GASTROINTESTINAL AGENTS

The Gastrointestinal (GI) Tract includes the mouth, stomach, small intestine (duodenum, jejunum, and ileum), large intestine (cecum and colon), rectum, anus, and its accompanying exocrine glands (the salivary glands, the pancreas, and the gallbladder).

Drugs affecting the GI system are used in the treatment of Gastric Acidity, Peptic Ulcers, and Gastro Esophageal Reflux Disease (GERD), Bowel Motility Disorders (gastroparesis [delayed gastric emptying due to partial paralysis of the stomach muscles], constipation, and diarrhea), and for the treatment of nausea and vomiting.

Agents used to treat gastrointestinal disturbance are known as gastrointestinal agents. Various inorganic agents used to treat GIT disorders include:

1. Products for altering gastric pH i.e. acidifiers and antacids

2. Protectives and adsorbents

3. Saline cathartics or laxatives

ACIDIFIERS

The pH of stomach is 1.5 -2 when empty and rises to pH 5-6 when food is ingested. The pH of stomach is so low because of the secretion of HCl. Gastric HCl act by destroying the bacteria in the ingested food and drinks. It softens the fibrous food and promotes the formation of the proteolytic enzyme pepsin. This enzyme is formed from pepsinogen at acidic pH (>6). Pepsin helps in the metabolism of proteins in the ingested food. Therefore lack of HCl in the stomach can cause Achlorhydria.

Achlorhydria or Hypochlorhydria refers to a condition characterized by the absence or extremely low levels of hydrochloric acid in the stomach. Hydrochloric acid is essential for the digestion of food, particularly the breakdown of proteins and the absorption of certain nutrients. Achlorhydria can be classified into two main types:

1. Primary Achlorhydria:

- ***Congenital Achlorhydria:*** This rare form of achlorhydria is present from birth and is usually due to a genetic mutation that impairs the production of hydrochloric acid.

- ***Acquired Achlorhydria:*** This type develops later in life and can be caused by various factors, including autoimmune conditions, chronic gastritis, or damage to the stomach lining. Conditions such as pernicious anemia, where there is a lack of intrinsic factor needed for vitamin B12 absorption, can also lead to acquired achlorhydria.

2. Secondary Achlorhydria:

- ***Drug-Induced Achlorhydria:*** Certain medications, such as proton pump inhibitors (PPIs) and H2 blockers, which are commonly used to treat conditions like gastroesophageal

reflux disease (GERD) and peptic ulcers, can reduce stomach acid production and lead to achlorhydria.

- ***Chronic Atrophic Gastritis:*** This is an inflammation of the stomach lining that can lead to a decrease in acid-producing cells, resulting in achlorhydria.

- ***H. pylori Infection:*** Helicobacter pylori is a bacterium that can infect the stomach lining, leading to inflammation and damage to acid-producing cells.

Common symptoms associated with achlorhydria include: indigestion, bloating, belching, feeling full quickly, nausea, constipation, diarrhea, weight loss, nutritional deficiencies, weakness, fatigue and increased risk of infections.

Achlorhydria can be treated by various acidifiers like ammonium chloride, dilute HCl, Calcium chloride etc.

Acidifying reagents/acidifiers are able to increase acidity in GIT. Some of the drugs are used to increase metabolic acidosis whereas some of these are used to increase the gastric hydrochloric acid.

❖***Gastric acidifiers:*** These are drugs which are used to restore temporarily the acidity of stomach in patients suffering from achlorhydria or hypochlorhydria.

❖***Urinary acidifiers:*** These are the drugs which are used to render acidic urine to enable treatment of some type of urinarytract disorders.

❖***Systemic acidifiers:*** These are the drugs which are able to neutralize the alkaline body fluids, particularly blood, in patients who are suffering from systemic alkalosis.

❖***Acids:*** Acids are used as pharmaceutical aids in the preparation, laboratory quality control etc.

Dilute Hydrochloric Acid

Molecular Formula: Dilute HCl

Molecular weight: 36.5 g/mol

Synonym: Muriatic acid, spirit of salt

IP Limit: Dilute HCl contains not less than 9.5% and not more than 10.5%w/w of hydrochloric acid.

The acid should be diluted with 25-50 volumes with water or juice and sipped through a glass tube to prevent reaction upon dental enamel. It is taken during or after meals given in conjunction with iron therapy in hyper chronic anemia.

Preparation:

It is prepared by mixing 274gm of HCl and 726 gm of purified water.

Method of Preparation of HCl:

1. It is manufactured by the action of warming sodium chloride salts with concentrated sulphuric acid.

$$NaCl + H_2SO_4 \rightarrow NaHSO_4 + HCl$$

2. During the manufacture of caustic soda by electrolysis of sodium chloride solution, large quantities of hydrogen and chlorine are obtained as by-products. These gases are combined to yield hydrogen chloride.

$$H_2 + Cl_2 \rightarrow 2HCl$$

Physical Properties:

1. It is a colourless liquid and strongly acidic.
2. It has pungent odour.
3. It is miscible with water, alcohol having a specific gravity of 1.18
4. Even in high diluted form, it is very strongly acidic to litmus.
5. Dilute hydrochloric acid is a good conductor of electricity due to the presence of ions (H^+ and Cl^-) in the solution.

Chemical Properties:

1. It is a strong acid and attacks metals, forming their hydrochlorides with the evolution of hydrogen gas.

$$2HCl + 2Na \rightarrow 2NaCl + H_2$$

$$2HCl + Fe \rightarrow FeCl_2 + H_2$$

$$2HCl + Zn \rightarrow ZnCl_2 + H_2$$

$$2HCl + Pb \rightarrow PbCl_2 + H_2$$

$$2HCl + Cu \rightarrow CuCl_2 + H_2$$

Uses:

1. It is used as gastric acidifier when levels of hydrochloric acid in gastric juice are low.
2. Externally used as a solvent and catalyst.
3. This acid purifies table salts. It is also useful to control the pH of pharmaceutical products, water, and foods.
4. It is in use for cleaning tiles in bathrooms and kitchens and it is also useful as a disinfecting agent. In the textile industry, HCl is useful for bleaching clothes and processing in the leather tanning industry.
5. Dilute hydrochloric acid is applied for removing rust from metal surfaces. It reacts with iron oxide (rust), making it soluble and allowing for rust removal.
6. In water softening systems, dilute HCl is used to regenerate ion exchange resins by removing accumulated hardness ions.

Ammonium Chloride:

Molecular formula*:* NH4Cl

Molecular weight: 53.5 g/mol

Synonym: sal ammoniac

IP Limit: Ammonium Chloride contains not less than 99.0 per cent and not more than 100.5 per cent of NH4Cl, calculated on the dried Basis

Preparation:

1. Ammonium chloride is prepared by reacting ammonia (NH3) with hydrochloric acid (HCl) to form white crystalline ammonium chloride.

$$NH_3 + HCl \rightarrow NH_4Cl$$

2. Ammonium chloride prepared through the Solvay process.

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

3. It can also be produced by reaction of sodium chloride with ammonium bicarbonate.

$$NaCl + NH_4HCO_3 \rightarrow NH_4Cl + NaHCO_3$$

Physical Properties:

1. It occurs as white, fine or coarse crystalline powder.
2. It is odourless.
3. It is having cooling saline taste.
4. It is very soluble in water and glycerol.
5. It is sparingly soluble in alcohol.
6. Its aqueous solution is weakly acidic having pH of 4.6
7. Density: 1.5274 g/cm^3 and Melting point: 338^0 C
8. It is hygroscopic in nature.

Chemical Properties:

1. Ammonium chloride appears to sublime upon heating but actually decomposes into ammonia and hydrogen chloride gas.

$$NH_4Cl \rightarrow NH_3 + HCl$$

2. Ammonium chloride reacts with a strong base like sodium hydroxide to release ammonia gas.

$$NH_4Cl + NaOH \rightarrow NH_3 + NaCl + H_2O$$

3. Similarly, ammonium chloride also reacts with alkali metal carbonates at elevated temperatures, giving ammonia and alkali metal chloride.

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

Assay:

Principle:

This is assayed by acid base titration. Ammonium chloride hydrolyses into ammonium hydroxide and hydrochloric acid. This hydrolysis is catalyzed by formaldehyde and forming hexamine. Finally the acid is titrated using an alkali.

$$NH_4Cl + H_2O \rightarrow NH_4OH + HCl$$

$$4NH_4OH + 6HCHO \rightarrow C_6H_{12}N_4 + 10\ H_2O$$

$$HCl + NaOH \rightarrow NaCl + H_2O$$

Procedure:

Accurately weighed 0.1 gm of ammonium chloride is taken and 50ml of water is added to dissolve. 50 ml of neutralized formaldehyde solution is added to the above solution. The hydrochloric acid liberated is titrated with standard sodium hydroxide solution using phenolphthalein as an indicator. End point is the appearance of permanent pale pink colour.

Uses:

1. Ammonium chloride serves as an expectorant, helping to relieve congestion and coughing.
2. It can also be used to acidify urine in specific medical conditions and as a diuretic in some cases.
3. In addition, it's employed as an antidote for certain poisonings.
4. Ammonium salts are an irritant to the gastric mucosa and may induce nausea and vomiting.
5. Ammonium chloride is used as a systemic acidifying agent in treatment of severe metabolic alkalosis.
6. The main application of ammonium chloride is as a nitrogen source in fertilizers.
7. Ammonium chloride is used as a flux in preparing metals to be tin coated, galvanized or soldered.