

PHARMACEUTICAL INORGANIC CHEMISTRY- BP104T

UNIT: 2 (ACIDS, BASES AND BUFFERS)

CLASS: 3

TOPIC: ELECTROLYTES USED IN REPLACEMENT THERAPY

CALCIUM GLUCONATE

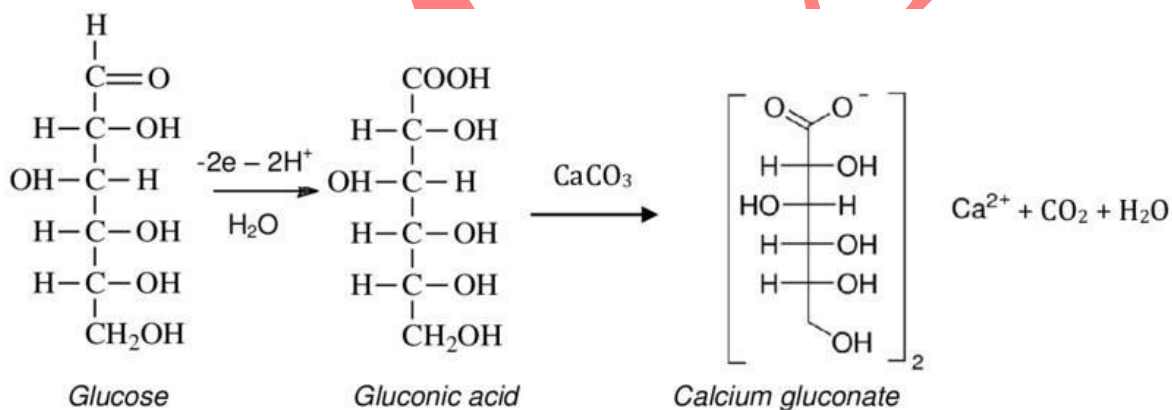
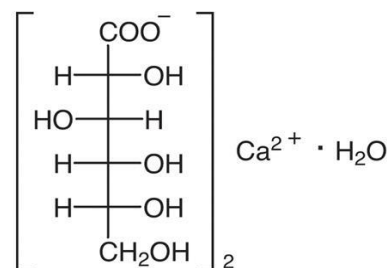
Molecular Formula: $C_{12}H_{22}O_{14}Ca \cdot H_2O$

Molecular weight: 448.40gm

Synonyms: Calcium D-gluconate, gluconic acid, calcium salt

Standards: Calcium gluconate contains not less than 98.0% and not more than 102% of calcium gluconate.

Method of preparation: It can be easily prepared by boiling solution of gluconic acid with excess of calcium carbonate. The precipitates obtained are then filtered and product is concentrated to crystallization.



Properties:

- It occurs as white, tasteless, odorless, crystalline or granular powder.
- It is stable in air, but loses water with decomposition on heating.
- It is soluble in water, more soluble in boiling water but insoluble in alcohol and other solvent.

Uses:

- It is used as calcium replenisher.

- Its injection is found to be useful in the treatment of urticaria and black widow spider bite.
- Its tablet also finds use in supplementary diet of convalescent and expectant mother

Some marked preparations of Calcium gluconate:

1. **Calcium Gluconate Injection:** It is sterile solution of calcium gluconate in water for injection. The amount of calcium gluconate must be in between 8.5-9.4% w/v. Calcium D-Saccharate is added as a stabilizer which also prevents the formation of precipitation of calcium gluconate.
2. **Calcium Gluconate Tablet:** Chewable Tablets are available in the strength of 0.325g, 0.5g, 0.65g, 1.0g.

Electrolyte Combination Therapy

- When a patient undergoes a surgery, he is unable to take normal diet. Therefore, he is given infusions containing saline and glucose. However, this is sufficient for a short-term therapy.
- But when the patient is deficient or in protracted illness, he also needs additional electrolytes which are intended for the fluid maintenance of the body. Usually the combination of electrolytes are prepared and given to the patient according to his requirement. This type of treatment is called electrolyte combination therapy.

Electrolyte combination Products are categorized in two categories:

1. **Fluid Maintenance:** The fluid or solutions of electrolytes have to be administered intravenously which provide the normal requirement of water and electrolytes.
2. **Electrolyte replacement:** in case of excessive vomiting, diarrhea or prolonged fever, electrolyte combination finds use in replacement therapy. Many electrolytes' combinations and varying concentrations are available as a dry powder to get dissolved in specified amount of water also known as "oral electrolyte solution".

Compound Sodium Lactate Injection

Synonyms: Ringer-Lactate solution for injection

Composition:

- Lactic Acid - 2.4 ml
- Sodium hydroxide - 1.15 g
- Dilute hydrochloric acid - Sufficient quantity
- Sodium Chloride - 6.0 g
- Potassium Chloride - 0.4 g

- Calcium chloride, hydrated - 0.4 g
- Water for injection sufficient to produce 1000 ml

Preparation: Sodium hydroxide is first of all dissolved in 200 ml of water for injection. To this lactic acid is added. It is now heated in an autoclave at 115°C for 1 hour. The solution is cooled and neutralized with hydrochloric acid. The other ingredients are dissolved in 700ml of WFI and the two solutions are mixed. Sufficient WFI is added for producing 1000ml. The solution is filtered. It is immediately sterilized by autoclaving or by filtration.

Properties: It is clear, colorless solution which is acidic in nature.

pH: Between 5 to 7

Test for Purity: It is tested for reaction, heavy metals and pythogens.

Compound Sodium Chloride Injection

Synonyms: Ringer's injection

Composition:

- Sodium Chloride - 8.6 g
- Potassium Chloride - 0.3 g
- Calcium chloride - 0.3 g
- Water for injection sufficient to produce 1000 ml

Preparation: The ingredients are dissolved in the water for injection. The solution is filtered until it becomes clear. Finally, it is sterilized by heating in an autoclave.

Oral Rehydration Salt (ORS)

- Oral rehydration therapy was developed in 1940
- ORS came in market from 1970
- Recommended by World Health Organization (WHO)
- Oral Rehydration Salts is a fluid replacement for the condition called dehydration, electrolyte imbalance due to diarrhea.
- It works by increase the uptake of sodium and water by the intestine.
- Potassium is very important it promote the water and sodium absorption.
- A large number of formulation of oral rehydration preparations are available in market, which contains glucose, sodium chloride, potassium chloride, and either sodium bicarbonate or sodium citrate.
- These dry powder preparations are to be mixed in specific amount of water and are used for oral rehydration therapy.

Composition of ORS:

Ingredients	ORS Formula	WHO/UNICEFORS (Bicarbonate formula)	WHO-UNICEF ORS (Sodium citrate formula)
Sodium chloride	1.0g	3.5g	3.5g
Potassium chloride	1.5g	1.5g	1.5g
sodium bicarbonate	1.5g	2.5g	-----
Sodium citrate	-----	-----	2.9g
Glucose	40g	22g	20g

PHYSIOLOGICAL ACID-BASE BALANCE

- The number of hydrogen-ions present in the solution may be regarded as a measure of the acidity of the solution. But pH is related to negative logarithm of acidity of (H⁺) ion concentration. Thus, pH may be considered to measure the acidity of the solution.
- All body fluids have definite pH values which must be maintained within relatively narrow limits (within which the cells functions normally).
- The normal range of pH values of few selected fluids are:

Blood 7.4-7.5

Duodenal fluid 5.5-7.5

Saliva 6.4-7.4

Gall bladder bile 5.5-7.7

Urine 4.5-8.0

Pancreatic juice 7.5-8.2

Gastric Juice 1.5-1.8

- The intracellular fluids also have varying pH depending upon the types of the cell. For Example in osteoblasts it may be slightly alkaline (pH 8.0) and in cells of prostate gland it may be acidic (pH 5.0).
- The individual pH in an organ is maintained by secretions of alkalis or acids to suit optimum level.
- The low pH in the stomach is best to the functioning of the enzyme pepsin present in gastric juice which breakdown proteins.
- Saliva has a pH range 6.4-7.4 which is the optimum value for the action of ptyalin (the enzyme present in saliva which initiates the digestion of carbohydrates)
- The metabolic process of the body cells produces acids or acidic substances (for eg. Carbonic acid from CO₂ and water, sulphuric acid and phosphoric acid from, proteins and phosphor proteins, lactic acid and pyruvic acid from anaerobic metabolism) and alkalis (for eg. Bicarbonate ions from salt of organic acids c.f. citrate, lactate etc) which tend to alter the pH of the tissue fluid and blood.

- The term Alkalosis refers to excess removal of H^+ from the body fluid, in contrast to the excess addition of H^+ , which is referred to as Acidosis.
- There are mainly three regulatory mechanisms which maintain the pH of the each system and equilibrium with one another.

These are:

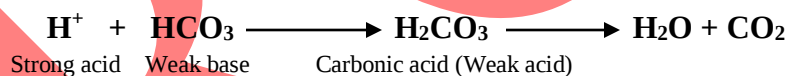
1. Buffer of the body fluids
2. Respiratory mechanism
3. Renal regulation

1. Buffer System:

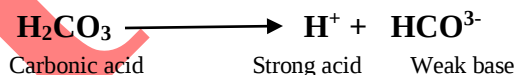
- Buffers are the chemicals capable to maintain a constant pH. Buffer system is consists of a weak acid and the salt of that acid.
- They resist the rapid change in the pH of body fluid by converting strong acids and bases into weak acids and bases. Buffer is thus able to remove excess H^+ from the body fluid but not from body.
- The major buffer systems existing in the body fluids are as follows:

i. Carbonic acid-Bicarbonate Buffer system ($H_2CO_3/NaHCO_3$):

It occurs in plasma and kidneys. Important regulator of blood pH. If there occurs an excess of H^+ , the bicarbonate (HCO_3^-) ion acts as a weak base and accept H^+ to form carbonic acid. They latter dissociate further to yield CO_2 and water molecules.

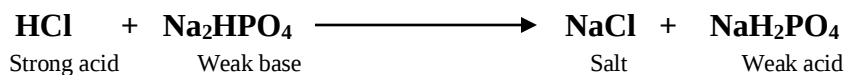


While if there occurs shortage of H^+ , the carbonic acid (another compound of buffer system) ionises to release more H^+ and maintain the pH.

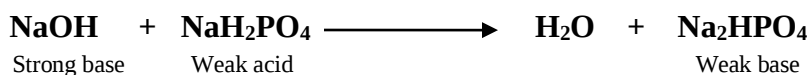


ii. Phosphate Buffer System (Na_2HPO_4/NaH_2PO_4):

- This buffer system mainly works in cells and kidneys and helps to maintain the physiological pH 7.4. Higher concentration of phosphate ions are found in intracellular fluid, thus consider as an important regulator of pH of cytosol.
- The system consists of monohydrogen phosphate/ dihydrogen phosphate (HPO_4^{2-} / $H_2PO_4^-$) anions.
- If there occur an excess of H^+ , the monohydrogen phosphate ion acts as the weak base by accepting the proton



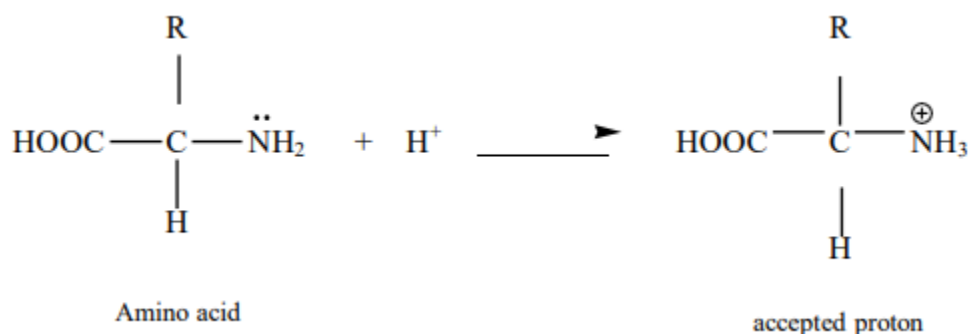
While dihydrogen phosphate ions can act as the weak acid and is able to neutralize the alkaline condition



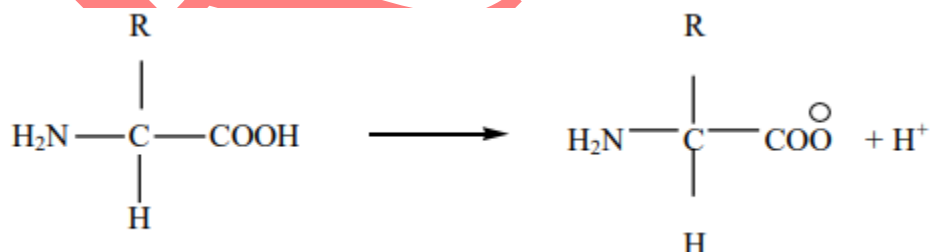
iii. Protein (Hemoglobin) Buffer System:

It is considered to be the most abundant buffer in body cells and plasma. Protein is compound 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 acts as a base and accept the proton.



While the free carboxyl group can release proton so as to neutralize an alkaline condition



Thus, proteins are able to serve both the functions of acid and base components of a buffer system due to its amphoteric nature. At physiological pH, histidine and cysteine are considered to be the most important amino acid buffer. Since hemoglobin which is a protein is composed of 37 histidine in the structure it is effective physiological buffer.

2. Respiratory mechanism:

- When respiration is decreased, there is an accumulation of CO_2 in the body which used up the alkali reserve of the blood resulting in the acidosis. On the other hand, if there is “over-breathing”, which results in excessive excretion of CO_2 , the condition of alkalosis may develop.
- Thus, acidity and CO_2 increases are both powerful stimulants of respiratory mechanism and cause an increase in the rate and depth of respiration.
- The H_2CO_3 is converted to CO_2 & H_2O and the CO_2 is rapidly breathed out. On the other hand, an increase in base, leads to decrease in acidity and H_2CO_3 content, resulting in retention of CO_2 and thus maintain within normal range

3. Renal mechanism:

- Kidneys have the ability to form ammonia which combines with the acids produced during the protein metabolism and is excreted in urine.
- The pH of urine is highly variable between 4.8 to 8.0 normally, it is towards acid side but varies with the nature of diet, exercise etc.
- While unstable H_2CO_3 is removed mainly by respiratory mechanism, the fixed acids like phosphoric, sulphuric and hydrochloric acids have to be removing through kidneys.

2 MARKS QUESTIONS

1. Write the method of preparation and uses of calcium gluconate injection?
2. What is electrolyte combination therapy?
3. Write the composition of ORS

5 MARKS QUESTIONS

1. Discuss the physiological acid-base balance?
2. Explain the method of preparation, and uses of calcium gluconate injection?
3. Write a short note on Oral Rehydration Salt

10 MARKS QUESTIONS

1. Discuss the mechanism of physiological acid base mechanism in the body
2. Write the principle, method of preparation, assay and uses of calcium gluconate