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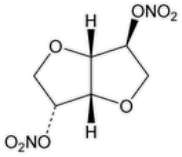
# Diluted Isosorbide Dinitrate



$C_6H_8N_2O_8$ 236.14

D-Glucitol, 1,4:3,6-dianhydro-, dinitrate;

1,4:3,6-Dianhydro-D-glucitol dinitrate CAS RN®: 87-33-2; UNII: IA7306519N.

## DEFINITION

Diluted Isosorbide Dinitrate is a dry mixture of isosorbide dinitrate ($C_6H_8N_2O_8$) with Lactose, Mannitol, or suitable inert excipients to permit safe handling. It may contain up to 1.0% of a suitable stabilizer, such as Ammonium Phosphate. It contains NLT 95.0% and NMT 105.0% of the labeled amount of isosorbide dinitrate ($C_6H_8N_2O_8$). It usually contains approximately 25% of isosorbide dinitrate.

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

## IDENTIFICATION

- **A.**

**Sample solution:** Transfer to a medium-porosity, sintered-glass filtering crucible a quantity of Diluted Isosorbide Dinitrate, equivalent to about 50 mg of isosorbide dinitrate, and pass three 5-mL portions of acetone through it. Evaporate the combined extracts at a temperature not exceeding 35°, with the aid of a gentle current of air, and dry the residue under vacuum over calcium chloride at room temperature for 16 h. Prepare a solution (1 in 40) of the residue so obtained, in chloroform.

**Standard solution:** A similar preparation from the residue obtained from USP Diluted Isosorbide Dinitrate RS

**Acceptance criteria:** The IR absorption spectrum of the *Sample solution*, determined in a 0.1-mm cell, exhibits maxima only at the same wavelengths as that of the *Standard solution*.

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

## ASSAY

- **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 |
| 18.0 | 60 | 40 |
| 18.1 | 0 | 100 |

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 20.5 | 0 | 100 |
| 21.0 | 100 | 0 |
| 26 | 100 | 0 |

**Diluent:** Methanol and water (15:85)

**Standard solution:** 0.25 mg/mL of isosorbide dinitrate prepared as follows. Transfer a suitable 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. Dilute with *Diluent* to 60% of the flask volume, and sonicate with occasional shaking until all solids dissolve. Dilute with *Diluent* to volume.

**Sample solution:** 0.25 mg/mL of isosorbide dinitrate prepared as follows. Transfer a suitable portion of Diluted Isosorbide Dinitrate, equivalent to 25 mg of isosorbide dinitrate, to a 100-mL volumetric flask. Add 10 mL of methanol and sonicate. Dilute with *Diluent* to 60% of the flask volume, and sonicate with occasional shaking until all solids are dissolved. Dilute with *Diluent* to volume.

**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:** 3 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 isosorbide dinitrate ($C_6H_8N_2O_8$) in the portion of Diluted Isosorbide Dinitrate 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)

$C_U$ = concentration of isosorbide dinitrate in the *Sample solution* (mg/mL)

**Acceptance criteria:** 95.0%–105.0%

## IMPURITIES

- **Organic Impurities**

**Solution A, Solution B, Mobile phase, Diluent,** and **Chromatographic system:** Proceed as directed in the *Assay*.

**Standard stock solution:** 0.3 mg/mL of isosorbide dinitrate prepared as follows. Transfer a suitable portion of USP Diluted Isosorbide Dinitrate RS, equivalent to 30 mg of isosorbide dinitrate, to a 100-mL volumetric flask. Add 10 mL of methanol and sonicate. Dilute with *Diluent* to 60% of the flask volume, sonicate with occasional shaking, and dilute with *Diluent* to volume.

**Standard solution:** 7.5 µg/mL of isosorbide dinitrate from the *Standard stock solution* in *Diluent*

**Sensitivity solution:** 0.375 µg/mL of isosorbide dinitrate from the *Standard solution* in *Diluent*

**Sample solution:** 750 µg/mL of isosorbide dinitrate prepared as follows. Transfer a suitable quantity of Diluted Isosorbide Dinitrate, equivalent to 37.5 mg of isosorbide dinitrate, to a 50-mL volumetric flask. Add 5 mL of methanol, mix, and sonicate. Add *Diluent* to fill 60% of the flask volume, and sonicate with occasional shaking. Allow the solution to equilibrate to room temperature and dilute with *Diluent* to volume.

**System suitability**

**Samples:** *Standard solution* and *Sensitivity solution*

[NOTE—See *Table 2* for relative retention times.]

**Suitability requirements**

**Tailing factor:** NMT 2.0, *Standard solution*

**Relative standard deviation:** NMT 2.0%, *Standard solution*

**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*

**Analysis**

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

Calculate the percentage of each impurity in the portion of Diluted Isosorbide Dinitrate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

$r_U$ = peak response of each impurity 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* (µg/mL)

$C_U$ = concentration of isosorbide dinitrate in the *Sample solution* (µg/mL)

$F$ = relative response factor (see *Table 2*)

**Acceptance criteria:** See *Table 2*. Reporting threshold: 0.05%.

**Table 2**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Isosorbide mononitrate related compound A[a] | 0.15 | 0.61 | 0.15 |
| Isosorbide mononitrate[b] | 0.21 | 0.61 | 0.15 |
| Isosorbide dinitrate | 1.0 | — | — |
| Any individual unspecified impurity | — | 1.0 | 0.10 |
| Total impurities | — | — | 1.0 |

[a] 1,4:3,6-Dianhydro-D-glucitol 2-nitrate.

[b] 1,4:3,6-Dianhydro-D-glucitol 5-nitrate.

## SPECIFIC TESTS

• **LOSS ON DRYING ⟨731⟩**

**Analysis:** Dry under vacuum over calcium chloride at room temperature for 16 h.

**Acceptance criteria:** NMT 1.0%

## ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers.

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Diluted Isosorbide Dinitrate RS

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| DILUTED ISOSORBIDE DINITRATE | Documentary Standards Support | SM22020 Small Molecules 2 |
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | SM22020 Small Molecules 2 |

**Chromatographic Database Information:** Chromatographic Database

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