Gastrointestinal Agents

Acidifying agents and Antacids

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Keywords
Acidifying agents, antacids,

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. acidifying agents and antacids
2. Protectives and adsorbents
3. Saline cathartics or laxatives

Acidifying Agents

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. Two types of achlorhydria are known:

1) where the gastric secretion is devoid of HCl, even after stimulation with histamine phosphate

2) where gastric secretion is devoid of HCl, but secreted upon stimulation with histamine phosphate.

The cause of achlorhydria in first case may be subtotal gastrectomy, atrophic gastritis, carcinoma, gastric polyp etc while in later case it may be chronic nephritis, tuberculosis, hyperthyroidism, chronic alcoholism, sprue, pellagra etc. The symptoms vary with associated disease but they generally include mild diarrhoea or frequent bowl movement, epigastric pain and sensitivity to spicy food.

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

Dilute Hydrochloric Acid

HCl M.W 36.5

I.P. Limit: It contains not less than 9.5% and not more than 10.5% w/w of HCl.

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 chromic anemia.

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

Test for Identification:

1) When added to $KMnO_4$ with dilute nitric acid, chlorine is evolved.
2) To acidified solution add silver nitrate solution, shake and allow to stand, curdy white precipitate is formed, which is insoluble in HNO_3 but soluble after being washed with water in ammonium hydroxide from which it is reprecipitated by the addition of HNO_3.

Assay: Weigh accurately 6gm, add 30 ml of distilled water mix and titrate with 1N NaOH using methyl red as indicator. Each ml of 1N NaOH is equivalent to 0.03646gm of HCl.

Antacids

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:

1) gastritis (a general inflammation of gastric mucosa)
2) peptic ulcer or oesophageal ulcer (lower end of oesophagus)
3) gastric ulcer (stomach)
4) duodenum ulcers

Peptic ulcers occur due to defective oesophageal sphinter as in hiatal hernia. Gastric ulcers occur in lesser curvature and are found in first portion of duodenum.

Symptoms include uncomfortable feeling from over eating, heart burn, growing hungry between meals.Complications involved are hemorrhage (being more common with duodenal ulcers), perforation. Depending upon the severity and location of an ulcer treatment will range from diet and antacids and /or anticholinergic therapy to complete bed rest to surgery. Small meals after short interval help in reducing acidity, stimulants of gastric acid must be avoided like coffee, alcohol, spicy food, oil or fried food.

Antacid therapy:

Antacids are alkaline bases used to neutralize the excess gastric HCl associated with gastritis or peptic ulcer. Since gastric HCl secretion is continuous, so is the administration of antacids.

Role of antacids:

1) Primarily in pain relief
2) Higher doses given continuously can promote ulcer healing
3) Superior to H_2 blockers in bleeding peptic ulcers

Criteria for antacids:

i) The antacid should not be absorber/or cause systemic alkalosis
ii) It should not be constipative or laxative
iii) It should exert effect rapidly and over a long period of time
iv) The antacid should buffer in the range of pH 4-6
v) Reaction of antacid with HCl should not cause large evolution of gas.

Side effects of long term antacid therapy:

a) If pH raises too high rebound acidity to neutralize the alkali occurs.
b) Antacids which absorbed systemically exert alkaline effect on body's buffer system.
c) Some antacids cause constipation while others have laxative effect.
d) Sodium containing antacids are problem for patients on sodium restricted diet.

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

- ***Classification of antacids***
  - Antacids can be classified into two main category:

i. Based on chemical nature of Antacid properties.

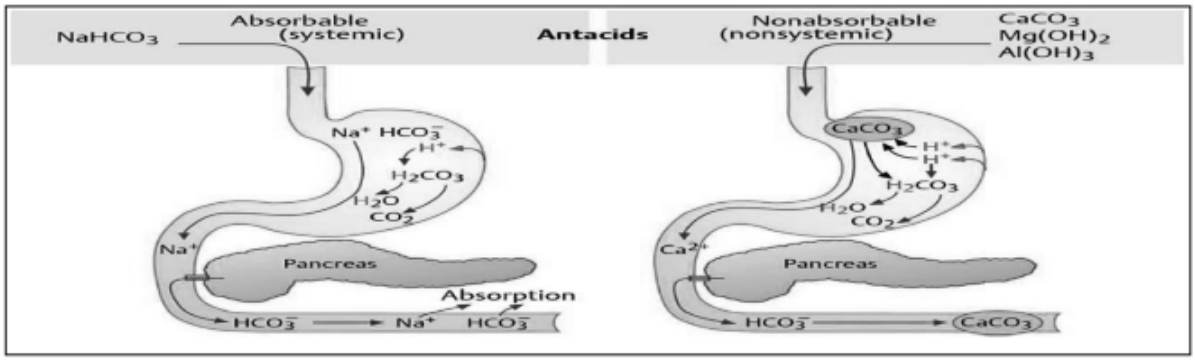
Absorbable Antacids	Non-Absorbable Antacids
○ The absorbable antacids (chemical antacids) show the most rapid onset of action and provide faster relief of symptoms. ○ However they may cause an "acid rebound". ○ Absorbable Antacids inappropriate for patients afflicted with hypertension or kidney failure.	○ The non-absorbable antacids though less prone to cause a rebound effect ○ Moreover as these antacids are more potent and effective in a semi liquid or liquid form than in a capsule or table ○ The usually high presence of aluminum and magnesium hydroxides in non-absorbable antacids can be effectively used to prevent significant stress ulcer bleeding in post-operative patients or those with severe burns.
Example	*Example*
▪ Sodium bicarbonate (baking soda) ▪ Magnesium oxide (magnesia) ▪ Magnesium carbonates ▪ Calcium carbonates ▪ Bourget mixture (sodium bicarbonates, sulphate, phosphate) ▪ Rennie mixture (calcium carbonates, magnesium carbonates); ▪ Tums mixture (calcium carbonates, magnesium oxide).	▪ Aluminum Phosphate ▪ Aluminum Hydroxide ▪ Magnesium Silicate ▪ Magnesium Hydroxide ▪ Aluminum-Magnesium Combination

ii. Based on pharmacological properties of Antacid.

Non-systemic antacids	Systemic antacids
○ Non-systemic antacids are compounds that are not absorbed into the systemic circulation. ○ Their anionic group neutralizes the H^+ ions in gastric acid. This releases their cationic group which combines with $\mathbf{HCO_3^-}$ from the pancreas to form an insoluble basic compound that is excreted in feces. ○ Thus these agents do not produce metabolic alkalosis.	○ Systemic antacids are absorbed into the systemic circulation. ○ They have a cationic group that does not form insoluble basic compounds with $\mathbf{HCO_3^-}$. ○ Thus the $\mathbf{HCO_3^-}$ can be absorbed producing a metabolic alkalosis.
Example	*Example*
▪ Aluminum Hydroxide ▪ Magnesium Hydroxide	▪ Sodium bicarbonate

Non-absorbable antacids have many others favorable properties
▪ Absorb pepsin, resulting in reduced proteolytic activity of gastric acid.
▪ Connect lysolecithin and bile acid, which have a damaging effect on the gastric mucosa.
▪ Possess cytoprotective function through the activation of prostaglandin synthesis, which stimulate a secretion of mucin and bicarbonates, improve microcirculation.
▪ Possess ambient function, forming a protective film on the gastric mucosal surface.
▪ Able to bind epithelial growth factor and fix it in the ulcerous defect region effectively stimulating cell proliferation, angenesis and angiogenesis.

- ***Mechanism of antacid:***
  - Antacids were developed based on the hydroxides and carbonates of the group II and III metals, as well as the bicarbonates of the alkali metals. All antacids contain at least one of the following metals: aluminum, calcium, magnesium, sodium, potassium, or bismuth. Antacids help neutralize excess acid produced in the stomach, i.e. the hydrogen ion concentration is reduced.
  - Each antacid has a specific active ingredient. This ingredient whether metallic or nonmetallic has a different effect on the gastric acid. They act similar to when an acid reacts with a hydroxide; a salt and water are produced as in the following equation: **HCl** (aq) + **NaOH** (aq) → **NaCl** (aq) + **H_2O**
  - **Sodium Bicarbonate: HCl** (aq) + **$NaHCO_3$ (aq)** → **NaCl** (aq) + **H_2O + CO_2.**
  - **Calcium Carbonate: HCl** (aq) + **$CaCO_3$** (aq) → **NaCl** (aq) + **H_2O + CO_2.**
  - **Magnesium Compounds: MgO + H_2O → Mg $(OH)_2$; HCl** (aq) + **Mg $(OH)_2$ → $MgCl_2$ + H_2O**
  - **Aluminum Compounds: $Al(OH)_3$ + HCl → $AlCl_3$ + H_2O**



- ***Side effects of long term antacid therapy:***
  - If pH raises too high rebound acidity to neutralize the alkali occurs.
  - Antacids which absorbed systemically exert alkaline effect on body's buffer system.
  - Some antacids cause constipation (Aluminium containing antacid) while others have laxative effect (Magnesium containing antacid).
  - Sodium containing antacids are problem for patients on sodium restricted diet (for hypertension patient).
  - Antacids containing calcium may cause hypercalcemia, which promotes kidney stones formation and reduces parathormone production.
- ***Requirement of combinations of antacids therapy:***
  - Systemic Antacid leads to alkalosis, may worsen edema and congestive heart failure because of sodium ion load, thereby they are not frequently used.
  - Whereas non-systemic antacid are more potent and effective as compare to systemic antacid, but They are insoluble and poorly absorbed systemically.
  - In Magnesium salt, Magnesium carbonate is most water soluble and reacts with HCl at a slow rate, while Magnesium hydroxide has low solubility and has the power to absorb and inactivate pepsin and to protect the ulcer base.
  - Aluminium hydroxide is a weak and slow reacting antacid. The aluminium ions relax smooth muscles and cause constipation.
  - Calcium carbonate is a potent antacid with rapid acid neutralizing capacity, but on long term use, it can cause hypercalcemia, hypercalciuria and formation of calcium stone in kidney.
  - Every single compound among antacid have some side effect especially when used for longer period or used in elderly patients. 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.

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

- ***Indications and principles of clinical use:***

  - **Gastro Esophageal Reflux Disease** (GERD) Antacids neutralize hydrochloric acid, inactivate pepsin, absorb bile acids, stimulate the synthesis of bicarbonates and raise the tone of the lower esophageal sphincter.
  - **Gastric and duodenal ulcers**
  - **Acute and Chronic gastritis / gastroduodenitis**
  - **Gastropathy caused by nonsteroidal anti-inflammatory drugs (NSAIDs - gastropathy):** Antacids can be taken alone or in addition to anti-secretory drugs in order to prevent gastro- and duodenopathies affected by the administration of nonsteroidal anti-inflammatory drugs (NSAIDs).
  - Antacids are recommended for healthy people with discomfort or epigastric pain.
  - Antacids are used in the intensive care units to prevent so-called "stress ulcers".

- ***Antacids interaction with other drugs:***

  - Antacids that contain calcium, magnesium and aluminum ions are chelators. They bind a great number of drugs such as digitoxin, tetracycline, indomethacin, aspirin, cimetidine, ranitidine, famotidine, theophylline etc.
  - Antacids also reduce the bioavailability of few drugs like barbiturates, sulfonamides, penicillin.
  - To avoid undesirable interactions, antacids are usually used 2 hours before or after taking any medication.

Systemic antacids:
Systemic antacids are antacids which get systemically absorbed e.g. sodium carbonate is water soluble and potent neutralizer, but it is not suitable for the treatment of peptic ulcer because of risk of ulcer perforation due to production of carbon dioxide in the stomach. Systemic absorption leads to alkalosis, may worsen edema and congestive heart failure because of sodium ion load.

Non Systemic antacids
They are insoluble and poorly absorbed systemically. In Magnesium salt, Magnesium carbonate is most water soluble and reacts with HCl at a slow rate, while Magnesium hydroxide has low solubility and has the power to absorb and inactivate pepsin and to protect the ulcer base. Aluminium hydroxide is a weak and slow reacting antacid. The aluminium ions relax smooth muscles and cause constipation. It absorbs pepsin at pH>3 and releases it at lower pH. It also prevents phosphate absorption. Calcium carbonate is a potent antacid with rapid acid neutralizing capacity, but on long term use, it can cause hypercalcemia, hypercalciuria and formation of calcium stone in kidney.

Every single compound among antacid have some side effect especially when used for longer period or used in elderly patients. 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.
(ii) Magnesium and calcium containing preparation where one is laxative and the later one is constipative in nature.

Compounds used as Antacids

(i)Sodium Bicarbonate (Baking soda)
$NaHCO_3$ M.W. 84.01

I.P. limit: It contains not less than 99% and not more than 101% of $NaHCO_3$

Properties: White crystalline powder, odorless, with saline and slight alkaline taste, Stable in dry air, sparingly soluble in water, insoluble in alcohol.

Preparation:
1. By passing strong brine containing high concentrations of ammonia through a carbonating tower where it is saturated with carbon dioxide under pressure. The

ammonia and carbon dioxide reacts to form ammonia bicarbonate which is allowed to react with NaCl to precipitate $NaHCO_3$ which is separated by filtration.

$$NH3 + H_2O + CO_2 \longrightarrow NH_4HCO_3$$

$$NH_4HCO_3 + NaCl \longrightarrow NaHCO_3$$

2. It can also be prepared by covering sodium carbonate crystals with water and passing carbon dioxide to saturation.

$$Na_2CO_3 + H_2O + CO_2 \longrightarrow NaHCO_3$$

Test for identification: To 5ml of 5%w/v solution in carbon dioxide free water add 0.1ml phenolphthalein solution a pale pink color is obtained. On heating a gas is evolved and the solution turns red.

For Sodium:

1. To sample solution add 15% w/v potassium carbonate, heat, no precipitate is obtained add potassium antimonite solution heat to boiling, cool and if necessary scratch the inside of test tube with a glass rod, a dense white precipitate is produced.
2. Acidified the sample solution with 1M acetic acid and add excess of magnesium uranyl acetate solution yellow crystalline precipitate is obtained.

For bicarbonate: to sample add magnesium sulphate no precipitate is produced. On boiling a white colored precipitate is formed.

Assay: Weigh accurately 1gm and dissolve in 20ml 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 $NaHCO_3$

Use: It is used as antacid, and in electrolyte replacement.

(ii) Aluminium Hydroxide

$Al(OH)_3$ M. W. = 78.0

Aluminium hydroxide gel is an aqueous suspension of hydrated aluminium oxide with different amounts of basic aluminium carbonate and bicarbonate.

I.P. limit: It contains not less than 3.5% and not more than 4.4% of $Al_2 O_3$

Properties: Aluminium hydroxide is a white, light odorless, tasteless amorphous powder. It is soluble in dilute mineral acids and in solution of alkali hydroxides but practically insoluble in water. It forms gel on prolonged contact with water at pH 5.5-8.0. It absorbs acids and carbon dioxide. The aluminium hydroxide gels are ideal buffers in the pH 3-5 range due to its amphoteric nature.

Preparation: It is prepared by dissolving sodium carbonate in hot water and the solution is filtered. To the filtrate add clear solution of alum (aluminium salt, chloride or sulphate) in water with constant stirring. Add more of water and remove all gas. The Aluminium Hydroxide precipitate out, collect the precipitate, wash and suspend in sufficient purified water flavoured with 0.01% peppermint oil and preserve with 0.1% sodium benzoate.

$$Al_2 (SO_4)_3 + 3Na_2CO_3 + 3H_2O \longrightarrow 2Na_2SO_4 + Al(OH)_3 + 3CO_2$$

Test for identification: A solution in 2N HCl gives the characteristic reactions of aluminium salts. To sample add 5drops of freshly prepared 0.05%w/v solution of quinalizarin in 1% w/v solution of NaOH heated to boiling, cool, acidify with excess of acetic acid a reddish violet color is produced.

Assay: Accurately weigh 5gm and dissolve in 3ml HCl by warming on water bath, cool to

below 20 °C and dilute to 100ml with water. To 20ml of this solution add 40ml of 0.05M disodium EDTA, 80ml water, 0.15ml methyl orange/red and neutralize by the dropwise addition of 1M sodium hydroxide. Again warm on water bath for 30 min, add 3gm hexamine and titrate with 0.05M lead nitrate using 0.5ml xylenol orange as indicator.
Each ml of 0.05M disodium EDTA ≡0.002549 gm of Al2 O3

Uses: Aluminium hydroxide is used as antacid in the management of peptic ulcer, gastritis, gastric hyperacidity. It is also used as skin protectant and mild astringent.

(iii) Aluminium Phosphate
$AlPO_4$ M.W. =122.0

Aluminium phosphate consists of hydrated aluminium orthophosphate.

I.P. limit: It contains not less than 80.0% of Al PO_4

Properties: It occurs in nature as the minerals angelite, coeruleolactile, evansite, lucinite, sterretite, wavellite etc. It is white infusible powder with some aggregates. It is insoluble in solutions of alkali hydroxide or acetic acid, water, alcohol etc; very slightly soluble in concentrated HCl and nitric acid. A 4% suspension in water has a pH of 5.5- 6.5. Aluminium phosphate gel is a white, viscous suspension from which small amount of water may separate on standing. The gel has a pH in the range of 6.0-7.2.

Preparation:

1. It may be prepared by treating aluminium sodium oxide ($NaAlO_2$) with phosphoric acid (H_3PO_4)

$$NaAlO_2 + 2H_3PO_4 \longrightarrow 2AlPO_4 + 2H_2O + 2NaH$$

2. It can also be prepared by drying under suitable conditions the product of interaction in aqueous of an aluminium salt with an alkali phosphate such as sodium phosphate.

Test for Identification:
For aluminum: A solution in 2N HCl gives the reactions characteristic of aluminium salts. To sample add 5drops of freshly prepared 0.05%w/v solution of quinalizarin in 1% w/v solution of NaOH heated to boiling, cool, acidify with excess of acetic acid a reddish violet color is produced.
For phosphate: To neutral sample solution add silver nitrate solution, a light yellow precipitate forms, the color of which is not changed by boiling and is readily soluble in 10M ammonia and dilute HNO_3.

Assay: To acidify solution of weighed amount of the aluminium phosphate (0.8gm), 7.7gm disodium acetate is added, pH is adjusted to 4.5 with glacial acetic acid and dithizone in ethanol is added and sufficient quantity of ethanol is added. Titrate the solution with 0.05M zinc chloride until color turns red. A blank titration is also performed and the volume consumed by sample is calculated. Each ml of 0.05M disodium EDTA≡ 6.098 mg of $AlPO_4$

Use: It is used as antacid.

(iv) Dihydroxy Aluminium Ammonium Acetate
$C_2H_6Al\ NO_4\ xH_2O$

I.P limit: It contains not less than 35.5% and not more than 38.5% of aluminum trioxide calculated on dried bases, contains small amounts of aluminum oxide and amino acetic acid.

Properties: It exists as very fine powder, bland taste, insoluble in water but forms suspension with water.

Preparation: It is prepared by adding solution of aluminum isopropoxide in isopropanolol to

an aqueous solution of glycine.

Test for Identification:
For aluminium: A solution of sample in 2N HCl gives the characteristic reactions of aluminium salts. To the sample, add 5drops of freshly prepared 0.05%w/v solution of quinalizarin in 1% w/v solution of NaOH heated to boiling, cool, acidify with excess of acetic acid, a reddish violet color is produced.
For acetate: Heat the sample with an equal amount of oxalic acid, acidic vapours with characteristic smell of acetic acid are liberated

Assay: Transfer about 2.5gm of accurately weighed dihydroxy aluminium ammonium acetate and add 15ml of HCl and warm if necessary, to dissolve the sample completely. Transfer the solution with the aid of water to 500ml volumetric flask and dilute with water to volume and mix. Transfer 20ml and add 25ml 0.05M disodium EDTA and 20ml of acetic acid ammonium acetate buffer. Heat near boiling for 5min, cool and add 50ml of alcohol and 2ml of dithizone. Titrate with 0.05M zinc sulphate until green violet color turns rose pink. Perform blank and calculate the volume consumed by sample. Each ml of 0.05M disodium EDTA≡ 2.549 mg of $Al_2 O_3$

Use: It is used as antacid.

(v) Dihydroxy Aluminium Sodium Carbonate
$CH_2Al\ Na\ O_5$ M.W.=143.99

I.P limit: It contains not less than 90% and not more than 110.0% of $Al_2 O_3$

Preparation: It is prepared by reaction between an alkoxide and sodium bicarbonate in water.

Test for Identification:

For aluminum: A solution in 2N HCl gives the reactions characteristic of aluminium salts. To sample add 5drops of freshly prepared 0.05%w/v solution of quinalizarin in 1% w/v solution of NaOH heated to boiling, cool, acidify with excess of acetic acid, a reddish violet color is produced.

For Carbonate: Suspend sample in 2ml of water in a test tube, add 2M acetic acid close the tube immediately with a stopper fitted with a glass tube bent at two right angles, heat gently and collect the gas in 5ml of 0.1M barium hydroxide a white precipitate is formed which is dissolves on addition of excess of dilute HCl.

For Sodium: To sample solution add 15% w/v potassium carbonate, heat, no precipitate is formed add potassium antimonite solution heat to boiling, cool and if necessary scratch the inside of test tube with a glass rod, a dense white precipitate is produced.

Assay: Weigh accurately powder not less than 200mg add 10ml of 2N HNO_3 cover and boil for 1 min, add 25ml of 0.1M disodium EDTA again boil for 1min cool, then add 10ml acetic acid ammonium acetate buffer and 50ml of acetone and 2ml of dithizone, adjust pH to 4.5 by the addition of ammonium hydroxide and titrate with 0.05M zinc sulphate maintaining pH at 4.5. Perform blank and calculate the volume consumed by sample.
Each ml of 0.05M disodium EDTA≡ 5.098 mg of $Al_2 O_3$

Use: It is used as antacid.

(vi)Calcium Carbonate (precipitated chalk)
$Ca\ CO_3$ M.W. = 100

Calcium carbonate is found in nature as limestone, marble, calcite, vaterite, aragonite and shell of sea animals.

I.P. limit: It contains not less than 98% and not more than 100.5% with reference to dried

substance.

Properties: It occurs as a white, odorless tasteless microcrystalline powder which is stable in air. It exists in two crystal form and both are of commercial importance, one Aragonite and other is Calcite.

Precipitated chalk is prepared as a fine precipitate by adding a solution of ammonium carbonate and ammonia or sodium carbonate to a solution of calcium nitrate.

Preparation:

1) It can be prepared by mixing and boiling calcium and sodium carbonate solution and allowing the resulting precipitate to settle. The precipitate is collected, washed with boiling water until free from chloride and dried.

$$CaCl_2 + Na_2CO_3 \longrightarrow CaCO_3 + 2Na\,Cl$$

2) By passing carbon dioxide through lime water

$$CaO + CO_2 + H_2O \longrightarrow CaCO_3$$

Test for Identification:

For Calcium: Dissolve substance in 5M acetic acid and add 0.5ml of potassium ferrocyanide solution. The solution remains clear. Add ammonium chloride white crystalline precipitate is formed.

For Carbonate: Suspend sample in 2ml water in a test tube, add 2M acetic acid close the tube immediately with a stopper fitted with a glass tube bent at two right angles, heat gently and collect the gas in 5ml of 0.1M barium hydroxide a white precipitate is formed which is dissolves on addition of excess of dilute HCl.

Assay: Accurately weigh 0.1gm, dissolve in 3ml of dilute HCl, add 10ml of water. Boil the solution for 10min, cool, dilute with 50 ml with water. Titrate the solution with 0.05M disodium EDTA to with a few ml of the expected end point and add 8ml of NaOH solution and 0.1g of calcon mixture. Continue the titration until the color changes from pink to blue.
Each ml of 0.05M disodium EDTA≡ 0.005004g of $CaCO_3$

Uses: It is used as fast acting antacid, in calcium deficiency, dentrifries and in combination with magnesium containing antacids due to its constipative properties.

(vii)Tribasic Calcium Phosphate

$CaO\ {}_3P_2O_5\ H_2O$ M.W.=328.2

I.P limit: Tribasic calcium phosphate consist of variable mixture of calcium phosphate having approximate composition of $10CaO\ 3P_2O_5\ H_2O$ not less than 34% and not more than 40% of calcium and an amount of phosphate equivalent to not less than calcium phosphate calculated with reference to ignited substance.

Properties: It is a white odourless, tasteless, amorphous powder practically insoluble in water, alcohol or acetic acid but readily soluble in dilute HCl and HNO_3

Preparation:

1. It is manufactured from bones which are calcined until white, powdered and digested with sulphuric acid. The insoluble tribasic calcium phosphate is converted to soluble phosphoric acid and insoluble calcium sulphate. The solution is filtered and the filtrate treated with calcium hydroxide to precipitate calcium phosphate.
2. Decomposition of calcium chloride and sodium phosphate in presence of aqueous ammonia at high temperature yield calcium phosphate. The white precipitate is filtered washed and freed from chloride and dried.

Test for Identification:
For Calcium: Dissolve substance in 5M acetic acid and add 0.5ml of potassium ferrocyanide solution. The solution remains clear. Add ammonium chloride white crystalline precipitate is formed.
For phosphate: To neutral sample solution add silver nitrate solution, a light yellow precipitate forms, the color of which is not changed by boiling and is readily soluble in 10M ammonia and dilute HNO_3.

Assay:
For calcium: Weigh accurately 0.2gm and dissolve in HCl, triethanol amine and hydroxynaphthol blue indicator are added and titrate with 0.05M disodium EDTA until blue colour is obtained. Each ml of 0.05M disodium EDTA ≡ 0.002004gm calcium.

For phosphate: Acidify the aqueous solution of substance 0.2gm with dilute nitric acid, filter and add strong ammonium solution to produce slight precipitate. The precipitate is dissolved in dilute nitric acid, ammonium molybdate is added and precipitate is filtered, washed with potassium nitrate solution and redissolved in 1N sodium hydroxide add phenolphthalein and titrate the excess alkali with 1N sulphuric acid. Each ml of 1N NaOH ≡ 0.006743 gm of calcium phosphate.

Use: It is used as antacid, as non hygroscopic diluent, as an abrasive in tooth pastes.

(viii) Magnesium Carbonate
$(MgCO_3)_4 : Mg(OH)_2 : 5H_2O$ M.W. = 508

Magnesium carbonate is a hydrated basic magnesium carbonate containing 40-45% of magnesium oxide. It occurs in nature as the meniral magnate and lansfordite.
Heavy Magnesium Carbonate: 15 g occupy a volume of about 30ml
Light Magnesium Carbonate: 15 g occupy a volume of about 150ml

I.P. limit: It contains not less than 40% and not more than 45% of magnesium oxide

Properties: Both heavy and light magnesium carbonate are hydrated. Both are white, odorless powder practically insoluble in water and alcohol but solubilizes in dilute acids with strong effervescence.

Preparation: It is prepared by mixing hot solution of magnesium sulphate and sodium carbonate. The mixture is evaporated to dryness and the residue consisting of magnesium carbonate and sodium sulphate is digested for half an hour with boiling water. The precipitate of magnesium carbonate is collected on filter paper, washed with water until free from sulphate and then dry.

$$5MgSO_4\ 7H_2O + 5Na_2CO_3\ 10\ H_2O \longrightarrow (MgCO_3)_4\ Mg\ (OH)_2\ 5H_2O + 5\ Na_2SO_4 + 5O_2 + 79\ H_2O$$

Test for Identification:
For Carbonate: Suspend sample in 2ml water in a test tube, add 2M acetic acid close the tube immediately with a stopper fitted with a glass tube bent at two right angles, heat gently and collect the gas in 5ml of 0.1M barium hydroxide a white precipitate is formed which is dissolves on addition of excess of dilute HCl.

For Magnesium: to solution of sample add dilute nitric acid solution a white precipitate is produced that is redissolved by adding 1ml of 2M ammonium chloride, add 0.25M disodium hydrogen phosphate a white crystalline precipitate is produced.

Assay: Accurately weigh 15g of magnesium carbonate and dissolve in a mixture of 20ml of water and 2ml 2M HCl. To this solution add 50ml of water and 10ml strong ammonia ammonium chloride solution titrate this with 0.05M disodium EDTA using mordant black II mixture as indicator until blue color is obtained. Each ml of 0.05M disodium EDTA≡ 0.002015g MgO

Uses: It is used as antacid and mild laxative. It is used as pharmaceutical aid (dispensing volatile oil for use in inhalants).

(ix) Magnesim Oxide (Magnesia)
MgO M.W. = 40.3

I.P. limit: It contains not more than 98% of magnesium oxide

It occurs in nature as mineral periclase. It occurs in two varieties heavy magnesium oxide which is relatively dense white powder with 15 g occupying volume of about 30ml while light magnesium oxide is very bulky with 15 g occupying volume of about 150ml.

Properties: Both heavy and light magnesium oxide are odorless taste slightly alkaline, practically insoluble in water yield a solution which is alkaline. It readily dissolves in dilute acids with slight effervescence. In presence of acid, the oxide forms the magnesium hydroxide, therefore the chemistry and pharmacology are same as those of magnesium hydroxide.

Preparation:

1. It can be prepared by heating gently magnesium carbonate to redness.
   $(MgCO_3)_4\,Mg(OH)_2\,5H_2O \longrightarrow MgO + CO_2 + H_2O$
2. It is also prepared by heating light magnesium carbonate to redness.
   $(MgCO_3)_4\,Mg(OH)_2\,3H_2O \longrightarrow 4MgO + 3CO_2 + 3H_2O$

Test for identification:
For Magnesium: to solution of sample add dilute nitric acid solution a white precipitate is produced that is redissolved by adding 1ml of 2M ammonium chloride, add 0.25M disodium hydrogen phosphate a white crystalline precipitate is produced.

Assay: The assay of magnesium oxide is performed by complexometry. Accurately weigh 15g of magnesium oxide and dissolve in a mixture of 20ml of water and 2ml 2M HCl. To this solution add 50ml of water and 10ml strong ammonia ammonium chloride solution titrate this with 0.05M disodium EDTA using mordant black II mixture as indicator until blue color is obtained. Each ml of 0.05M disodium EDTA≡ 0.002015g MgO

Uses: It is used as antacid and laxative. It is ingredient of universal antidote along with tannic acid and charcoal. It is used for compounding and preserving fluid extract because of its absorptive power.

(x)Magnesium Phosphate
$Mg_3\,(PO_4)_2\,5H_2O$ M.W. = 352.93

I.P. limit: It contains not less than 98% and not more than 101.5% substance ignited at 425°C to constant weight.

Properties: It is white, odourless, tasteless powder readily soluble in dilute mineral acids but practically insoluble in water. The chemistry is same as tribasic calcium phosphate.

Test for Identification:
For Magnesium: to solution of sample add dilute nitric acid solution a white precipitate is produced that is redissolved by adding 1ml of 2M ammonium chloride, add 0.25M disodium hydrogen phosphate a white crystalline precipitate is produced.

For phosphate: To neutral sample solution add silver nitrate solution, a light yellow precipitate forms, the color of which is not changed by boiling and is readily soluble in 10M ammonia and dilute HNO_3.

Assay: Weigh accurately 200mg previously ignited to 425°C to constant weight and dissolve in mixture of 25ml of water and 10ml of 2N HNO_3. Filter if necessary, wash any precipitate add sufficient 6Nammonium hydroxide to the filtrate to produce a slight precipitate and then add 1ml of 2N HNO_3. Adjust temperature to 50° add 7ml ammonium molybdate and maintain temperature for 30min with occasional stirring. Wash the precipitate once or twice with water by decantation. Transfer precipitate to the filtrate, wash with KNO_2 solution until the last washing is not acid to litmus. Transfer precipitate and filter to precipitate vessel add 50ml of water and 40ml of 1N NaOH, agitate until the precipitate is dissolved, add phenolphthalein and titrate excess of alkali with 1N H_2SO_4. Each ml of 1N NaOH ≡ 5.716mg of magnesium phosphate.

Uses: It is used as antacid and laxative.

(xi)Magnesium Trisilicate
$2MgO\ 3SiO,\ xH_2O$ M.W. (anhydrous) =260.86

I.P. limit: It contains not more than 29% of magnesium oxide and not more than 65% of silicon dioxide both calculated with reference to the ignited substance.

Properties: Fine, white, odorless, tasteless powder, free from grittiness. Magnesium silicate hydrate is a compound of magnesium oxide and silicon dioxide with varying amount of water.

Preparation: It is prepared by precipitation from solution of magnesium sulphate and sodium silicate.

$$2MgSO_4 + 2Na_2O\ 3SiO_2 + X\ H_2O \longrightarrow 2MgO\ 3SiO_2\ XH_2O + Na_2\ SO_4 + H_2O$$

Test for identification:
For Magnesium: to solution of sample add dilute nitric acid solution a white precipitate is produced that is redissolved by adding 1ml of 2M ammonium chloride, add 0.25M disodium hydrogen phosphate a white crystalline precipitate is produced.
For silicate: in a lead or platinum crucible mix by means of a copper wire to obtain a thin slurry the prescribed amount (0.25gm) of substance with 10mg of sodium fluoride and a few drops of sulphuric acid cover the crucible with thin transparent plate of plastic under which a drop of water is suspended and warm gently within a short time a white ring is formed around the drop of water

Assay:
For Magnesium Oxide: Weigh accurately 1gm substance and dissolve in 35ml of water allow to stand for 15min on water bath. Cool the contents to room temperature filter and wash the residue with water and dilute the combined filtrate and washing to 250ml with water. Neutralize 50ml of this solution with about 8ml of 10M NaOH and then add 10ml ammonia buffer pH 10, 50mg mordant black II mixture. Heat the contents to 40 °C and titrate with

0.05M disodium EDTA until color changes to deep blue.Each ml of 0.05M disodium EDTA≡ 0.002015g MgO

For silicon dioxide: weigh accurately 0.7gm of substance add 10 ml of 1M sulphuric acid, 10ml water and heat on water bath for 1.5hrs. shaking frequently and replacing the evaporated water. Allow to cool decant on to an ashless filter paper (7cm in diameter). Wash the precipitate by decantation with three quantities each of 5ml of hot water, transfer it to the filter paper and wash it with hot water, until 1ml of the filtrate remains clear on addition of 2ml of barium chloride solution and 0.5ml of 2N HCl. Ignite the filter paper and its contents in a tarred platinum crucible at 900 °C to constant weight. The residue is silicon dioxide.

Uses: It is used as non systemic antacid and adsorbent.

References:

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