UNIT-II

ACIDIFERS

In patients suffering from achlorhydria, there is deficient secretion of hydrochloric acid in the stomach. In such cases, acidifiers are useful in providing the necessary acidity for the proper digestion of food. Systemic acidifiers are those which, when given usually by injection, act by reducing the alkali reserve in the body and so are useful in reducing metabolic alkalosis.

HYDROCHLORIC ACID, HCl

Test for Purity:

1. Arsenic
2. Heavy metals
3. Bromide and iodide
4. Sulphite
5. Sulphate
6. Free chlorine
7. Residue on evaporation

Storage:

Hydrogen chloride gas volatilizes from Hydrochloric Acid when exposed to atmosphere till a constant boiling mixture of 20.24% boiling at 110 C is formed. Therefore hydrochloric acid should be stored in glass-stopped containers securely closed at a temperature not exceeding 30 C.

Medicinal and Pharmaceutical Uses:

Pharmaceutical Aid (acidifying agent)

Hydrochloric acid is used in cases of achlorhydria (lack of hydrochloric acid in the gastric juice) in the form of dilute hydrochloric acid, I.P.

It is also used in the manufacture of glucose from corn starch, for extracting glue (gelatin) from bones and as a reagent in the laboratory.

DILUTE HYDROCHLORIC ACID, HCl

Test for Purity, Storage and Uses: Same as HYDROCHLORIC ACID.
ANTACIDS

Antacids are drugs used to neutralize the hydrochloric acid secreted in the stomach in the gastric juice. They raise the pH of the gastric contents to above 3.5 and give symptomatic relief of pain (in gastric and duodenal ulcers) by lowering the acidity and consequently relieving the muscle spasm. They do this by acting as weak bases.

An ideal antacid should not have any side effects other than its main action of neutralizing gastric acid. For example, it should not have a constipating or laxative effect. It should not cause, if absorbed, systemic alkalosis (in this condition, the pH of the body fluids and tissues is high). It should not cause precipitation of phosphate in the gastrointestinal tract and depletion of phosphorus in the body. It should not also interfere with the absorption of other drugs such as tetracycline from the gut. It should not also delay the absorption of drugs which are weak acids or speed up the absorption of basic drugs. This happens when the pH of the gastric contents is raised.

In the case of antacids, the acid neutralizing capacity is important. This may be determined by allowing the antacid to remain in contact with 0.1M hydrochloric acid at 37°C in a thermostatically controlled bath and measuring the pH at successive time intervals. Finally, the concentration of the acid is out by determining the remaining acid by titration with 0.1M sodium hydroxide after one hour.

CLASSIFICATION OF ANTACIDS

Antacids are divided into:

1. Non-systemic Antacids: These, as stated above, directly neutralize the acid in the stomach and give relief in gastric and duodenal ulcers.
   
   a) Aluminium hydroxide gel
   b) Dried aluminium hydroxide gel
   c) Aluminium phosphate
   d) Magnesium hydroxide
   e) Magnesium trisilicate
   f) Light and heavy magnesium carbonate
   g) Magaldrate
   h) Calcium carbonate.
   i) Bismuth subcarbonate.

2. Systemic Antacids: These may be absorbed from the gut into the blood circulation and cause alkalosis. So they may also be called as systemic alkalisers when they are used by injection to relieve acidosis in the blood, especially in diabetic coma.
   
   a) Sodium bicarbonate
   b) Potassium citrate
COMBINATIONS OF ANTACIDS

There are three complication usually seen when antacids are used. First, many antacids exert an action on the bowel. For example some have a mild laxative effect (eg. Magnesium hydroxide) and some are constipating (e.g. aluminum hydroxide). Secondly if the cation (the metallic ion) is absorbed, systemic alkalosis (a condition in which the alkalinity of body fluids and tissues is abnormally high) may be produced (eg. sodium bicarbonate). Calcium ions may produce hypercalcemia (the presence in the blood of an abnormally high concentration of calcium). (Magnesium and aluminum cause precipitation of phosphate in the gastrointestinal tract and depletion of phosphorus. Finally antacids may affect the absorption of other drugs which may be administered along with antacids such as anticholinergics and antibiotics. These drugs may be adsorbed by the antacids. Antacids may also alter the pH of gut gastric contents thereby delaying the absorption of weak acids and speeding the absorption of basic drugs.

If dyspepsia (indigestion) leading to gas formation in the gut is present, use of a drug like methylpolysiloxane (dimethicone or simethicone) is necessary. Therefore because of the defects associated with the antacids as discussed in the previous paragraph, it is apparent that it is wiser to use a combination of antacids so that the defects can be minimized. For example magnesium hydroxide and aluminum hydroxide may be combined to balance the constipating effect of the latter with the laxative effect of the former. On this basis the following combinations are in regular clinical use.

1. Magnesium and aluminium hydroxides (Magaldrate)
2. Magnesium and aluminium hydroxides, dimethicone (Dioval Forte Tabs)
3. Magnesium and aluminium hydroxides, methylpolysiloxane (Gelusil MPS)
4. Aluminium hydroxide gel, magnesium trisilicate (Gelusil)
5. Aluminium hydroxide gel, Magnesium hydroxide, magnesium trisilicate (Gelusil M)
6. Mag.hydroxide, dried alu, hydroxide gel, methylpolysiloxane, sod. carboxymethyl cellulose (Digene gel).
MAGNESUM TRISILICATE, 2MgO, 3SiO₂, xH₂O

Test for Purity:

1. Arenic
2. Heavy metals
3. Chloride
4. Sulphate
5. Acid absorption
6. Alkalinity
7. Water soluble salts
8. Loss on ignition

Storage:

Since it is slightly hygroscopic in nature, store in a well closed container.

Medicinal and Pharmaceutical Uses:

Good Antacid. It does not produce any rebound acidity like Sodium bicarbonate. It does not interfere with peptic digestion.
**ALUMINIUM HYDROXIDE GEL, Al(OH)$_3$**

**Preparation:** For preparing this a hot solution of potash alum is added slowly to a hot solution of sodium carbonate and not vice versa. The precipitate of aluminium hydroxide is washed thoroughly with hot water till it is free from sulphate. The gel is then adjusted to the required volume with distilled water.

$$3\text{NaCO}_3 + 2\text{KAl(SO}_4)_2 + 3\text{H}_2\text{O} = 3\text{NaSO}_4 + \text{K}_2\text{SO}_4 + 2\text{Al(OH)}_3 + 3\text{CO}_2$$

Potash alum

If sodium carbonate solution is added to potash alum solution, then it is difficult to wash out the sulphate completely. Due to adsorption by aluminium hydroxide, some carbonate may be present.

**Assay:** An accurately weighed quantity of the gel is dissolved in concentrated hydrochloric acid by warming and diluted with water. To an aliquot a known excess of 0.05M sodium edetate is added and the mixture is neutralized with 1M sodium hydroxide using methyl red as indicator. This neutral mixture is warmed on a water bath for half an hour to ensure complexation of aluminium by sodium edetate. Hexamine is added and it is back titrated with 0.05M lead nitrate using xylenol orange as indicator.

This is a complexometric titration and the sodium edetate is allowed to complex aluminium under conditions which metals such as calcium and magnesium do not interfere. The excess of sodium edetate left after complexation with aluminium is over is back titrated with 0.05M lead nitrate solution. Hexamine is added to raise the pH to the alkaline side to facilitate the complexometric titration of the excess of EDTA with 0.05M lead nitrate.

**Test for purity**

1. pH
2. Arsenic
3. Heavy metals
4. Chloride
5. Sulphate
6. Neutralising capacity
7. Neutralising capacity

pH should be between 5.5 and 8.

**Storage:** Store in tightly closed containers in a cool place and avoid antacid and protective in treating peptic ulcers. It is also used in cases of acute hyperacidity.

**Medicinal and Pharmaceutical Use:** Antacid. It is used as an antacid and protective in treating peptic ulcers. It is also used in cases of acute hyperacidity.

**DRIED ALUMINIUM HYDROXIDE GEL, Al(OH)$_3$**

**Test for Purity, Storage and Uses:** Same as ALUMINIUM HYDROXIDE GEL.
**ALUMINIUM PHOSPHATE, AlPO₄**

It consist of mainly of about 80% of hydrated aluminum orthophosphate.

**Test for Purity:**

1. Acidity and alkalinity
2. Arsenic
3. Heavy metals
4. phosphate

**Storage:**

Store in a well closed container

**Medicinal and Pharmaceutical Analysis:**

Antacid, dried aluminium phosphate is used as a slow-actind antacid.
MAGNESIUM HYDROXIDE, Mg(OH)₂

Tests for Purity

1. Colour of Solution
2. Arsenic
3. Heavy metals
4. Chloride
5. Sulphate
6. Calcium
7. Iron
8. Soluble substances; substances insoluble in acetic acid
9. Loss on ignition.

Storage: Store in well Closed containers

Medicinal Use: Antacid and osmotic laxative.

MAGNESIUM HYDROXIDE ORAL SUSPENSION, Mg(OH)₂

Test for Purity, Storage and Uses: Same as MAGNESIUM HYDROXIDE.
MAGNESIUM CARBONATE, MgCO₃

Magnesium carbonate occurs in two forms, that is, heavy magnesium carbonate and light magnesium carbonate. They are both hydrated basic magnesium carbonate and differ only in the content of water of hydration (the heavy variety having 4H₂O and the light one with 3H₂O) and in the bulk density.

HEAVY MAGNESIUM CARBONATE, 3MgCO₃, Mg(OH)₂, 4H₂O

Test for Purity

1. Arsenic
2. Calcium
3. Copper
4. Iron
5. Heavy metals
6. Chloride
7. Sulphate
8. Soluble substance
9. Substances insoluble in acetic acid.

Storage:

Store in well closed container.

Medicinal and Pharmaceutical Uses:

Antacid and osmotic laxative. It is used as a clarifying agent or filtering agent for alkaline solutions (eg. Tolu Syrup). It is also used as an abrasive in some tooth powders.

LIGHT MAGNESIUM CARBONATE, 3MgCO₃, Mg(OH)₂, 3H₂O

Test for Purity, Storage and Uses: Same as Heavy Magnesium carbonate.
CALCIUM CARBONATE, CaCO₃

Preparation:
Calcium carbonate is prepared by passing carbon dioxide through lime water (calcium hydroxide solution).

\[ \text{Ca(OH)}_2 + \text{CO}_2 = \text{CaCO}_3 + \text{H}_2\text{O} \]

However calcium carbonate is usually prepared by mixing boiling sodium carbonate and calcium chloride solutions and the resulting precipitate is allowed to subside.

\[ \text{CaCl}_2 + \text{Na}_2\text{CO}_3 = \text{CaCO}_3 + 2\text{NaCl} \]

The precipitated calcium carbonate is collected on a calico filter, washed with boiling water till it is free from chloride and dried.

Assay:
This is a complexometric assay. The sample is dissolved in dilute hydrochloric acid and titrated against 0.05M EDTA. Towards the end of titration, sodium hydroxide solution and the indicator calcon mixture are added and the titration is continued till the change of colour from pink to full blue takes place at the end point. Calcon mixture consists of calon (mordant black) and freshly ignited anhydrous sodium sulphate. It gives a purple-red colour with calcium ions in alkaline solution.

Test for Purity
1. Substances insoluble in acetic acid
2. Magnesium and alkali metals
3. Barium
4. Iron
5. Arsenic
6. Heavy metals
7. Chloride
8. Sulphide
9. Loss on drying

Storage:
Since it is stable in air, it may be stored in a well closed container.

Medicinal and Pharmaceutical Uses
Antacid. Precipitated chalk is used as a dentifrice (tooth powder) Prepared chalk (made by the process of elutriation) is usually in preference to precipitated chalk as an antacid. Because of its mild, non-irritating nature, it is also used in the treatment of some forms of diarrhea.

Limestone is used in the manufacture of cement, lime, washing soda and glass.
SILICONE POLYMERS

Compounds that are formed as a result of the bonding of silicon, oxygen and carbon by condensation are known as silicones. One of the building blocks of silicones is dimethyldihydroxysilane, (CH3)2Si(OH)2

Two dimethyldihydroxysilane molecules undergo condensation with elimination of molecule of water. Repeated condensation of the molecules results in the formation of macro molecules (big molecules) or polymers. These are known as silicones. The Si-O-Si linkage in these molecules is very strong.

The general formula of silicones may be given as [(CH3)2SiO-]n. Silicones obtained by starting with dimethyldihydroxysilane are known as silicones oils.

The silicones are stable even at very high and very low temperatures and are water repellent. Silicones are used for making water-proof cloth and lubricants which do not freeze even at very low temperatures. Activated Dimethicone is official in I.P

ACTIVATED DIMETHICONE

Activated Dimethicone is activated polydimethylsiloxane. It is also known as Simethicone. It has the formula (CH3)2Si-[OSi(CH3)2]-CH3.

Test for Purity

1. Acidity
2. Heavy metals
3. Defoaming activity

Storage:

Store in tightly closed containers.

Medicinal and Pharmaceutical Use:

Protective and Defoaming agent. Dimethicone is used for preparing Dimethicone cream (formerly official in B.P.C). This cream is used to protect the skin against colostomy and discharges and to prevent bed sores and napkin-rash. (Colostomy is an operation to make an artificial opening so that the colon opens on to the anterior abdominal wall. This operation is done when there is an obstruction in the colon). Dimethicone is also included in antacid mixtures to treat cases of flatulence.
MAGALDRATE, $\text{Al}_5\text{Mg(OH)}_{21}(\text{SO}_4)_{2}\cdot x\text{H}_2\text{O}$

Magaldrate is a product of chemical combination of aluminium hydroxide and magnesium hydroxide along with the sulphates of aluminium and magnesium. It contains a variable amount of water of hydration and corresponds to the formula given above.

Test for Purity:

1. Arsenic
2. Heavy metals
3. Soluble chloride
4. Soluble sulphate
5. Sodium
6. Aluminum hydroxide
7. Magnesium hydroxide
8. Sulfate
9. Loss on drying
10. Microbial limits

Storage:

Store in well closed container.

Medicinal Use:

Antacid. It is used in the form of magaldrate oral suspension and magaldrate tablets.
**SALINE CATHARTICS:**

Saline cathartics are also called as osmotic laxative. They are not much absorbed in the gastrointestinal tract and exert an osmotic effect leading to the retention of large quantity of water and stimulates the intestinal motor activity leading to evacuation of the bowels.

**MAGNESIUM SULPHATE, MgSO$_4$.7H$_2$O (EPSOM SALTS)**

**Preparation:**

It may be prepared by one of the following methods:

By neutralizing hot, dilute sulphuric acid with magnesium oxide or magnesium carbonate.

\[ \text{MgO} + \text{H}_2\text{SO}_4 = \text{MgSO}_4 + \text{H}_2\text{O} \]

**B.P AND I.P Assay:**

This is a volumetric method and a complexometric assay.

It is assayed by titration of the substance against M/20 sodium edetate using mordant black mixture as indicator. A mixture of strong ammonia and ammonium chloride is used as buffer. The end point is the appearance of blue colour.

**Test for Purity:**

1. Clarity and colour of solution
2. Acidity and alkalinity
3. Arsenic
4. Iron
5. Heavy metals
6. Chloride
7. Sulphide
8. Loss on drying

**Storage:**

It is efflorescent, so in a well closed container.

**Medicinal and Pharmaceutical Uses:**

Cathartic (drastic purgative). Osmotic laxative.

This salt is very widely used as a saline cathartic. Neither the sulphate nor the magnesium ion is readily absorbed. Therefore water is retained in the intestine. Because of this the quantity and fluidity of the intestinal contents are increased. This mechanically stimulates peristalsis and the bowels are emptied. It is also used in the treatment of electrolyte deficiency.
SODIUM PHOSPHATE, \( \text{Na}_2\text{HPO}_4\cdot12\text{H}_2\text{O} \)

Test for Purity:

1. Clarity and colour of the solution
2. Arsenic
3. Heavy metals
4. Iron
5. Chloride
6. Sulphate
7. Reducing substances
8. Sodium dihydrogen phosphate
9. Water

Storage:

Since the salt is strongly efflorescent, store in tightly closed containers.

Medicinal and Pharmaceutical Uses:

Systemic acidifier and buffering agent. It is also a saline laxative and cathartic.
GENERAL PRINCIPLES FOR TEST FOR PURITY

1. **pH** - It is determined on a suspension of the substance in carbon dioxide free water, using pH meter.

2. **Loss on Drying** - It is determined by drying the sample in an oven at 105°C.

3. **Calcium** - detected by boiling the solution of the sample for 5 mins, the solution should be clear. If calcium is present, calcium salts are precipitated out.

4. **Copper** – it is limited by dissolving the substance in hydrochloric acid and making alkaline with dilute ammonia solution. No blue colour is produced.

5. **Acidity and alkalinity** – determination is based on acid base titration. Alkalinity determined by titrating an aqueous solution of the substance with 0.1N hydrochloric acid using methyl red as indicator. Acidity determined by titrating an aqueous solution of the substance with 0.1N sodium hydroxide using phenolphthalein as indicator.

6. **Arsenic** – it may be impurity during preparation.

7. **Lead** - it may be the impurity during preparation. It can be determined by atomic absorption spectrophotometry.

8. **Silver** – it may the impurity during the preparation. It can be limited by precipitating as silver chloride and the opalescence produced is compared with a silver standard solution similarly treated.

9. **Adsorption power (adsorbents)** – it can be determined by shaking the sample with a solution of methylene blue and allowing to settle. It is centrifuged and the supernatant liquid is diluted with water to a definite volume. The solution is not more intensely coloured than the standard solution of methylene blue. If the absorptive power of the sample is good, most of the dye would have been adsorbed by it and the colour of the solution will be less intense than that of the standard solution.
10. **Swelling power (Kaolin)** – determined by titrating the sample with water. The mixture should not flow. The sample should have enough swelling power to absorb all the water and swell making it difficult for the mixture to flow.

11. **Coarse particles (kaolin)** – determined by preparing a suspension of the sample in a solution of sodium pyrophosphate and withdrawing after 5 mins an aliquot of the suspension below 5 cm. This repeated again and again adding water till a definite volume has been collected, the remainder is evaporated to dryness on a water bath and the residue evaporated to dryness on a water bath and the residue dried at 105°C and weighed. The remainder of the suspension contains the coarse particles.

12. **Fine particles (kaolin)** – determined by preparing a suspension of the sample in water, withdrawing a definite volume. Evaporating to dryness and drying to constant weight at 105°C. The remainder of suspension is allowed to stand for 4 hrs, a second similar volume is withdrawn from a depth below 5 cm, evaporate and dry at 105°C. The weight of the residue from the second portion is NLT 70% of the weight of the residue from first portion.

13. **Loss on ignition** – a more liberal limit of 15% is permitted.

14. **Chloride** –

15. **Reducing substances** – tested by adding a dilute solution of potassium permanganate and heating on a water bath for five mins. The red colour should not be completely discharged.

16. **Neutralizing capacity** – determined by allowing the gel to remain in contact with 0.1 M hydrochloric acid at 37°C in a thermostatically controlled bath and measuring the pH at successive time intervals. Finally the concentration of acid is increased further and the neutralizing capacity is found out by finding out the remaining acid by titration with 0.1M sodium hydroxide after one hour.

17. **Microbial limits (for orally administered preparations)** – the total microbial count should not exceed 1000 per ml and 1 ml of the mixture should also be free from E.Coli.
since this is an orally administered preparation, these microbial limits are prescribed from the point of view of safety.

18. **Soluble alkalies** – to determine soluble alkalies, the mixture is filtered and the filtrate is diluted and titrated with 0.05M sulphuric acid, using methyl red as indicator. This limit test has been prescribed to ensure proper washing of the precipitate to eliminate the presence of excess of sodium hydroxide.

19. **Soluble salts** – determined by taking the filterate and adding sulphuric acid. It is evaporated to dryness on a water bath and ignited gently to constant weight. This limit test has also been prescribed to ensure proper washing of the precipitate in order to remove the soluble bye product.

20. **Sodium** – estimated by flame photometry.

21. **Aluminum** – by complexometric titration, sample dissolved in dilute hydrochloric acid and mixed with known excess of 0.05M disodium edetate, aluminium form complex with EDTA. The excess unreacted EDTA is found out by titrating it with 0.05M zinc sulphate after addition of ammonia buffer. Dithizone is used as indicator. Blank titration is performed.

22. **Magnesium** – complexometric titration. Sample + dilute HCl + ammonium chloride + triethanilamine + ammonia-ammonium chloride buffer (to maintain pH to 10 – only at this pH a stable complex of Magnesium and EDTA will be formed) and erichrome black T as indicator. Titratre against 0.05M EDTA. Blank titration performed.

23. **Acid absorption** – it can be determined by suspending the sample in 0.1N hydrochloric acid and allowing to stand in a water bath at 37 C for 2 hrs shaking frequently. Bromophenol solution is added to an aliquot of the supernanant liquid and it is titrated with 0.1M sodium hydroxide until blue colour is produced. This test is to determine the unneutralized 0.1M hydrochloric acid left behind.