Gastrointestinal Agents

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GI Tract

- The **human gastrointestinal tract** is the stomach and intestine
- sometimes including all the structures from the mouth to the anus
- The GI tract always releases hormones to help regulate the digestive process.
- These hormones, including gastrin, secretin, cholecystokinin .

Gastrointestinal Agents

- Any inorganic substances which can be used in gastrointestinal disorder are called gastrointestinal agent

Classification of inorganic gastrointestinal agents :

1. Products for altering gastric pH:

A) Acidifying agents (induce acid secretion, e.g. histamine phosphate)

B) Gastric Antacids, e.g. $Al(OH)_3$, $NaHCO_3$

2. Protectives for intestinal inflammation, e.g. bismuth subcarbonate.

3. Adsorbents for intestinal toxins, e.g. activated charcoal

4. Cathartics or laxatives for constipation, e.g. magnesium sulfate.

Ammonium chloride

- **Molecular formula:** NH_4Cl **Molar mass:** 53.49 g/mol
- Physical Properties
- **Appearance:** White solid, hygroscopic

  Odor: Odorless
- **Preparation:** - Ammonium chloride prepared through the Solvay process:

  $CO_2 + 2\ NH_3 + 2\ NaCl + H_2O \rightarrow 2\ NH_4Cl + Na_2CO_3$

  - Ammonium chloride is prepared commercially by combining ammonia (NH_3) with either hydrogen chloride (gas) or hydrochloric acid (water solution):

  $NH_3 + HCl \rightarrow NH_4Cl$

- **Reactions** - Ammonium chloride appears to sublime upon heating but actually decomposes into ammonia and hydrogen chloride gas:

  $NH_4Cl \rightarrow NH_3 + HCl$

- **Assay** - Dissolve 1.000 g of Ammonium chloride in 20 ml of water and add a mixture of 5 ml of formaldehyde solution, with few drops of phenolphthalein solution. After 1 min to 2 min, titrate slowly with 1M sodium hydroxide.
- - 1 ml of 1M sodium hydroxide is equivalent to 53.49 mg of NH_4Cl
- **Uses:** - Ammonium chloride is used as an expectorant in cough medicine.
- - Ammonium salts are an irritant to the gastric mucosa and may induce nausea and vomiting.
- - Ammonium chloride is used as a systemic acidifying agent in treatment of severe metabolic alkalosis.
- - The main application of ammonium chloride is as a nitrogen source in fertilizers.

HYDROCHLORIC ACID

- **Molecular formula :** HCl **Molecular wt. :** 36.46
- **Synonyms :** Spirit of salt, Muriatic acid
- **Preparation :** It can be prepared by the action conc. Sulphuric acid on Sodium Chloride and passing the liberated Hydrogen Chloride through water.

  $NaCl + H_2SO_4 \longrightarrow NaHSO_4 + HCl$
- **Properties:** 1. It is nearly colorless clear and fuming liquid.

  2. It possesses pungent odor.

  3. It is soluble with water and alcohol.

  4. It is a strong acid.
- **Chemical properties :** 1. It reacts with sodium metal which results in the formation of sodium chloride and liberates hydrogen gas.

  $2Na + 2\ HCl \longrightarrow 2NaCl + H_2$
- **Uses :** 1. It is used as a pharmaceutical aid or as an acidifying agents.
- 2. Used as gastric acidifiers when levels of hydrochloric acid in gastric juice are low.

2. Antacids

- - Antacids (anti - against; acidus - acid) are weak alkaline compounds used to neutralize hydrochloric acid in the stomach.
- - Antacids are the substances which reduce gastric acidity resulting in an increase in the pH of stomach and duodenum. Gastric acidity occurs due to excessive secretion of HCl in stomach due to various reasons.
- - The pH of the stomach is 1.5- 2.5 when empty and raises to 5-6 when food is ingested.
- - Low pH is due to the presence of endogenous HCl, which is always present under physiological conditions.
- - When hyperacidity occurs the result can range from:
- i. Gastritis (a general inflammation of gastric mucosa)
- ii. Peptic ulcer or esophageal ulcer (lower end of esophagus)
- iii. Gastric ulcer (stomach)
- - **Symptom of hyperacidity:** ▪ Hydrochloric acid is secreted by the stomach to kill harmful organisms, aid digestion and activate digestive enzymes.

- Criteria of an ideal antacid preparation:

- The antacid should not be absorbable or cause systemic alkalosis
- The antacid should not be a laxative or causes constipation
- The antacid should exert its effect rapidly and over a long period of time
- The antacid should buffer in the pH 4-6 range
- The reaction of the antacid with gastric HCl acid should not cause a large evolution of gas
- The antacid should probably inhibit pepsin.

Requirement of combinations of antacids therapy:

- To avoid certain side effects associated with antacids, combinations of antacids are used such as:

i. Magnesium and aluminium containing preparation e.g. magnesium hydroxide a fast acting antacid with aluminium hydroxide which is a slow acting antacid.

Magnesium and calcium containing preparation where one is laxative and the later one is constipative in nature.

Sodium bicarbonate

- Molecular formula $NaHCO_3$ ▪ Molar mass 84.01 g/mol
- ▪ Synonym: Baking soda; Bread soda, Cooking soda, Bicarbonate of soda
- **Properties: Appearance :** White crystalline powder or granules
- **Odor :** Odourless
- ▪ **Preparation** – Na_2CO_3 may be obtained by the reaction of carbon dioxide with an aqueous solution of sodium hydroxide. The initial reaction produces sodium carbonate. Further addition of carbon dioxide produces sodium bicarbonate
- $CO_2 + 2\ NaOH \rightarrow Na_2CO_3 + H_2O$
- $Na_2CO_3 + CO_2 + H_2O \rightarrow 2\ NaHCO_3$
- - On an industrial scale it is obtained by Solvay process:
- $CO_2 + H_2O \rightarrow H_2CO_3$
- $NH_3 + H_2CO_3 \rightarrow NH_4HCO_3$
- $NaCl + NH_4HCO_3 \rightarrow NaHCO_3 + NH_4Cl$

- **Reaction -**
- Thermal decomposition: Above 500 C, sodium bicarbonate gradually decomposes into sodium carbonate, water and carbon dioxide. The conversion is fast at 2000C
- $2\ NaHCO3 \rightarrow Na2CO3 + H2O + CO2$
- - Sodium bicarbonate reacts with bases such as sodium hydroxide to form carbonates
- $NaHCO3 + NaOH \rightarrow Na2CO3 + H2O$
- **Assay -** Weigh accurately 1gm of Sodium bicarbonate and dissolve in 20 ml of water, titrate the solution with 0.5N sulphuric acid using methyl orange as indicator.
- - Each ml of 0.5N sulphuric acid ≡ 0.0425gm of NaHCO3

Uses - It is used as Systemic antacid and in electrolyte replacement.

- - Sodium bicarbonate may be used as a buffering agent, combined with table salt, when creating a solution for nasal irrigation.
- - 0.1% to 1% Sodium bicarbonate solution used as eye lotion.

Aluminum hydroxide gel

- **Molecular formula**: Al(OH)3 - **Molar mass:** 78.00 g/mol
- **Synonym:** Hydrated alumina, Ortho Aluminic acid, Aluminic
- **Properties: Appearance :** White amorphous powder
- - Aluminium hydroxide is amphoteric in nature, i.e, it has both basic and acidic properties.
- In presence of an alkali, it behaves as an acid:
- $Al(OH)_3 \rightleftharpoons 3H^+ + AlO_3$
- In presence of an alkali, it behaves as an acid:
- $Al(OH)_3 \rightleftharpoons 3OH^- + Al^{3+}$

▪ **Preparation -** It is prepared by hot solution of potash alum slowly with constant stirring to a hot solution of sodium carbonate.

- ▪ **Uses -** Aluminum salts remain in the stomach for long periods and slowly react with stomach acid to form aluminum chloride. Aluminum hydroxide may inhibit the action of pepsin.

- Aluminium hydroxide used as gastric antacid.

Magnesium hydroxide mixture

- **Molecular formula:** $Mg(OH)_2$
  Molar mass: 58.31 g/mol
- Mg^{2+} Salts or Oxide or Hydroxide acts as both antacids and laxative agents
- **Properties:**
- **Appearance :** White amorphous powder
- **Odor :** Odorless **Taste :** Tasteless
- **Preparation -** Combining a solution of many magnesium salts with basic water induces precipitation of solid $Mg(OH)_2$: $Mg^{2+} + 2\ OH^- \rightarrow Mg(OH)_2$
- **Laboratory Preparation:** $MgCO_3 + 2\ NaOH \rightarrow Mg(OH)_2 + Na_2CO_3$
- **Uses -** Used as weak antacid and laxative.
- Most commonly used antacids combine aluminum hydroxide and magnesium hydroxide. The combination decreases the adverse effects of diarrhea (with magnesium products) and constipation (with aluminum products).

Milk of Magnesia

- Double-Strength Milk of Magnesia, and Triple-Strength Milk of Magnesia contain not less than 90.0 percent and not more than 115.0 percent of the labeled amount of Mg(OH)2,
- the labeled amount being 80, 160, and 240 mg of Mg(OH)2 per mL, respectively as per USP Monographs.
- **Packaging and storage:** Preserve in tight containers, preferably at a temperature not exceeding 350C . Avoid freezing.
- (ii) **“SHAKE WELL BEFORE USED”**
- **Uses:** Milk of Magnesia is used for a short time to treat occasional constipation, it is used as Laxative.
- Milk of Magnesia is also used to treat symptoms caused by too much stomach acid such as heartburn, upset stomach or indigestion.

- **ANTIMICROBIALS**
- Anti microbial is a broad terminology describing activity against microbes.
- Specific terminology gives exact mode of action.
  1. **Antiseptics** are substances that kill or prevent the growth of micro organism. This is specific for preparation intended to be used for living tissues.
  2. **Disinfectant** is prevent infection by the destruction of pathogenic micro organism. It is generally used to inanimate objects.
  3. **Germicide** is an agent which kills micro organisms. More specific terminologies like ‘bactericide’ (against bacteria), ‘fungicide’ (against fungi), virucide (against virus) denotes exact action.
- **Bacteriostatics** is an agent which function by inhibiting the growth of bacteria. Thus bacteriostatic agents do not kill but stops the growth of bacteria

- **Mechanism of Action**
  - Inorganic compounds generally exhibit antimicrobial action by three different mechanism.
- They are 1) Oxidation mechanism
  2) Halogenation mechanism
  3) Protein precipitation

1. **Oxidation Mechanism:** This belongs to class of peroxides, peroxy acids, oxygen liberating like permanganate.

They act on proteins containing sulph hydryl group and oxidizes free sulfhydryl to disulphide bridge and inactivate its function.

These infective agent brings about oxidation of active functional group present in protein & enzyme vital to growth & survilance of microorganis.

This cause the change on conformation of protein

Halogenation Mechanisms: Compounds which liberates chlorine or hypochlorite or iodine act by this mechanism. They act on peptide linkages and alter it's property.

The destruction of specific function of protein results in death of micro organism.

Most of enzymes are proteineous in nature, protein molecule composed of variety of amino acids connected through the peptide (-CONH-) linkage.

Antiseptic have hypohalite functional group exerts their antimicrobial activity by chlorination of peptide linkage in protein molecule.

Protein Precipitation: Many cations exhibit protein binding or protein precipitation.

The interaction with protein occurs through polar group of protein which acts as ligands and metal cation as Lewis acid.

The complex formed may be strong chelate leading to inactivation of proteins.

POTASSIUM PERMANGANATE ($KMnO_4$)

- **Mol. Formula-** $KMnO_4$ **Mol. Wt. 158**
- It is having Not less than 99% of $KMnO_4$
- **Preparation**

Manganese dioxide is fused with solid potassium hydroxide along with potassium chlorate, a green mass potassium manganate is obtained. The mass is cooled is extracted with water and filtered.

$$3MnO_2 + 6KOH + KClO_3 \xrightarrow{\Delta} 3K_2MnO_4 + KCl + 3H_2O$$

The filtrate is treated with carbon dioxide followed by chlorine. By this potassium manganate is converted into potassium permanganate.

- **Physical Properties**

It occurs in the form of deep, dark purple, monoclinic prismatic crystals and moderately soluble in water. The taste is sweet and astringent.

- **Chemical Properties**

It is very powerful oxidizing agent both in dry state and in solution. Explosions may occur when it comes in contact with organic or other readily oxidizable materials.

It act as an oxidizing agent because it produces nascent oxygen in solution.

$$2KMnO_4 + 3H_2SO_4 \rightarrow K_2SO_4 + 2MnSO_4 + 3H_2O + 5(O) \text{ (acid solution)}$$

$$2KMnO_4 + H_2O \rightarrow 2MnO_2 + 2KOH + 3(O) \text{ (Alkaline (or) neutral solution)}$$

- **Use**

1. It is used as local anti infective.
2. It is used as mouthwash and gargle (more than 1 in 1000 solution).
3. It is also used as stomach wash in the treatment of Narcotic drug poisoning.

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BORIC ACID

- **M.F.** H_3BO_3
- **Syn :** Ortho Boric Acid
- **Preparation :** (i) Laboratory Method
- Adding a mixture of concentrated sulphuric acid and water to a boiling solution of borax, the solution is allowed to cool. The boric acid is filtered and then washed until they become free from sulphate ions.
- $Na_2B_4O_7 + H_2SO_4 + 5H_2O \rightarrow Na_2SO_4 + 4H_3BO_3$
- **Physical Properties**
- i. White odorless, crystalline powder, soft to touch.
- ii. Slightly acidic to taste.
- iii. Freely soluble in boiling water, boiling alcohol and glycerin

- **Chemical Properties**
- i. Boric acid is a weak acid.
- ii. On heating tetra boric acid produces the boric acid anhydride, boron trioxide
- B_2O_3 H_2 B_4O_7 –160–▫C→ $2B_2O_3$ + H_2O (Boron trioxide)
- Assay Boric acid is assayed by titrimetric method. It is a very weak acid.
- Use : Anti infective.

HYDROGEN PEROXIDE (H_2O_2)

- **Preparation**
  - It is prepared by adding a paste of barium peroxide in ice cold water to a calculated quantity of ice cold dilute sulphuric acid. The insoluble barium sulphate is filtered off.
    - $BaO_2 + H_2SO_4 \rightarrow BaSO_4\downarrow + H_2O_2$
  - It is also manufactured by electrolysis process. Electrolysis of sulphuric acid to proxy sulphuric acid which is hydrolyzed to give the product. Sulphuric acid is oxidized to give peroxydisulphuric acid ($H_2S_2O_8$)

- **Properties:**
- Hydrogen peroxide solution is a colorless liquid with slightly acidic taste. The solution is decomposes in contact with oxidizable matter, reducing agent, when made alkaline or even on standing.
  - $2H_2O_2 \rightarrow 2H_2O + O_2$
- The solution is stabilized by the addition of small amount of acid and adjusting the pH between 2 and 3. Polyvalent metal ions catalyze decomposition of hydrogen peroxide and complexing agent prevent it by acting as stabilizer.
- Hydrogen peroxide acts as oxidizing or reducing agent depending upon the chemical environment.

- **Assay**
  - It is estimated by titration with potassium permanganate in presence of 4 N sulphuric acid. Potassium permanganate is reduced to manganese sulphate. This determination depends on mutual oxidation – reduction as expressed by following equations.
- $2KMnO_4 + 3H_2SO_4 \rightarrow K_2SO_4 + 2MnSO_4 + 3H_2O + 5(O)$

  $H_2O_2 + (O) \rightarrow H_2O + O_2$
- Hydrogen peroxide is oxidized to oxygen by nascent oxygen produced from the reaction between potassium permanganate and dilute sulphuric acid. The appearance of permanent pale pink color indicates the end point.

- **Use**
  1. Used as an Antiseptic and topical Anti-infective.
  2. It is used to clean the wounds and ears.

CHLORINATED LIME [Ca(OCl) Cl]

- **Syn:** Bleaching powder
  - Calcium choro hypochlorite.
- **Preparation**
  - It is obtained by the action of chlorine on calcium hydroxide. Slaked lime is spread on stable shelves in a container and chlorine gas is introduced at the top of the chamber and passed through the contents of the shelves. This is done at 25°C to minimize the formation of calcium chloride.
- $Ca(OH)_2 + Cl_2 \rightarrow Ca(OCl)\ Cl + H_2O$
- **Properties**
  - It is dull white powder with characteristic odour, on exposure to air it absorbs moisture and decomposes by liberating chlorine. It is sparingly soluble in water and insoluble in alcohol.
  - When bleaching powder is added to water hypochlorite goes into solution and oxygen is liberated. The oxidizing and bleaching properties are shown.

- **Use:**

1. It is used as disinfectant, deodorant.
2. Commonly used in chlorination of water and in treatment of swimming tank.

IODINE (I_2)

- **Preparation**
  - Iodine is manufactured by extracting kelp (sea weed ash) with water and the solution is concentrated. The sulphate and chloride of sodium and potassium are crystallized out, leaving soluble sodium and potassium iodides in the mother liquor.
  - Sulphuric acid is added to the mother liquor and Sulphur which is liberated from small amount of thiosulphate and sulphide is allowed to settle. The mother liquor is decanted and to this MnO_2 is then added and the Iodine is distilled out.
- $2NaI + 3H_2SO_4 + MnO_2 \rightarrow MnSO_4 + 2\ NaHSO_4 + I_2 + 2H_2O$

- **Physical Properties**
  - It occurs as heavy, bluish-black rhombic plates with metallic luster.

  It melts at higher temperature.

  It is practically insoluble in water but soluble in alcohol.

  It is freely soluble in chloroform and ether.

- **Chemical Properties**

1. It combines directly with some non-metals and with many metals.
2. $2P + 3\ I_2 \rightarrow 2PI_3$
   $Fe + I_2 \rightarrow FeI_2$

- Reducing agent reacts with aqueous iodine solution and gets oxidized.
- Iodine reacts with alkali to form an iodide and iodate when heated.

$$3I_2 + 6NaOH \xrightarrow{\Delta} 2NaI + NaIO_3 + 3H_2O$$

SOLUTIONS OF IODINE

- Iodine is insoluble in water but it is soluble in water in presence of potassium or sodium iodide due to the formation of poly iodides. The following are the solution preparations containing iodine.
  1. Strong iodine solution (10% W/V solution of iodine)
  2. Weak iodine solution (2% W/V solution of iodine)
  3. Aqueous iodine solution (5% W/V solution of iodine)
  4. Iodine tincture USP.
  5. Mandl's paint.
- **Use:** All the above solutions are used as antiseptics and disinfectants.

POVIDONE – IODINE (PVP – IODINE)
(Polyvinyl Pyrrolidone – Iodine Complex)

- It is a complex of polyvinyl pyrrolidone and iodine containing not less than 9% and not more than 12% W/V of available I_2 (iodine).

The complex is yellowish brown amorphous powder and has slight characteristic odour, its aqueous solution is acid to litmus

Uses

- Major advantages over other iodine preparation is lack of tissue irritation. Solutions are used for surgical scrubs and for pre operative antisepsis for the skin.
- It is also used in gargles and mouth washes for the treatment of infections in the oral cavity.