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Isosorbide Dinitrate Extended-Release Tablets

DEFINITION

Isosorbide Dinitrate Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of isosorbide dinitrate (C₆H₈N₂O₈).

IDENTIFICATION

Change to read:

- **A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#)**▲ (USP 1-Aug-2023)

Sample solution: Transfer a suitable quantity of finely powdered Tablets to a glass-stoppered centrifuge tube. Add 10 mL of [sodium hydroxide](#) solution (1 in 250), shake to wet the powder, add 15 mL of [hexane](#), and shake again. Centrifuge the mixture, and transfer the upper phase to a beaker. Evaporate the solvent, and dry the residue under vacuum over [calcium chloride](#) at room temperature for 16 h. Where separation of interferences is required, proceed as follows. Transfer a quantity of finely powdered Tablets, equivalent to 20 mg of isosorbide dinitrate, to a glass-stoppered centrifuge tube. Add 10 mL of [sodium hydroxide](#) solution (1 in 250), shake to wet the powder, add 15 mL of solvent [hexane](#), and shake again. Centrifuge the mixture, and transfer the upper phase to a beaker. Place in a freezer, at a temperature of -14°, the beaker and a short-stem funnel fitted with a cotton plug that previously has been [chloroform](#) washed and dried. After 30 min, filter the solution while still in the freezer. Evaporate the solvent, and dry the residue in vacuum over [calcium chloride](#) for 16 h, dissolved in 0.4 mL of [chloroform](#).

Standard solution: Prepare a solution with [USP Diluted Isosorbide Dinitrate RS](#) following a similar preparation as the *Sample solution*.

Acceptance criteria: The IR absorption spectrum of the *Sample solution* exhibits maxima only at the same wavelengths as that of the *Standard solution*. If separation of interference is required, the IR absorption spectrum of the *Sample solution* determined in a 0.1-mm cell shows all of the significant absorption bands present in the spectrum obtained for a similar preparation from the *Standard solution*. The major peaks are at 1650 cm⁻¹, 1284 cm⁻¹ and 1275 cm⁻¹ (a doublet), 1106 cm⁻¹, and 844 cm⁻¹.

Add the following:

- ▲ **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.▲ (USP 1-Aug-2023)

ASSAY

Change to read:

- **PROCEDURE**

▲ **Solution A:** [Methanol](#) and [water](#) (6:94)

Solution B: [Methanol](#) and [water](#) (50:50)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
2.5	100	0
18	60	40
18.1	0	100
20.5	0	100
21	100	0
26	100	

Diluent: [Methanol](#) and [water](#) (15:85)

Standard solution: 0.25 mg/mL of isosorbide dinitrate prepared as follows. Transfer a portion of [USP Diluted Isosorbide Dinitrate RS](#) equivalent to 25 mg of isosorbide dinitrate to a 100-mL volumetric flask. Add 10 mL of [methanol](#) and sonicate for NLT 5 min. Add *Diluent* to 60% of the flask volume and sonicate for NLT 15 min with occasional shaking until the solids are dissolved. Dilute with *Diluent* to volume.

Sample solution: Nominally 0.25 mg/mL of isosorbide dinitrate prepared as follows. Transfer a portion of finely powdered Tablets (NLT 20) equivalent to 50 mg of isosorbide dinitrate, to a 200-mL volumetric flask. Add 20 mL of [methanol](#), shake immediately, and sonicate for about 5 min to avoid clumping. Add *Diluent* to 60% of the flask volume and sonicate for about 15 min with occasional shaking. Shake for another 30 min on a shaker and allow the solution to come to room temperature. Dilute with *Diluent* to volume. Centrifuge a portion of the solution and use the clear supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 5-cm; 5-μm packing [L1](#)

Column temperature: 30°

Flow rate: 2 mL/min

Injection volume: 75 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of isosorbide dinitrate ($C_6H_8N_2O_8$) in the portion of Tablets taken:

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

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

r_S = peak response of isosorbide dinitrate from the *Standard solution*

C_S = concentration of isosorbide dinitrate from [USP Diluted Isosorbide Dinitrate RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of isosorbide dinitrate in the *Sample solution* (mg/mL)▲ (USP 1-Aug-2023)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#).

Test 1

Medium: [Water](#); 500 mL

Apparatus 2: 50 rpm

Time: 1, 2, 4, and 6 h

Solution A: 13.2 g/L of [ammonium sulfate](#) in [water](#). Adjust with 1 N [sulfuric acid](#) to a pH of 3.0.

Mobile phase: [Methanol](#) and *Solution A* (50:50)

Standard solution: A known concentration of isosorbide dinitrate in *Medium* from [USP Diluted Isosorbide Dinitrate RS](#)

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Column: 5-mm × 25-cm; packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

▲ Calculate the concentration (C_U) of isosorbide dinitrate ($C_6H_8N_2O_8$) in the sample withdrawn from the vessel at each time point (t):