

Introduction to Limit Tests

What are Limit Tests?

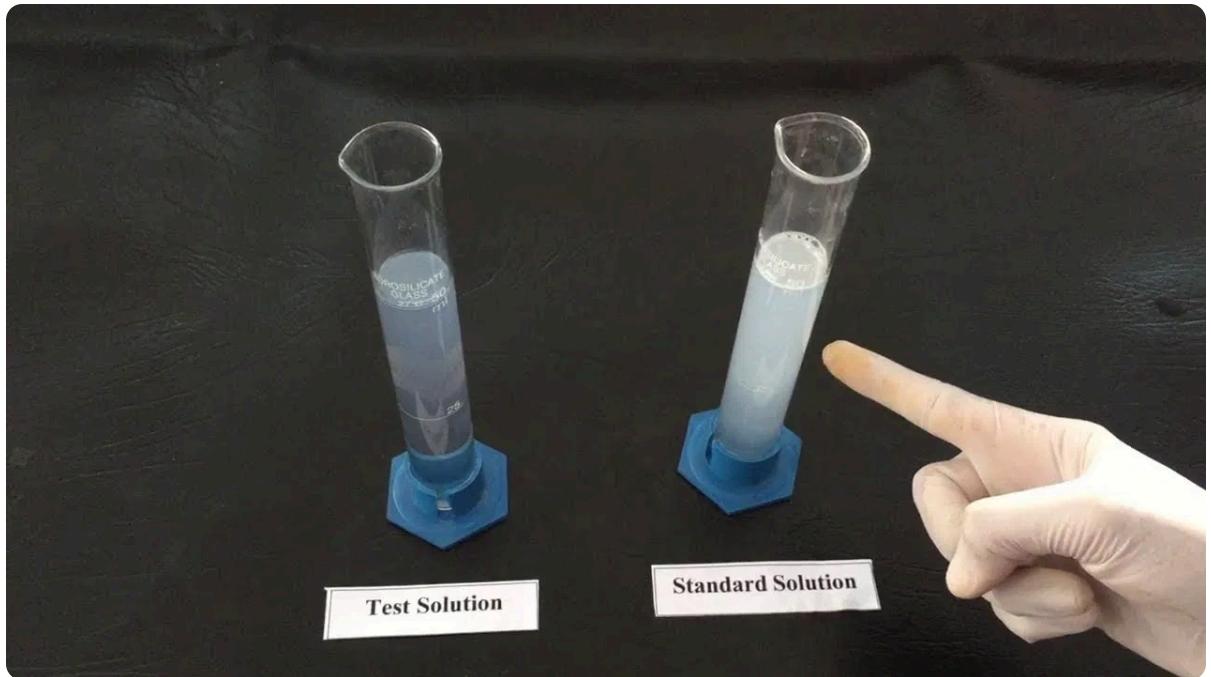
Limit tests are quantitative or semi-quantitative analyses designed to identify and control small amounts of impurities in pharmaceutical substances.

Purpose of Limit Tests:

- To determine whether impurities are within acceptable limits
- To ensure quality and safety of pharmaceutical products

Types of Limit Tests

- Chloride
- Sulphate
- Iron
- Arsenic
- Lead
- Heavy Metals



General Principles of Limit Tests

Key Concepts

Quantitative vs. Semi-quantitative:

Limit tests determine whether impurities are below or above a specified limit rather than exact quantities.

Comparison Methodology:

Test samples are compared with standard solutions containing known amounts of impurities.

Acceptance Criteria:

Pass/Fail methodology based on visual comparison:

- Pass: Test sample shows less intensity than standard
- Fail: Test sample shows more intensity than standard

Limit test for CHLORIDE



Common Laboratory Equipment



Nessler Cylinders



Test Tubes



Comparison Apparatus

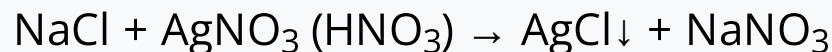


Pipettes

Limit Test for Chloride

Principle

The precipitation reaction is the basis for the chloride limit test. In the presence of dilute nitric acid, silver nitrate reacts with soluble chloride to produce silver chloride, appearing as solid particles (opalescence) in the solution.



Procedure Overview

1. Prepare test and standard solutions in Nessler cylinders
2. Add dilute nitric acid and silver nitrate to both
3. Compare the opalescence after 5 minutes

Visual Indicator:

The intensity of opalescence (cloudiness) indicates the amount of chloride present. If the test sample shows less opalescence than the standard, it passes the test.

Principle

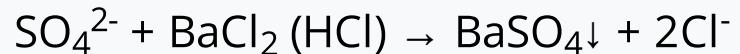
1. Limit test of sulphate is based on the reaction of soluble sulphate with barium chloride in presence of dilute hydrochloric acid to form barium sulphate which appears as solid particles (turbidity) in the solution.
2. The precipitate barium sulphate formed is insoluble in dil. Acetic acid and gives opalascence/turbidity.
3. A known amount of Pot. Sulphate is added in both standard and test in order to increase the sensitivity, rapid and complete precipitation by seeding.



Limit Test for Sulphate

Principle

The sulphate limit test uses a precipitation method. In the presence of hydrochloric acid, barium chloride reacts with sulphate ions to form insoluble barium sulphate, causing turbidity in the solution.



Procedure Overview

1. Prepare test and standard solutions
2. Add dilute HCl to both solutions
3. Add barium chloride solution and mix
4. Compare turbidity after 5 minutes

Visual Indicator:

The degree of turbidity depends on the amount of sulphate in the solution. Test results that are less turbid than the standard indicate a sample that contains sulphates within acceptable limits.

**Limit Test
for IRON**

STANDARD

TEST

In Just 4 Min

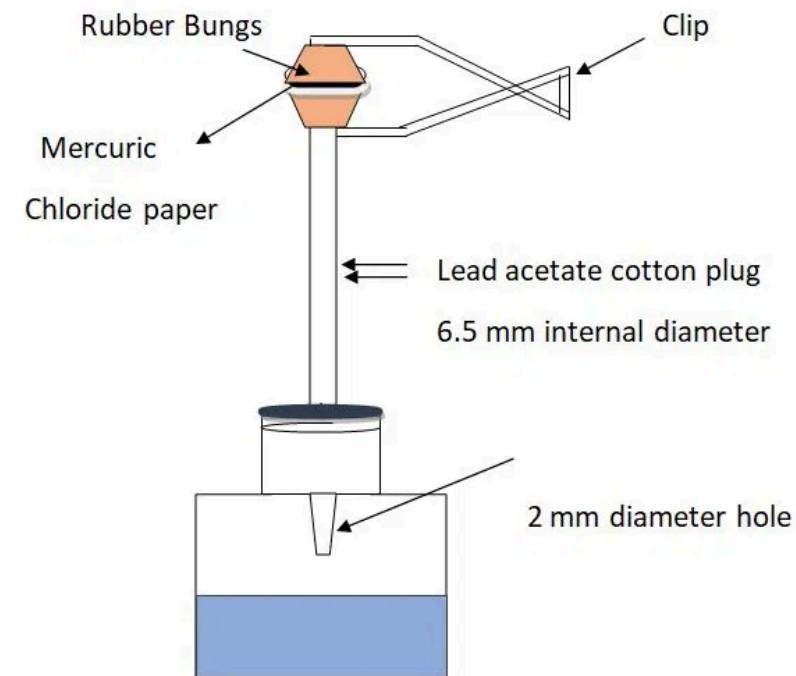
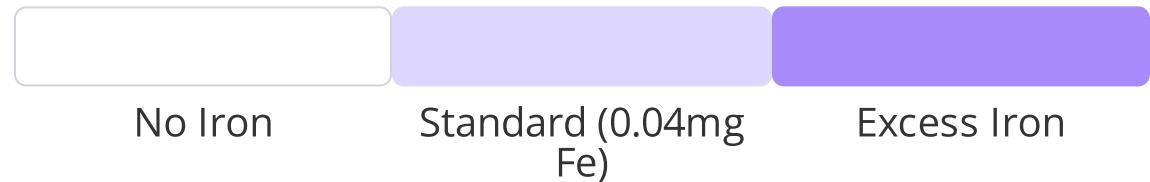
Pharmaceutical Inorganic Chemistry

Limit Test for Iron

Principle

The limit test for iron is based on the formation of a purple color when iron reacts with thioglycolic acid in a solution buffered with ammonium citrate.

Color Formation:



Procedure Overview

1. Dissolve sample in water
2. Add ammonium citrate solution
3. Add thioglycolic acid
4. Compare color with standard iron solution

Standard Comparison:

The color produced is compared with a standard color containing a known amount of iron (0.04mg of Fe).

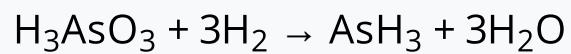
Limit Test for Arsenic

Principle: Gutzeit Test

The arsenic limit test is based on the formation of yellow stains on mercuric chloride paper when arsine gas reacts with hydrogen ion in the presence of reducing agents.



(Arsenic acid → Arsenious acid)



(Arsenious acid → Arsine gas)

Safety Considerations:

- Arsine gas is highly toxic
- Perform test in well-ventilated area
- Avoid direct contact with reagents

Apparatus Components



Test Bottle



Mercuric Chloride Paper



Lead Acetate Cotton



Zinc Granules

LIMIT TEST OF LEAD

AN INFORMATIVE VIDEO LECTURE ON LIMIT TEST FROM PHARMACEUTICAL ANALYSIS

BY AMAR RAVAL

GPAT NIPER DI PHARMACIST

Limit Test for Lead

Principle

The limit test for lead is based on the reaction of lead in alkaline solution with diphenyl thiocarbazole (dithizone) to form a lead-dithizone complex that produces a distinctive color.

Color Indicators:



Dithizone (Green)

Lead-Dithizone
(Violet)

Final Complex (Red)

Procedure Overview

1. Prepare sample in alkaline solution
2. Add dithizone reagent in chloroform
3. Shake and allow layers to separate
4. Compare color with standard lead solution

Applications:

Used to detect lead contamination in pharmaceuticals, particularly in substances used for parenteral preparations where lead toxicity is a significant concern.



Limit Test for Heavy Metals

In Just 4 Min

Pharmaceutical Inorganic Chemistry

Limit Test for Heavy Metals

Principle

In an acidic medium, metallic impurities react with hydrogen sulphide to produce a brownish-colored solution. The test detects lead, mercury, bismuth, arsenic, antimony, tin, cadmium, silver, copper, and molybdenum.

Indian Pharmacopoeia Standard:

Metal impurity is expressed as parts of lead per million parts of the substance. The maximum acceptable concentration is 20 ppm.

Testing Methods

Method A:

For colorless substances

Method B:

For colored substances

Method C:

For substances which form colored and colorless solutions with sodium

Method D:

For remaining substances



Applications and Significance

Importance in Quality Control

Regulatory Requirements:

Pharmacopoeias worldwide mandate limit tests to ensure drug safety and efficacy.

Pharmacopoeial Standards:

Indian Pharmacopoeia, USP, BP, and EP all include specific limit test protocols with defined acceptance criteria.

Modern Alternatives:

- Atomic Absorption Spectroscopy (AAS)
- Inductively Coupled Plasma (ICP)
- High-Performance Liquid Chromatography (HPLC)
- Ion Chromatography



Modern pharmaceutical quality control laboratory

Key Takeaways

Limit tests remain fundamental in pharmaceutical analysis despite advances in instrumentation, providing simple, cost-effective methods for quality control in pharmaceutical manufacturing.