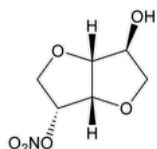


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Diluted Isosorbide Mononitrate



$C_6H_9NO_6$ 191.14

D-Glucitol, 1,4:3,6-dianhydro-, 5-nitrate;

1,4:3,6-Dianhydro-D-glucitol 5-nitrate CAS RN[®]: 16051-77-7; UNII: LX10H63030.

DEFINITION

Diluted Isosorbide Mononitrate is a dry mixture of isosorbide mononitrate ($C_6H_9NO_6$) with lactose or other suitable excipients to permit safe handling. It contains NLT 95.0% and NMT 105.0% of the labeled amount of isosorbide mononitrate ($C_6H_9NO_6$).

[CAUTION—Exercise proper precautions in handling undiluted isosorbide mononitrate, which is a powerful explosive and can be exploded by percussion or excessive heat. Only exceedingly small amounts should be isolated.]

IDENTIFICATION

Change to read:

- A. ▲ [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197A or 197K▲ (USP 1-May-2024)

Sample: Shake a suitable amount of Diluted Isosorbide Mononitrate, equivalent to about 25 mg of isosorbide mononitrate, with 10 mL of [acetone](#) for 5 min. Filter, evaporate to dryness at a temperature below 40°, dry the residue in a vacuum over [phosphorus pentoxide](#) for 16 h, and use the residue.

Standard: Prepare as directed for the *Sample* using a suitable amount of [USP Diluted Isosorbide Mononitrate RS](#).

Acceptance criteria: Meets the requirements

- B. The retention time of the major peak of the *Sample solution* corresponds to that of *Standard solution A*, as obtained in the Assay.

ASSAY

Change to read:

PROCEDURE

Mobile phase: [Methanol](#) and [water](#) (5:95)

Standard solution A: 2.0 mg/mL of isosorbide mononitrate prepared as follows. Transfer a suitable amount of [USP Diluted Isosorbide Mononitrate RS](#) to a suitable volumetric flask, dissolve in a suitable volume of [water](#), add a volume of [methanol](#) equivalent to 4% of the flask volume, and dilute with [water](#) to volume.

▲ (USP 1-May-2024)

Standard solution B: 0.05 mg/mL of isosorbide mononitrate related compound A prepared ▲ as follows. Transfer a suitable amount of [USP Diluted Isosorbide Mononitrate Related Compound A RS](#) to a suitable volumetric flask, dissolve in a suitable volume of [water](#), add a volume of [methanol](#) equivalent to 4% of the flask volume, and dilute with [water](#) to volume.▲ (USP 1-May-2024)

System suitability solution: 0.02 mg/mL of isosorbide mononitrate and 0.005 mg/mL of isosorbide mononitrate related compound A prepared as follows. Transfer 1.0 mL of *Standard solution A*, 10.0 mL of *Standard solution B*, and 4.0 mL of [methanol](#) to a 100-mL volumetric flask, and dilute with [water](#) to volume. Filter a portion of the solution, discarding the first few milliliters of the filtrate.

Sample solution: Nominally 2.0 mg/mL of isosorbide mononitrate from Diluted Isosorbide Mononitrate prepared as follows. Transfer a suitable amount of Diluted Isosorbide Mononitrate to a suitable volumetric flask, dissolve in 50% of the flask volume of [water](#), add a volume of [methanol](#) equivalent to 4% of the flask volume, and dilute with [water](#) to volume. Filter a portion of the solution, discarding the first few milliliters of the filtrate.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 220 nm

Column: 4-mm × 12.5-cm; ▲5-μm▲ (USP 1-May-2024) packing [L1](#)

Flow rate: 1.5 mL/min, increase to 3.0 mL/min at about 8.5 min. ▲[NOTE—Make sure that the isosorbide mononitrate peak has completely eluted before increasing the flow rate.]▲ (USP 1-May-2024)

Injection volume: 50 µL

▲**Run time:** NLT 5 times the retention time of isosorbide mononitrate▲ (USP 1-May-2024)

System suitability

Samples: *Standard solution A* and *System suitability solution*

▲[NOTE—The relative retention times for isosorbide mononitrate related compound A and isosorbide mononitrate are 0.8 and 1.0, respectively.]▲ (USP 1-May-2024)

Suitability requirements

Resolution: NLT 2.0 between isosorbide mononitrate related compound A and isosorbide mononitrate, *System suitability solution*

Relative standard deviation: NMT ▲0.73%,▲ (USP 1-May-2024) *Standard solution A*

Analysis

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

Calculate the percentage of the labeled amount of isosorbide mononitrate ($C_6H_9NO_6$) in the portion of Diluted Isosorbide Mononitrate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of isosorbide mononitrate from the *Sample solution*

r_S = peak response of isosorbide mononitrate from *Standard solution A*

C_S = concentration of isosorbide mononitrate in *Standard solution A* (mg/mL)

C_U = nominal concentration of isosorbide mononitrate in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

IMPURITIES

Add the following:

▲• LIMIT OF NITRATE

[NOTE—Use water with a resistivity of NLT 18 megohm-cm to prepare the solutions.]

Mobile phase: 20 mM [potassium hydroxide](#) in [water](#). [NOTE—*Mobile phase* can be generated electrolytically using an automatic eluant generator.]

Sensitivity solution: 0.5 µg/mL of [USP Potassium Nitrate RS](#) in [water](#)

Standard solution: 5.0 µg/mL of [USP Potassium Nitrate RS](#) in [water](#)

Sample solution: Nominally 1000 µg/mL of isosorbide mononitrate from Diluted Isosorbide Mononitrate in [water](#)

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: Conductivity with suppression

Columns

Guard: 4.0-mm × 5-cm; 13-µm packing [L120](#). [NOTE—Alternatively, a 4.0-mm × 0.5-cm column that contains 5.0-µm packing [L91](#) may be used.]

Analytical: 4.0-mm × 25-cm; 7.5-µm packing [L113](#). [NOTE—Alternatively, a 4.0-mm × 15-cm column that contains 5.0-µm packing [L91](#) may be used.]

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 100 µL

Run time: NLT 2 times the retention time of nitrate

System suitability

Sample: *Sensitivity solution*

Suitability requirements

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nitrate as potassium nitrate relative to the labeled amount of isosorbide mononitrate in the portion of Diluted Isosorbide Mononitrate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$