

4.4 POISON AND ANTIDOTES

A poison may be defined as any substance administered in whatever way (by mouth, injection, inhalation, skin, mucous membrane) produces ill health, disease or death.

The diagnosis of poisoning is often difficult. But acute poisoning may be accidental, occupational, suicidal or criminal.

Self-medication is also a major cause of drug poisoning.

The poisoning either accidental or intentional requires immediate support and symptomatic management to avert any threat to life. The perfect management and treatment solely depends upon the identification of ingested poison or corrosive substance so that specific antidote which counteract that poison, can be used.

Classification of Poisoning:

1. **Intentional poisoning:** A person taking or giving a substance with intention of causing harm to that person. e.g. Suicide, assault.
2. **Unintentional poisoning :** If the person taking or giving a substance without knowing its toxic effects. e.g. Accidentally.
3. **Undetermined:** When the distinction between intentional and unintentional is not clear. e.g. Poisoning due to insecticides or pesticides.

Other Causes:

1. Most common cause of poisoning is heavy metals which occur by metallic contamination of food and water by leaching process.
2. Due to overdose of drug inhalation.
3. Intentionally cyanide poisoning.

Signs and Symptoms of Poisoning:

1. Reduced breathing rate
2. Nausea, vomiting and diarrhoea
3. Increased or decreased heart rate.
4. Dilated or shrunken pupils.
5. Muscle cramps
6. Partial consciousness.

Heavy Metal Poisoning:

Heavy metal poisoning occurs due to intake of salts of arsenic, lead, mercury, iron and cadmium. Depending upon the content and type of heavy metal, toxic effect can be seen in the future.

Treatment:

Activated charcoal is given initially for absorbing heavy metal or poisons. Then the emetics are given to eliminate any poison left in the stomach.

Some inorganic compounds precipitate the heavy metals and prevent their absorption in blood circulation. e.g. Activated charcoal, light kaolin, copper sulphate, magnesium sulphate etc.

Cyanide Poisoning:

Cyanide poisoning may occur by inhalation of fumes of hydrocyanic acid (HCN), ingestion of inorganic cyanide salt or cyanide releasing substances like cyanamide, cyanogen chloride, peach of apricot, bitter almond, photographic chemical and silver polishes.

Consumption of 300 mg of potassium cyanide may cause death.

Physiology of Cyanide in body:

Cyanide readily combines with ferric ion of cytochrome oxidase, which prevents the electron transfer and stops the cellular respiration or oxidation-reduction reaction.

Treatment:

Sodium nitrite and Sodium thiosulphate injections both the antidotes one by one are administered for the treatment of cyanide poisoning.

Antidotes

Antidotes are the substances which react specifically with the ingested poison or toxic substance or with potent drugs in case of overdose.

They are used to neutralize the effect of poison in the body.

Classification : According to their mechanism of action, they are classified as:

- 1. Physiological Antidotes:** They are also called antagonists. They produce the effect opposite to that of the poison. They are used after some of the poison is absorbed in the circulation. e.g. Sodium nitrite (used in cyanide poisoning), Atropine and Physostigmine are two antidotes for each other.
- 2. Chemical Antidotes:** They react by combining with the poison and change its chemical nature by converting the poison into inactive or harmless compounds. e.g. Sodium thiosulphate (which convert the systemic toxic cyanide into non-toxic thiocyanate), EDTA (chelating agent for heavy metal poisoning).
- 3. Mechanical Antidotes:** They act by preventing the absorption of poison into the body or expel out the poison by emesis or eliminate through urine. e.g. Activated charcoal absorbs the poison prior to absorption into intestinal wall. Copper sulphate, magnesium sulphate and sodium monohydrogen phosphate (Na_2HPO_4) inactivate the poison prior to absorption and precipitate the toxic material as insoluble salt.

Antidotes for selected unabsorbed inorganic poisons and drug overdose

Poison/Drug in overdose	Antidote	Mechanism
Acid (Corrosive)	Antacid or Weak alkali (Milk of Magnesia). Avoid inducing vomiting.	Chemical antagonism. Acid-base neutralization.
Alkalis (Caustics)	Weak acid (lemon juice or diluted vinegar)	Chemical antagonism. Acid-base neutralization.
Iron salts	Desferroxamine, sodium carbonate, 1% lavage	Chelation
Copper and lead salts	Penicillamine	Chelation
Mercury salt	Dimercaprol (BAL)	Chelation

4.4.1 Sodium Nitrite Injection

Molecular Formula: NaNO_2

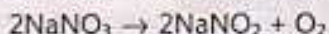
Molecular Weight: 69 g

Synonyms: Nitrous acid Sodium Salt, Etinitrit

Standards: It contains not less than 97% and not more than 101% of sodium nitrite calculated on dried basis.

Methods of Preparation:

1. It is prepared by strongly heating sodium nitrate.



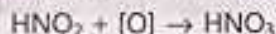
2. It can also be prepared by heating sodium nitrate with lead.



Physical Properties:

1. It is yellow or white crystalline powder.
2. It has saline taste and freely soluble in water but less soluble in alcohol.
3. It is odourless in nature.
4. When it is exposed to air, it readily forms sodium nitrate.

Assay: 1 gm of sodium nitrite is dissolved in 100 ml of water, pipette out 10 ml of the solution and transfer to another solution containing KMnO_4 , 100 ml of water and 5 ml of H_2SO_4 . The solution is warmed to 40°C and allowed to stand for 5 minutes. To this 25 ml of 0.1 N oxalic acid is added and again heated to 80°C . The excess oxalic acid is titrated with 0.1 N potassium permanganate. At the end point, colour changes from colourless to pink.



Each 1 ml of 0.1 N $\text{KMnO}_4 = 3.450$ gm of NaNO_2

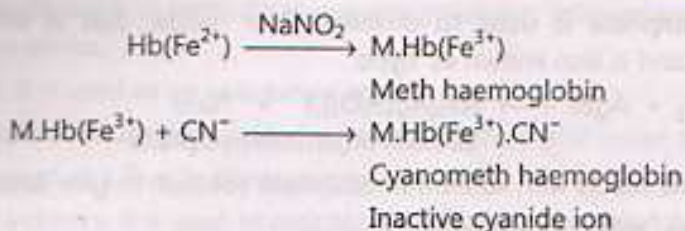
Uses:

1. Nitrite ions release the smooth muscle of blood vessels and give the vasodilator action.
2. It is mainly used in cyanide poisoning.
3. It is also used in anti-rust solution to prevent the rusting of surgical instruments.

Mechanism of Antidote Action:

In cyanide poisoning, the injection of sodium nitrite is given primarily, which causes the oxidation of ferrous ions (Fe^{2+}) of haemoglobin to ferric ion (Fe^{3+}) of methhaemoglobin.

This methhaemoglobin then combines with the serum cyanide and produce cyanometh haemoglobin and protect the enzyme from harmful cyanide ions.

**Test for Purity:**

The sample is tested for the presence of heavy metals not more than 0.002% and loss on drying not more than 0.25%.

Incompatibilities:

It is incompatible with acetanilide, antipyrine, phenazone, caffeine citrate, chlorate, hypophosphite, iodide, mercury salt, permanganate, tannic acid, vegetable decoction, infusion or tincture.

Dose of Injection: 10 - 15 ml of 3% solution i.v.

4.4.2 Sodium Thiosulfate Injection

Molecular Formula: $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$

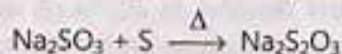
Molecular Weight: 248.18 g

Synonyms: Sodium hyposulfite, Anti-chlor.

Standards: It contains not less than 99% and not more than 101% of $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$

Methods of Preparation:

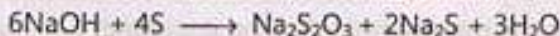
1. It can be prepared by boiling sodium sulphite with sulphur.



2. It can also be prepared by passing SO_2 gas in a mixture of sodium sulphide (8%) and sodium carbonate (6%).



3. Sodium thiosulphate is also prepared by reacting sodium hydroxide with sulphur.



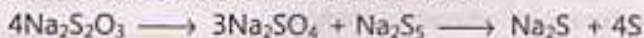
4. It can also be prepared by passing sulphur dioxide into sodium sulphide solution.

**Physical Properties:**

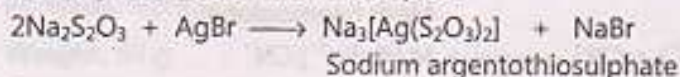
1. It occurs as large, transparent prismatic crystalline powder.
2. It effervesces in dry air.
3. It is practically soluble in water and insoluble in alcohol.
4. It starts melting at 50°C and at 100°C , loses its all moles of water.

Chemical Properties:

1. Its aqueous solution decomposes slowly as:



- Sodium thiosulphate is used to dissolve silver halide, that is why it is used in photography and is also known as 'hypo'.

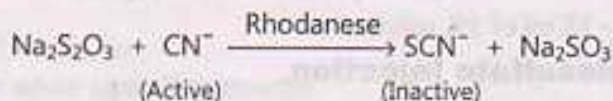


- Barium chloride reacts with sodium thiosulphate solution to give white precipitates of barium thiosulphate.



Mechanism of Antidote:

After 5 min. of injection of sodium nitrite, a slow i.v. infusion of sodium thiosulfate is given which causes dissociation of cyanometh haemoglobin and set free cyanide ion. This cyanide ion (CN^-) is converted into thiocyanate ion (SCN^-) by sodium thiosulphate in the presence of enzyme Rhodanese and thiocyanate ion (SCN^-) is then excreted out from body by kidney.

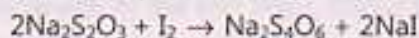


Identification Tests:

- Add few drops of iodine solution to 10% w/v solution of sodium thiosulphate. The solution will appear colourless.
- A solution (1 in 20) gives the reaction of sodium and thiosulphate ion.

Assay: Its assay is based upon **iodometric titrations**.

Take about 0.5 gm of the sample and dissolve in 20 ml of water, and the solution is titrated against 0.05 M iodine using starch solution as an indicator, when at the end point, the excess iodine reacts with starch paper turning it to a blue colour.



Each 1 ml of 0.05 M iodine = 0.02482 gm of sodium thiosulphate.

Test for Purity:

The sample is tested for the presence of following impurities:

- Heavy metals not more than 10 ppm.
- Absence of sulphide and sulphite.
- Sulphates must not be more than 0.2%
- The pH of aqueous solution of 10%w/v of sodium thiosulphate is 6.0-8.4.

Incompatibility: Mixing it with solutions containing other metal cation is a source of incompatibility due to the precipitation of metal thiosulphate. In acidic medium, these precipitates may darken due to the formation of respective sulphides.

Uses:

- Its use as an antioxidant is limited to solution containing iodides.
- It is used as a standard titrant in iodimetric analysis.

3. It is basically used as antidote in cyanide poisoning intravenously after the injection of sodium nitrite.
4. Topically, it is used as an anti-fungal agent.
5. It is also effective antidote in lead, bismuth, mercury and iodine poisoning.
6. It is also used as a fixer in photographic work.
7. In textile industry, it is used as antichlor in bleaching process.

Dose: The I.P. recommended dose of injection which is equivalent of 0.3-1.0 gm (3-10 ml) and is administered by i.m. and i.v. route.

Storage: Sodium thiosulphate injection should be stored in tightly closed containers and container must be of single dose.

4.4.3 Activated Charcoal

Charcoal is a dark grey residue consisting of carbon and any remaining ash obtained by removing water and other volatile constituent from animal and vegetable substances.

Methods of Preparation:

1. It is prepared by burning wood in absence of air. The residue obtained consists of nearly pure carbon.
2. **Activation of Charcoal:** The absorptive power of charcoal could be tremendously increased by treating it with various substances such as steam, air, carbon dioxide, oxygen, zinc chloride, sulphuric acid, phosphoric acid or a combination of these substances, at temperature ranging from 500°-9000°C. In this process, the activating substance presumably removes substances previously absorbed on charcoal and in some instances at least, breaking down the granules of carbon into smaller ones having a greater total surface of approximately 100 m².
3. **Other sources:** Sucrose, lactose, rice, starch, coconut, pericarp, bone, blood and various industrial wastes can be used for preparing charcoal.

Properties:

1. It is fine, black, odourless and tasteless powder.
2. It is free from gritty matter.
3. It is insoluble in water and other organic solvents.

Uses:

1. It is used as an emergency antidote in many forms of poisoning.
2. It is used as protective and adsorbent.
3. It is also used as a burning fuel.
4. Due to its high surface area, it is also used as a filter-aid.
5. It is also a constituent for gum powder.
6. It is used as disinfectant in wounds.
7. It is used to filter toxins from blood and kidney diseases.

8. It is used to purify blood transfusions.
9. It is used in overdose of aspirin.
10. Its antidote activity is also reported in case of snake, spider and insect bite.

4.5 ASTRINGENTS

The 'Astringent' word is derived from the Latin word **adstringere** meaning 'to bind fast'.

These 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. It also has local styptic and antiseptic action. Astringents applied over the wound in small quantity to stimulate the growth of new tissues but in higher concentrations it produces irritation or corrosive effect. This corrosive property is useful in removal of warts (undesired tissues).

Astringents are normally used in much diluted forms and are used topically:

- ✓ Clean the face and prevent acne breakouts.
- ✓ Stop bleeding
- ✓ Treat 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 as 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 create a barrier against infection.

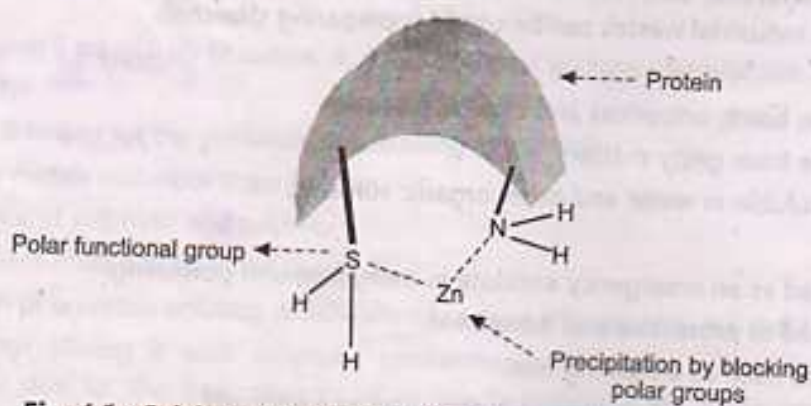


Fig. 4.1 : Seizing of Polar functional groups by Astringents

Astringent Compounds - Causes:

1. Constriction of capillaries and small blood vessels in stopping of blood by coagulation.