Stage 4 Harmonization
Official: December 1, 2024

Lactose Monohydrate

Portions of the monograph text that are national *USP* text, and are not part of the harmonized text, are marked with symbols (⧫) to specify this fact.

Change to read:

DEFINITION

Lactose Monohydrate is the monohydrate of *O*-β-D-galactopyranosyl-(1→4)-α-D-glucopyranose. ▲⧫▲ (NF 1-Dec-2024)[NOTE—Lactose Monohydrate may be modified as to its physical characteristics. It may contain varying proportions of amorphous lactose.]▲⧫▲ (NF 1-Dec-2024)

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS ⟨197⟩, *Infrared Spectroscopy*:** 197K

- **⧫B. THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST ⟨201⟩**

  Diluent: Methanol and water (3:2)

  Standard solution A: 0.5 mg/mL of USP Lactose Monohydrate RS in *Diluent*

  Standard solution B: 0.5 mg/mL each of USP Dextrose RS, USP Lactose Monohydrate RS, USP Fructose RS, and USP Sucrose RS in *Diluent*

  Sample solution: 0.5 mg/mL of Lactose Monohydrate in *Diluent*

  Adsorbent: 0.25-mm layer of chromatographic silica gel

  Application volume: 2 µL

  Developing solvent system: Ethylene dichloride, glacial acetic acid, methanol, and water (10:5:3:2)

  Spray reagent: 5 mg/mL of thymol in a mixture of alcohol and sulfuric acid (19:1)

  Analysis

  Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*

  Allow the spots to dry, and develop the plate in a paper-lined chromatographic chamber equilibrated with *Developing solvent system* for about 1 h prior to use. Allow the chromatogram to develop until the solvent front has moved about three-quarters of the length of the plate. Remove the plate from the chamber, dry in a current of warm air, and redevelop the plate in fresh *Developing solvent system*. Remove the plate from the chamber, mark the solvent front, and dry the plate in a current of warm air. Spray the plate evenly with *Spray reagent*. Heat the plate at 130° for 10 min.

  System suitability: The test is not valid unless the chromatogram of *Standard solution B* shows four clearly discernible spots, disregarding any spots at the origin.

  Acceptance criteria: The principal spot from the *Sample solution* corresponds in appearance and R_F value to that from *Standard solution A*.⧫

IMPURITIES

- **RESIDUE ON IGNITION ⟨281⟩**

  Analysis: A sample ignited at a temperature of 600 ± 50°

  Acceptance criteria: NMT 0.1%

SPECIFIC TESTS

- **Clarity and Color of Solution**

  Sample solution: 1 g in 10 mL of boiling water

  Analysis: The *Sample solution* is clear and nearly colorless. Determine the absorbance of this solution at a wavelength of 400 nm.

  Acceptance criteria: The absorbance divided by the path length, in cm, is NMT 0.04.

Change to read:

- ▲ ▲ (NF 1-Dec-2024)**Microbial Enumeration Tests** ⟨61⟩ and **Tests for Specified Microorganisms** ⟨62⟩**:** The total aerobic microbial count does not exceed ▲ ▲ (NF 1-Dec-2024) 10^2 cfu/g, the total combined molds and yeasts count does not exceed ▲50▲ (NF 1-Dec-2024) cfu/g, and it meets the requirements of the test for absence of *Escherichia coli*.▲ ▲ (NF 1-Dec-2024)

- **Optical Rotation** ⟨781S⟩*, Procedures, Specific Rotation*

  Sample solution: Dissolve 10 g by heating in 80 mL of water to 50°. Allow to cool, and add 0.2 mL of 6 N ammonium hydroxide. Allow to stand for 30 min, and dilute with water to 100 mL.

  Acceptance criteria: +54.4° to +55.9°, calculated on the anhydrous basis, determined at 20°

- **Acidity or Alkalinity**

  Sample solution: Dissolve 6 g by heating in 25 mL of carbon dioxide-free water, cool, and add 0.3 mL of phenolphthalein TS.

  Acceptance criteria: The solution is colorless, and NMT 0.4 mL of 0.1 N sodium hydroxide VS is required to produce a pink or red color.

Change to read:

- ▲ ▲ (NF 1-Dec-2024)**Loss on Drying** ⟨731⟩

  Analysis: Dry a sample at 80° for 2 h.

  Acceptance criteria

  Monohydrate: NMT 0.5%

  ▲♦▲ (NF 1-Dec-2024)**Monohydrate, modified:** NMT 1.0%♦

- **Water Determination** ⟨921⟩*, Method I*

  Sample solution: Prepare a preparation containing Lactose Monohydrate in a mixture of methanol and formamide (2:1).

  Acceptance criteria: 4.5%–5.5%

Change to read:

- **Protein and Light-Absorbing Impurities**

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Sample solution: 1% (w/v)

▲**Instrumental conditions**

Mode: UV

Wavelength range: 210–300 nm▲ (NF 1-Dec-2024)

Acceptance criteria: The absorbance divided by the path length, in centimeters, is NMT 0.25 in the range of 210–220 nm and is NMT 0.07 in the range of 270–300 nm.

ADDITIONAL REQUIREMENTS

Change to read:

- **▲▲Packaging and Storage:** Preserve in tight containers.▲▲ (NF 1-Dec-2024)

Change to read:

- **▲▲▲ (NF 1-Dec-2024)Labeling:** Where the labeling states the particle size distribution, it also indicates the d_{10}, d_{50}, and d_{90} values and the range for each. For modified Lactose Monohydrate, also label it to indicate the method of modification.▲▲ (NF 1-Dec-2024)

Change to read:

- **USP Reference Standards** ⟨11⟩

  USP Dextrose RS

  USP Fructose RS

  USP Lactose Monohydrate RS

  USP Sucrose RS

▲ (NF 1-Dec-2024)

Page Information:

Not Applicable

Current DocID: