Limit Test for Heavy Metals

The Indian pharmacopoeia (1996) prescribes limit test of heavy metals for some drugs. The heavy metals like cobalt, tin, manganese, bismuth, lead, antimony etc., are present in the pharmacopoeial substances. The Indian pharmacopoeia (1996) prescribes methods for the limit test of heavy metals.

1. **Method 'A' :**

Principle : This method is used for the colourless substance. In acidic medium when hydrogen sulphide is reacted with heavy metals, the metal sulphites are produced. These are distributed in colloidal state and produce brown colour. The 'test' colour is compared with "standard".

$$\underset{\text{Heavy metal}}{M} + H_2S \xrightarrow[\text{medium}]{\text{acidic}} \underset{\text{(Brown colouration)}}{MS + H_2}$$

Standard Solution : Take 1.0 ml of lead standard solution in 50 ml Nessler cylinder and dilute with water to 25 ml. Adjust with dilute ammonia solution or dilute acetic acid so that pH is maintained between 3.0 and 4.0, then dilute with water to 35 ml and mix.

Test Solution : In 50 ml of Nessler cylinder take 25 ml of the solution or specified quantity of substance being examined, prepared for the test as directed in the individual monograph in sufficient water to produce 25 ml. Adjust with dilute acetic acid or dilute ammonia solution so that pH is maintained between 3.0 to 4.0, dilute with water to 35 ml and mix.

Procedure : In both Nessler cylinders add 10 ml of freshly prepared H_2S solution, mix, dilute to 50 ml with water, allow to stand for 5 minutes and see downward over a white surface.

The colour produced in the "Test Solution" should not be more intense than that produced in the "Standard solution".

2. **Method 'B'**

Principle : Method 'B' is used for the coloured substance. The coloured substances are converted into colourless before preparing their solution with special treatment (Sulphuric acid, ignition, nitric acid, digested with hydrochloric acid, and finally react with water). This method is based on the reaction between H_2S and heavy metals in an acidic medium and metal sulphide is produced.

$$\underset{\text{Heavy Metal}}{} H_2S \xrightarrow[\text{Medium}]{\text{Acidic}} \underset{\text{(Brown Colouration)}}{\text{Sulphides of heavy metals}}$$

Standard Solution : Take 1.0 ml of standard lead solution in 50 ml of Nessler cylinder and dilute with water to 25 ml. Adjust with dilute ammonia solution or dilute acetic acid, so that pH is maintained between 3.0 and 4.0. Then dilute with water to 35 ml and mix.

Test Solution : Weigh in a silica crucible, the quantity of the substance as specified in the individual monograph. Add sulphuric acid to wet the sample, ignite carefully at a low temp.

4. It react with concentrated ammonia

$$2\,NH_3 + 3I_2 \longrightarrow NI_3 \bullet NH_3 + 3\,HI$$

5. It adsorbs on the surface of starch and starch solution turns violet.

Purity test

1. *For bromides and chlorides* : Triturate 3 gm iodine with 20 ml of water, filter, wash the filtrate, and dilute filtrate to 30 ml and add 1 gm of zinc powder. The solution decolourises filter and wash the filtrate with sufficient water to produce 40 ml to 10 ml of this solution, add 3 ml of 10 M ammonia and 6 ml of silver nitrate solution, and dilute to 20 ml with water. To 10 ml of filtrate add 1.5 ml of nitric-acid. The opalescence produced should not be more than opalescence produced by mixing 0.25 ml of 0.01 M hydro chloric acid (not more than 250 PPM).

Incompatibility

It is incompatible with alkalies and alkali carbonates.

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

Assay : It is assayed by direct iodimetric type of redox titration. Iodine is weighed in iodine flask containing 1 gm potassium iodide of 2 M acetic acid and 50 ml of water. Titrate with 0.1 N sodium thiosulphate using starch as indicator.

Factor : Each ml of 0.1 M $Na_2S_2O_3 \equiv 0.01263$ gm of Iodine.

$$2Na_2S_2O_3 + I_2 \longrightarrow Na_2S_4O_6 + 2NaI$$

Uses : Iodine is used as an antimicrobial agent acts by formation of hypoiodous acid (HIO) which is six times more effective than hypochlorous acid (HOCl). It is used for disinfecting unbroken skin, application to mucous membrane in pharyngitis and follicular tonsillitis in combination with glycerol.

Iodine deficiency causes goitre due to iodine deficiency in human diet. For this purpose iodized salts with sodium iodides are given but should be avoided in pregnancy and lactation.

(b-5) Iodine Solution

There are various types of Iodine solutions used as germicidal action.

1. Aqueous Iodine solution B.P./I.P.(1966) (strong iodine U.S.P)
2. Weak Iodine solution B.P./I.P. (1966).
3. Strong Iodine solution I.P. (1966)
4. Iodine Tincture U.S.P.

1. *Aqueous Iodine solution B.P./I.P.(1966) (strong-Iodine U.S.P)* : It is also called as Lugol's solution. It does not contain alcohol.

$$NaBO_2 + 2H_2O \longrightarrow NaOH + H_3BO_3$$

Boric acid

$$Na_2B_4O_7 + 7H_2O \longleftrightarrow 4H_3BO_3 + 2NaOH$$

2. *Heating* : On heating it losses water of crystallization above its M.P. and swells up to form porous mass, which on further heating melts and solidifies to a transparent glossy mass.

$$Na_2B_4O_7 \bullet 10H_2O \longrightarrow Na_2B_4O_7 + H_2O$$

$$Na_2B_4O_7 \longrightarrow 2\,NaBO_2 + B_2O_3$$

Sodium meta borate — Boric anhydride

|——— glassy mass———|

3. It reacts with conc. HCl or conc. H_2SO_4 to form boric acid

$$Na_2B_4O_7 + 2HCl + 5H_2O \longrightarrow 2\,NaCl + 4H_3BO_3$$

$$Na_2B_4O_7 + H_2SO_4 + 5H_2O \longrightarrow Na_2SO_4 + 4H_3BO_3$$

4. On heating with ammonium chloride if form boron nitrite.

$$Na_2B_4O_7 + 2\,NH_4Cl \longrightarrow 2NaCl + 2BN + B_2O_3 + 4H_2O$$

Incompatibility : Borax is incompatible with mercuric chloride, zinc sulphate, other metallic salt and also precipitate alkaloids from their solutions. e.g. : Cocaine HCl solution is precipitated by borax.

Storage : It should be stored in air-tight containers in a cool place.

Uses : It is a weak antibacterial agent simillar to boric acid. It is used in the treatment of inflammatory conditions of eye, gargles and mouth washes, lozenges for astringent action (ingredient in compound thymol glycerin lozenges).

(b-9) Silver Nitrate

Chemical formula : $AgNO_3$

Molecular Weight : 169.89

Standards : It contains not less than 99% and not more than 100.5% of silver nitrate.

Preparations : Silver nitrate is prepared by the action of hot concentrated nitric acid on silver metal. The solution is heated to dryness till silver nitrate crystallizes.

$$Ag + 2HNO_3 \longrightarrow AgNO_3 + NO_2 + H_2O$$

Silver metal — Silver nitrate

Physical Properties : It is a white crystalline powder or colourless crystals; odourless; very soluble in water, soluble in 95% ethanol but very slightly soluble in ether and glycerol.

renal dialysis. The internal intake of fluorides is considered to be better than topical application as anticaries. Absorbed fluoride comes out with saliva and acts on tooth as anticaries.

(E-1) SODIUM FLUORIDE

Chemical formula : NaF

Molecular Weight : 41.99.

Standards : It contains not less than 98.5% and not more than 100.5% of NaF with reference to dried substance.

Preparations

1. It is prepared by treatment of hydrofluoric acid with sodium carbonate in lead container.

$$2HF + Na_2CO_3 \longrightarrow 2NaF + H_2O + CO_2$$

2. It is also prepared by the double decomposition of calcium fluoride with sodium carbonate, the insoluble calcium carbonate is filtered out.

$$CaF_2 + Na_2CO_3 \longrightarrow 2NaF + CaCO_3$$

Calcium fluoride

Physical Properties : It occurs as a colourless crystals or white powder; odourless; soluble in water and insoluble in ethanol (95%).

Purity test : Test for acidity or alkalinity : The boiling solution of sodium fluoride is titrated with 0.1 M sodium hydroxide until a red colour is produced. Not more than 1.5 ml of 0.1 M NaOH is required.

Storage : It should be stored in air tight containers.

Uses : Sodium fluoride is used in the treatment of prophylaxis of dental caries in communities where the intake of fluoride from drinking water and food is minimum. Sodium fluoride in 2% aqueous solution is used topically or applied to children's teeth. Sodium fluoride is used as a constituent of some insecticides and rhodenticides.

(E-2) STANNOUS FLUORIDE

Chemical formula : SnF_2

Molecular Weight : 156.69

Synonym : Tin Fluoride

Preparations

1. From stannous oxide : It is prepared by evaporating a solution of stannous oxide with hydrofluoric acid in the absence of oxygen in a lead retard.

$$SnO + 2HF \longrightarrow SnF_2 + H_2O$$

Stannous oxide Stannous fluoride