



Name of Subject : Pharmaceutical Inorganic Chemistry

Subject Code : 818805

Name of Chapter : Miscellaneous agents

Name of Topic : Expectorants, Emetics, Haematinics, Poison and Antidote, Astringents

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## Expectorants

**Que: Write a short note on expectorants.**

### **Expectorants:**

Expectorants are the agents that removes sputum from the respiratory tract.

They do this either by:

1. Increasing the fluidity of sputum (reducing the viscosity) or
2. Increasing the volume of fluid that should be expelled out from the respiratory tract by coughing.

### **Examples:**

Ammonium chloride ( $\text{NH}_4\text{Cl}$ ), Potassium Iodide (KI), Sodium Iodide (NaI).

- As dose of the expectorant is high, so if patient is sensitive then vomiting may occur.
- So it is advisable that the dose should be given that could be tolerated by the patient.
- Flavors, sweeteners like pharmaceutical aids and cough suppressants should be given along with the dose of expectorant.

## Classification:

According to **mechanism of action**, they can be classified in to two classes:

### 1. Sedative expectorants:

- They **irritate stomach** that produce their effect through stimulation of gastric reflexes.
- Ex. Bitter drugs like **Ipecac, senega, Indian squill**. Compounds like **antimony potassium tartarate, ammonium chloride, potassium citrate, potassium iodide, sodium iodide**.

### 2. Stimulant expectorants:

- They directly or indirectly **stimulate secretory cells of the respiratory tract**.
- As they stimulate secretion, **more fluid get produced** in respiratory tract that dilute sputum.
- Ex. Drugs such as **Eucalyptus, lemon, anise**, active constituents like **terpine hydrate, anethole**.

# Que: Give monograph of ammonium chloride and potassium iodide

## 1. Ammonium chloride:

**Mol Formula:**  $\text{NH}_4\text{Cl}$  **Mol wt:** 53.49 gm/mol.

**Limits of purity:** It contains not less than 99.5% w/w of  $\text{NH}_4\text{Cl}$ .

### Preparation:

1). It can be prepared by **neutralizing** ammonia with HCl. This solution will be evaporated till crystalline mass of ammonium chloride is obtained.



2). Also prepared by **heating** ammonium sulphate with sodium chloride.



### Properties:

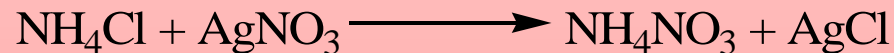
- **White** fine or **crystalline** powder.
- **Hygroscopic**.
- Soluble in **water** and **glycerine**.

## Assay:

### Method 1:

Previously, ammonium chloride was assayed by precipitation titration by Volhard's method.

- Take 0.2 gm ammonium chloride.
- Dissolve it in 40 ml water.
- Acidify it with 3 ml nitric acid.
- Add 50 ml 0.1N AgNO<sub>3</sub> and 5 ml nitrobenzene and shake it.
- The excess of silver nitrate is titrated with 0.1N ammonium thiocyanate using ferric ammonium sulphate as an indicator.

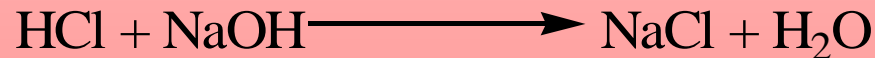
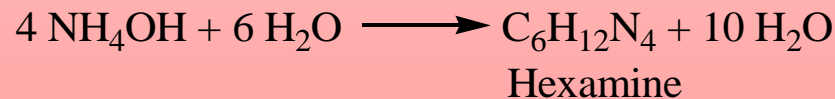
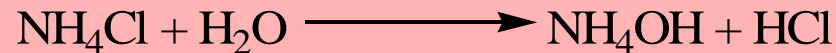


- Each ml of 0.1 N AgNO<sub>3</sub> is equivalent to 0.005349 gm of NH<sub>4</sub>Cl.

## Method 2:

Now, ammonium chloride is assayed by acid base titration that is simpler and as it does not require silver nitrate so it is cheaper also.

- Take 0.1 gm  $\text{NH}_4\text{Cl}$  in conical flask.
- Add 50 ml distilled water.
- Add 5 ml neutral formaldehyde solution. (formaldehyde contains small amount of formic acid so it bears slight acidic character. So it is neutralized by sodium hydroxide solution with phenolphthalein solution).
- Keep aside the solution for 2 minutes.
- Titrate the liberated hydrochloric acid with standard 0.1 N sodium hydroxide solution using phenolphthalein solution as an indicator.
- Each ml of 0.1 N sodium hydroxide solution is equivalent to 0.005349 gm of  $\text{NH}_4\text{Cl}$ .



## Dose:

- For systemic acidifier, dose is **1 to 2 gm four times a day** in form of injection or tablets.
- For expectorant, **0.3-0.5 gm** dose is required.

**Storage:** Store in highly closed containers.

## Uses:

- Gastric acidifier
- Diuretic
- Mild expectorant
- Diaphoretic.

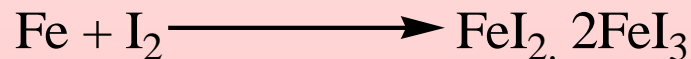
## 2. Potassium Iodide

**Mol. Formula:** KI                      **Mol. Weight:** 166 gm/mol.

It is having not less than 99 %ww of KI.

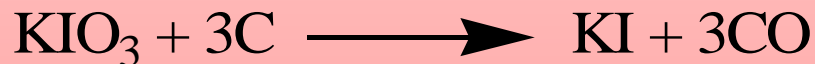
## Preparation:

1). Industrially, prepared by action of iodine on moist iron filling and forms ferro-ferric iodide ( $\text{FeI}_2 \cdot 2\text{FeI}_3$ ). Then it will decomposed with potassium carbonate to give potassium iodide.



2). Also prepared by treating a hot solution of potassium hydroxide with iodine that gives mixture of potassium iodide and potassium iodate.

The mixture then treated with charcoal powder that will give potassium iodide.





## Properties:

- Colorless
- Transparent or opaque crystals or white granular powder
- Odourless
- Saline and bitter taste
- Soluble in water, glycerin, alcohol and acetone.

## Uses:

- Used internally to supply iodine for treatment of thyroid deficiency.
- As expectorant in cough mixture.
- Saline diuretic.
- It has mild antifungal activity.
- Also used in the preparation of reagents containing complex iodides like potassio-mercuric iodide, potassio-bismuth iodide.

**Storage:** Stored in well closed container.

# Emetics

Que: Write a short note on emetics. OR Define emetics and explain how they work with giving some examples of them.

## Emetics:

- Emetics are the agents that bring about forceful expulsion of contents of stomach through oral cavity.
- They are a valuable part of treatment in poisoning cases.
- Emetics can act either by
  1. Local irritation of gastric mucosa: Ex. Ammonium bicarbonate, or
  2. Directly on the chemoreceptor trigger zone in the 4<sup>th</sup> ventricle of medulla.

- **Emetics** are added in **low doses** to cough preparations to **stimulate respiratory secretions**.
- In case of **poisoning**, **emetics** are given to patients that **physically expel the toxic poisonous substances** and **reduce its harmful effects** and **save patient's life**.
- If patient is **unconscious** then **gastric lavage will be required**.
- Many **salts in larger doses** can exert **emesis** action whereas **some bitter salts** even in **smaller doses** can exert **emesis** action.
- **Examples:** Antimony potassium tartarate, Copper sulphate, Zinc sulphate, Ammonium bicarbonate.

# Emetics

Que: Define emetics. Give monograph of copper sulphate and sodium potassium tartarate

## Emetics:

- Emetics are the agents that brings about forceful expulsion of contents of stomach through oral cavity.
- They are a valuable part of treatment in poisoning cases.

## 1). Copper sulphate

**Synonym:** Cupric sulphate

**Mol. Formula:**  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$       **Mol. Wt:** 249.7 gm/mol.

It contains not less than 98.5% and not more than 101% of  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ .

## Preparation:

1). It can be prepared by treating **granulated copper** with **sulphuric acid** in presence of **air**.



2). It can be prepared by treating **metallic copper** with **sulphuric acid**.



3). It can be prepared by treating **oxides of copper** with **dilute sulphuric acid**.



## Properties:

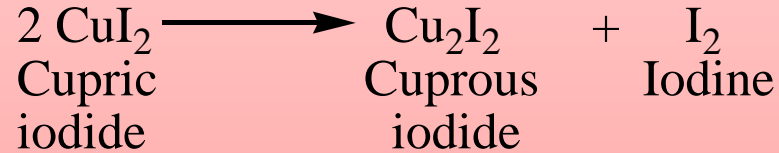
- Deep blue color
- Triclinic crystals of pentahydrate or crystalline granules or powder.
- Soluble in water. Slowly soluble in glycerol and insoluble in alcohol.
- Stable up to  $60^{\circ}\text{C}$ .
- When heated up to  $100^{\circ}\text{C}$ , it releases two water molecules.
- When heated up to  $140^{\circ}\text{C}$ , it releases another water molecule.
- When heated up to  $200^{\circ}\text{C}$ , it releases further two water molecules and becomes white anhydrous salt.
- Its aqueous solution is acidic to litmus paper.

## Assay: (Iodometry titration)

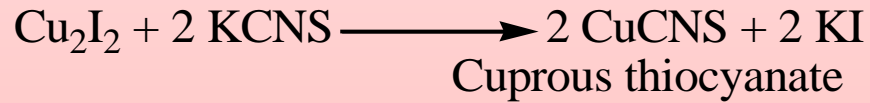
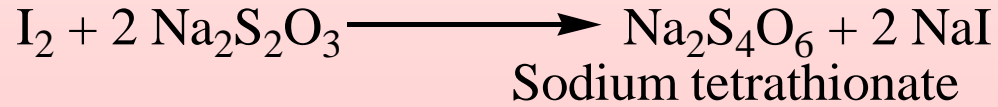
Based on the principle on the instability of cupric iodide that formed in the reaction between  $\text{CuSO}_4$  and KI that decomposes to give  $\text{Cu}_2\text{I}_2$  with

liberation of **free iodine**.

- Take accurately weighed **copper sulphate** powder in conical flask.
- Add **water** to dissolve it.
- Add **KI** to this.
- Add **acetic acid**.
- **Iodine** that liberated will be titrated with **standard sodium thiosulphate** solution by using **starch paste** as an indicator until faint blue color developed.



Add 2 gm potassium thiocyanate (KCNS) and continue the titration until blue color disappears.



1 ml of 0.1 N  $\text{Na}_2\text{S}_2\text{O}_3$  is equivalent to 0.02497 gm of  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ .

**Storage:** Protected from air, heat and moisture.

**Use:**

- Used as an emetic in a dose of 300 mg in 30 ml of water.
- As chemical antidote in phosphorus poisoning.
- Externally used as an astringent and fungicide.
- Ingredient of Benedict's and Fehling's solution.



## 2). Sodium potassium tartarate

**Synonym:** Rochelle salt

**Mol. Formula:**  $C_4H_4O_6NaK.4H_2O$       **Mol. Wt.:** 282.2 gm/mol.



It is having not less than **99.0 %w/w** and not more than **104.0 %w/w** of  $C_4H_4O_6NaK.4H_2O$ .

### **Preparation:**

• Obtained by neutralizing a solution of **sodium carbonate** with **potassium bitartarate**. The solution is boiled for some time and then allowed to cool. **Carbon dioxide** will be evolved. The solution is filtered and concentrated to crystallisation.



## Properties:

- It gives characteristic reactions of sodium and potassium.
- On heating, it gives burning sugar like odor. Also remaining residues are alkaline to litmus paper and give effervescence with acids.

## Uses:

- Emetic.
- Administered in solution for its saline cathartic action in a dose of 10 gm.
- Ingredient of compound effervescent powder.
- Food additive.

## Haematinics and Ferrous sulphate

**Que: Define haematinics. Write preparation, properties, assay principle and uses of Ferrous sulphate.**

### **Haematinics:**

In case of anemia, hemoglobin content in the blood decreases.

The agents that increase hemoglobin content in the blood are known as haematinics.

### **Ferrous sulphate:**

**Mol. Formula:**  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$     **Mol. Wt.:** 278 gm/mol.

It contains not less than 98.0 not more than 103.0 per cent of  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ .

### **Preparation:**

Prepared by treating iron with excess amount of dilute sulphuric acid. Green crystals of ferrous sulphate will be obtained.



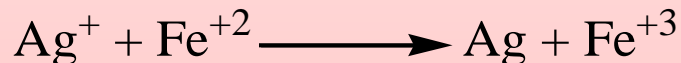
### **Properties:**

- Greenish crystalline powder.
- On exposed to air, it gets oxidized and form ferric salt.

- On heating, it decomposes and gives ferric oxide, sulphur dioxide and sulphuric acid.



- It reduces salt of silver and gold.



- It reacts with sodium carbonate and releases  $\text{CO}_2$ .



### Assay:

- Take 1 gm sample in conical flask.
- Add 30 ml water and 20 ml dilute sulphuric acid
- Titrated with 0.1 N ceric ammonium nitrate using ferroin sulphate solution as an indicator till red color changes in to light blue.
- Each ml of 0.1 M ceric ammonium sulphate  $\equiv$  0.0278 gm of  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ .



**Uses:**

As Haematinic it increases hemoglobin content in the blood in iron deficiency.  
Overdose can cause shock, GI irritation and discoloration in teeth.

**Storage:** In a tightly closed container.

## Haematinics and Ferrous gluconate

**Que:** Define haematinics. Write preparation, properties and uses of Ferrous gluconate.

### Haematinics:

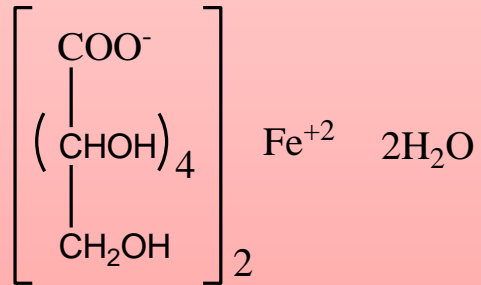
In case of anemia, hemoglobin content in the blood decreases.

The agents that increase hemoglobin content in the blood are known as haematinics.

### Ferrous gluconate

Mol. Formula:  $C_{12}H_{22}O_{14}Fe \cdot 2H_2O$     Mol. Wt.: 482.2 gm/mol.

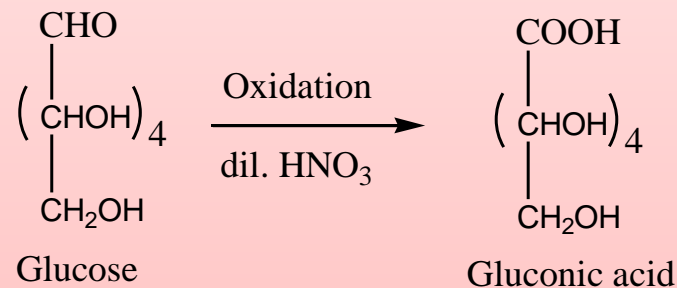
Structure:



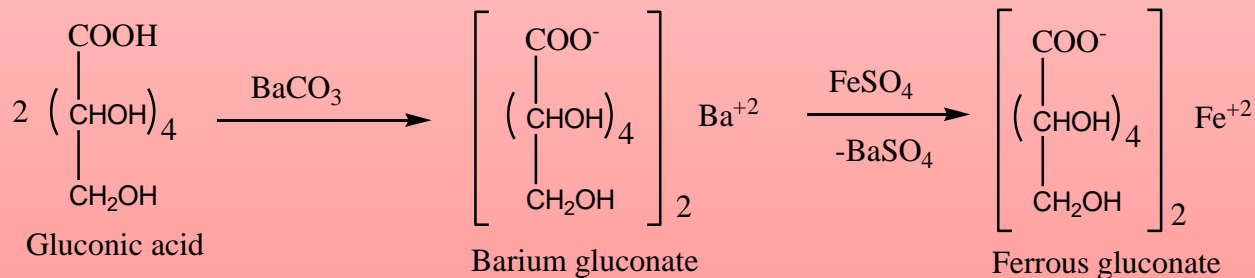
It contains not less than 95% of  $C_{12}H_{22}O_{14}Fe$

## Preparation:

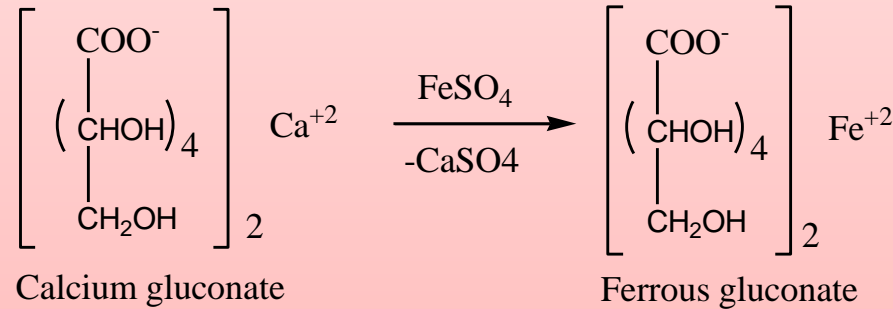
1). It is prepared by treating glucose with dilute nitric acid. So by oxidation reaction, gluconic acid will be formed.



Gluconic acid is then treated with barium carbonate so barium gluconate will be formed which then treated with ferrous sulphate solution so that barium sulphate will be precipitated out. This barium sulphate is filtered and clear filtrate is concentrated and cooled. Precipitates of ferrous gluconate will be obtained that will be filtered.



2). It is also prepared by treating calcium gluconate with ferrous sulphate solution so that calcium sulphate will be precipitated out. This calcium sulphate is filtered and clear filtrate is concentrated and cooled. Precipitates of ferrous gluconate will be obtained that will be filtered.



### Properties:

- Yellowish grey or pale greenish fine powder.
- Burnt sugar like odor.
- Soluble in water but insoluble in alcohol.
- It's aqueous solution is acidic in nature.



### **Storage:**

Stored in well closed container protected from light.

### **Use:**

Haematinic

It can be used in preparation of ferrous gluconate tablets.

It causes less side effects.

### **Dose:**

0.3 to 0.6 gm

\*\*\*\*\*

## Poison and Antidote

**Que. Explain Antidotes. Write types of Antidotes with examples. Write preparation, properties, assay and uses of sodium thiosulphate.**

**Poison:** Poisons are the toxic chemical substances that is harmful to our body.

**Antidote:** Antidotes are the substances that react against ingested poison or toxic substances or overdose of any potent drug and nullifies its side effects.

• They act by either:

❖ Neutralizing the poison or its toxic effect or

❖ Pharmaceutically (Antagonism action) or Chemically (formation of chelates, acids or derivatives) they convert the poison in to nontoxic or less toxic compound.

• Based on mechanism of action, Antidotes can be classified in to three classes:

1. Physiological antidotes
2. Chemical antidotes and
3. Mechanical antidotes

# Antidote: Types

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graph TD; A[Antidote: Types] --> B[1. Physiological antidote:]; A --> C[2. Chemical antidote:]; A --> D[3. Mechanical antidote:];
```

## 1. Physiological antidote:

- They gives effect **opposite** to that of **poison**

**or**

- they **physiologically counteract** the effect of **poison**.

- Ex. **Sodium nitrite**

## 2. Chemical antidote:

- They **combine** with **poison** and changes its **poisonous nature** and **nullifies** the **effect of poison**.

- Ex. **Dimercaprol, Dimercaptosuccinic acid, Ethylene diamine tetraacetic acid (EDTA)**

## 3. Mechanical antidote:

- They either:

- **Prevents absorption** of **poison** in the body

**or**

- They **expel** out the **poison** by **emesis** **or**

- They eliminates the **poison** through **urine**.

- Ex. **Activated charcoal**

# Sodium thiosulphate: preparation, properties, assay and uses

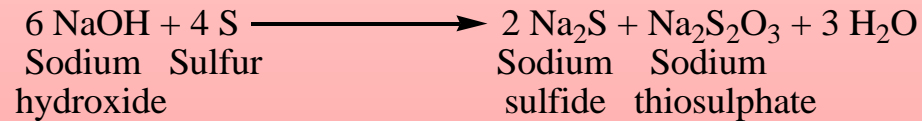
## Sodium thiosulphate, IP

### Properties:

- White crystalline solid powder
- Odorless
- Highly water soluble
- pH of the 1% solution should be in between 6 to 8.4.
- Mol. Wt.: 158.11 gm/mol
- Density: 1.667 g/cm<sup>3</sup>

### Preparation:

- 1). Prepared by treatment between sodium hydroxide and sulfur in heating condition.



- 2). Prepared by treatment between sodium sulfite and sulfur in heating condition.

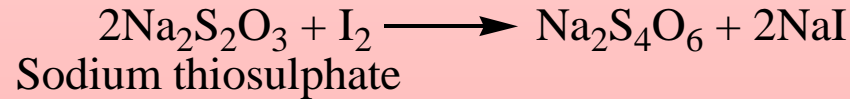


## Assay: (Iodimetry titration)

It can be assayed by titration with **standard iodine solution** using **starch** as an **indicator**.

- Take **0.8 gm sodium thiosulphate powder** and dissolve in **30 ml distilled water** in conical flask.
- Titrate this with **0.1 N standard Iodine solution**.
- Add **3 ml starch** solution as an **indicator** towards the end point.
- End point can be detected by **discharge of yellow color of iodine**.

Each ml of **0.1 N iodine** is equivalent to **0.02482 gm of sodium thiosulphate**.



## Uses:

- In **cyanide poisoning**.
- **Reducing agent**
- Standard **titrant** in iodimetric analysis.

**Storage:** Stored in **tightly closed container**.

## Que. Write a note on cyanide poisoning and its treatment

### Cyanide poisoning:

Cyanide poisoning occurs by either:

- ❖ Cyanide poison taken **accidentally** or
- ❖ Cyanide poison taken **intentionally** to commit the **suicide**.

• **Cytochrome oxidase** is an enzyme that responsible for **electron transfer reactions**. This is necessary for the **cellular respiration**.

• In case of Cyanide poisoning, cyanide binds with **ferric ion of cytochrome oxidase**.

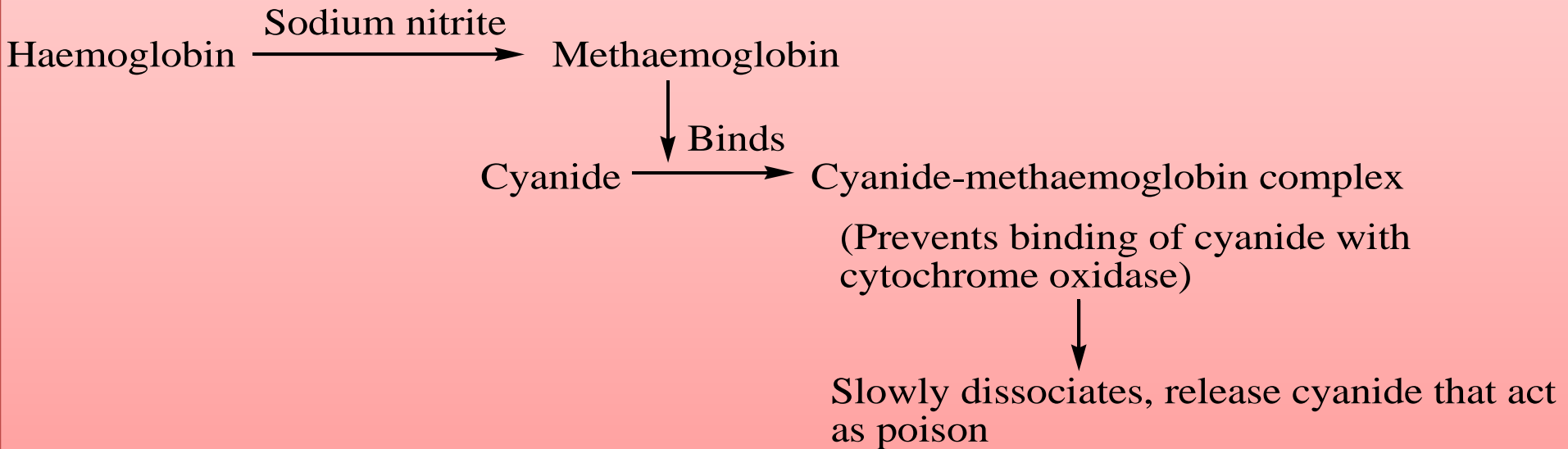
• This leads to **stoppage of electron transfer reactions** which **inhibits cellular respiration** as well as **metabolic reactions**.

• If cyanide poisoning is not treated immediately, it could be **fatal** and even lead to **death** of a person also.

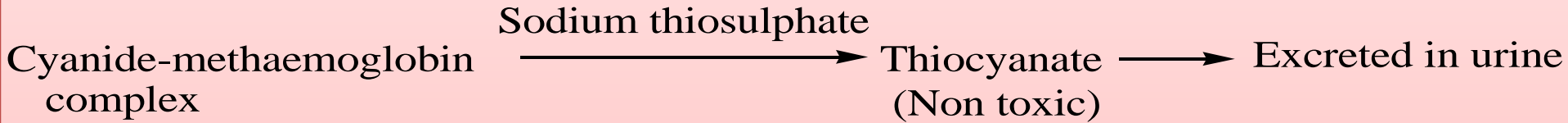
• **Two antidotes** in combination can be used to treat cyanide poisoning:

- ❖ **Sodium nitrite** and
- ❖ **Sodium thiosulphate**

- First, intravenous infusion of 10 ml, 3% w/v sodium nitrite injection can be given over 3 minute period that followed by intravenous injection of 25 ml, 50% w/v sodium thiosulphate.
- Sodium nitrite converts haemoglobin to methaemoglobin that binds with cyanide ions and forms cyanide-methaemoglobin complex. This complex prevents cyanide poisoning of cytochrome oxidase.
- But, this cyanide-methaemoglobin complex slowly gets dissociates and releases cyanide again which still acts as poison.



• **Sodium thiosulphate** immediately converts this **cyanide-methaemoglobin complex** in to nontoxic **thiocyanate** that can be excreted by the kidney and relieves the patient from cyanide poisoning.



• **Dicobalt edetate** can also be useful in place of sodium nitrite. This dicobalt edetate forms **cobaltcyanoedetate complex** that is nontoxic which is followed by i.v. infusion of **sodium thiosulphate**.

Compounds used in the treatment of cyanide poisoning

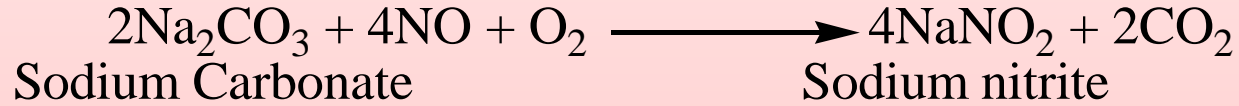
### 1. **Sodium nitrite, USP**

**Mol. Formula:**  $\text{NaNO}_2$ , **Mol. Wt.** 68.99 gm/mol

It contains 97% to 101% of  $\text{NaNO}_2$ .



**Preparation:** It can be prepared by treating nitrogen oxide gas (NO) with Sodium carbonate ( $\text{Na}_2\text{CO}_3$ ).



### **Properties:**

- White granular or crystalline powder.
- Soluble in water. Sparingly soluble in alcohol

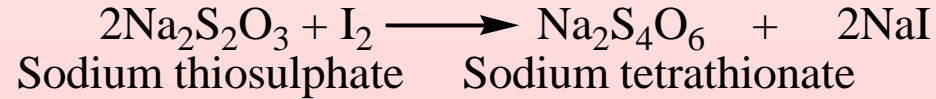
### **Uses:**

- Vasodilator.
- In cyanide poisoning
- It has hypotensive effect.
- As food preservative.

## **2. Sodium thiosulphate, IP**

**Limits:** pH of the 1% solution should be in between 6 to 8.4.

**Assay:** It can be assayed by Iodometry titration with standard iodine solution using starch as an indicator.



### Uses:

- In cyanide poisoning.
- Reducing agent
- Standard titrant in iodimetric analysis.

**Storage:** Stored in tightly closed container.

### 3. Sodium thiosulphate Injection, IP

Strength is 100 mg/ml and single dose equivalent to 0.3 to 1 gm (3 to 10 mL) given by Intravenous or intramuscular route.

### Uses:

In cyanide poisoning after iv infusion of sodium nitrite.

### Storage:

Stored in single dose container.

## Poison and Antidote

Que. Define Poison and antidote and write preparation, properties and uses of activated charcoal.

**Poison:** Poisons are the toxic chemical substances that is harmful to our body.

**Antidote:** Antidotes are the substances that react against ingested poison or toxic substances or overdose of any potent drug and nullifies its side effects.

### **Activated charcoal**

#### **Preparation:**

- 1). It is prepared by burning of organic materials. The obtained residue will be crushed and powdered.
- 2). Prepared by distillation of organic materials. The obtained residue will be crushed and powdered.

## Properties:

- Fine, black, odorless, tasteless.
- Smooth powder.
- Insoluble in all solvents.
- It has more surface area for adsorbent properties.

## Actions and Use:

- Adsorbent
- Used in poisoning
- Adsorb heavy metal as well as drugs such as hypnotics, sedatives, alkaloids and gases like carbon monoxide, carbon dioxide and nitrous oxide
- Used in diarrhoea to adsorb toxins

## Dose:

- Given in form of tablets in a ratio of 5:1 or 10:1 (charcoal to poison).

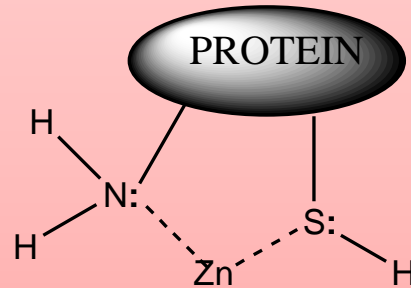
## Astringents

**Que. Define Astringents. Write a short note on it. Give monograph of zinc sulphate and potash alum.**

**Astringents:** Astringents are the substances that bring about protein precipitation reaction on the surface of skin.

- These agents have low cell permeability so protein precipitation reaction is limited only to the skin surface and the interstitial cell surface.
- They do contraction and wrinkling of the tissue and by blanching.
- Topically, In low concentration, they stimulate growth of a new tissue while in high concentration, they bring about corrosive action on tissue.
- Metal ion that act as Lewis acid can work by this mechanism.

- They act on polar functional group of protein or enzyme that act as ligand and brings about protein precipitation.
- Complex will be formed by binding of metal ion with protein (ligand) that will be strong chelate and causes drastic change in the properties of protein. This will lead to inactivation of protein.
- Examples: Alum, aluminium citrate, calamine, zinc oxide, zinc sulphate.



Binding of metal ion  
with protein (ligand)

- They exhibit their action by;
  - 1). Styptic action: stopping of blood by coagulation of blood and constriction of small capillaries.
  - 2). Antiinflammatory action: by decreasing supply of blood to the tissues.
  - 3). Antiperspirant action: By decreasing secretion of perspiration by reducing pore size of skin.
  - 4). Antimicrobial action: By protein precipitation mechanism. Some other uses of astringents:
    - 1). To treat diarrhoea.
    - 2). Possess deodorant properties.
    - 3). Decrease sweating and make skin tougher.
    - 4). Promote healing process.

Some other uses of astringents:

- 1). To treat diarrhoea.
- 2). Possess deodorant properties.
- 3). Decrease sweating and make skin tougher.
- 4). Promote healing process.

## **1). Zinc sulphate**

**Synonym:** White vitriol

Mol. Formula:  $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$                       Mol. Wt.: 287.6 gm/mol.

It is having not less than 99.5% and not more than equivalent of 102.0% of  $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ .

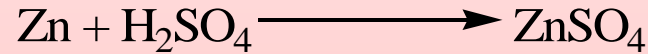
### **Preparation:**

1). By treating zinc sulphide (zinc blende) in presence of air under specified conditions. The heated mass is dissolved in hot water, filtered and solution is concentrated for crystallization.





2). For pharmacopoeial preparation, it is prepared by treatment of zinc metal with dil. Sulphuric acid. The reaction mixture is filtered and concentrated for crystallization.



### **Properties:**

- Colorless transparent crystals, prisms or needles or granular crystalline powder.
- Odorless with astringent and metallic taste.
- Very soluble in water and glycerin and insoluble in alcohol.
- Aqueous solution is acidic to litmus.

**Dose:** 0.6 to 2 gm.

**Storage:** Stored in well-closed containers in a cool place.

### **Uses:**

- Internally used as emetic.
- Externally, it is used as an astringents in form of solutions and powders.

## 2). Sodium potassium tartarate

**Synonym:** Potash alum

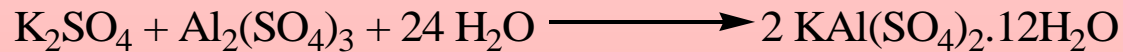
Mol. Formula:  $\text{KAl}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$

Mol. Wt: 474.4 gm/mol.

It contains aluminium not less than 99.5%  $\text{KAl}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ .

### **Preparation:**

Prepared by adding concentrated solution of potassium sulphate to a hot solution of an equimolar proportion of aluminium sulphate. Obtained solution is concentrated and cooled for crystallization.



### **Properties:**

- Colorless, transparent or granular crystals.
- Sweet astringent taste.
- Soluble in water but insoluble in alcohol.
- When heated at 200 °C, it releases water and becomes anhydrous.

## Uses:

- Externally, used as an astringent.
- Antiseptic
- Used as a local styptic action.
- After shave, it is used as wetting and rubbing due to its astringent and antiseptic action.
- Pharmaceutical aid.

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