Major Extra and Intracellular Electrolytes

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^{-}

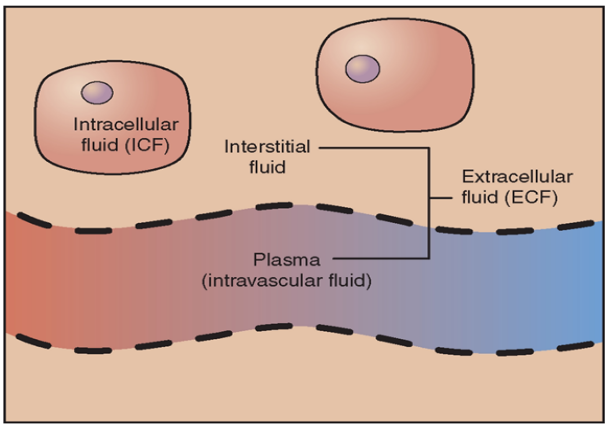
- But in our body, electrolytes are certain charged nutrients present in our body that have many important functions like:
  - Electrolytes regulate our nerve and muscles function, our body's hydration, blood pH, blood pressure, and rebuilding of damaged tissue.
  - The body cells require a perfect pH , osmotic balance and ionic balance. This balance is maintained by the body fluids which contains inorganic and organic solutes. These solutes can be electrolytes, acid, bases, blood products, carbohydrates, amino acids, proteins.

Electrolytic Fluid Compartments:

- Body contain 60-70% of water

Body Fluids

Intracellular Fluid
(Fluid inside the cell)
[45-50% of body weight]

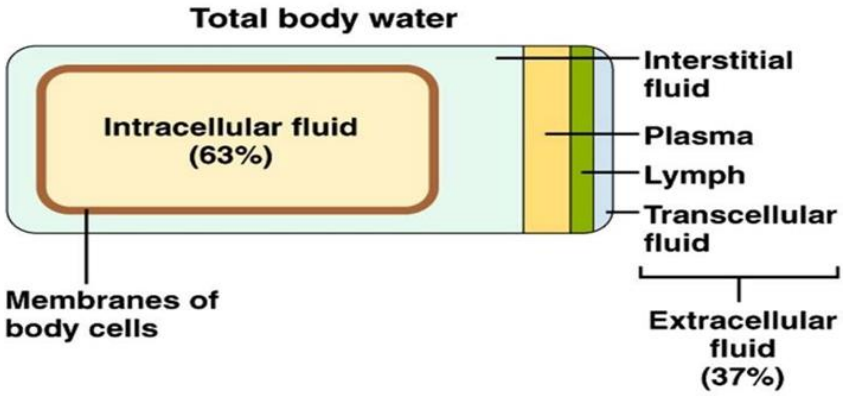


Extracellular Fluid

Interstitial Fluid
(Between the cell)
[12-15% of body weight]

Plasma or Vascular fluid
(Fluid within blood vascular system)
[4-5% of body weight]

- The term 'extracellular fluid' includes both interstitial and vascular fluids.
- These three compartments are separated from each other by membranes that are permeable to water and many organic and inorganic solutes.
- They are nearly impermeable to macromolecules such as proteins and are selectively permeable to certain ions such as Na^+, K^+, Mg^{2+}



Functions of Electrolytes:

- Maintain electrolytic balance, including acid-base balance and osmotic equilibrium in various body fluid.
- To facilitate specific metabolic functions by supplying the specific ion to the body fluids associated with the concerning cell or organ.
- To regulate the total amount of water in body fluids.
- Our heart, muscles and nerve cells use electrolytes to maintain voltage across their cell membranes and to carry electrical impulses to other cells.
- A muscle contraction needs calcium (Ca^{++}), sodium (Na^+), and potassium (K^+) to be present. Deficiency and excess of electrolyte level lead to either weak muscles, or muscles that contract too severely.

Electrolytic Imbalance and its causes:

- Body have capacity to adjust slight variation in concentration of electrolytes in fluid compartments. Mainly electrolytic level is kept constant by our kidneys and other hormones.
- Whenever there is a change in concentration of ions in any compartment, water will migrate across the cell membrane to re-establish osmotic equilibrium. If body is unable to adjust the concentration of fluid electrolytes then externally "electrolytic replacement therapy" is used.
- Body electrolytic levels tend to alter when water levels in the body changes- when our level of hydration goes up or down.

- Several other causes include:

Kidney disease	Vomiting or prolong periods
Poor diet	severe dehydration
Diarrhea	Congestive heart failure

Edema (fluid get accumulated in intestinal space between cell due to low osmotic pressure)
Acid-Base imbalance

Symptoms of electrolytic Imbalance:

- The symptoms will depend on which electrolyte is out of balance, and whether that level is too high or too low.
- An altered level of magnesium, sodium, potassium, or calcium may produce one or more of the following symptoms:

Irregular heart beat	Weakness
Bone disorder	Blood pressure change
Confusion	Seizures
Nervous system disorder	Convulsion
Muscle spasm	

Major Physiological Ions and their functions:

8 Major Physiological Ions	
Cations	**Anions**
Sodium (Na^+)	Chloride (Cl^-)
Calcium (Ca^{2+})	Bicarbonate (HCO^{3-})
Potassium (K^+)	Phosphate (HPO^{4-})
Magnesium (Mg^{2+})	Sulphate ($SO4^{2-}$)

A. MAJOR EXTRACELLULAR IONS

CHLORIDE (Cl^-)

Amount present in body: 50 mEq/Kg;
Recommended daily Requirement: 5-10 g as NaCl

Major Food Source: Common table salt, Animal food

Absorption from GIT and Fate in Body (Metabolism): Completely absorbed, eliminated from blood by glomerular filtration and possibly reabsorbed by the kidney tubules

Principle Physiological/ Metabolic Function: Maintenance of proper hydration, osmotic pressure, normal electrolyte balance, acid-base balance, Gastric HCl

Deficiency: ***Hypochloemia*** occur due to kidney disease, metabolic acidosis (due to diabetes or renal failure or prolong vomiting)

Excessive Presence: ***Hyperchloremia*** in dehydration, decreased renal blood flow associated with congestive heart failure (CHF), severe renal damage and excessive Cl^- intake.

SODIUM (Na^+),

Amount present in body: 1.8 g/Kg;
Recommended daily Requirement: Approx. 3-5 g.

Major Food Source: Table salt, baking soda, animal food and some vegetables.

Absorption From GIT and Fate in Body (Metabolism): Completely absorbed, excreted in sweat and urine, kidney regulates sodium contents of the body, hormone aldosterone increases reabsorption in renal tubules.

Principle Physiological/ Metabolic Function: Maintenance of normal hydration & osmotic pressure, acid-base balance, cell membrane permeability, muscle contraction, carbon dioxide transport, transmission of nerve impulses.

Deficiency: ***Hyponateremia*** may occur with excess loss of urine (diuresis) in diabetes insipidus, Addison's disease (with reduced secretion of anti-diuretic hormone, aldosterone) diarrhea & vomiting, renal damage.

Excessive Presence: ***Hypernateremia*** may occur in hyperadrenalism (Cushing's syndrome) with increased aldosterone production, severe dehydration, certain types of head injury, hypertension.

CALCIUM (Ca^{++})

Amount present in body: 22 g/Kg (99% in bones, rest mainly in extracellular fluid);
Recommended daily Requirement: About 1 g.

Major Food Source: Milk and milk products, eggs, green vegetables and some fishes.

Absorption From GIT and Fate in Body (Metabolism): Poorly absorbed (20-40%), variable absorption depend upon body requirements and affected by several factors c.f. *increased* in vit. D, lactose, acidity; *decrease* by fat, oxlate, low dietary phosphorous intake; excreted in faeces, parathyroid hormone controls blood Ca^{++} and phosphate level and mobilization in bones.

Principle Physiological/ Metabolic Function: Hardening of bones and teeth; coagulation of blood, muscle contraction, cell membrane permeability.

Deficiency: ***Hypocalcemia*** rickets in children's, poor growth, osteoporosis in adults, hyperexcitability, Cushing's syndrome (hyperactive adrenal cortex)

Excessive Presence: ***Hypercalcemia*** fatique, muscle weakness, constipation, anorexia (loss of appetite), cardiac irregularities, renal failure [hypercalcemia is associated with hyperparathyroidism, hypervitaminosis D and some bone neoplastic (cancer) diseases.

BICARBONATE (HCO_3^-)

Amount present in body: 25-30 mEq/l in blood or plasma;

Major Food Source: Certain citrus fruits, milk etc. which *in vivo* converted into HCO_3^-

Absorption From GIT and Fate in Body (Metabolism): Bicarbonate salt (eg $NaHCO_3$) if taken orally neutralized by gastric acid in stomach. Organic acid radicals lactate, citrate etc. are converted into bicarbonate *in vivo.* Most CO_2 is exhaled by lungs but some as per body requirement converted into carbonic acid (H_2CO_3) and bicarbonate ion (HCO_3^-) constituting important physiological buffer.

Principle Physiological/ Metabolic Function: Maintenance of physiological acid-base balance, CO_2 transport, maintenance of proper hydration, gastric acid, electrolyte balance.

Deficiency: Metabolic acidosis especially in uncontrolled diabetes with ketosis, renal disease, poisoning by an acid salt, loss of intestinal fluid in vomiting, diarrhoea. Increased respiration (hyperpnea).

Excessive Presence: Metabolic Alkalosis due to ingestion of large quantities of alkalis in treatment of acidity, peptic ulcer, metabolic acidosis, high intestinal obstruction, prolong

vomiting or excessive removal of gastric secretion. In Cushing's disease and during corticotropin or cortisone administration, in hypokalemia.

B. MAJOR INTRACELLULAR IONS

PHOSPHATE (PO_4^{3-})

Amount present in body: 12 g/Kg;
Recommended daily Requirement: 800 mg

Major Food Source: Milk and milk products, oatmeal, whole grains, legumes, nuts, egg yolk, meat especially in liver and kidney.

Absorption From GIT and Fate in Body (Metabolism): Easily absorbed by intestine, excretion is mainly through urine via kidney (unlike calcium) only small amount are excreted in faces.

Principle Physiological/ Metabolic Function: like calcium, it is predominant constituent of bones and teeth; building block of several important substance including those used by the cell for energy (ATP), cell membranes, DNA & RNA, secondary messengers, modulation of enzyme activity, biological buffer etc.

Deficiency: ***Hypophosphatemia*** may be associated with vitamin D deficiency, hyperparathyroidism and prolong use of aluminium hydroxide gel antacids. It may leads to rare osteomalacia and cardiac arrhythmia.

Excessive Presence: ***Hyperphosphatemia*** may be associated with hypervitaminsois D, renal failure, hypoparathyroidism, it may lead to formation of kidney stone with possible kidney damage.

POTASSIUM (K^+)

Amount present in body: 2.6 g/Kg;
Recommended daily Requirement: Approx. 1.5-4.5 g.

Major Food Source: Milk and milk products, fruits, vegetables, legumes, whole grain, meat.

Absorption From GIT and Fate in Body (Metabolism): Rapidly absorbed, excess excreted by kidney. Presence in intracellular compartment is 23 times higher than extracellular and this ration is maintained by active transport mechanism; through *sodium potassium* pump.

Principle Physiological/ Metabolic Function: Electrolyte, acid-base and water balance, buffer constituent, muscle contraction, membrane transport, carbon dioxide transport.

Deficiency: *Hypokalemia* *(hypopotassemia)* leading to depressed myocardial function, flaccid and feeble muscle and hypotension may occur from vomiting, diarrhoea, dehydration, burns, haemorrhages, intravenous infusion of potassium-lacking solution (dilution effect), excessive use of diuretics.

Excessive Presence: *Hyperkalemia* *(hyperpotassemia)* though less common, can occur with impaired renal functions (lack of excessive K^+ excretion) and potassium retention due to acidosis.

MAGNESIUM (Mg^{2+})

Amount present in body: 0.5 g/Kg;
Recommended daily Requirement: Approx. 350 mg.

Major Food Source: Green vegetables, legumes, whole grain, nuts, beans, meat, milk.

Absorption From GIT and Fate in Body (Metabolism): Not readily absorbed from GIT, absorption retarded by alkaline media, unabsorbed Mg^{2+} is excreted through urine, bile and intestinal secretion.

Principle Physiological/ Metabolic Function: Essential component of some enzyme involving phosphate metabolism, constituent of bones and teeth; essential for protein synthesis, smooth functioning of neuromuscular function.

Deficiency: *Hypomagnesemia* can occur due to malnutrition, dietary restriction, chronic alcoholism, malabsorption, GIT disorder, medication and parathyroid hormone imbalance. Personality changes confusion, choreiform movement, tremors, cardiac disorders including vasodilation.

Excessive Presence: *Hypermagnesemia* (increase in blood levels of magnesium) depress the nervous system and higher levels can induce anaesthesia and paralysis of skeletal muscle.

Electrolytes Used for Replacement Therapy

The electrolyte concentration is maintained constant in body fluids. If a person undergoes surgery, remains ill or remain in an undesirable condition for a long time, the body cannot

maintain or correct the electrolyte balance, then done by external administration which is termed as **"Replacement Therapy"**.

There are various conditions which leads to disturbance of electrolytic balance and ultimately disturb the physiological system. Major causes are:

1. Any accident, haemorrhage, surgery, etc.
2. Diarrhoea, vomiting, dehydration due to GIT infection.
3. Drugs induced electrolytes elimination e.g. using thiazide or high ceiling diuretics leads to loss of K+
4. Metabolic disorder leading to alkalosis or acidosis.
5. Deficiency of essential ions or excessive elimination (e.g. hyponatremia, hypokalemia, hypocalcemia, hypomagnesemia etc)

However, there are two types of solutions of electrolytes which are used in replacement therapy.

(a) A solution for rapid initial replacement:

This solution is having sodium in the concentration range of 130-150 mEq/l, 98-110 mEq/l of chloride, 28-55 mEq/l of bicarbonate, 4-12 mEq/l of potassium, 3-5 mEq/l of calcium and 3 mEq/l of magnesium.

These electrolyte concentration thus closely resemble with the electrolyte concentration which are found in extracellular fluids.

(b) A solution for subsequent replacement:

The electrolyte composition of such solution is 40-120 mEq/l Na, 30-105 mEq/l Cl, 16-53 mEq/l HCO_3, 16-35 mEq/l K, 1-15 mEq/l Ca, 3-6 mEq/l Mg and 0-13 mEq/l of phosphorous.

Sodium Chloride

Molecular Formula: NaCl
Molecular weight: 58.5
Synonyms: Rock salt, common salt, Table salt
Natural Source: Rock salt, Sea water.
Standards: Sodium chloride contains not less than 99.0% and not more than 100.5% of NaCl, calculated on dried basis.

Method of preparation:
In laboratory it is prepared by reaction between a strong acid (HCl) and a strong base (NaOH). The sodium chloride present in dissolved form; solid is obtained by evaporation of water.

Industrially, it is prepared (i) by evaporating purified saline (sea water) diposits and further purification. (ii) by purifying rock salt

Properties:

1. It occurs in the form of white or colorless crystals.
2. It is odorless and having saline (salty) taste.
3. It is soluble in water but insoluble in alcohol.
4. With silver nitrate solution, it gives white insoluble precipitate of silver chloride which is soluble in ammonia.

$$NaCl + AgNO_3 \rightarrow AgCl\downarrow + NaNO_3$$

Uses:

1. It is source of both sodium and chloride ions.
2. 0.9% solution of NaCl solution is isotonic with blood, used in wet dressing and irrigating body cavity.
3. It is used alone or in combination with other salts or glucose when body fluid electrolytes are depleted.
4. Used as electrolyte replenisher.
5. When hypertonic solution is given orally, it induces vomiting and thus can use in case of poisoning as a first aid.

Storage: It is stored in tightly closed container in dry place as it absorb moisture.

Some marked preparations of Sodium Chloride:

1. Sodium Chloride Eye Lotion (B.P)

- ❑ It contains 0.85-0.95% w/v of NaCl.
- ❑ It is prepared by dissolving sodium chloride in purified water, filtered, transferred to final container, avoiding the entry of micro-organisms and sterilized by heating in an autoclave.

2. Sodium Chloride Solution (B.P)

- ❑ It contains 0.9% w/v sodium chloride, prepared in purified water and clarified by filtration.
- ❑ When normal saline is prescribed then above solution is dispensed. If the label states that it is sterile solution, then it should comply for test for sterility.

3. Sodium Chloride Hypertonic Injection:

- ❑ It is having 1.6% w/v of sodium chloride. (pH 5-7.5)

Composition:

Sodium chloride - 16 gm

Water for injection sufficient to produce 1000 ml

4. Sodium Chloride Injection

- ❑ It is sterile isotonic solution of sodium chloride in water for injection. It contains not less than 0.85% and not more than 0.95% w/v of NaCl. It contains no antimicrobial agents.

Composition:

Sodium Chloride - 9 gm

Water for injection sufficient to produce 1000 ml.

Preparation:

The sodium chloride injection is prepared from the above ingredients by dissolving Sodium chloride in water for injection, filtered and immediately sterilizing by heating in an autoclave or by filtration.

Properties:

It is clear and colorless solution.

Storage:

It should be stored in single-dose containers of glass or plastic.

Uses:

1. It is used alone or in combination with other salts or glucose when body fluid electrolytes are depleted.

2. It is used as electrolyte replenisher.

5. Sodium Chloride and Dextrose Injection

- It is sterile solution of sodium chloride and dextrose in water for injection.
- It contains not less than 95% and not more than 105% of the stated amount of sodium chloride and dextrose.

Preparation:

It is prepared by dissolving the calculated quantities of sodium chloride and dextrose in purified water. Finally it is sterilized immediately by autoclaving or by filtration.

Properties:

It is clear, colorless solution.

Storage & labeling:

It is stored in single dose container in a cool place. The label should state the strength as percentage w/v of sodium chloride and dextrose. When it is intended for I.V. use, the label must also state the appropriate concentration in mEq/l of sodium and chloride ions.

Uses:

It is used as a fluid, nutrient and electrolyte.

6. Mannitol and sodium chloride Injection:

- It is sterile solution of sodium chloride and mannitol in various proportion of the above ingredients. E.g. 5 and 10 % mannitol with 0.3 % NaCl, 15 and 20% mannitol with 0.45% NaCl.

Uses:

Electrolyte replenisher cum diuretic.

Replacement of Potassium

Potassium Chloride

Molecular Formula: KCl
Molecular weight: 74.55 g/mol
Synonyms: kalii Chloridum
Natural Source: Sylvin and Carnallite (Minerals)
Standards: Potassium chloride contains not less than 99.0% and not more than 100.5% of KCl, calculated on dried basis.
Method of preparation:

1. It is mainly prepared from the natural minerals, carnallite (KCl.MgCl2.6H2O) the raw salt deposit is first of all grounded and then treated with hot water when the less soluble KCl crystallizes out on cooling. The process has to be repeated for achieving almost complete recovery of KCl from the mother liquor and wash water.
2. In the laboratory, it is prepared by the action of HCl on potassium carbonate or bicarbonate.

$$K_2CO_3 + 2HCl \rightarrow 2KCl + H_2O + CO_2$$
$$KHCO_3 + HCl \rightarrow KCl + H_2O + CO_2$$

Properties:

1. It occurs as colorless prismatic or cubical crystals or as a white granular powder.
2. The salt is odorless and having a saline taste.
3. It is soluble in water, insoluble in alcohol and ether.
4. It melts at 772°C. its 10 percent aqueous solution is neutral to litmus paper.

Uses:

1. It is used as an electrolytic replenisher.
2. It also finds use when hypokalemia or hypochloremia alkalosis exists as has been the case after prolong diarrhea or vomiting.
3. It is sometimes used as diuretics also.
4. As an antidote, it is used in digitalis poisoning.
5. Potassium chloride has been an ingredient of sodium chloride injection, Ringer's solution, ORS etc.

Storage: It is stored in tightly closed container in dry place as it absorbs moisture.

Some marked preparations of Sodium Chloride:

1. **Potassium Chloride and Sodium Chloride I.V. Infusion (B.P.)**

- ❑ It is a sterile solution containing 95.0 to 105.0% of the stated amount of sodium chloride and potassium chloride. The solution is prepared in water for injection and sterilized by heating in autoclave.
- ❑ Usual strength available are infusions containing 0.15, 0.20 and 0.30% w/v KCl, each containing 0.9 % w/v of NaCl, in 500 and 1000 ml containers**.**

2. Potassium Chloride and Glucose intravenous Infusion (B.P.)

- ❑ It is a sterile solution in water for injection containing KCl 95.0 to 105.0 of the stated amount of glucose and potassium chloride.
- ❑ Usual strengths available are intravenous infusions containing 0.15, 0.2 and 0.3 per cent w/v of KCl, each containing 5.0% w/v glucose in 500ml and 1000ml containers.

3. Potassium chloride, Sodium Chloride and Glucose intravenous infusion (B.P.)

- ❑ It is a sterile solution of water for injection containing:

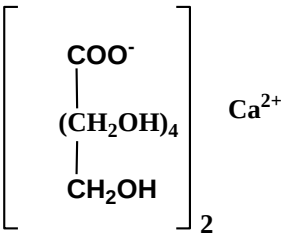
  KCl - 0.3%
  NaCl - 0.18%
  Glucose - 40%

4. Effervescent KCl Tablet:

- ❑ It Contains:

  KCl - 600mg
  $KHCO_3$ - 400mg
- ❑ KCl sustain release tablet of 600mg.

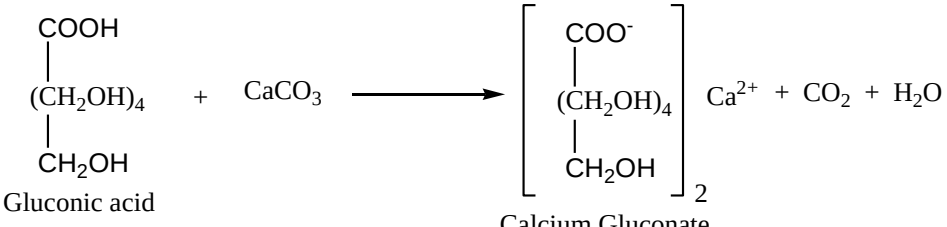
Calcium Gluconate



Molecular Formula: $C_{12}H_{22}O_{14}Ca.H_2O$
Molecular weight: 448.40
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:

1. It occurs as white, tasteless, odorless, crystalline or granular powder.

2. It is stable in air, but loses water with decomposition on heating.
3. It is soluble in water, more soluble in boiling water but insoluble in alcohol and other solvent.

Uses:

1. It is used as calcium replenisher.
2. Its injection is found to be useful in the treatment of urticaria and black widow spider bite.
3. Its tablet also finds use in supplementary diet of convalescent and expectant mother.

Some marked preparations of Sodium Chloride:

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 prevent 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 categories in two categories:

1. Fluid Maintenance: The fluid or solution 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 prolong fever, electrolyte combination find use in replacement therapy. Many electrolytes' combinations and varying concentration are available a dry powder to get dissolve in specified amount of water also k/a "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 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-UNICEF ORS (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 Eg 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 phosphoproteins, 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 ($HCO3^-$) ion acts as a weak base and accept H^+ to form carbonic acid. They latter dissociate further to yield CO_2 and water molecules.

$$\underset{\text{Strong acid}}{H^+} + \underset{\text{Weak base}}{HCO_3^-} \longrightarrow \underset{\text{Carbonic acid (Weak acid)}}{H_2CO_3} \longrightarrow H_2O + CO_2$$

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

$$\underset{\text{Carbonic acid}}{H_2CO_3} \longrightarrow \underset{\text{Strong acid}}{H^+} + \underset{\text{Weak base}}{HCO_3^-}$$

ii. Phosphate Buffer System (Na_2HPO_4/NaH_2PO_4):

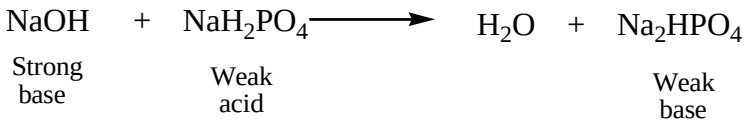
This buffer system mainly works in cells and kidneys and helps to maintain the physiological pH 7.4. Higher concentration of phosphate ions are found in intracellular fluid, thus consider as an important regulator of pH of cytosol.

The system consists of monohydrogen phosphate/ dihydrogen phosphate ($HPO4^{2-}$/ $H2PO4^-$) anions.

If there occur an excess of H+, the monohydrogen phosphate ion acts as the weak base by accepting the proton

$$\underset{\text{Strong acid}}{HCl} + \underset{\text{Weak base}}{Na_2HPO_4} \longrightarrow \underset{\text{Salt}}{NaCl} + \underset{\text{Weak acid}}{NaH_2PO_4}$$

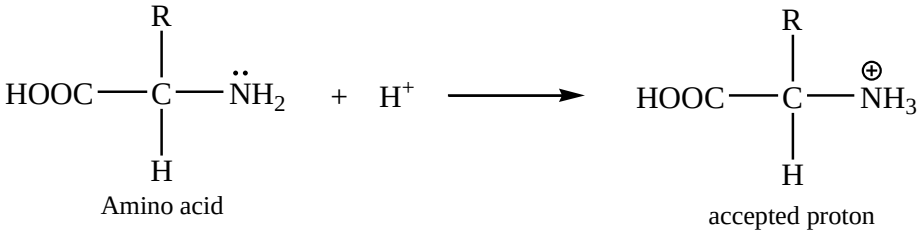
While dihydrogen phosphate ions can act as the weak acid and is able to neutralize the alkaline condition



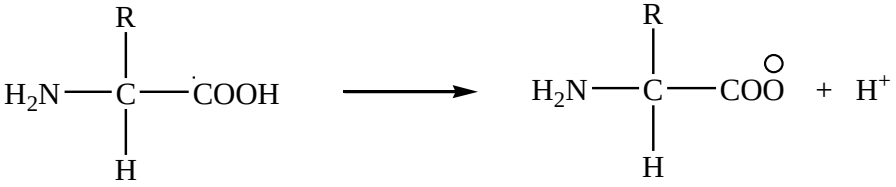
iii. Protein (Hemoglobin) Buffer System:

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 (NH_2) 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 with in 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 remove through kidneys.