ANTIMICROBIAL AGENTS

An antimicrobial is a chemical agent that is used to kill or inhibit the growth of pathogenic microorganisms such as bacteria, fungi and protozoa. They are normally ineffective in the sporing state of microorganisms. These agents are either microbicidal or microbiostatic.

Classification:

It is broadly classified into six categories based on its mode of action.

- Antiseptic
- Disinfectant
- Germicides
- Bacteriostatic
- Sanitizers

Antiseptic

These are the type of antimicrobial agents that are applied to living tissue/skin to reduce the possibility of infection, sepsis or putrefaction. They act either by inhibiting multiplication and metabolic activities of microorganisms or by killing microorganisms.

An ideal antiseptic should destroy bacteria, spores, fungi, viruses or other microorganisms without causing any harm to the host tissue.

They must be safe to be applied on almost all body tissues and can be used in the preparation of mouthwashes, soaps, deodorants, throat and nasal sprays, and vaginal douches. Generally, antiseptics are protein denaturants and act on bacterial enzymes.

Disinfectant

These substances kill the pathogenic microorganisms to prevent infection. Disinfectants are usually applied on non-living objects. All the disinfectants are bactericidal in nature.

These are used to maintain hygienic conditions in home and hospitals. Disinfection can also be achieved through heat, irradiation or chemicals. Their microbial action is non-selective in nature and therefore they also destroy non-pathogenic microbes.

All disinfectant solutions undergo degradation, if stored for prolonged time period or at elevated temperature. Few chemical disinfectants are known to cause irritation or corrosion to the skin or tissues.

Germicides

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

These agents act by oxidation of protoplasm by denaturation of bacterial enzymes and their proteins.

Bacteriostatic

These are used to inhibit bacterial growth. These drugs or agents do not kill but hamper bacterial growth.

Sanitizers

Sanitizers are substances used to reduce or eliminate the microorganisms on surfaces, objects, or skin. They play a crucial role in preventing the spread of infectious diseases. They are used to maintain general public health standards. There are two main types of sanitizers. They are hand Sanitizers and surface sanitizers.

Mechanism of Action

Following three mechanisms are generally employed to exhibit antimicrobial action of inorganic compounds.

- Oxidation
- Halogenation
- Protein Precipitation

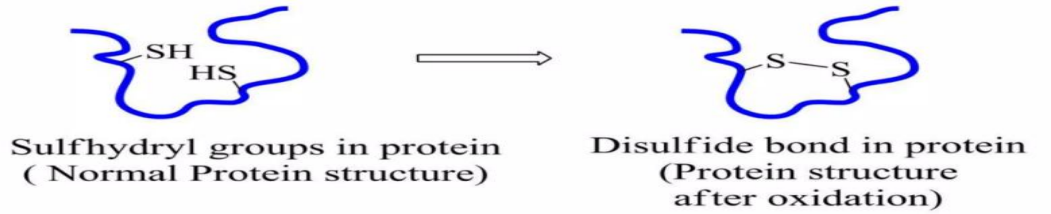
Oxidation

Different compounds belonging to the category of peroxides of peroxyacids, oxygen liberating like permanganate and certain oxo-halogen anions exhibit this mechanism.

Ex. Potasssium permanganate, Hydrogen peroxide

These agents oxidize the active functional groups present in proteins or enzymes important for the growth and survival of microbes. It results to alteration in configuration of bacterial protein and hence affects their functions.

For example, a free sulfhydryl group is necessary for activity of a variety of proteins and enzymes. However, this free nature of sulfhydryl group is destroyed through oxidation and results in the formation of a disulphide bond.



Sulfhydryl groups in protein (Normal Protein structure)

Disulfide bond in protein (Protein structure after oxidation)

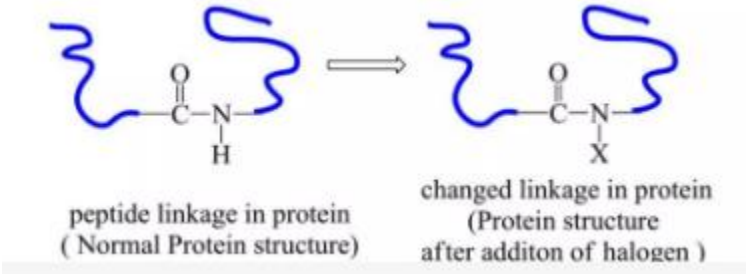
Halogenation

Compounds liberating chlorine and hypochlorite or iodine act by this mechanism.

Ex. Chlorinated lime, Iodine, Povidone Iodine

These agents commonly act on peptide linkage and affect its capabilities and properties. A damage to a functional group present in protein results in microbial death.

Enzymes are proteinaceous compounds and a protein molecule is composed of a long chain of amino acids joined by a peptide (-CONH-) linkage.



peptide linkage in protein (Normal Protein structure)

changed linkage in protein (Protein structure after additon of halogen)

The hydrogen-bonding responsible for proper orientation of the protein molecule is altered due to the substitution of halogen on the nitrogen of peptide linkage. Thus, proper functions of the protein are not carried out.

Protein precipitation

Most of the metal ions act by protein binding or protein precipitation. ex. Silver nitrate. The polar group of protein (act as ligands) and metal ions (act as Lewis acid) determines the nature of interaction with protein. However, the resultant complex may be strong chelate that may inactivate the protein.

This action is usually non-specific since protein precipitants are unable to differentiate between protein of microbe and that of the host. Germicidal action is only attained at such ionic concentration that largely restricts the reaction to the parasite cell. Depending on the concentration and extent of reaction actions like astringent, irritant, corrosive or even caustic action may be seen on the host.

Potassium Permanganate

Molecular Formula: $KMnO_4$

*Molecular Weight:*158 g/mol

Synonymn: Permanganate of potash, Condy's crystals

IP limit: Potassium permanganate contains not less than 99.0% and not more than 100.5% of $KMnO_4$.

Preparation:

Manganese dioxide is fused with excess of potassium hydroxide in the presence of oxidizing agent such as potassium chlorate.

$$\mathbf{6KOH + 3MnO_2 + KClO_3 \rightarrow 3K_2MnO_4 + KCl + 3H_2O}$$

The green residue consisting of potassium manganate is extracted with water. From this potassium permanganate is made by any one of the following three methods:

1. By passing carbon dioxide:

$$\mathbf{6K_2MnO_4 + 2CO_2 \rightarrow 2KMnO_4 + MnO_2 + 2K_2CO_3}$$

2. All the manganate may be converted into permanganate by passing chlorine through the solution.

$$\mathbf{2K_2MnO_4 + Cl_2 \rightarrow 2KMnO_4 + 2KCl}$$

3. By electrolyzing a warm solution of the manganate.

$$\mathbf{2K_2MnO_4 + 2H_2O \rightarrow KMnO_4 + 2KOH + H_2}$$

Physical Properties

- It is found in the form of dark purple coloured monoclinic prism.
- It is odourless.
- Density of potassium permanganate is around 2.7 g/cm^3.
- Soluble in water
- Freely soluble in boiling water.
- Solution of potassium permanganate is sweet and tastes like astringent.
- It is almost opaque by transmitted light and having a blue metallic lusture by reflected light.

Chemical Properties

1. On heating potassium permanganate at 240^0C very pure oxygen is evolved and a black powdery residue of potassium manganate and manganese dioxide is left.

$$\mathbf{2KMnO_4 \rightarrow K_2MnO_4 + MnO_2 + O_2}$$

2. Potassium permanganate acts as an oxidizing agent because it is able to produce nascent oxygen in solution.

$$\mathbf{2KMnO_4 + H_2O \rightarrow 2MnO_2 + 2KOH + 3(O)}$$

3. Iodine is liberated from potassium iodide by an acid solution of potassium permanganate.

$$\mathbf{2KMnO_4 + 10KI + 8H_2SO_4 \rightarrow 6K_2SO_4 + 2MnSO_4 + 5\ I_2 + 8H_2O}$$

Uses

- It is used an antimicrobial agent with antibacterial and antifungal properties.
- It is used as an antiseptic.
- In low concentrations it is used for cleansing of wounds.
- It is used as an oxidizing agent.
- It is used as an antidote in barbiturate poisoning, chloral hydrate poisoning and alkaloidal poisoning.
- Used in the treatment of urethritis

Boric Acid

Molecular Formula: H_3BO_3

Molecular Weight: 61.83 g/mol

Synonymn: Boracic acid, orthoboric acid

IP limit: It contains not less than 99.5% and not more than 100.5% of boric acid.

Preparation:

It is prepared by treating hot concentrated solution of borax with hydrochloric acid or sulphuric acid. The boric acid is allowed to crystallize after filtration.

$$\mathbf{Na_2B_4O_7 + H_2SO_4 + 5H_2O \rightarrow 4H_3BO_3 + Na_2SO_4}$$

$$\mathbf{Na_2B_4O_7 + 2HCl + 5H_2O \rightarrow 4H_3BO_3 + 2NaCl}$$

Physical properties

- Boric acid occurs in three forms
    1. Transparent, smooth, pearly scales
    2. Triclinic crystals
    3. A white, bulky powder
- It is odourless
- It is slightly acidic or bitter in taste.
- It is soluble in water and alcohol.
- It is stable in air.
- Its melting point is 171^0C.
- Its boiling point is 300^0C.

Chemical properties

1. When boric acid is heated at 100^0C or slightly above it is converted to metaboric acid by loss of a water molecule.

$$\mathbf{H_3BO_3 \rightarrow HBO_2 + H_2O}$$

2. With sodium hydroxide it forms sodium metaborate due to its acidic nature.

$$\mathbf{H_3BO_3 + NaOH \rightarrow NaBO_2 + 2H_2O}$$

3. On reaction with sodium carbonate it liberates carbon dioxide and borax is formed.

$$\mathbf{4H_3BO_3 + Na_2CO_3 \rightarrow Na_2B_4O_7 + CO_2 + 6H_2O}$$

Uses

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

Hydrogen peroxide

Molecular Formula: H_2O_2

Molecular Weight: 34.01 g/mol

Synonymn: Dioxidane; Oxidanyl; Perhydroxic acid

Standard: Hydrogen peroxide 100ml solution contains not less than 26.0%w/w and not more than 28%w/w of H_2O_2 corresponding to about 100 times its volume of available oxygen.

Preparation:

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

$$\mathbf{BaO_2 + H_2SO_4 \rightarrow H_2O_2 + BaSO_4}$$

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

$$\mathbf{2\ BaO_2 + 2\ H_3PO_4 \rightarrow Ba_3\ (PO_4)_2 + 3\ H_2O_2}$$

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

$$\mathbf{Na_2O_2 + H_2SO_4 \rightarrow Na_2SO_4 + H_2O_2}$$

Physical properties

- Hydrogen peroxide solution is colourless and odourless.
- It taste is sligthly acidic.
- It is a strong oxidizing agent.
- It is miscible with water.

Chemical properties

1. Decomposition: Pure hydrogen peroxide decomposes slowly, but when heated at 100^0C it liberate oxygen.

$$\mathbf{H_2O_2 \rightarrow 2\ H_2O + O_2}$$

2. Oxidation properties: Hydrogen peroxide is a strong oxidising agent and react many organic materials.

$$\mathbf{PbS + 4\ H_2O_2 \rightarrow PbSO_4 + 4\ H_2O}$$

3. Reduction properties: Hydrogen peroxide behaves as reducing agents towards other oxidizing agents.

$$\mathbf{Ag_2O\ + H_2O_2 \rightarrow 2\ Ag + 2\ H_2O + O_2}$$

Assay

Principle:

This is a redox titration. Both hydrogen peroxide and acidified potassium permanganate are oxidizing agents, which reduce each other and liberate gaseous oxygen. Potassium permanganate act as indicator and produces pink colour at the end point.

$$2KMnO_4 + 3H_2SO_4 + 5H_2O_2 \rightarrow K_2SO_4 + 8H_20 + 5O_2 + 2MnSO_4$$

Procedure

Accurately weighed amount of sample is diluted with water and dilute sulphuric acid is added to the above solution. The resultant solution is titrated with potassium permanganate solution until a faint pink colour is produced.

Uses

- Hydrogen peroxide used as an antiseptic, germicidal and disinfectant.
- It is used for removing ear wax.
- It is an effective antidote for phosphorus and cyanide poisoning.
- It is used for bleaching the hair.
- Its 1.6% solution is used as deodorant, gargles and mouth wash.
- Hydrogen peroxide is also used for tooth whitening.

Chlorinated Lime

Molecular Formula: $Ca(ClO)_2$

Molecular Weight: 143.0 g/mol

Synonymn: Hypochlorous acid, Bleaching powder, Calcium oxychloride, Calcium hypochlorite

Standard: Chlorinated lime contains not less than 30 %w/w available chlorine.

Preparation:

1. Chlorinated lime is produced industrially by treating calcium hydroxide with chlorine gas.

$$2\ Cl_2 + 2\ Ca(OH)_2 \rightarrow Ca(ClO)_2 + CaCl_2 + 2\ H_2O$$

Physical properties

- It is a dull white powder with characteristic odour.
- On exposure to air it becomes moist and rapidly decomposes to release Hypochlorous acid.
- Its solubility in water is 21g/100 mL and it reacts with the water when dissolved.
- The melting point of calcium hypochlorite is 100°C
- Its boiling point is 175°C.
- It is highly soluble in alcohol.

Chemical properties

1. Calcium hypochlorite reacts with carbon dioxide to form calcium carbonate and release dichlorine monoxide.

$$Ca(ClO)_2 + CO_2 \rightarrow CaCO_3 + Cl_2O$$

2. Calcium hypochlorite reacts with hydrochloric acid to form calcium chloride, water and chlorine.

$$Ca(ClO)_2 + 4\ HCl \rightarrow CaCl_2 + 2\ H_2O + 2\ Cl_2$$

Assay

Principle

This is an iodometric titration. In the presence of acid, the chlorinated lime liberates the available chlorine. Iodine is produced when the liberated chlorine reacts with potassium iodide. The quantity of iodine produced is estimated by titrating it with sodium thiosulphate.

$$Ca(ClO)_2 + 2CH_3COOH \rightarrow (CH3COO)_2Ca + H_2O + Cl_2$$
$$2KI + Cl_2 \rightarrow 2KCl + I_2$$
$$2Na_2S_2O_3 + I_2 \rightarrow Na_2S_4O_6 + 2NaI$$

Procedure

An aqueous suspension of the substance is treated excess of potassium iodide and acidified with acetic acid. Acetic acid liberates chlorine from chlorinated lime. The liberated chlorine displaces an equivalent amount of iodine from potassium iodide. The liberated iodine is titrated with 0.1 N sodium thiosulphate using starch mucilage as indicator. The end point is the colour of solution changes from violet to colourless.

Uses

- Calcium hypochlorite has rapid bactericidal action. It kills most of bacteria, some fungi, yeast, algae, viruses and protozoa.
- Calcium hypochlorite is commonly used to sanitize public swimming pools.
- Surgical chlorinated soda solution (Dankin's solution) is employed for wound disinfectant.
- Mixture of chlorinated lime and boric acid solution (Eusol) used as disinfectant lotions and wet dressings.
- In wastewater treatment plants, chlorinated lime is used to disinfect sewage and control the growth of harmful microorganisms

Iodine and its preparations

Iodine

Molecular Formula: I_2

Molecular Weight: 126.9 g/mol

Preparation:

1. Common methods of preparing Iodine: Iodine is formed by adding liquid bromine into an aqueous solution of potassium iodide or passing chlorine gas.

$$\mathbf{2KI + Br_2 \rightarrow I_2 + 2KBr}$$

$$\mathbf{2KI + Cl_2 \rightarrow I_2 + 2KCl}$$

2. From Sea weeds: Iodine in the form of iodide is present in sea weeds. 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.

$$\mathbf{2NaI + Cl_2 \rightarrow I_2 + 2NaCl}$$

Physical properties

- Iodine occurs as greyish black small crystals with metallic luster.
- It possesses irritating odour and bitterly pungent in taste.
- It is volatile at room temperature.
- It is stored in bottles and glass stoppers. This is because the vapour attacks both cork and rubber.
- It melts at 114^0C but sublimes at temperature below its melting point.
- It is slightly soluble in water, but more soluble in alcohol.

Chemical properties

1. Iodine reacts with iron to convert it to ferrous iodide.

$$\mathbf{Fe + I_2 \rightarrow FeI_2}$$

2. With alkali iodine gives the corresponding iodides and iodates on heating.

$$\mathbf{I_2 + 6NaOH \rightarrow 5NaI + NaIO_3 + 3H_2O}$$

Uses

- It is a topical anti infective agent, has bactericidal action.
- It is used as germicide.
- Iodine ointment is generally used as counter irritant and disinfectant.

- Iodine is an essential element for human body, deficiency of iodine leads to development of goiter.

Preparations of Iodine

1. Povidone Iodine

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

Physical Properties:

- The complex is yellowish-white brown amorphous powder.
- It is soluble in water and alcohol.
- Povidone-lodine solution is a transparent liquid having a reddish brown colour.
- Its non-irritating effects on tissues, low oral toxicity, its water solubility and its low iodine vapour pressure make it superior to iodine solutions.
- Povidone-lodine 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 lodine is a liquid make up of two parts Potassium iodide (Kl) for every one part elemental iodine 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.
- It is used to treat thyrotoxicosis prior to surgery.
- It helps to protect the thyroid gland from harmful effects of radioactive iodine and to treat iodine deficiency.
- When applied to the cervix, it is used in screening for cervical cancer.

- It is used as a disinfectant, it may be applied to small wounds such as a needle stick injury.

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 thyroid gland when certain types of radiopharmaceuticals are used.
- 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 in oral route.
- Potassium iodide has the chemical formula KI. Commercially it is made by potassium hydroxide with iodine.

Potassium Iodide Solution (100 gm in 100ml solution)

- It is used as Iodine supplement.
- It is used as an expectorant.
- It is also used in Sporotrichosis treatment.

Mandl's paint

- It contains 1.25%w/v solution of iodine in Glycerin. Glycerin is used to hold the iodine in the applied area (throat).
- Mandl's Paint is used as throat paint for the treatment of laryngitis, pharyngitis, sore throat and tonsils.
- It can be used on sore throats and ulcers to ease them.