

# Gastro intestinal agents

Gastro intestinal 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  $\text{KMnO}_4$  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  $\text{HNO}_3$  but soluble after being washed with water in ammonium hydroxide from which it is reprecipitated by the addition of  $\text{HNO}_3$ .

**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 sphincter 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<sub>2</sub> 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.

### **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

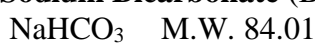
They are insoluble and poorly absorbed systemically. In Magnesium salt, Magnesium carbonate is most water soluble and reacts with HCl at a slow rate, while Magnesium hydroxide has low solubility and has the power to absorb and inactivate pepsin and to protect the ulcer base. Aluminium hydroxide is a 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)

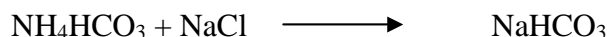
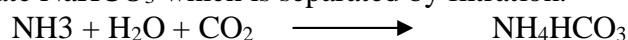


**I.P. limit:** It contains not less than 99% and not more than 101% of  $\text{NaHCO}_3$

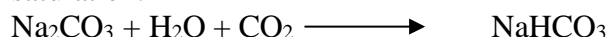
**Properties:** White crystalline powder, odorless, with saline and slight alkaline taste, Stable in dry air, sparingly soluble in water, insoluble in alcohol.

#### 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  $\text{NaHCO}_3$  which is separated by filtration.



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



**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  $\equiv$  0.0425gm of  $\text{NaHCO}_3$

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

### (ii) Aluminium Hydroxide gel

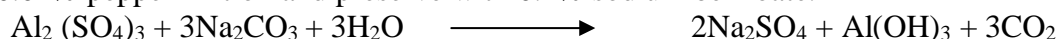
$\text{Al}(\text{OH})_3$  M. W. = 78.0

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  $\text{Al}_2\text{O}_3$

**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.



**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  $\equiv$  0.002549 gm of  $\text{Al}_2\text{O}_3$

**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) Tribasic Calcium Phosphate

$\text{CaO } 3\text{P}_2\text{O}_5 \text{ H}_2\text{O}$  M.W.=328.2

**I.P limit:** Tribasic calcium phosphate consist of variable mixture of calcium phosphate having approximate composition of  $10\text{CaO } 3\text{P}_2\text{O}_5 \text{ H}_2\text{O}$  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<sub>3</sub>

**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<sub>3</sub>.

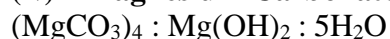
**Assay:**

**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  $\equiv$  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  $\equiv$  0.006743 gm of calcium phosphate.

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

**(iv) Magnesium Carbonate**



M.W. = 508

Magnesium carbonate is a hydrated basic magnesium carbonate containing 40-45% of magnesium oxide. It occurs in nature as the mineral magnesite and lansfordite.

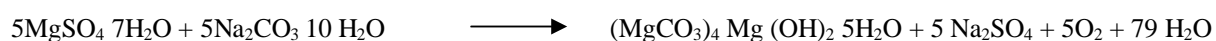
Heavy Magnesium Carbonate: 15 g occupy a volume of about 30ml

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.



**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  $\equiv$  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).

## (ii) Kaolin



Heavy kaolin is purified natural hydrated aluminium silicate of variable composition. Light kaolin is native hydrated aluminum silicate freed from most of its impurities by elutriation and dried. It may contain a suitable dispersing agent.

**Preparation:** Kaolin is widely distributed in nature contaminated with ferric oxides. It is prepared when the rock is mined, evacuated and the impurities are washed with water and then powdered. The rock is elutriated with water and large sized particles are separated. The turbid liquid is allowed to settle; heavy kaolin containing large particles and colloidal kaolin containing particles of small size are separated and dried. For pharmaceutical use it is purified by treatment with HCl and H<sub>2</sub>SO<sub>4</sub> or both and then washed with water.

**Test for Identification:** Fuse 2gm of substance with 4gm anhydrous sodium carbonate. Warm residue with water and filter, acidify the filtrate with HCl evaporate to dryness and warm the residue with dilute HCl, residue of silica is obtained and the acid solution after neutralization gives reaction for aluminum.

**For aluminium:** To 0.5 gm in a metal crucible add 1gm HNO<sub>3</sub> and 3gm anhydrous sodium carbonate, heat to melt and allow cool, adding 20ml of boiling water to this residue and filtering. To filtrate add 1ml of 10M NaOH and filter. To filtrate add 3ml of ammonium chloride solution a gelatinous white precipitate is obtained.

**For silicate:** Fuse 1gm of substance with 2g anhydrous sodium carbonate and warm the residue with 10ml of water, filter, wash with water and reserve the residue. To combined filtrate and washings add 3ml of HCl a gelatinous precipitate is obtained.

**Use:** It is used as adsorbent in diarrhoea caused by agents capable of being absorbed e.g due to food poisoning. Also used in chronic ulcerative colitis. As poultice, dusting powder, clarifying and decolorizing medium, as filtering medium, as tablet diluent.

### **Saline Cathartics**

Saline cathartics or purgatives are agents that quicken and increase evacuation from the bowl. Laxatives are mild cathartics. Cathartics are used:

- to ease defecation in patients with painful hemorrhoids or other rectal disorders and to avoid excessive straining and concurrent increase in abdominal pressure in patients with hernias Or
- to avoid potentially hazardous rise in B.P. during defecation in patients with hypertension, cerebral coronary or other arterial disease Or
- to relieve acute constipation Or
- to remove solid material from intestinal tract prior to certain roentgenographic studies.

Laxative should only be used for short term therapy as prolonged use may lead to loss of spontaneous bowl rhythm upon which normal evacuation depends, causing patient to become dependent on laxatives, the so called laxative effect.

Constipation is the infrequent or difficult evacuation of the feces. It may be due to a person resisting the natural urge to defecate, causing the fecal material which remains in the colon to lose fluid and to become relatively dry and hard. Constipation can also be due to intestinal atony, intestinal spasm, emotions, drugs and diet. Many a time constipation can be helped by eating food such as natural laxatives or food with large roughages. Four types of laxatives are known:

1. Stimulants
2. Bulk forming
3. Emollient
4. Saline cathartics

**Stimulants** act by local irritation on the intestinal tract which increase peristaltic activity. They include phenolphthalein, aloin, cascara extract, rhubarb extract, senna extract, podophyllin, castor oil, bisacodyl, calomel etc.



**Bulk forming laxatives** are made from cellulose, sodium carboxyl methyl cellulose and karaya gum.

The **emollient laxatives** act either as lubricants facilitating the passage of compacted fecal material or as stool softeners. E.g mineral oil, d-octyl sodium sulfosuccinate, an anionic surface active agent.

**Saline cathartics** act by increasing the osmotic load of the GIT. They are salts of poorly absorbable anions  $\text{-H}_2\text{PO}_4^-$  (biphosphate),  $\text{-HPO}_4^{2-}$  (phosphate), sulphates, tartarates, and soluble magnesium salt.

Saline cathartics are water soluble and are taken with large quantities of water. This prevents excessive loss of water from body fluids and reduces nausea vomiting if a too hypertonic solution should reach the stomach. They act in the intestine and a full cathartic dose produces a water evacuation within 3-6 hrs. Because of their quick onset of action they are given early in the morning before breakfast.

They are used for bowel evacuation before radiological, endoscopic and surgical procedures and also to expel parasite and toxic materials.

Small amounts of these drugs may be absorbed in the blood causing occasional toxicity. The absorption of magnesium may cause marked CNS depression while that of sodium worsens the existing congestive cardiac failure (CCF).

### Compounds used as Saline cathartics

**(i)Sodium Acid Phosphate** (sodium biphosphate)

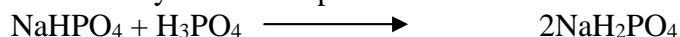
$\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$  M.W. = 156.01

**LP limit:** It contains not less than 98.0% and not more than 100.5% of  $\text{NaH}_2\text{PO}_4$  calculated with reference to the dried substance.

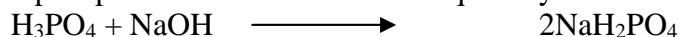
**Properties:** Colorless, odorless, crystalline powder with saline acidic taste. Freely soluble in water and practically insoluble in alcohol. Slightly deliquescent.

### Preparation:

1. It is prepared by adding phosphoric acid to hot concentrated solution of disodium phosphate until liquid ceases to give precipitate with barium chloride. The solution is then concentrated to the crystallization point.



2. By reaction with phosphoric acid with calculated quantity of sodium hydroxide.



### Test for Identification:

**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  $\text{HNO}_3$ .

**For sodium:** To 2ml of solution add 2ml of 15% w/v of  $\text{K}_2\text{CO}_3$  heat to boil, no precipitate is produced. Add 3ml of potassium antimonite solution and heat to boil. Allow to cool in ice and if necessary scratch the inside of the test tube with glass rod white precipitate is produced.

**Assay:** Weigh accurately 2.5 gms dissolve in 40ml water and titrate with carbonate free 1M NaOH. Determine end point potentiometrically. Each ml of 0.5M sodium hydroxide  $\equiv$  0.0780g of  $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$

**Use:** It is used as saline cathartic and as buffer in pharmaceutical preparations. As urinary acidifier, source of phosphorous.

**(ii) Disodium Hydrogen Phosphate** (phosphor soda)

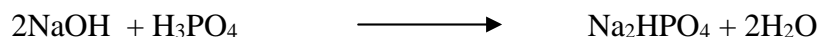
$\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$  M.W. = 358.14

**I.P limit:** It contains not less than 98.0% and not more than 101% of  $\text{NaH}_2\text{PO}_4$  calculated with reference to the dried substance.

**Properties:** Colorless, odorless, crystalline powder. Soluble in water and practically insoluble in alcohol. Very efflorescent.

**Preparation:**

1. It is prepared by reaction of orthophosphoric acid calculated quantity of sodium hydroxide.



2. From bone ashes or mineral phosphorite, which is treated with sulphuric acid

**Assay:** Weigh accurately 4gm of substance and dissolve in 25ml of water add 25ml 1N HCl and titrate potentiometrically with 1M NaOH to first inflection point of the pH curve (n1) continue titration until second inflection of curve is reached. The total volume of NaOH required is n2 ml. calculate percent content from the expression

$$1420(25-n1)/w (100-d) \quad d \text{ is percentage of water content.}$$

**Use:** Widely used as saline cathartic. Orally as antihypercalcemic It is a pharmaceutical aid used as buffering agent.

**(iii) Magnesium Sulphate**

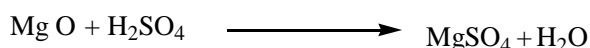
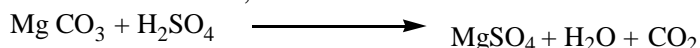
$\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$  M.W. = 246.47

**I.P. limit:** It contains not less than 99.0% and not more than 100.5% of magnesium sulphate calculated with reference to dried substance.

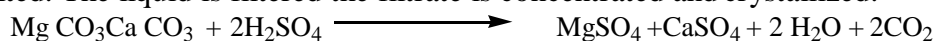
**Properties:** It forms colorless prismatic crystals. It dissolves in water, is practically insoluble in alcohol. It has cooling saline bitter taste.

**Preparation:**

- 1) It can be prepared by neutralizing hot dilute sulphuric acid with magnesium or its oxides or carbonate. The solution is filtered; the filtrate is concentrated and recrystallized.



- 2) On commercial scale it is manufactured by reacting sulphuric with dolomite. Magnesium sulphate so formed is dissolved in the solution and the sparingly soluble calcium sulphate is deposited. The liquid is filtered the filtrate is concentrated and crystallized.



Dolomite

**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 sulphate:** To 5ml of sample solution add 1ml of dilute HCl and 1ml barium chloride solution white precipitate. Add 1ml of iodine solution to the suspension, the suspension remains yellow (distinction from sulphites and dithionites) but decolorizes on adding stannous chloride (distinction from iodates).

**Assay:** Weigh accurately about 6.3gm of sample dissolve in 50ml of water, add 10ml of strong ammonia ammonium chloride solution and titrate with 0.05M disodium EDTA using 0.1gm of moderate black II mixture as indicator until blue color is obtained.  
Each ml of 0.05M disodium EDTA  $\equiv$  0.00602 gm of  $MgSO_4$

**Uses:** It is used as osmotic laxative, in treatment of electrolyte deficiency, in wet dressing in boils, in treatment of cholecystitis, sea sickness, hypertension etc.

**(v) Magnesium hydroxide mixture”**

$(MgCO_3)_4 : Mg(OH)_2 : 5H_2O$

M.W. = 508

Magnesium carbonate is a hydrated basic magnesium carbonate containing 40-45% of magnesium oxide. It occurs in nature as the mineral magnesite and lansfordite.

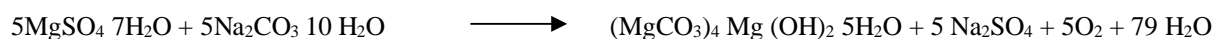
Heavy Magnesium Carbonate: 15 g occupy a volume of about 30ml

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.



**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  $\equiv$  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).

**(vi) Magnesium 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.  
 $(\text{MgCO}_3)_4 \text{Mg}(\text{OH})_2 \cdot 5\text{H}_2\text{O} \longrightarrow \text{MgO} + \text{CO}_2 + \text{H}_2\text{O}$
2. It is also prepared by heating light magnesium carbonate to redness.  
 $(\text{MgCO}_3)_4 \text{Mg}(\text{OH})_2 \cdot 3\text{H}_2\text{O} \longrightarrow 4\text{MgO} + 3\text{CO}_2 + 3\text{H}_2\text{O}$

**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  $\equiv$  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.

**(iii) Kaolin**  
 $\text{Al}_2\text{O}_3 \cdot 2\text{SiO}_2 \cdot 2\text{H}_2\text{O}$

Heavy kaolin is purified natural hydrated aluminium silicate of variable composition. Light kaolin is native hydrated aluminum silicate freed from most of its impurities by elutriation and dried. It may contain a suitable dispersing agent.

**Preparation:** Kaolin is widely distributed in nature contaminated with ferric oxides. It is prepared when the rock is mined, evacuated and the impurities are washed with water and then powdered. The rock is elutriated with water and large sized particles are separated. The turbid

liquid is allowed to settle; heavy kaolin containing large particles and colloidal kaolin containing particles of small size are separated and dried. For pharmaceutical use it is purified by treatment with HCl and H<sub>2</sub>SO<sub>4</sub> or both and then washed with water.

**Test for Identification:** Fuse 2gm of substance with 4gm anhydrous sodium carbonate. Warm residue with water and filter, acidify the filtrate with HCl evaporate to dryness and warm the residue with dilute HCl, residue of silica is obtained and the acid solution after neutralization gives reaction for aluminum.

**For aluminium:** To 0.5 gm in a metal crucible add 1gm HNO<sub>3</sub> and 3gm anhydrous sodium carbonate, heat to melt and allow cool, adding 20ml of boiling water to this residue and filtering. To filtrate add 1ml of 10M NaOH and filter. To filtrate add 3ml of ammonium chloride solution a gelatinous white precipitate is obtained.

**For silicate:** Fuse 1gm of substance with 2g anhydrous sodium carbonate and warm the residue with 10ml of water, filter, wash with water and reserve the residue. To combined filtrate and washings add 3ml of HCl a gelatinous precipitate is obtained.

**Use:** It is used as adsorbent in diarrhoea caused by agents capable of being absorbed e.g due to food poisoning. Also used in chronic ulcerative colitis. As poultice, dusting powder, clarifying and decolorizing medium, as filtering medium, as tablet diluent.

### **Saline Cathartics**

Saline cathartics or purgatives are agents that quicken and increase evacuation from the bowl. Laxatives are mild cathartics. Cathartics are used:

- to ease defecation in patients with painful hemorrhoids or other rectal disorders and to avoid excessive straining and concurrent increase in abdominal pressure in patients with hernias Or
- to avoid potentially hazardous rise in B.P. during defecation in patients with hypertension, cerebral coronary or other arterial disease Or
- to relieve acute constipation Or
- to remove solid material from intestinal tract prior to certain roentgenographic studies.

Laxative should only be used for short term therapy as prolonged use may lead to loss of spontaneous bowl rhythm upon which normal evacuation depends, causing patient to become dependent on laxatives, the so called laxative effect.

Constipation is the infrequent or difficult evacuation of the feces. It may be due to a person resisting the natural urge to defecate, causing the fecal material which remains in the colon to lose fluid and to become relatively dry and hard. Constipation can also be due to intestinal atony, intestinal spasm, emotions, drugs and diet. Many a time constipation can be helped by eating food such as natural laxatives or food with large roughages. Four types of laxatives are known:

1. Stimulants
2. Bulk forming
3. Emollient
4. Saline cathartics

**Stimulants** act by local irritation on the intestinal tract which increase peristaltic activity. They include phenolphthalein, aloin, cascara extract, rhubarb extract, senna extract, podophyllin, castor oil, bisacodyl, calomel etc.

**Bulk forming laxatives** are made from cellulose, sodium carboxyl methyl cellulose and karaya gum.

The **emollient laxatives** act either as lubricants facilitating the passage of compacted fecal material or as stool softeners. E.g mineral oil, d-octyl sodium sulfosuccinate, an anionic surface active agent.

**Saline cathartics** act by increasing the osmotic load of the GIT. They are salts of poorly absorbable anions  $\text{-H}_2\text{PO}_4^-$  (biphosphate),  $\text{-HPO}_4^{2-}$  (phosphate), sulphates, tartarates, and soluble magnesium salt.

Saline cathartics are water soluble and are taken with large quantities of water. This prevents excessive loss of water from body fluids and reduces nausea vomiting if a too hypertonic solution should reach the stomach. They act in the intestine and a full cathartic dose produces a water evacuation within 3-6 hrs. Because of their quick onset of action they are given early in the morning before breakfast.

They are used for bowel evacuation before radiological, endoscopic and surgical procedures and also to expel parasite and toxic materials.

Small amounts of these drugs may be absorbed in the blood causing occasional toxicity. The absorption of magnesium may cause marked CNS depression while that of sodium worsens the existing congestive cardiac failure (CCF).

### Compounds used as Saline cathartics (i)Sodium

**Acid Phosphate** (sodium biphosphate)



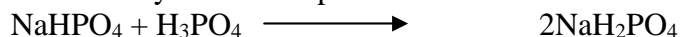
M.W. = 156.01

**LP limit:** It contains not less than 98.0% and not more than 100.5% of  $\text{NaH}_2\text{PO}_4$  calculated with reference to the dried substance.

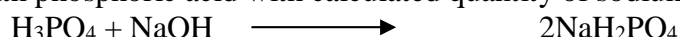
**Properties:** Colorless, odorless, crystalline powder with saline acidic taste. Freely soluble in water and practically insoluble in alcohol. Slightly deliquescent.

#### Preparation:

3. It is prepared by adding phosphoric acid to hot concentrated solution of disodium phosphate until liquid ceases to give precipitate with barium chloride. The solution is then concentrated to the crystallization point.



4. By reaction with phosphoric acid with calculated quantity of sodium hydroxide.



#### Test for Identification:

**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  $\text{HNO}_3$ .

**For sodium:** To 2ml of solution add 2ml of 15% w/v of  $\text{K}_2\text{CO}_3$  heat to boil, no precipitate is produced. Add 3ml of potassium antimonite solution and heat to boil. Allow to cool in ice and if necessary scratch the inside of the test tube with glass rod white precipitate is produced.

**Assay:** Weigh accurately 2.5 gms dissolve in 40ml water and titrate with carbonate free 1M NaOH. Determine end point potentiometrically. Each ml of 0.5M sodium hydroxide  $\equiv$  0.0780g of  $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$

**Use:** It is used as saline cathartic and as buffer in pharmaceutical preparations. As urinary acidifier, source of phosphorous.

**Disodium Hydrogen Phosphate** (phosphor soda)

$\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$

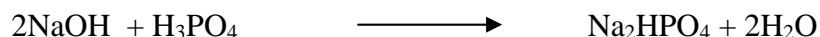
M.W. = 358.14

**I.P limit:** It contains not less than 98.0% and not more than 101% of  $\text{NaH}_2\text{PO}_4$  calculated with reference to the dried substance.

**Properties:** Colorless, odorless, crystalline powder. Soluble in water and practically insoluble in alcohol. Very efflorescent.

**Preparation:**

3. It is prepared by reaction of orthophosphoric acid calculated quantity of sodium hydroxide.



4. From bone ashes or mineral phosphorite, which is treated with sulphuric acid

**Assay:** Weigh accurately 4gm of substance and dissolve in 25ml of water add 25ml 1N HCl and titrate potentiometrically with 1M NaOH to first inflection point of the pH curve (n1) continue titration until second inflection of curve is reached. The total volume of NaOH required is n2 ml. calculate percent content from the expression

$$1420(25-n1)/w (100-d) \quad d \text{ is percentage of water content.}$$

**Use:** Widely used as saline cathartic. Orally as antihypercalcemic It is a pharmaceutical aid used as buffering agent.

(iv) **Magnesium Sulphate**

$\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$

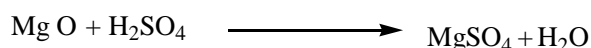
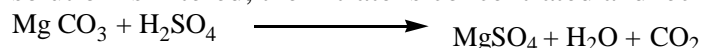
M.W. = 246.47

**I.P. limit:** It contains not less than 99.0% and not more than 100.5% of magnesium sulphate calculated with reference to dried substance.

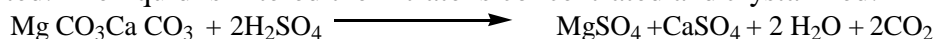
**Properties:** It forms colorless prismatic crystals. It dissolves in water, is practically insoluble in alcohol. It has cooling saline bitter taste.

**Preparation:**

- 3) It can be prepared by neutralizing hot dilute sulphuric acid with magnesium or its oxides or carbonate. The solution is filtered; the filtrate is concentrated and recrystallized.



- 4) On commercial scale it is manufactured by reacting sulphuric with dolomite. Magnesium sulphate so formed is dissolved in the solution and the sparingly soluble calcium sulphate is deposited. The liquid is filtered the filtrate is concentrated and crystallized.



Dolomite

**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 sulphate:** To 5ml of sample solution add 1ml of dilute HCl and 1ml barium chloride solution white precipitate. Add 1ml of iodine solution to the suspension, the suspension remains yellow (distinction from sulphites and dithionites) but decolorizes on adding stannous chloride (distinction from iodates).

**Assay:** Weigh accurately about 6.3gm of sample dissolve in 50ml of water, add 10ml of strong ammonia ammonium chloride solution and titrate with 0.05M disodium EDTA using 0.1gm of moderate black II mixture as indicator until blue color is obtained.  
Each ml of 0.05M disodium EDTA  $\equiv$  0.00602 gm of  $MgSO_4$

**Uses:** It is used as osmotic laxative, in treatment of electrolyte deficiency, in wet dressing in boils, in treatment of cholecystitis, sea sickness, hypertension etc.









