintains the ionic gradient

- Na^+/K^+-ATPase pump: uses ATP to keep Na^+ mainly outside and K^+ mainly inside the cell (3 Na^+ out, 2 K^+ in per cycle).
- Regulation: Na^+ by RAAS + ADH; K^+ by aldosterone + insulin; Ca^{2+} by PTH, calcitonin, and vitamin D.

Replacement Therapy

Replacement Therapy

Replacement therapy is used to **replace fluids or essential electrolytes** that are low in the body.

1. Sodium Chloride (NaCl)

- Used to replace **fluid and sodium**.
- **0.9% NaCl** → isotonic fluid replacement.
- **3% NaCl** → hypertonic solution used in **severe hyponatraemia**.

2. Potassium Chloride (KCl)

- Used to treat **hypokalaemia (low potassium)**.
- **Never give KCl as a rapid or undiluted IV injection.**
- Rapid administration can cause **dangerous heart problems or cardiac arrest**.

3. Calcium Chloride

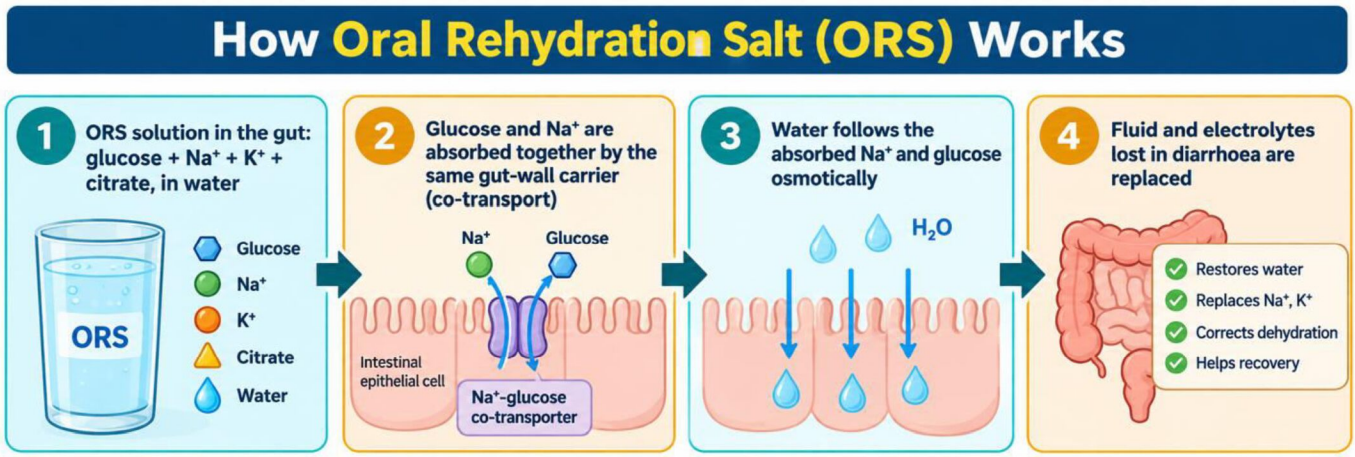
- Used for:
  - **Hypocalcaemia**
  - **Hyperkalaemia**, where it helps protect the heart.
- It is **irritant to tissues**, so extravasation should be avoided.

4. Magnesium Sulphate ($MgSO_4$)

- Used to treat **hypomagnesaemia (low magnesium)**.
- Also used in **pre-eclampsia and eclampsia** to help prevent or control seizures.

5. Compatibility Precaution

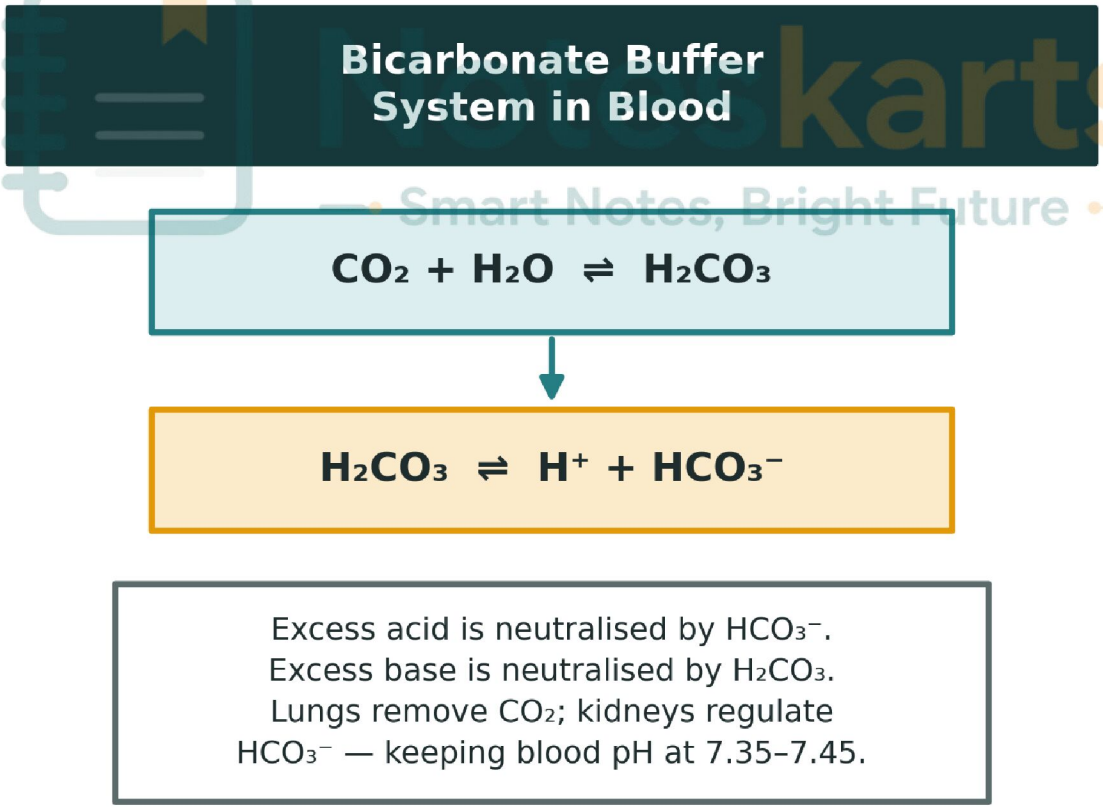
- **Calcium salts should not be mixed directly** with solutions containing:
  - **Bicarbonate**
  - **Phosphate**
- They can form **insoluble precipitates**.
- Keep them separate unless **compatibility has been confirmed**.



How ORS works: glucose-sodium co-transport

- ORS (WHO reduced-osmolarity formula, per litre): NaCl 2.6 g, glucose 13.5 g, KCl 1.5 g, trisodium citrate 2.9 g — works via glucose-Na^+ co-transport (SGLT1), remains active during diarrhoea.

2.4 Physiological Acid-Base Balance



The bicarbonate buffer system in blood

Bicarbonate Buffer System

- The **bicarbonate buffer system** is the **main buffer system in blood**.
- It maintains blood pH through the following equilibrium:

$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

- **H_2CO_3** = Carbonic acid
- **HCO_3^-** = Bicarbonate ion

Role in Acid–Base Balance

- **Excess acid** is neutralised by **HCO_3^- (bicarbonate)**.
- **Excess base** is neutralised by **H_2CO_3 (carbonic acid)**.
- **Lungs** regulate **CO_2** rapidly, within minutes.
- **Kidneys** regulate **HCO_3^-** more slowly, over hours to days.
- Normal blood pH is approximately **7.35–7.45**.

Henderson–Hasselbalch Equation for Blood

$pH = 6.1 + \log([HCO_3^-] / (0.03 \times pCO_2))$

Where:

- **$[HCO_3^-]$** = bicarbonate concentration in mEq/L
- **pCO_2** = partial pressure of carbon dioxide in mmHg
- **6.1** = pKa of the bicarbonate buffer system
- **0.03** = solubility coefficient of CO_2 in blood

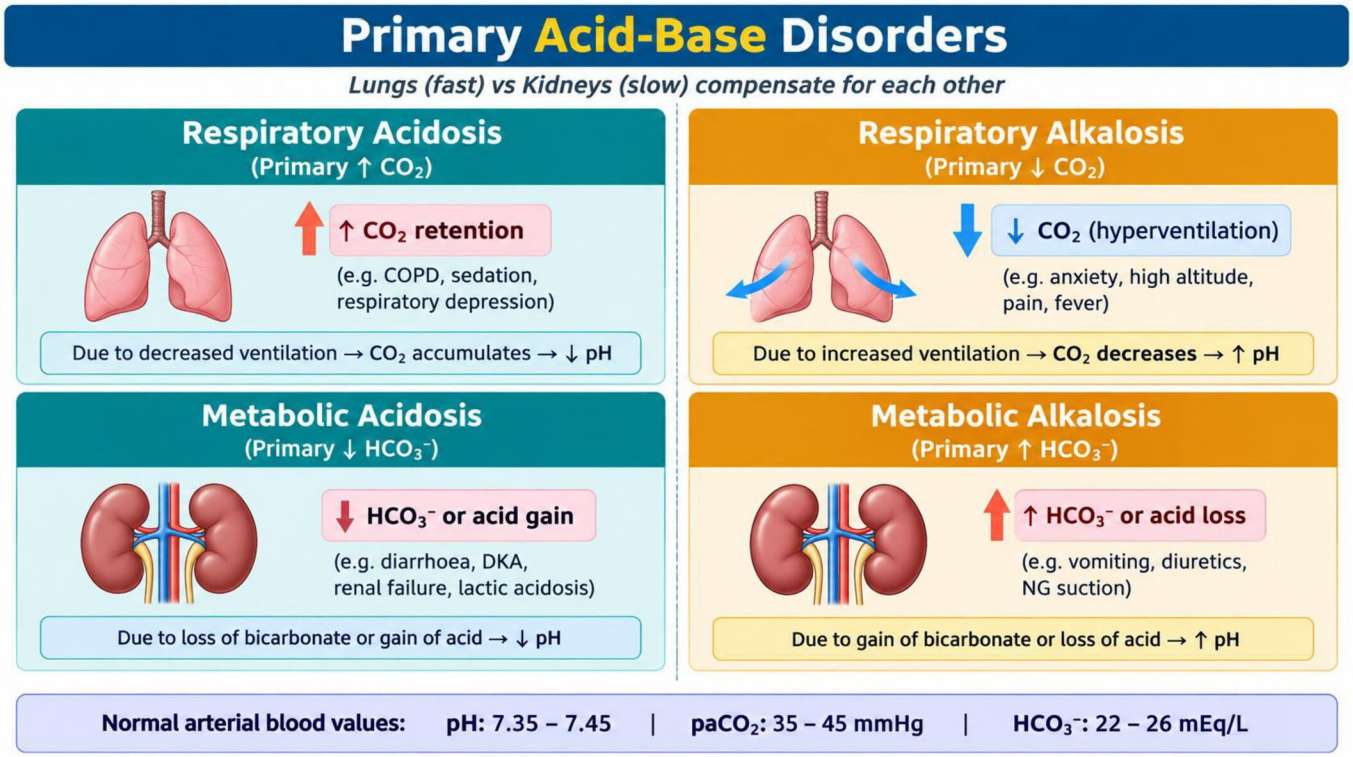
Other Buffer Systems

- **Phosphate buffer:** $H_2PO_4^-$ / HPO_4^{2-}
- **Protein buffers:** Plasma proteins and haemoglobin
- These are particularly important:
  - **Inside cells**
  - In the **kidney tubules**
  - In **urine**

WORKED EXAMPLE — BLOOD PH

HCO_3^- = 24 mEq/L, pCO_2 = 40 mmHg. Find blood pH.

pH = 6.1 + log(24/(0.03×40)) = 6.1 + log(20) = 6.1 + 1.30 = 7.40 (normal)



The four primary acid-base disorders

Disorder	Primary Change	Common Cause	Compensation
Respiratory acidosis	↑ pCO_2	COPD, respiratory depression	Kidneys retain HCO_3^- (slow)
Respiratory alkalosis	↓ pCO_2	Hyperventilation	Kidneys excrete HCO_3^- (slow)
Metabolic acidosis	↓ HCO_3^-	Diarrhoea, DKA, renal failure	Lungs ↑ ventilation (fast)
Metabolic alkalosis	↑ HCO_3^-	Vomiting, diuretics	Lungs ↓ ventilation (fast)

- Anion gap = $Na^+ - (Cl^- + HCO_3^-)$; normal ≈ 8–12 mEq/L. High gap → unmeasured acid (lactate/ketones); normal gap → direct HCO_3^- loss (e.g. diarrhoea).
- Compensation brings pH back toward normal but rarely restores it completely, and never overshoots into the opposite abnormality — a useful check when interpreting a blood gas result.
- Mixed acid-base disorders (more than one primary process at once) are recognised when the degree of compensation seen doesn't match what would be expected for a single, pure disorder.

WORKED EXAMPLE — ANION GAP

Na^+ = 138, Cl^- = 100, HCO_3^- = 14 mEq/L.

Anion gap = 138 − (100+14) = 24 mEq/L — high, indicating an unmeasured acid (e.g. lactate or ketones).

COMMON MISTAKES

Assuming buffer capacity is the same at any pH — in fact capacity is sharply peaked around pH = pKa and falls away quickly beyond about one pH unit on either side.

Forgetting that Molarity and Normality differ for polyprotic/multivalent species — always check n before converting.

Giving potassium chloride as a rapid IV push — always dilute and infuse slowly.

▸ Key Terms — Unit II

Term	Meaning
pKa	pH at which a weak acid is exactly half dissociated
Isotonic	Same effective solute concentration (osmotic effect) as body fluids
E value	Grams of NaCl producing the same osmotic effect as 1 g of a given drug
Anion gap	$Na^+ - (Cl^- + HCO_3^-)$; helps classify metabolic acidosis
Compensation	The body's secondary response that partially corrects a primary acid-base disturbance