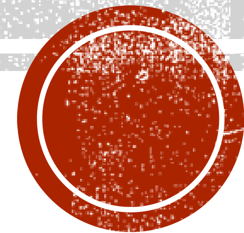
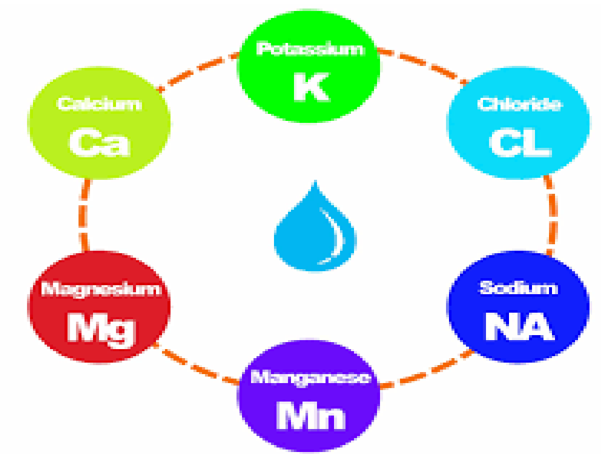
MAJOR EXTRA & INTRACELLULAR ELECTROLYTES.



By- Miss. Sampada L. Deshmukh
Assistant Professor
(Pharmaceutical chemistry)

ELECTROLYTES



- Substance when dissolved in solution separates into ions & is able to carry an electrical current
- Cation - positively charged electrolyte e.g. Ca++
- Anion - negatively charged electrolyte e.g. Cl
- No of Cations must equal to no of Anions for homeostasis to exist in each fluid compartment
- ELECTROLYTES IN BODY FLUID COMPARTMENTS:
- Intracellular: K, Mg, P
- Extracellular: Na, Cl, HCO3

PHYSIOLOGICAL IONS

1. Sodium

- **-Location:** Extracellular compartment as salt Na+
- -Normal level- 136- 142 mEq/L
- **Functions:**
- Absorbed & excreted by cells (maintain charge balance between the body fluids)
- Along with Cl, maintain osmotic balance of all body fluids
- In kidney, maintain blood urine volume level.
- **Hyponatremia-** low level of sodium in body. Due to extreme urine loss (in diabetic insipidus), kidney damage, diarrhea, vomiting, excessive Sweating.
- Symptoms- headache, muscle weakness, respiratory depression.
- **Hypernatremia-** high level of sodium in body, due to dehydration, high sodium intake.
- Symptoms- intense trust, fatigue.
- Treatments- diuretics, cardiotonic drug, low salt diet.

2. Calcium

- Location- 1% in extracellular & 99% in bones & teeth
- **Functions-**
- Blood clotting
- Muscle contraction
- Release of Ach from neurons
- Bones & teeth
- **Hypocalcemia-** decrease calcium level in body, due to lower absorption, Vit. D deficiency, bone cancer
- Symptoms- tetanic spasms, convulsions.
- **Hypercalcemia-** high calcium level in body, due to hypervitaminosis D, bone neoplastic disease.
- Symptoms- muscle weakness, constipation, cardiac irregularities.

3. Chloride

- **Location-** It is majorly found in all body fluid, nearly 66% of ion content in plasma is chloride ion.
- Normal level- about 50 mEq/ Kg
- **Functions**
- Absorbed & excreted by cells (maintain charge balance between body fluids)
- Along with sodium, maintain osmotic balance of all body fluids
- Take part in formation of gastric acid.
- **Hypochloremia-** decrease level of chloride level in body, due to metabolic acidosis seen in diabetic mellitus & renal failure, lack of reabsorption from kidney, excessive vomiting- loss of gastric acid (HCl)
- Symptoms- alkalosis, respiratory depression, muscle spasm
- **Hyperchloremia-** increase chloride level in body due to excess loss of bicarbonate ions, dehydration, CHF

4. Potassium

- **Location-** It is majorly found in intracellular fluid
- **Normal level-** 3.8- 5.0 mEq/L
- **Functions**
- Contraction of muscles, especially cardiac muscle
- Maintain osmotic balance
- Transmission of nerve impulses
- **Hypokalemia-** decrease potassium level in body due to lower absorption, malnutrition, diarrhea, more urine loss, heart disease.
- **Hyperkalemia-** increase potassium ion level in body due to kidney damage, dehydration, cardia disease, CNS depression.
- Symptoms- bradycardia, mental confusion, muscle weakness.

5. Magnesium

- **Location-** It is majorly found in intracellular fluid, about 54% in bones & about 45% in ICF
- **Functions**
- To activate enzymes which are involved in Protein metabolism
- Neuronal transmission
- Myocardial function
- **Hypomagnesemia-** decrease magnesium ion level in body due to lower absorption, malnutrition, diarrhea, chronic alcoholism
- Symptoms- muscle weakness, confusion, nausea, cardiac arrhythmia
- **Hypermagnesemia-** increase magnesium ion level in body due to Addison's disease, acute diabetic acidosis, renal failure
- Symptoms- hypotension, cardiac arrest.
- **Other ions-** sulphate, bicarbonate, phosphate etc.

ELECTROLYTE REPLACEMENT THERAPY

- It is also called as electrolyte replenisher. Due to serious symptoms of the loss of electrolytes, it is essential to maintain the normal level by external supply of electrolytes, this therapy is called as electrolyte replacement therapy.
- There are two types of electrolyte solutions are used in replacement therapy-
- **I) Electrolyte solution for rapid initial replacement-** solutions contains electrolyte with concentration resemble with the electrolyte concentration found in extracellular fluids.
- **II) Electrolyte solution for subsequent replacement-** lower concentration of electrolyte in solution.
- **1. Sodium replacement-**
- The depletion of sodium cause various forms of hyponatremias. A patient who suffers severe symptoms cause by hyponatremia should receive either 3% or 0.9% sodium chloride solution, until severe symptoms resolve
- The main objective of replacement to raise the serum sodium concentration to 120 mEq/L. there are various sodium chloride preparations are available.

1. Sodium chloride:

Formula: NaCl **Molecular weight-** 58.44

Standards : Sodium chloride not less than 99.0% and not more than 100.5% of NaCl, calculated with reference to the dried substance.

Method of Preparation: In laboratory it is prepared from common salt in water by passing hydrochloric acid gas. The crystals are precipitated out.

- Industrially it is prepared by 1) by evaporating purified saline (sea water) deposits & further purification. 2) and by purifying rock salt.
- It can also be prepared in laboratory in small scale by the acid-base reaction. In which strong acid (HCl) reacts with strong base (NaOH) & finally it gives sodium chloride.

Properties:

Physical properties: it is colorless crystals or white, crystalline powder.

- It is freely soluble in water & slightly more soluble in boiling water, practically insoluble in ethanol.

Chemical properties:

- With oxidizing agent, it gets oxidized & liberates chlorine gas.
- $2Cl + MnO2 + 2H2SO4 \longrightarrow Mn + 2SO4 + 2H2O + Cl2$

- **Identifications:** It gives reactions characteristics of sodium and chloride.
- **Test of purity:** It has tested for acidity and alkalinity, Ba, Ca and Mg, Fe and heavy metals, bromide, iodide, sulphate and loss on drying.
- **Assay:** The 0.1 g of substance is dissolved in 50ml of water in a glass stoppered flask. To it, 50ml of 0.1 N silver nitrate solution, 3ml of nitric acid, 5ml of nitrobenzene & 2ml of ferric ammonium sulphate solution are added. Now the solution is shaken well and is then titrated with 0.1 N ammonium thiocyanate solution until the water becomes reddish- yellow.
- Each ml of 0.1 N $AgNO_3$ = 0.005844 g of NaCl.
- **Storage:** It is stored in tightly closed container in dry place as it absorb moisture.
- **Uses:** 1. it can be used as electrolyte replenisher, as it is isotonic solution.
- 2. In combination with other electrolyte & dextrose, it is used as dialysis solution in renal failure.
- 3. It is used as a saline diuretic in the form of enteric coated tablet.

Sodium chloride preparations:

- **1. sodium chloride injection I.P** (normal saline)

It contains 0.9% sodium chloride without any antimicrobial agent (PH 4.5- 7.0)

- **2. Sodium chloride hypertonic injection I.P-**

It contains 1.6% w/v sodium chloride (PH 5- 7.5)

- **3. Compound sodium chloride injection (ringer solution)**

It contain following ingredients:

Sodium chloride- 0.869 g

Potassium chloride- 0.030 g

Calcium chloride- 0.048 g

Water for injection q. s. 100ml

- **4. Bacteriostatic sodium chloride injection USP.**

It is sterile solution of sodium chloride (0.9% w/v) in water for injection containing suitable antimicrobial agent. It is used as sterile vehicle.

5. Sodium chloride & Dextrose Injection I.P

It is solution of dextrose & sodium chloride in water for injection containing no antimicrobial agent (PH 3.5-6.5). It is used as a nutrient & as an electrolyte replenisher.

- **6. sodium chloride tablet I.P**

It contain 95.0 to 105 % w/v of sodium chloride and is available in strength of 180, 300 & 500 mg of sodium chloride. It is used as an electrolyte replenisher.

- **7. Sodium chloride and mannitol injection**.

It is sterile solution of sodium chloride and mannitol in water for injection. It is used as a diuretic agent.

2. Potassium chloride

Formula: KCl **Molecular weight- 74.55**

Standard: potassium chloride contains not less 99.0% and not more than 100.5 % of KCl, calculated with reference to the dried substance.

Preparation:

1. It is prepared from natural mineral, carnallite (KCl, MgCl2.6H2O). The raw mineral is ground and then treated with hot water. The less soluble KCl precipitate out. The process is repeated till all the KCl is recovered from liquid.
2. On laboratory scale, it is prepared by action of HCl on potassium carbonate or bicarbonate.

$$K2CO3 + 2HCl \longrightarrow 2KCl + H2O + CO2\uparrow$$

$$KHCO3 + HCl \longrightarrow KCl + H2O + CO2\uparrow$$

3. It can also be prepared in the laboratory in small scales by reacting potassium hydroxide (KOH) with hydrochloric acid (HCl).

$$KOH + HCl \longrightarrow KCl + H2O$$

Properties:

It is colorless crystalline, or white crystalline powder; odorless. It has a saline taste. It melts at 772 C. the 10% aqueous solution is neutral to litmus.

It is freely soluble in water; practically insoluble in ethanol and ether.

Uses:

- It is used in prevention and treatment of potassium depletion and hypokalemia and diuretic-induced hypokalemia.
- Potassium chloride is sometimes used as an excipient in pharmaceutical formulations.
- It is used in diabetic ketoacidosis.
- It is used in hypertension, potassium supplementation results in reduction of both systolic and diastolic blood pressure.

- **Preparations of Potassium chloride:**

1. Potassium chloride and Dextrose Injection:

Potassium chloride and dextrose, intravenous infusion, is a sterile solution of potassium chloride and either anhydrous glucose, in water for Injections.

2. Potassium chloride, sodium chloride and dextrose Injection:

Potassium chloride, sodium chloride and dextrose Injection intravenous infusion.

3. Bumetanide and slow potassium tablets:

This preparation is official in BP 2007. It contains bumetanide and potassium chloride. They are formulated so that the potassium chloride is released over a period of several hours.

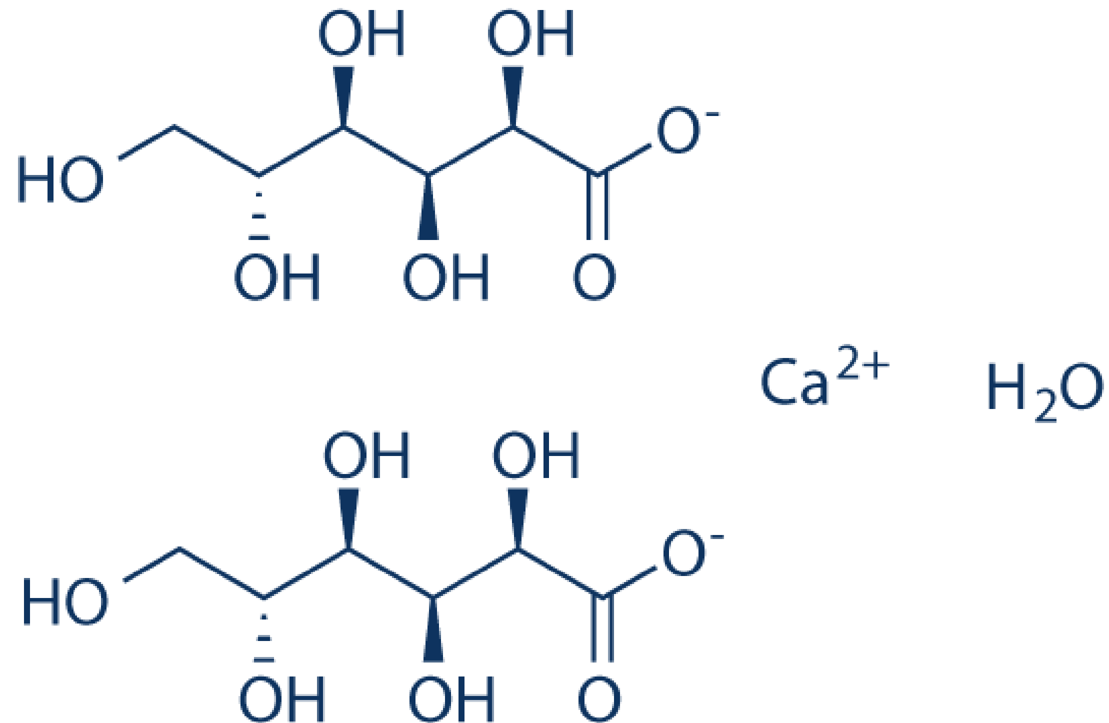
4. Sterile potassium chloride concentrate:

It is sterile solution of potassium chloride in water for Injections.

3. Calcium gluconate

Formula: C12H22CaO14. H2O **Molecular weight:** 448.40

Structure: calcium gluconate is calcium D-gluconate monohydrate.



Physical properties:

- White crystals, granules or powder, stable in air, does not lose its

(C12H22O14Ca. H2O) water of crystallization on drying.

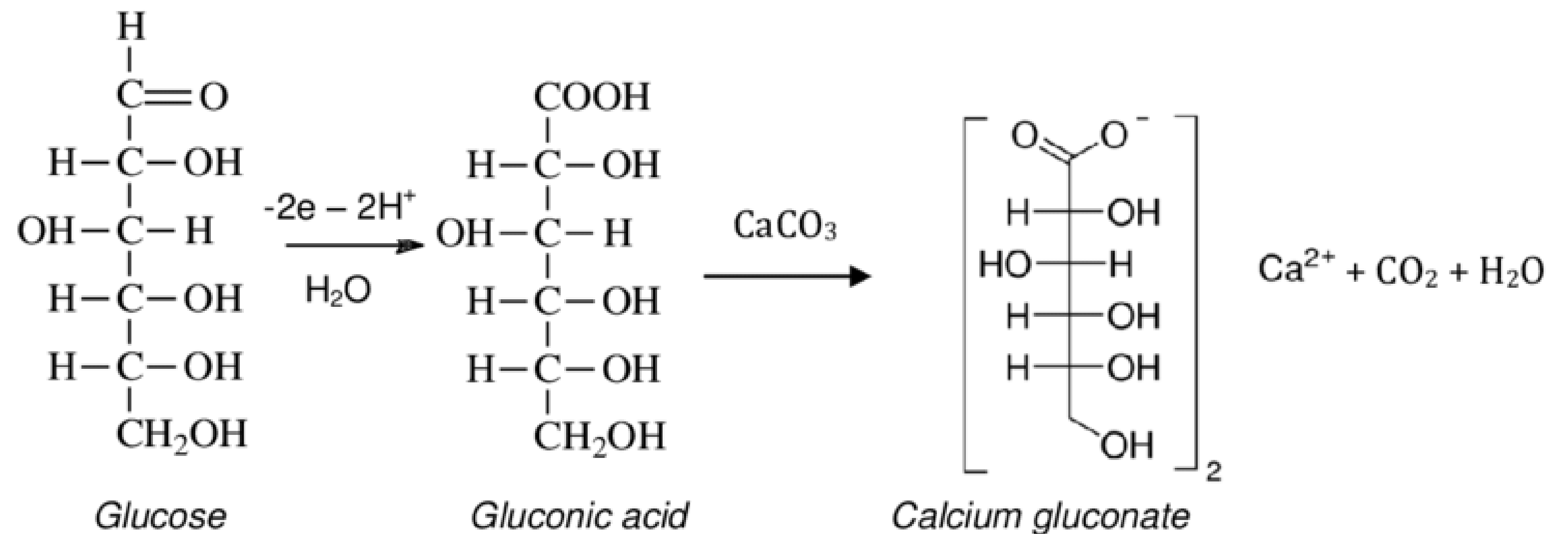
- Neutral to litmus paper.

Chemical properties:

- When treated with dil. HCl, it is decomposed into gluconic acid and calcium chloride.

Method of Preparation:

- It is prepared by boiling a solution of gluconic acid with Calcium carbonate.
- Product is filtered and dried.



- **Assay:**
- Principles: Complexometric titration.
- -0.5 g sample is dissolved in warm water, cool and add 5 ml of 0.05 M $MgSO_4$ and 10 ml of strong ammonia solution.
- -Titrant: 0.05 M Disodium EDTA
- -Indicator: Mordant Black II mixture.
- - End point: until deep blue color develops.
- -From the volume of 0.05 M disodium EDTA required, subtract the volume of the $MgSO_4$ solution added for actual reading.
- - Factor: 1 ml 0.05 M disodium EDTA= 0.02242 g of Calcium gluconate.
- **Uses:** It is used in management of hypocalcemia and calcium deficiency state.
- In insect bite: calcium gluconate 10 % solution, is given intravenously as an alternative to the use of conventional muscle relaxant, for the management of pain and muscle spasm associated with insect bite.
- In severe acute hypocalcemia.

- **Preparations of calcium gluconate:**
- **1. Calcium gluconate injection:**

Calcium gluconate injection is a sterile solution of calcium gluconate in water for Injection. Not more than 5 % of the calcium gluconate may be replaced with a suitable calcium salt as stabilizing agent.

- **2. Calcium gluconate tablets:**

Usual strengths: 325 mg; 500 mg; 650 mg; 1 g

- **3. Effervescence calcium gluconate tablets:**

- **Oral rehydration salt (ORS)**
- Oral rehydration salts are dry, homogenously mixed powders containing Dextrose, sodium chloride, potassium chloride and either sodium bicarbonate or sodium citrate for use in oral rehydration therapy after being dissolved in the requisite amount of water.

- It is combination of oral electrolytes.

- **Composition:**
- - contains essential electrolytes those are important to maintain the normal function of the body.
- - Also contains sufficient amount of water.
- - The concentration of electrolytes may be varying depending on the loss of particular electrolytes.
- **Uses:**
- In the heavy loss of water (dehydration) and loss of electrolytes.
- Condition like severe vomiting, diarrhea and prolonged fever.

- **Oral Rehydration Salt Powder IP 2007:**

As the stability of ORS containing sodium bicarbonate under tropical condition is very poor, formulations containing sodium bicarbonate are less suitable; sodium bicarbonate may be packaged separately in such cases to improve storage stability. ORS may contain suitable flavoring agent and, where necessary, suitable flow agent, in the minimum quantity, required to achieve a satisfactory product. But may not contain artificial sweetening agent like mono or polysaccharide, saccharin or aspartate.

Usual strength of ORS

Formula	(gm/L) ORS- A	ORS- Citrate
Sodium chloride	1.25	3.5
Potassium chloride	1.5	1.5
Sodium citrate	2.9	2.9
Anhydrous Dextrose	2.9	2.9
Dextrose monohydrate	29.7	22.0

- ORS- A , commonly used in India for treatment of non-choleraic diarrhea &
- ORS- Citrate, recommended by Diarrheal Disease Control Programmed of the World Health Organization (WHO).

PHYSIOLOGICAL ACID BASE BALANCE

- Our body fluids are having a balanced quantity of acids and bases. It becomes essential to maintain normal PH range because the biochemical reaction which take place in the living system are very sensitive to even small changes in acidity or basicity.
- Generally acidic metabolites are formed in higher quantity then basic metabolites because CO2, protein and amino acids contributes to acidic metabolites generation. These are then neutralize by bicarbonate ions.
- PH of blood remains constant around 7.3- 7.4 because of the mechanism of controlling PH by buffering system. An optimum PH is required by every system of body to perform various physiological functions and reactions.
- Most of metabolic reaction occurs in narrow range of PH. The required PH of plasma is maintained by the three regulatory mechanism.
- The buffer system may consist of weak acid and the salt of that acids. Buffer system of body does not allow rapid and drastic changes in the PH of a body fluid by converting strong acids & bases into weak acids & bases. Buffers are thus able to remove the excess Hydrogen from the body fluids but not from the body.

- **1. Buffer system/ buffering mechanism**

a) Carbonic acid & bicarbonate ion (HCO3 & H2CO3)

- found in plasma & kidney

b) Phosphate buffer system (HPO4/ H2PO4)

-Found in cell & kidney

c) Protein buffer system

- On dissociation of some amino acid which form OH & H+ ion which take part in buffering of body fluid.

2. Respiratory mechanism

On stimulation of respiratory center, the rate of breathing is altered, remove CO2 in the body fluid leads to change in PH.

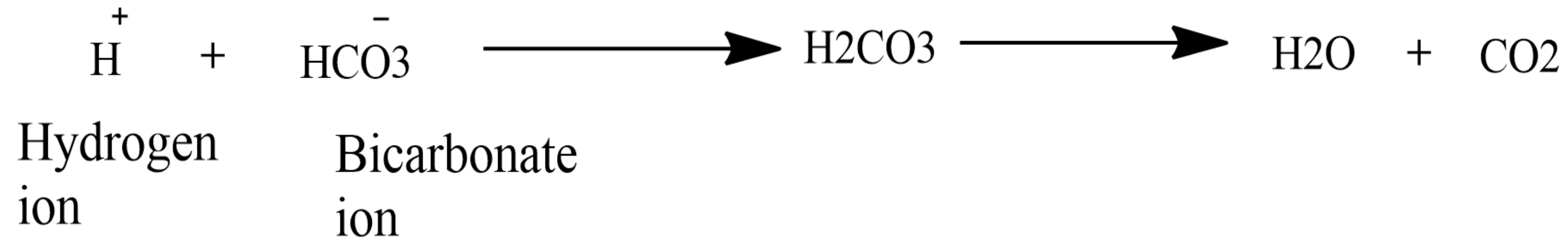
3. Renal mechanism

Absorption of certain ion & elimination of other through urine by kidney control the acid-base balance of kidney.

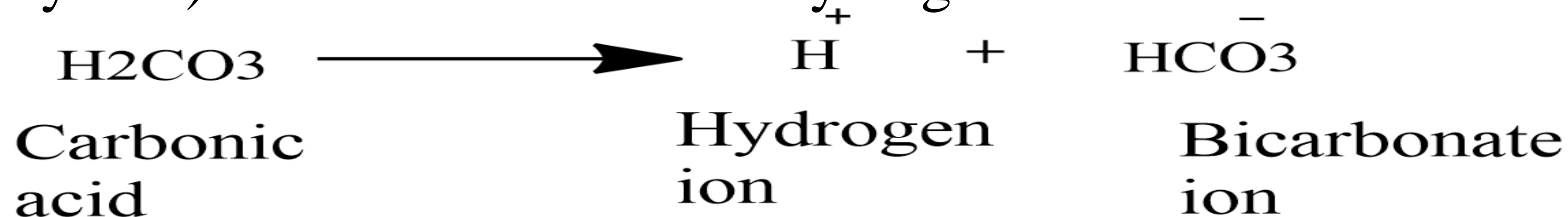
1. Carbonic acid-bicarbonate buffer system

Chief Buffer system of Blood.

- It occurs in plasma and kidney.
- It is considered to be an important regulation of blood PH. If there occurs an excess of Hydrogen, the bicarbonate (HCO3) ion acts as a weak base and accepts hydrogen to form carbonic acid. The latter dissociate further to yield carbon dioxide and water molecule. The carbonic acid formed later dissociates to yield carbon dioxide and water.



- While if there occurs shortage of hydrogen, the carbonic acid (another component of buffer system) ionize to release more hydrogen ion & maintain the PH.



- In lungs, for example, oxygen reacts with the protonated deoxyhemoglobin, releasing protons. Theses protons combine with bicarbonate, forming carbonic acids, which then dissociates to yield carbon dioxide and water. Then the carbon dioxide gets exhaled out.
- Normal metabolism gives rise to more acids than bases, but the blood is made more acidic. Therefore the body needs more bicarbonate salt than it needs carbonic acid. Hence at physiological PH 7.4, the plasma is having about 24 mEq/L of bicarbonate in comparison to about 1.2 mEq/L of carbonic acid. (ratio of 20: 1)

Bicarbonate Buffer System in the Regulation of Plasma pH

Decreased respiratory rate elevates P_{CO_2}

$CO_2 + H_2O$

LUNGS

Removal of H^+

BICARBONATE RESERVE

H_2CO_3 → H^+ + HCO_3^-

Na^+ HCO_3^- → $NaHCO_3$

Other buffer systems release H^+

Generation of H^+

Secretion of HCO_3^-

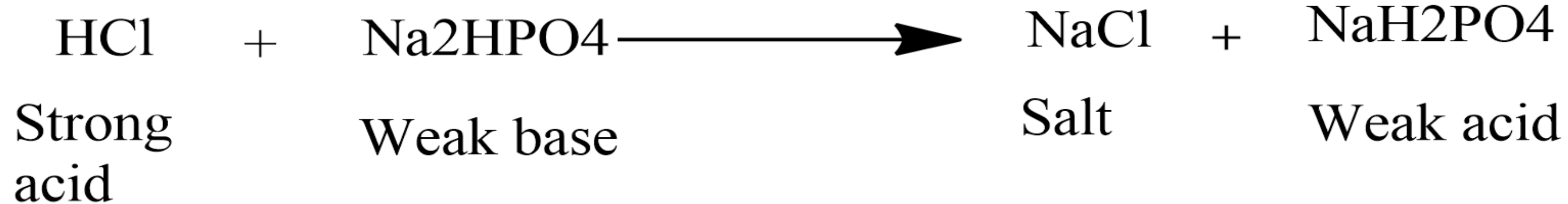
KIDNEYS

(b) The response to alkalosis

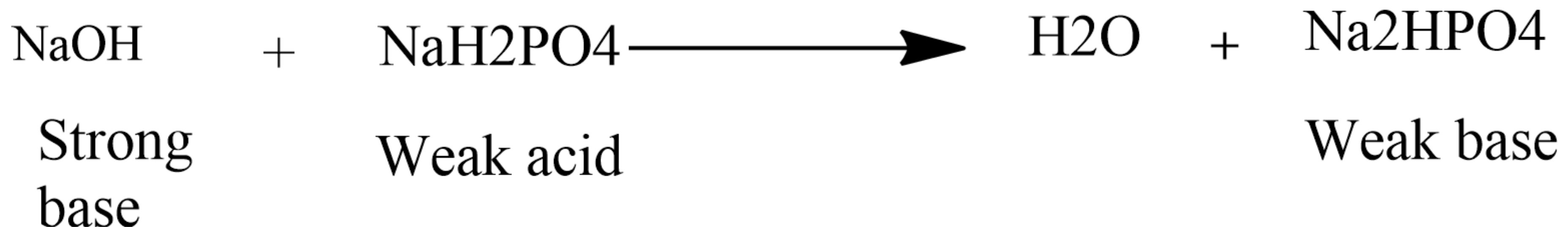
2. Phosphate buffer system

It is also able to maintain physiological PH at 7.4. as the phosphate concentration is highest in intra-cellular fluid, the phosphate buffer system is considered to be an important regulator of PH. This system occurs in the cells and kidneys. The system consist of monohydrogen phosphate/ dihydrogen phosphate (HPO4/H2PO4). It is known to act in the same manner as the carbonic acid- bicarbonate buffer system acts.

- If there occurs an excess of hydrogen, the monohydrogen phosphate ion acts as the weak base by accepting the proton.



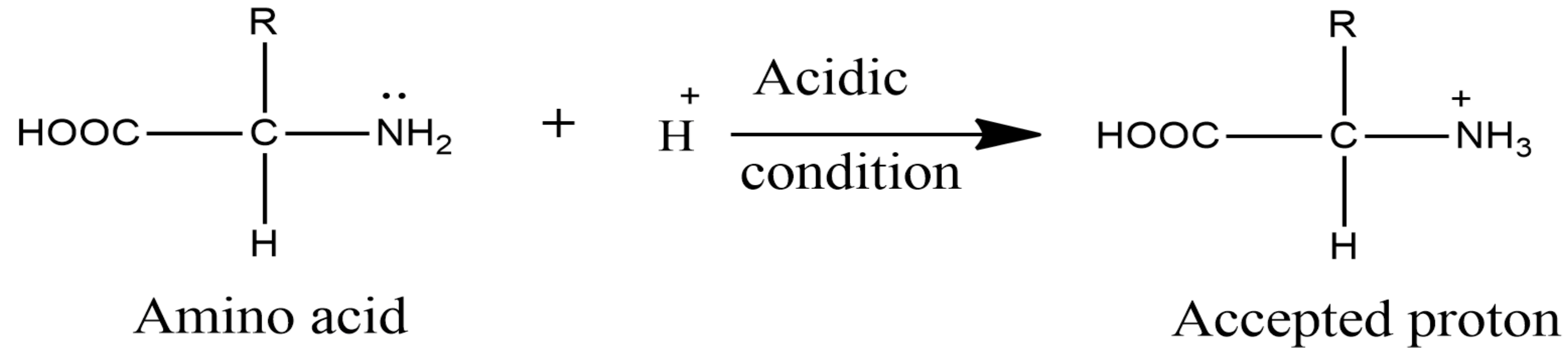
- While the dihydrogen phosphate ion can act as the weak acid and is able to neutralize the alkaline condition, as



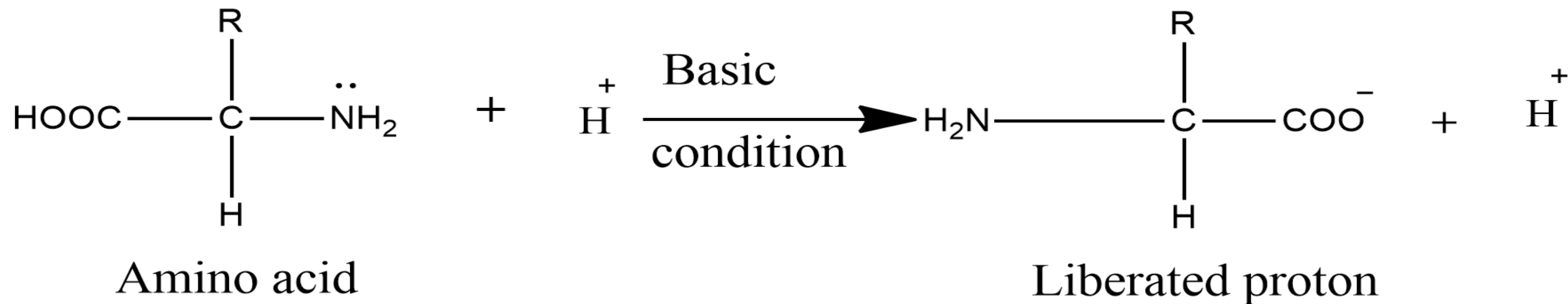
- For example, in kidney, NaH_2PO_4 gets formed if excess hydrogen ion in the kidney tubules combines with Na_2HPO_4. the sodium ion released in this reaction forms sodium bicarbonate by accepting bicarbonate ion.
- The $NaHCO_3$ then enters the blood. The kidney are also able to synthesize new HCO_3 and reabsorb bicarbonate ion that have been filtered so this important buffer does not get lost in the urine.
- The hydrogen ion that replaces sodium ion become part of the NaH_2PO_4 that goes into the urine. Thus, kidney are able to maintain pH by the acidification of urine. At physiological pH, the HPO_4/H_2PO_4 ratio in the intracellular fluid is about 4:1. while in the kidney it is nearly 1:100 because the urine pH is in acidic (4.5- 4.8) range.

3. Protein (Hemoglobin) buffers system

- It is considered to be the most abundant buffer in body cells and plasma. Proteins are composed of amino acids that are having at least one carboxyl group (COOH) and at least one amino (NH2) group. When there occurs an excess of hydrogen ions, the amino group act as a base and accepts the proton.



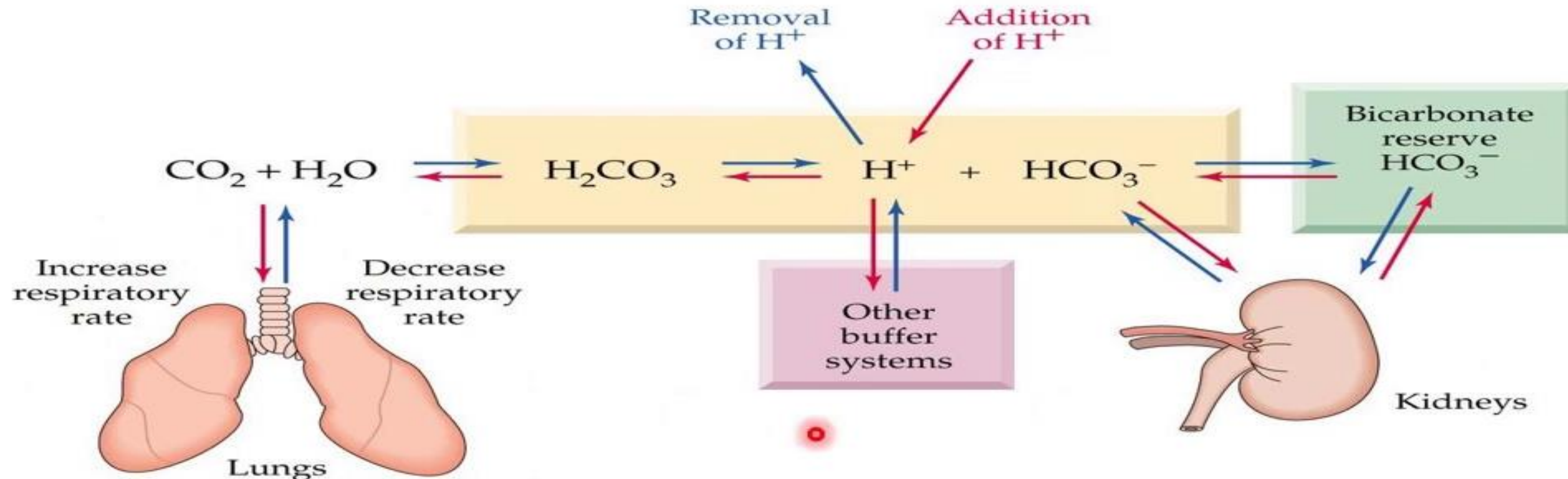
- While the free carboxyl group can release protons so as to neutralize an alkaline condition.



Thus, protein is able to serve both the function of acid and base components of a buffer system because of its amphoteric nature.

- **2. Respiratory mechanism:**
- The body's second best defense against acid-base disturbance is control of extracellular fluid CO_2 concentration by the lungs.
- When respiration get decreased, the accumulation of CO_2 combines with water present in blood to form carbonic acid (H_2CO_3) which further dissociates to give Hydrogen ion and give rise to acidosis.

Similarly in case of over breathing, excess of CO2 excreted by lung, which give rise to alkalosis.



3. Renal mechanism:

Kidney perform a major task to remove the excess of acid present in the body that is why PH of urine usually found to be acidic. Kidney is able to generate ammonia (NH3) which neutralize the acidic product of protein metabolism, these products are then excreted out from the body in urine. Fixed acids like sulphuric, phosphoric and hydrochloric acids are generally excreted out by kidney while unstable carbonic acid is removed mainly by respiratory mechanism.

KIDNEY'S ROLE in ACID-BASE BALANCE

URINE

HCO_3^-

(BICARBONATE)

H^+

BLOOD

- **Stability of buffers (From acids, bases & buffer chapter)**
- It is required to make up and treat buffer solutions with care. A typical shelf life for commercial technical buffers is 2 years unopened and 3- 6 months open. However, this is not valid for alkaline buffers (PH of buffer is 10 or higher). Alkaline solution will change their PH when they come into contact with carbon dioxide in air. The typical shelf-life for alkaline buffers is 1 month open.
- So to maintain the stability of buffer solutions, following points must be taken care of;
- Check any expiration date on commercial buffer solution before using it.
- During making a buffer solution, put a date on label and also an expiration date.
- Keep the buffer solutions in closed plastic container or within stoppered flask.
- Store the buffers at room temperature, 15 to 25C.
- For alkaline buffers, it is recommended to put the bottles in the refrigerator.
- The temperature of buffers is important because it is a function of its PH. At lower temperature, the evaporation of the water in the buffers is slower than a higher temperature, which help to maintain the concentration of the buffer constant for a longer period of time.

- **Storage:** store the buffers;
- At room temperature, 15 to 30 C or
- Refrigerated, 2 to 8 C
- Store the prepared buffer solutions in chemically resistant, tight container such as type I glass bottles. Use these solutions within 3 months.