

### 3.7 ANTI-MICROBIAL AGENTS

These are the agents which are used to destroy or inhibit the growth of pathogenic micro-organisms. They are of six types and their mechanism of action is given below:

1. Antiseptics
2. Disinfectant
3. Germicides
4. Bacteriostatic
5. Sanitizers
6. Sterilization

#### **Antiseptics:**

These are the agents which prevent sepsis by destroying or inhibiting the growth of micro-organism on the living tissues.

An ideal antiseptic should destroy bacteria, spores, fungi, viruses, or any other microorganism without causing any harm to the tissue of the host. Antiseptics can also be used in prevention to the hands of surgeons, dentists, nurses and others in their routine procedure.

#### **Disinfectant:**

These are the substances which prevent infection by the destruction of pathogenic microorganisms and are generally employed for inanimate objects and materials such as instrument, room, hospitals, home equipment etc. to get rid of microorganisms. All the disinfectants are bactericidal in nature.

**Germicides:**

These are the substances which kill the microorganisms; the more specific term which is used is bactericide, fungicide, virucide and amoebicide.

**Sanitizers:**

These are the disinfectants used to maintain public health standards and called as sanitizers. Sanitation is mainly concerned with cleaning or washing away the organism.

**Sterilization:**

Sterilization is the process of complete destruction of all living microorganisms, including bacterial spores. It can be done by physical methods (application of heat or radiation) or by chemical means (use of chemical disinfectant).

**Mechanism of Action:**

Generally inorganic compounds are not used as anti-infective for systemic infection (antibiotics are used), they are used only for topical application.

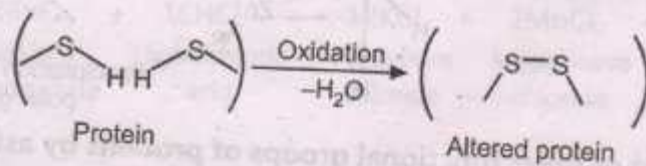
Inorganic compounds exhibit their action by:

1. Oxidation
2. Halogenation
3. Protein precipitation or binding

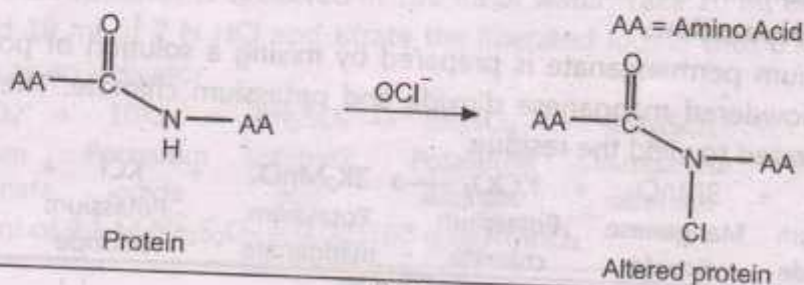
**Oxidation:**

Reducing group is present in most of the proteins and these groups are required for the growth and survival of microorganisms. These reducing groups are oxidized by oxidizing agents who alter the shape and confirmation of proteins and thereby alter its function and ultimately leading to the destruction of proteins.

Generally non-metal anions, peroxides, metal peroxides, permanganates, halogens act by this mechanism.

**Halogenation:**

Most of the enzymes are proteins in nature. Primary and secondary amide group present in protein at peptide linkage undergo chlorination with change in molecular shape and ultimately leading to the destruction of proteins. Generally hypochlorites or hypochlorites act by this mechanism.



**Protein Precipitation or Binding:**

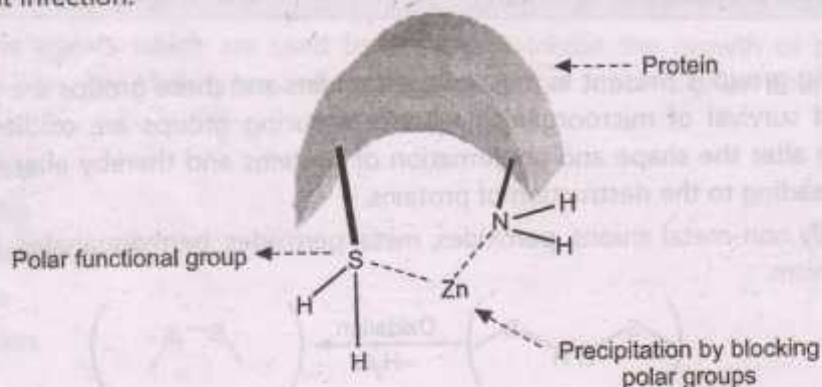
'Astringents' are the compounds which bring about protein precipitation and form a protective layer on the surface and hence stop bleeding by constricting the blood vessels. Astringents protect from external irritation and reduce cellular permeability and hence exert its local styptic and antiseptic action. Astringents are normally used in much diluted forms and are used topically to:

- ✓ Clean the face and prevent acne breakouts.
- ✓ Stop bleeding
- ✓ Haemorrhoids
- ✓ Relieve the discomfort and itching of insect bites.

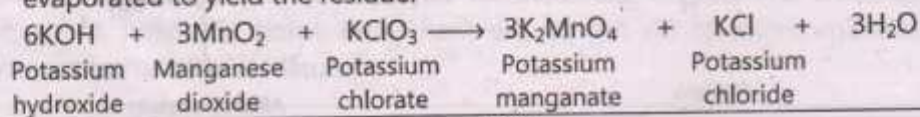
**Mechanism of Action:**

Transition metal cations have protein precipitation action and if a very dilute solution of such metal cation is used over a tissue, a mere surface action specially leading to "shrinkage" or "firming up" of the skin take place and this is called astringent action.

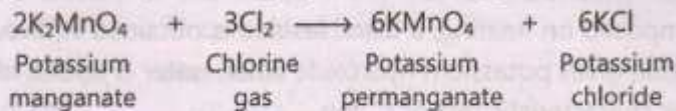
The metal would form complex with various polar groups present on the protein or an enzyme. This complexation of important functional groups at the action site of protein causes a drastic change in the properties of proteins. It hardens the epidermis and creates a barrier against infection.

**Sizing of polar functional groups of proteins by astringents****3.7.1 Potassium Permanganate****Molecular Formula:**  $\text{KMnO}_4$ **Molecular Weight:** 158.03 g**Synonym:** Permanganic acid.**Standards:** It contains not less than 99% and not more than 100.5% of  $\text{KMnO}_4$ .**Methods of Preparation:**

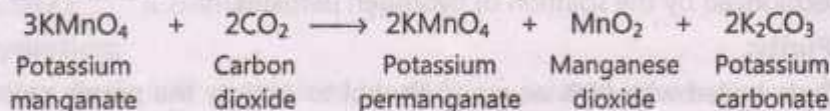
1. Potassium permanganate is prepared by mixing a solution of potassium hydroxide with powdered manganese dioxide and potassium chlorate. The mixture is boiled and evaporated to yield the residue.



2. By passing chlorine gas through potassium manganate solution.

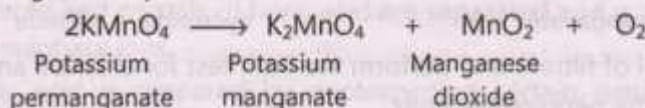


3. When carbon dioxide is passed in place of chlorine gas, then two-third of the manganate gets converted to potassium permanganate.

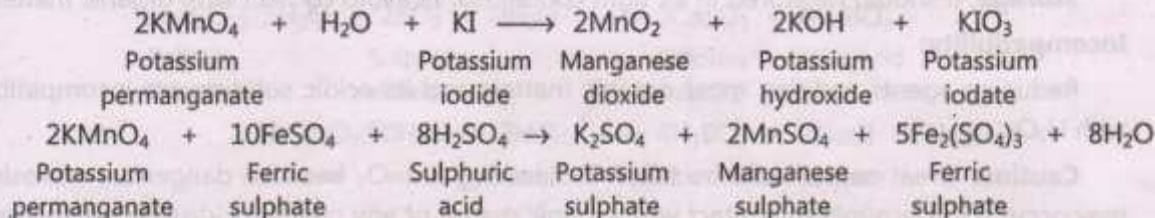


### Properties:

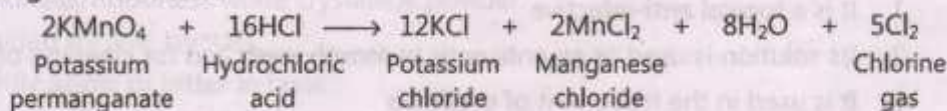
1. It occurs in the form of dark purple prismatic crystal with metallic lustre.
2. It is odourless but it tastes sweet and astringent.
3. It decomposes at higher temperature.



4. It is a powerful oxidizing agent.



5. When hydrochloric acid is added to the solution of potassium permanganate, chlorine gas is liberated.



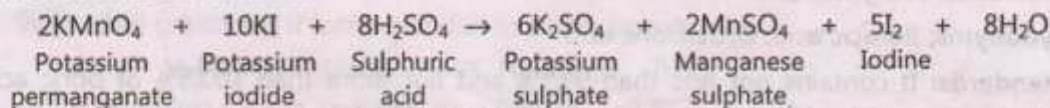
### Mode of Action:

Potassium permanganate releases the nascent oxygen i.e. [O], which by oxidative mechanism inhibits the actions of microorganism and their growth.

### Assay:

This assay is based on **iodometric type of redox titration**.

0.3 gm of the substance is dissolved in 100 ml of water. Take 20 ml of this solution, add 1 gm of KI and 10 ml of 2 N HCl and titrate the liberated iodine with 0.1 M  $\text{Na}_2\text{S}_2\text{O}_3$  using starch solution as an indicator.



Each 1 ml of 0.1 M  $\text{Na}_2\text{S}_2\text{O}_3 \equiv 0.003160$  g of  $\text{KMnO}_4$

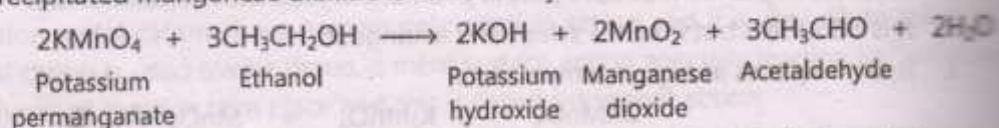
**Identification Tests:**

1. It gets decomposed on heating, a black residue is obtained with evolution of oxygen gas. The residue gives potassium hydroxide when water is added into it. The resulting solution gives characteristic test of  $K^+$  ion.
2. A solution of  $KMnO_4$  is acidified with sulphuric acid, and then heated to  $70^\circ C$ ; it gets decolorized by the solution of hydrogen peroxide.

**Test for Purity:**

$KMnO_4$  is boiled with 95% aqueous alcohol to destroy the purple colour so that colour should not interfere with the limit test.

The precipitated manganese dioxide is removed by filtration.



Take 20 ml of filtrate and perform the limit test for chloride and sulphate and the sample must comply the permissible limits.

**Storage:** It should be stored in air tight containers, to avoid contact with organic matter.

**Incompatibility:**

Reducing agents, iodides, most organic matters and its acidic solution are incompatible with  $H_2O_2$ .

**Caution:** Great care should be taken in handling  $KMnO_4$  because dangerous explosion may occur if it is brought in contact with organic matter or any rapidly oxidisable substance.

**Uses:**

1. It is a topical anti-infective.
2. Its solution is used as an antiseptic in mouth wash and for cleaning of ulcers.
3. It is used in the treatment of urethritis
4. Because of its oxidizing property, it is used as an antidote in many venoms, barbiturates, alkaloids etc.
5. Its solution is used in bath for eczema and acute dermatoses patients.
6. It is commonly used as an antiseptic in veterinary practices.

**3.7.2 Boric Acid**

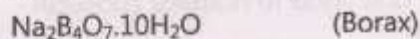
**Molecular Formula:**  $H_3BO_3$

**Molecular Weight:** 61.83

**Synonyms:** Boracic acid, Orthoboric acid

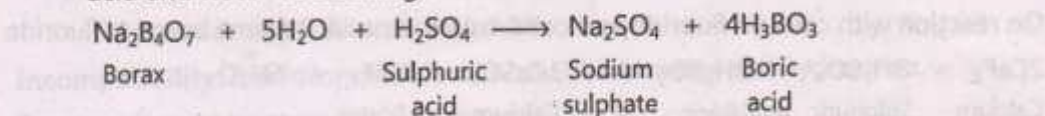
**Standards:** It contains not less than 99.5% and not more than 100.5% of boric acid with reference to dried substance.

Free boric acid occurs in sea water, many plants and nearly in all fruits. Although, its largest natural source occur in combined form.



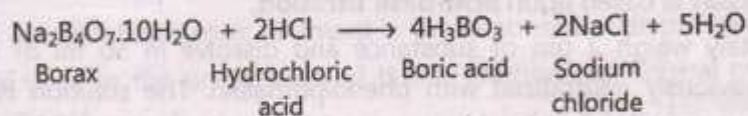
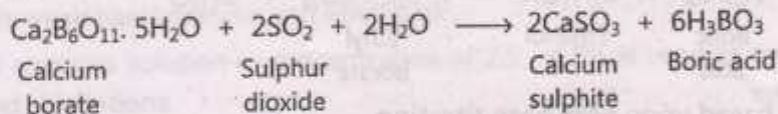
### Methods of Preparation:

1. In laboratory, boric acid is obtained by adding a mixture of concentrated sulphuric acid and water to a boiling solution of borax.



This solution is filtered and crystals of boric acid are separated and washed until they become free from sulphate ions.

2. Commercially boric acid is prepared by decomposing certain naturally occurring borates.

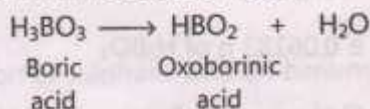


### Physical Properties:

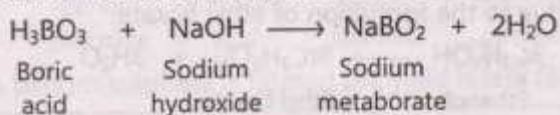
1. It is colourless, odourless white crystalline powder.
2. It is six sided triclinic crystals.
3. It is slightly acidic or bitter in taste.
4. It is soluble in water and alcohol.
5. It is stable in air and melting point is 171°C.
6. Its 1.9% solution in water is isotonic with serum

### Chemical Properties:

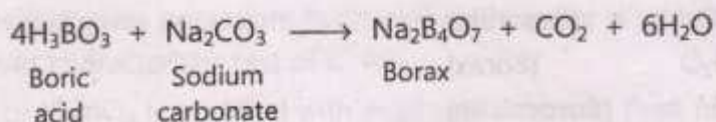
1. On heating to 100°C, it loses one molecule of water,



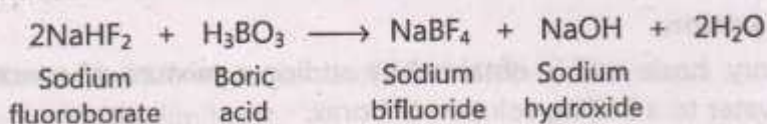
2. With alkali substance it forms salt due to its acidic nature.



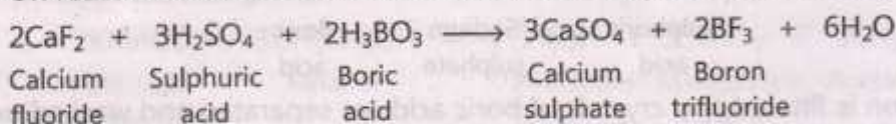
3. On reaction with sodium carbonate, it liberates carbon dioxide and borax ( $\text{Na}_2\text{B}_4\text{O}_7$ ) is formed.



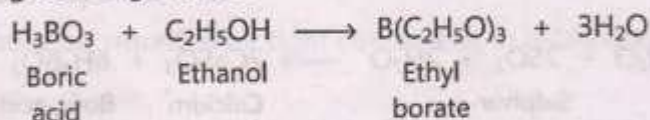
4. It reacts with alkali acids and fluorides to form sodium fluoborate ( $\text{NaBF}_4$ ).



5. On reaction with calcium fluoride and conc. sulphuric acid, it forms boron trifluoride.



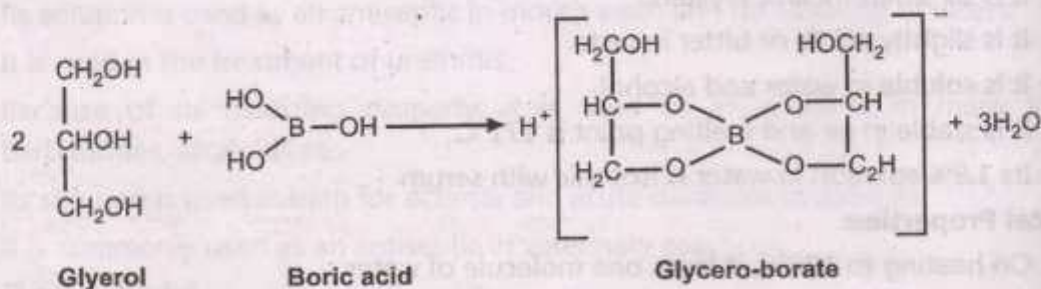
6. Ethanolic solution of boric acid when heated, gives ethyl borate. This ethyl borate burns with green edge flame.



**Assay:** Its assay is based upon acid-base titration.

Accurately weigh 2 gm of substance and dissolve in 50 ml of water and 100 ml of glycerol previously neutralized with phenolphthalein. The solution is titrated against 1 N NaOH using phenolphthalein solution as an indicator. At the end point, colour changes to red.

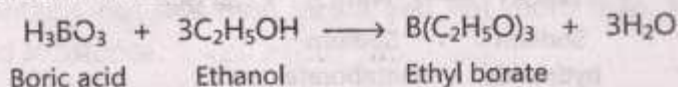
**Reaction:**



Each 1 ml of 1 N NaOH  $\equiv$  0.06183 g of  $\text{H}_3\text{BO}_3$

**Identification Tests:**

1. Solution of boric acid in alcohol in presence of few drops of conc.  $\text{H}_2\text{SO}_4$  burns with green border flame due to the formation of ethyl borate.



- An aqueous solution of boric acid on addition of HCl turns the turmeric paper to pink or brownish red, which upon being moistened with  $\text{NH}_3$  solution, changes to blue or greenish black.
- Aqueous solution of boric acid is faintly acidic.

**Test for purity:**

The sample is tested for the presence of following impurities:

- Arsenic should not be more than 10 ppm.
- Sulphate should not be more than 450 ppm.
- Heavy metals should not be more than 20 ppm.
- Loss on drying not more than 0.5%.

**Incompatibility:** It is incompatible with alkali carbonates and hydroxides.

**Storage:** It must be stored in air tight container in a cool place.

**Uses:**

- Boric acid is a local anti-infective and is used in the preparation of various dusting powders, antiseptic creams, ointments etc.
- It is weak bacteriostatic and fungistatic.
- Its aqueous solution in concentration of 2.5 - 4.5% is used as eye wash, mouth wash and skin lotions.
- It is used as emollient antiseptic ointment in the treatment of diaper rashes.
- Boric acid is used in the preparation of buffer solutions for topical medications to maintain acidic pH.

**Caution:** It is toxic if ingested, hence should not be used for internal preparations

**3.7.3 Hydrogen Peroxide**

**Molecular Formula:**  $\text{H}_2\text{O}_2$

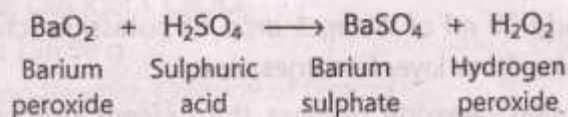
**Molecular Weight:** 34.01gm

**Standards:** Hydrogen peroxide solution 100 ml contains not less than 26%w/w and not more than 28%w/w of  $\text{H}_2\text{O}_2$ , corresponding to 100 times, its volume of available oxygen.

It is an aqueous solution of hydrogen peroxide, it contains not less than 6% w/w of hydrogen peroxide.

**Methods of Preparation:**

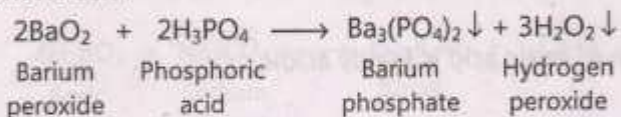
- It is prepared by the action of sulphuric acid on barium peroxide.



Insoluble barium sulphate is filtered off, yield is less (15-20%).

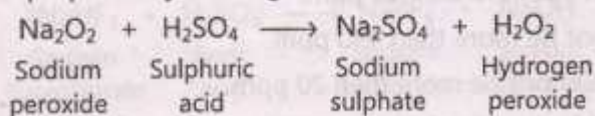


2. Hydrogen peroxide solution may be prepared by the reaction of barium peroxide with phosphoric acid.

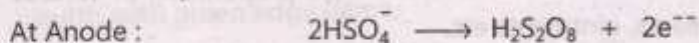
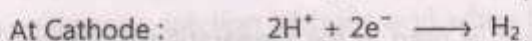
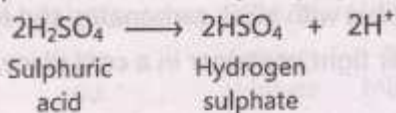


Barium phosphate is filtered.

3. It can also be prepared by treating sodium peroxide with sulphuric acid.

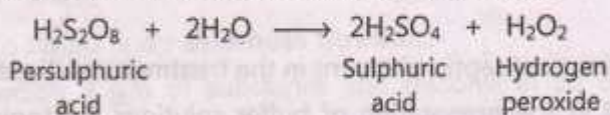


4. Most of the hydrogen peroxide now-a-days is prepared by electrolysis.



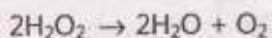
Persulphuric acid

Persulphuric acid is then distilled under vacuum with water.



### Physical Properties:

1. Hydrogen peroxide solution is colourless and odourless.
2. Its taste is slightly acidic.
3. It readily gets decomposed when come in contact with oxidisable organic metal.



The decomposition of hydrogen peroxide is promoted by catalysts Cu, Fe and Mn etc. while small quantity of sulphuric acid, phosphoric acid and alcohol retarded the decomposition of hydrogen peroxide.

4. It is a strong oxidizing agent and is miscible with water.

### Identification Tests:

1. When made alkaline and heated, it is decomposed with effervescence evolving oxygen.
2. To 1 drop of  $\text{H}_2\text{O}_2$ , add 20 ml of water, 1 drop of potassium chromate and 2 ml of solvent ether and shake. Ether layer becomes blue.

**Mode of Action:** Hydrogen peroxide releases the nascent oxygen i.e. [O], which by oxidative mechanism inhibits the action of microorganism and their growth.

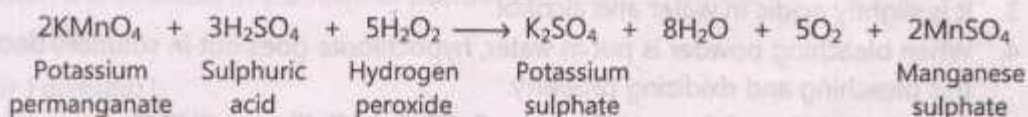
**Assay:**

Hydrogen peroxide ( $H_2O_2$ ) and potassium permanganate ( $KMnO_4$ ) both are oxidising agents and reduce each other with the evolution of gaseous oxygen. Hydrogen peroxide reduces  $KMnO_4$  solution and causes its decolourization. At the end point, excess drops of  $KMnO_4$  give pink colour, here  $KMnO_4$  itself act as an indicator.

This assay is based upon **volumetric titration method**, 10 ml of a sample is diluted to 250 ml in a volumetric flask with purified water.

To 25 ml of the solution, add 10 ml of 5 N  $H_2SO_4$ , then the whole content is titrated with 0.1 N  $KMnO_4$  solution until pink colour is obtained.

Each 1 ml of 0.1 N  $KMnO_4 \equiv 0.001701$  g of  $H_2O_2$



**Test for purity:** The sample of hydrogen peroxide is tested for the presence of organic stabilizers and non-volatile matter.

**Incompatibility:** It is incompatible with most organic substances and with alkalis, iodides, permanganates and other oxidisable matters.

**Storage:** It should be stored in light resistant black container in a cool place (temperature not exceeding  $50^\circ C$ ). The bottle should be closed with glass and suitable plastic caps.

**Uses:**

1. It is a strong antiseptic and destroys all pathogenic bacterias.
2. 6% solution of hydrogen peroxide is used as disinfectant. Its action is due to quick release of oxygen from it when it is applied to tissues.
3. It is also used for cleaning of cuts and wounds.
4. It is also used for removing ear wax.
5. It is an effective antidote for phosphorus and cyanide poisoning.
6. Its 1.6% solution is used as deodorant, gargles and mouth wash.
7. It is used for bleaching the hair.

**Formulation:** It is formulated in the form of solutions.

**3.7.4 Chlorinated Lime**

**Molecular Formula:**  $Ca(OCl)Cl$ ,  $CaOCl_2$

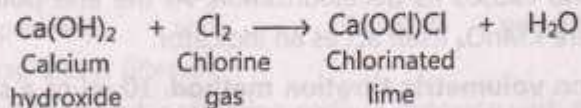
**Molecular Weight:** 136.98 g

**Synonyms:** Bleaching Powder, Chloride of lime.

**Standard:** Chlorinated lime should contain not less than 30% w/w of available chlorine.

**Method of Preparation:**

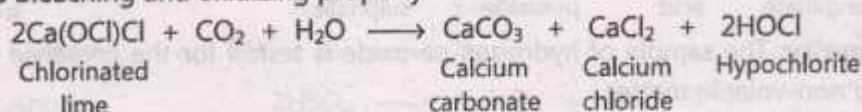
It is prepared by the action of chlorine on calcium hydroxide. Calcium hydroxide (slaked lime) is spread on the shelves in a suitable container. The chlorine gas is introduced at the top of chamber.



This process takes about 12-24 hrs.

**Properties:**

1. It is a dull white powder with characteristic odour.
2. When exposed to air, it absorbs moisture and gradually decomposed.
3. It is slightly acidic in water and alcohol.
4. When bleaching powder is put in water, hypochlorite goes out in solution, because of this bleaching and oxidizing property.

**Mode of Action:**

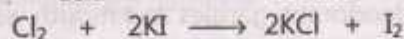
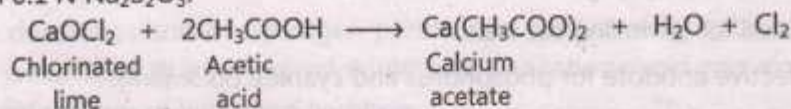
It works by chlorination of microorganism's protein, which ultimately leads to the destruction of protein and cell death.

**Identification Test:**

When the sample is treated with concentrated HCl, chlorine gas is evolved in large amount.

**Assay:**

**Principle:** Its assay is based on **redox titration method**. Chlorinated lime liberates the available chlorine as  $\text{Cl}_2$  gas by the action of acid. Then, this free chlorine is allowed to react with potassium iodide to liberate iodine, the quantity of liberated iodine is then estimated by titration with 0.1 N  $\text{Na}_2\text{S}_2\text{O}_3$ .



Sodium  
thiosulphate

Sodium  
tetrathionate

**Procedure:**

Take 4 g of chlorinated lime with small quantity of water and transfer it to 1 L flask and make up the volume to the mark. Measure 100 ml of this suspension and transfer in another flask. Then it is titrated with 3 gm KI solution, acidified with 5 ml acetic acid, the liberated iodine is titrated against 0.1 N sodium thiosulphate using starch solution as an indicator.

Each 1 ml of 0.1 N  $\text{Na}_2\text{S}_2\text{O}_3 \equiv 0.003545$  g of available chlorine.

**Test for purity:** It has been tested for its stability by heating it at 100°C for 2 hrs. It must not lose more than 3% w/w of available chlorine.

**Storage:** It should be stored in well closed container as it is slowly decomposed with the loss of chlorine.

**Uses:**

1. Chlorinated lime has the bactericidal action.
2. It is used as disinfectant in wounds.
3. It is used as cleansing agent for water closets (toilets), drains and effluents.
4. It is also used as an ingredient in the preparation of detergents.
5. It is powerful bleaching agent and is used in decolorizing most dyes.

**Formulation:** It is available in the form of powder and dilute solutions.

### 3.7.5 Iodine

**Molecular Formula:** I<sub>2</sub>

**Molecular Weight:** 126.9

**Standards:** It contains not less than 99.5% and not more than 100.5% of iodine.

Iodine compounds are very common in nature. Most of the sea-weeds contain iodine, perhaps the largest portion of iodine is contained in *Laminariadigitata*.

0.2% of iodine is present in the form of sodium iodate in crude *chile saltpetre*.

**Methods of Preparation:**

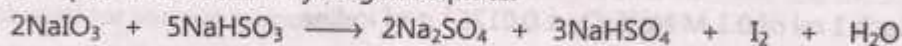
**1. From Sea weeds:** Iodine in the form of iodide is present in sea weeds such as *Laminariadigitata* and *Fucusvesiculosus*.

These sea weeds are dried and burnt. Their ash which is also called 'kelp' is extracted with water. This extract is purified to remove chlorides, sulphates, sulphides or thiosulphates. The purified extract is treated with exact amount of chlorine for the precipitation of iodine.



|                  |          |                    |        |
|------------------|----------|--------------------|--------|
| Sodium<br>iodide | Chlorine | Sodium<br>chloride | Iodine |
|------------------|----------|--------------------|--------|

**2. From Chile saltpeter:** Crude *Chile saltpeter* which is found in Chile (South America) contains sodium nitrate and sodium iodate. During its crystallization, sodium sulphate separate out as crystals whereas sodium iodate remains in mother liquor. Iodine is obtained by treating mother liquor with sodium hydrogen sulphite.



|                  |                             |                    |                             |        |       |
|------------------|-----------------------------|--------------------|-----------------------------|--------|-------|
| Sodium<br>iodate | Sodium<br>hydrogen sulphite | Sodium<br>sulphate | Sodium<br>hydrogen sulphate | Iodine | Water |
|------------------|-----------------------------|--------------------|-----------------------------|--------|-------|

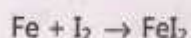
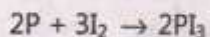
**Properties:**

1. Iodine occurs as bluish black small crystals with metallic luster.
2. It possesses a different irritating odour and bitterly pungent in taste.
3. It is volatile at room temperature and its vapour attack both cork and rubber.

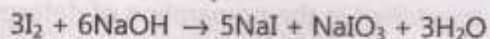
- It is slightly soluble in water, but insoluble in alcohol, ether, chloroform.
- At higher temperature, the density of iodine decreases as it dissociates.



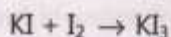
- It reacts directly with some non-metals and with heavy metals.



- With an alkali, iodine reacts to form an iodide and iodate with heat.

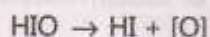
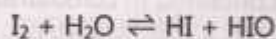


- Potassium iodide is able to dissolve large quantity of iodine due to the formation of  $I_3^-$  ions.



#### Mode of Action:

Iodine in aqueous solution act as a mild oxidising agent which is mediated through the formation of hypiodous acid (HIO), which further release the nascent oxygen [O], which dose the oxidation of microorganism's proteins.

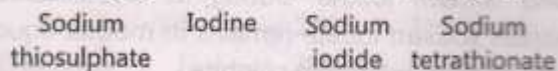
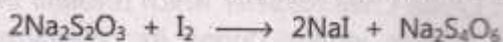


#### Identification Tests:

- When small amount of sample is ignited in the test tube, it gives violet colour vapours which condense at the internal surface of the test tube.
- Add a little sample in the solution of KI and starch, a deep blue colour is produced which disappear on heating but reappear on cooling.

**Assay:** Its assay is based on direct **iodometric titration**.

Iodine is weighed in iodine flask containing 1 gm of potassium iodide of 2 M acetic acid and 50 ml of water. Titrate it with 0.01 N sodium thiosulphate using starch as an indicator.



Each 1 ml of 0.1 M  $Na_2S_2O_3 \equiv 0.01263$  g of iodine.

**Test for Purity:** The sample is tested for the presence of impurity like chloride, bromide, cyanide and non-volatile material.

**Incompatibility:** It is incompatible with alkalies, and alkali carbonates.

**Storage:** It should be stored in earthenware container having waxed bungs or in ground glass stoppered bottles.

**Uses:**

1. It is topical anti-infective, has a powerful bactericidal action.
2. It is also used as a local germicide.
3. Iodine ointment is generally used as counter-irritant and disinfectant.
4. Iodine is an essential element for human body, deficiency of iodine leads to the development of goiter.

**3.7.6 Preparations of Iodine****Povidone Iodine**

Povidone Iodine is a complex of iodine and povidone (polymer) also known as Polyvinylpyrrolidone (PVP) and iodopovidone. It is an antiseptic used for skin disinfection before and after surgery and on the hands of the healthcare providers. It may also be used for minor wounds. It may be applied to the skin as a liquid or a powder. This complex contain from 9% to 12% available iodine. It works by releasing iodine which results in the death of a range of microorganisms. It belongs to the class of 'iodophore' class of compounds. Iodophores are the complex of iodine, which act as carrier and liberate iodine wherever it is required (solubilising agents).

**Physical Properties:**

1. The complex is yellowish-white brown amorphous powder.
2. It is soluble in water and alcohol.
3. Povidone-Iodine solution is a transparent liquid having a reddish brown colour.
4. Its non-irritating effects on tissues, low oral toxicity, its water solubility and its low iodine vapour pressure makes it superior to iodine solutions.
5. Povidone-Iodine solutions are non-staining and can be washed clear from the skin and clothing.

**Lugol's Iodine**

Lugol's iodine was first made in 1829 by the French physician Jean Lugol. It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system. Lugol's Iodine is a liquid make up of two parts potassium iodide (KI) for every one part elemental iodine ( $I_2$ ) in water. Lugol's Iodine is available as a generic medication and over the counter.

**Lugol's Iodine**, also known as aqueous iodine and strong iodine solution, is a medication and disinfectant used for various purposes:

1. It is used to treat thyrotoxicosis prior to surgery.
2. It helps to protect the thyroid gland from harmful effects of radioactive iodine and to treat iodine deficiency.
3. When applied to the cervix, it is used in screening for cervical cancer.
4. As a disinfectant, it may be applied to small wounds such as a needle stick injury.
5. A small amount may also be used for emergency disinfection of drinking water.

### Potassium Iodide

Potassium iodide is a chemical compound, medication, and dietary supplement. As a medication it is used to treat hyperthyroidism, in radiation emergencies, and to protect the thyroid gland when certain types of radiopharmaceuticals are used. In the developing world it is also used to treat skin sporotrichosis and phycomycosis. As a supplement it is used in those who have low intake of iodine in the diet. It is given by mouth.

Potassium iodide has the chemical formula KI. Commercially it is made by mixing potassium hydroxide with iodine.

**Potassium iodide solution** (100 g in 100 ml solution) is used as iodine supplement, an expectorant 0.3 ml, *sporotrichosis* treatment, 0.6 ml thrice a day. The amount increases each day by 0.06 ml at each dose until maximum tolerance is reached. The treatment should be continued for 6-8 weeks for complete cure.

### Exercise

#### (A) Short Answer Type Questions:

1. Write a note on gastrointestinal tract agents in detail.
2. What are antacids? Classify them with suitable examples.
3. Write preparation, uses and assay of : (a)  $\text{H}_2\text{O}_2$  (b)  $\text{KMnO}_4$
4. Why antacids are given in combination always, explain with some marketed preparations.
5. Write a detail note on:  
(a) Bentonite as cathartic  
(b) Magnesium hydroxide mixture as antacid

#### (B) Long Answer Type Questions:

1. Discuss various mechanisms of action of antimicrobial agents with suitable examples.
2. Give preparation, properties, uses and assay of the following compounds:  
(a) Sodium bicarbonate (b) Chlorinated lime
3. Write a detail note on:  
(a) Acidifying agents (b) Marketed preparations of iodine
4. Define cathartics and give classification of cathartics with example and also give a detail note on Epsom salt.
5. Write complete chemistry of the following compounds:  
(a) Ammonium chloride (b) Boric acid

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