Inorganic Pharmaceutical Chemistry

3rd Stage – 1st Semester

Lecture 4

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Major Intra and Extra Cellular Electrolytes

Electrolytes

Substances whose molecules dissociate into ions when they are placed in water.

Cations (+) Anions (-)

Medically significant / routinely ordered electrolytes include:

Cation: Positively Charged particles.

Sodium	(Na^{+})
Potassium	(K^{+})
Calcium	(Ca^{++})
Magnesium	(Mg^{++})

Anion: Negatively charged particles.

Chloride	(Cl^{-})
Bicarbonate	(HCO_3^{-})
Phosphate	(PO_4^{-2})

- **Body Fluids Compartments:**

a- Intracellular Fluid (ICF) compartment: (about 67%)

It is the system that includes all fluid enclosed in cells by their plasma membranes.

b- Extracellular Fluid (ECF): (about 33%)

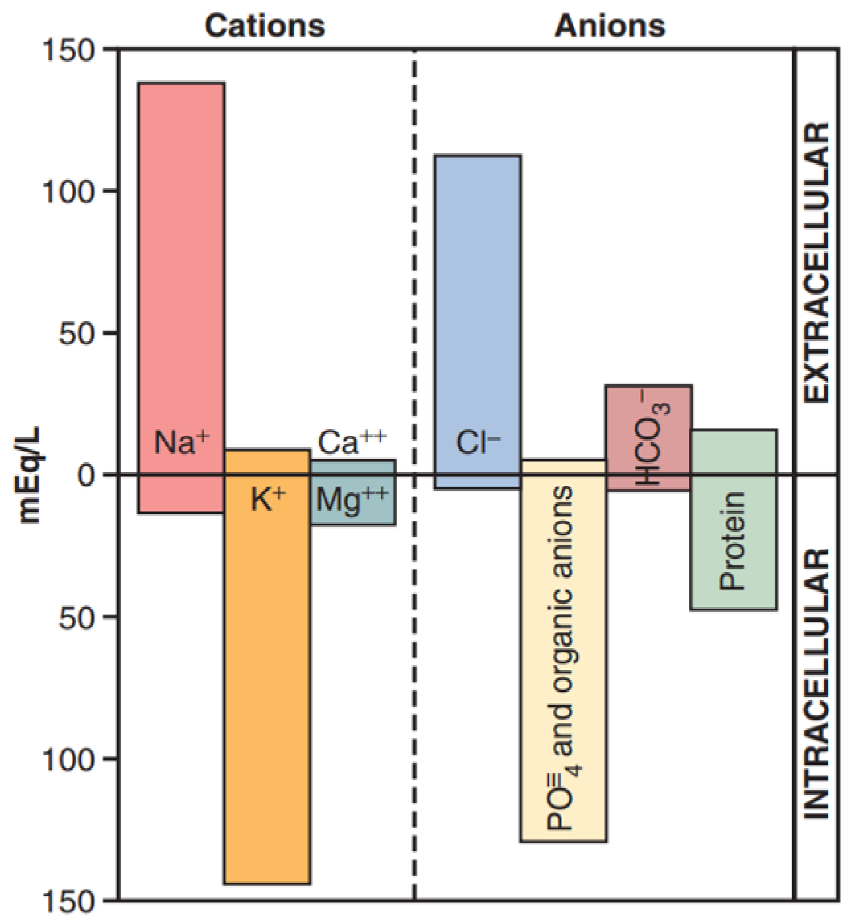
It surrounds all cells in the body. Extracellular fluid has two primary constituents:

1- Plasma: the fluid component of the blood

2- Interstitial Fluid (IF) that surrounds all cells not in the blood.

c- Transcellular Fluid:(about 1%): is the portion of total body water contained within the epithelial-lined spaces.

- Some electrolytes present in the extracellular fluids while other present in the intracellular fluids.



- The most important point is the charge balance, two types of balance are present:
  1- balance between +ve charges, Balance between negative charges in the same compartment
  2- Each cation should be with anion (in extracellular and intracellular).
  Some diseases occur with changes in balance, should be treated

- **Electrochemical Equivalence**
  mEquivalent (mEq/L) = moles x valence

  Monovalent Ions (Na^+, K^+, Cl^-):
  1 milliequivalent (mEq/L) = 1 millimole

  Divalent Ions (Ca^{++}, Mg^{++}, and HPO_4^{2-})
  1 milliequivalent = 0.5 millimole

- **Electrolyte Functions:**
  - Volume and osmotic regulation. (Na^+)
  - Myocardial rhythm and contractility. (K^+, Mg^{+2}, Ca^{+2})
  - Cofactors in enzyme activation. (Ca^{+2})
  - Regulation of ATPase ion pumps. (Mg^{+2})
  - Acid-base balance. (HCO_3^-, PO_4^{-2})
  - Blood coagulation. (Ca^{+2})
  - Neuromuscular excitability. (Na^+: depolarization, K^+: Repolarization)
  - Production of ATP from glucose. (Mg^{+2})

I- Sodium:

The major monovalent cation of ECF. Sodium serum normal values: 135-145 mEq/L

Functions:

- Most abundant extracellular cation.
- Regulates body water distribution.
- Aids nerve impulse transmission.
- Aids transfer of calcium into cells.

Concentration depends on:

- intake of water in response to thirst
- excretion of water due to blood volume or osmolality changes

Regulation of sodium:

- Kidneys can conserve or excrete Na^+ depending on ECF and blood volume
- by aldosterone which promotes excretion of K^+ in exchange for reabsorption of Na^+
- by the renin-angiotensin system: this system will stimulate the adrenal cortex to secrete aldosterone.

Note: The renin–angiotensin system (RAS), or renin–angiotensin–aldosterone system (RAAS), is a hormone system that regulates blood pressure and fluid and electrolyte balance.

Disorders related to Sodium:

- **Hyponatremia:** < 135 meq/L, Increased Na^+ loss, caused by:

- Aldosterone deficiency such as Addison's disease (hypo-adrenalism, result in decreased release of aldosterone)
- Diabetes Mellitus: In acidosis of diabetes, Na^+ is excreted with ketones
- Potassium depletion: K^+ is normally excreted, if none, then Na^+
- Loss of gastric contents
- Increased water retention results in dilution of serum or plasma Na^+
- Renal failure
- Nephrotic syndrome

- **Hypernatremia:** rise in serum sodium concentration to a value > 145 meq/L, caused by:

- Excess water loss resulting in dehydration (relative increase): Sweating, Diarrhea, Burns
- Dehydration from inadequate water intake, including thirst mechanism problems
- Diabetes insipidus: (ADH deficiency leads to water loss)
  Diabetes insipidus is caused by a lack of antidiuretic hormone (ADH), also called vasopressin, which prevents dehydration, or the kidney's inability to respond to ADH. ADH enables the kidneys to retain water in the body.
- Cushing's syndrome: overproduction of Aldosterone.

II- Potassium:

The major monovalent cation of ICF. Only 2% of potassium is in the plasma. Potassium concentration inside the cells is 20 times greater than it is outside. This is maintained by the Na^+ pump, (exchanges 3 Na^+ for 1 K^+)

$$\frac{INSIDE}{OUTSIDE} = \frac{20}{1}$$

Serum Potassium Normal Level: Adults 3.6-5.2 mEq/L, Newborns slightly higher 3.7-5.9 mEq/L

<u>Functions:</u>

- Most abundant intracellular cation. (Intracellular cation acts to balance Sodium "extracellular Cation")
- Necessary for transmission and conduction of nerve impulses.
- Maintenance of normal cardiac rhythm.
- Necessary for smooth and skeletal muscle contraction.

<u>Regulation:</u>

- Diet: easily consumed (banana for example)
- Kidneys: Potassium is readily excreted, but gets reabsorbed in the proximal tubule - under the control of Aldosterone.

Disorders related to Potassium:

- **Hypokalemia:**

- Decrease in K^+ concentration resulting in neuromuscular weakness and cardiac arrhythmia
- Severity is considered as mild when the serum potassium level is 3 to 3.4 mmol/L, moderate when the serum potassium level is 2.5 to 3 mmol/L, and severe when the serum potassium level is less than 2.5 mmol/L

<u>Causes Of Hypokalemia:</u>

- excessive fluid loss (diarrhea, vomiting, diuretics)
- overproduction of aldosterone: aldosterone promotes Na^+ reabsorption, then K^+ is excreted instead (Cushing's syndrome)
- Intravenous (IV) insulin therapy**:** Insulin IV promotes rapid cellular potassium uptake (i.e) K^+ moves into RBCs to preserve electrical balance, causing plasma potassium to decrease.

- **<u>Hyperkalemia</u>**:
  - Increased K^+ concentration, it is defined as a serum or plasma potassium level above the upper limits of normal limit.
  - Mild hyperkalemia is usually asymptomatic, while high potassium levels may cause life-threatening cardiac arrhythmias, muscle weakness, or paralysis.

<u>Causes Of Hyperkalemia:</u>

- Renal diseases: impaired excretion of potassium ions
- Acidosis: acidosis causes low pH and increased hydrogen ions, then these hydrogen ions enter into the cells and potassium ions leave the cells and enter the blood resulting in increased plasma level of potassium (hyperkalemia). Hydrogen ions compete with K^+ to enter into the cells and to be excreted by kidneys.
- Diabetes mellitus: decreased insulin promotes cellular K^+ loss. In untreated Diabetes Mellitus, shift of K^+ to the cell will decrease, impaired K^+ excretion due to impaired renal tubular function.
- Long use of Potassium sparing diuretics: inhibit the reabsorption of sodium (and water) from the distal tubule by antagonizing aldosterone. They reduce potassium excretion

III- Calcium:

Extracellular divalent cation. Normal = 4.5-5.8 mEq/L

Functions:

- Plays role in nerve impulse transmission. Increases force of muscle contractions.
- Functions as an enzyme co-factor in blood clotting. Necessary for structure of bone and teeth.

Disorders related to calcium:

- Hypocalcemia [$Ca^{++} < 4.5$ mEq/L]

Causes Of Hypocalcemia:

- Acute pancreatitis: decreased absorption of Ca^{++} from the GIT
- Chronic Diarrhea: decreased absorption of Ca^{++} from the GIT
- Hypoparathyroidism: absorption of Ca^{++} from GIT will decrease, resorption or mobility of Ca^{++} from bone to blood will decrease
- Lack of vitamin D intake: will decrease reabsorption of Ca^{++}
- Long-term steroid therapy
- Addison's disease - hypo- adrenal; hypo- aldosterone result in increased loss of Ca^{++}

- **Hypercalcemia** [Ca^{++} > 5.8 mEq/L]

Causes Of Hypercalcemia:

- Hyperparathyroidism: absorption of Ca^{++} from GIT will increase, resorption or mobility of Ca^{++} from bone to blood will increase
- Increased vitamin D intake: will increase reabsorption of Ca^{++}
- Osteoporosis and osteomalacia: bones continue to release Ca^{++} into the blood

IV- **Magnesium:**

Intracellular divalent cation. Normal serum level = 1.5–2.5 mEq/L

<u>Functions</u>:

- Activates (ATP-ase) the primary energy source for the sodium potassium pump.
- Plays important role in the relaxation of smooth muscle.
- Stabilizes cardiac muscle cells - decreases fibrillation threshold.

- **Hypomagnesemia:** [$Mg^{++} < 1.50$ mEq/L]

<u>Causes Of Hypomagnesemia:</u>

- Low intake of Mg^{++} in the diet
- Chronic diarrhea
- Massive diuresis
- Hypoparathyroidism

- **Hypermagnesemia**: [$Mg^{++} > 2.5$ mEq/L]

<u>Causes Of Hypermagnesemia:</u>

- Renal failure and dehydration
- Excessive use of Mg-containing antacids or laxatives (OTC drugs)

V- Chloride:

The major monovalent anion of Extracellular Fluid. Normal Serum Level: 100 -110 mEq/L

Functions:

- Chloride moves passively with Na^+ or against HCO_3^- to maintain neutral electrical charge. Cl^- Balanced with Na^+: +ve and –ve, with Carbonate: -ve and –ve
- Body hydration
- Osmotic pressure
- Electrical neutrality & other functions

Disorders related to Cl^-:

- **Hypochloremia:**
  - Decreased serum Cl^-
  - Loss of gastric HCl (chronic vomiting)
  - Renal diseases
  - Metabolic alkalosis: increased $HCO3^-$ & decreased Cl^-
- **Hyperchloremia**
  - Increased serum Cl^-
  - dehydration (relative increase)
  - excessive intake (IV)
  - congestive heart failure
  - renal tubular disease
  - metabolic acidosis decreased HCO_3^- & increased Cl^-

VI- Bicarbonate:

Monovalent anion of Extracellular Fluid. The normal level of serum HCO_3^- is 22-29 mEq/L

Functions:

- Principle buffer of body pH. (extracellular)
- Neutralizes acids.
- Plays important role in acid / base balance.
- Acts as chemical sponge to soak up Hydrogen ions. (Acidic metabolic waste). For every one Hydrogen ion twenty bicarbonate ions are released to maintain balance.

Regulation: -

Bicarbonate is regulated by excretion and reabsorption at the renal tubules

Acidosis : ↓ renal excretion

Alkalosis : ↑ renal excretion

Kidney regulation requires the enzyme carbonic anhydrase - which is present in renal tubular cells & RBCs

$$\text{Reaction: } CO_2 + H_2O \overset{\text{carbonic anhydrase}}{\leftrightharpoons} H_2CO_3 \rightarrow H^+ + HCO^{-3}$$

VII- Phosphate:

- Phosphate ($H_2PO_4^-$, HPO_4^{2-}, PO_4^{3-})
- Important ICF anion; Normal plasma level 1.7-2.6 mEq/liter
- Most (85%) is stored in bone as calcium salts
- also combined with lipids, proteins, carbohydrates, nucleic acids (DNA and RNA), and high energy phosphate transport compound (ATP, GTP)

<u>Function:</u>

important acid-base buffer in body fluids

<u>Regulation</u>:

- It is regulated in an inverse relationship with Ca^{2+} by PTH and Calcitonin
- Homeostatic imbalances. Phosphate concentrations shift oppositely from calcium concentrations and symptoms are usually due to the related calcium excess or deficit.