

**Aim:** Modified Limit Test for Chlorides and Sulphates

**References:**

1. Indian Pharmacopoeia (IP) 2022, Vol I & II, Appendix 2.3.1, Limit Tests.
2. British Pharmacopoeia (BP) 2023, Appendix VIII, Limit Tests for Chlorides and Sulphates.
3. United States Pharmacopoeia (USP) 43-NF 38, General Chapter <231> Heavy Metals.

**Objective:**

To perform the modified limit test for chlorides and sulphates in a pharmaceutical sample to ensure the concentration of these impurities is within acceptable limits, with enhanced sensitivity and reduced interference from other ions.

**Materials and Reagents**

**1. For Modified Chlorides Test:**

- Nitric acid ( $\text{HNO}_3$ ) - concentrated and dilute
- Silver nitrate solution ( $\text{AgNO}_3$ , 5% w/v)
- Dextran sulfate solution (0.1% w/v) or equivalent stabilizing agent
- Standard sodium chloride solution (0.05845% w/v)
- Purified water
- Nessler cylinder

**2. For Modified Sulphates Test:**

- Hydrochloric acid ( $\text{HCl}$ ) - concentrated and dilute
- Barium chloride solution ( $\text{BaCl}_2$ , 5% w/v)
- Gelatin solution (1% w/v) or polyvinyl alcohol (PVA, 1% w/v)
- Standard potassium sulphate solution (0.1089% w/v)
- Purified water
- Nessler cylinder

### **Apparatus:**

- Nessler cylinders (50 mL)
- Measuring cylinders
- Glass rods
- Beakers (100 mL)
- Pipettes
- Analytical balance

### **Procedure**

#### **1. Modified Limit Test for Chlorides:**

##### **Preparation of Standard Solution:**

- **Standard Sodium Chloride Solution (0.05845% w/v):** Dissolve 58.45 mg of sodium chloride (NaCl) in sufficient purified water to make 100 mL of solution.

##### **Preparation of Test Solution:**

- Dissolve the specified quantity of the test substance in 15 mL of water. If the substance is insoluble in water, use a suitable solvent as directed in the pharmacopeia.
- Add 1 mL of concentrated nitric acid to the solution, mix well, and allow it to stand for 5 minutes.
- Add 0.2 mL of dextran sulfate solution to stabilize the turbidity.
- Add 1 mL of 5% silver nitrate solution, and dilute the solution to 50 mL with purified water.

##### **Preparation of Blank Solution:**

- Prepare a blank using the same quantity of reagents (1 mL of nitric acid, 0.2 mL of dextran sulfate solution, 1 mL of silver nitrate solution) but without the test substance. Make up to 50 mL with purified water.

### **Procedure:**

1. Transfer 10 mL of the test solution into a Nessler cylinder.
2. Add the prepared reagents as described above and dilute to 50 mL.

3. Prepare a standard solution using the standard sodium chloride solution following the same steps.
4. Compare the turbidity or opalescence of the test solution with that of the standard solution against a black background after 5 minutes.

**Observation:**

- The opalescence or turbidity of the test solution should not exceed that of the standard solution, indicating the presence of chlorides within the permissible limit.

**2. Modified Limit Test for Sulphates:**

**Preparation of Standard Solution:**

- **Standard Potassium Sulphate Solution (0.1089% w/v):** Dissolve 108.9 mg of potassium sulphate ( $K_2SO_4$ ) in sufficient purified water to make 100 mL of solution.

**Preparation of Test Solution:**

- Dissolve the specified quantity of the test substance in 15 mL of water or the appropriate solvent.
- Add 2 mL of concentrated hydrochloric acid to remove any interfering ions and let it stand for 10 minutes.
- Add 0.2 mL of gelatin or PVA solution to stabilize the precipitate.
- Add 1 mL of 5% barium chloride solution and dilute to 50 mL with purified water.

**Preparation of Blank Solution:**

- Prepare a blank using the same reagents (2 mL of HCl, 0.2 mL of gelatin or PVA solution, 1 mL of  $BaCl_2$  solution) without the test substance and dilute to 50 mL with purified water.

**Procedure:**

1. Transfer 10 mL of the test solution into a Nessler cylinder.
2. Add the prepared reagents as described above and dilute to 50 mL.
3. Prepare a standard solution using the standard potassium sulphate solution following the same steps.

4. Compare the turbidity of the test solution with that of the standard solution against a black background after 5 minutes.

**Observation:**

- The turbidity of the test solution should not exceed that of the standard solution, indicating the presence of sulphates within the permissible limit.

**Calculation:**

The modified limit tests for chlorides and sulphates do not require direct numerical calculations as they are based on a visual comparison of turbidity or opalescence against a standard. However, any deviations or visual discrepancies should be documented carefully.

**Result:** The sample passes the modified limit test if the turbidity of the test solution does not exceed that of the standard solution, indicating compliance with impurity limits for chlorides and sulphates.

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