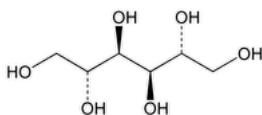


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Mannitol

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.



$C_6H_{14}O_6$ 182.17
D-Mannitol CAS RN®: 69-65-8.

DEFINITION

Mannitol contains NLT 97.0% and NMT 102.0% of mannitol ($C_6H_{14}O_6$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- A. **▲ SPECTROSCOPIC IDENTIFICATION TESTS †(197), Infrared Spectroscopy: 197K▲** (CN 1-MAY-2020)

If the spectra shows differences, proceed as directed.

Standard solution: Dissolve 25 mg of [USP Mannitol RS](#) in a glass vial with 0.25 mL of distilled water without heating. The solution is clear.

Evaporate to dryness by one of the following methods. Heat in a microwave oven with a power range of 600–700 W for 20 min, or heat in an oven at 100° for 1 h, then gradually apply vacuum until a dry residue is obtained. Non-sticky, white, or slightly yellowish powders are obtained.

Sample solution: Dissolve 25 mg of Mannitol in a glass vial with 0.25 mL of distilled water without heating. The solution is clear. Evaporate to dryness by one of the following methods. Heat in a microwave oven with a power range of 600–700 W for 20 min, or heat in an oven at 100° for 1 h, then gradually apply vacuum until a dry residue is obtained. Non-sticky, white, or slightly yellowish powders are obtained.

Analysis: Record new spectra using the residues from the *Standard solution* and the *Sample solution*.

ASSAY

• PROCEDURE

Mobile phase: Degassed water

System suitability solution A: 25.0 mg/mL each of sorbitol and [USP Mannitol RS](#)

System suitability solution B: 1.0 mg/mL each of maltitol and isomalt

Standard solution A: 50.0 mg/mL of [USP Mannitol RS](#)

Standard solution B: Dilute 2.0 mL of the *Sample solution* with water to 100.0 mL.

Standard solution C: Dilute 0.5 mL of *Standard solution B* with water to 20.0 mL.

Sample solution: 50.0 mg/mL of Mannitol

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 7.8-mm × 30-cm; packing L19

Temperatures

Detector: 40° (maintain at a constant temperature)

Column: 85 ± 2°

Flow rate: 0.5 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of the mannitol peak. [NOTE—The retention time for mannitol is about 20 min.]

System suitability

Samples: *System suitability solution A*, *System suitability solution B*, *Standard solution B*, and *Standard solution C*

Suitability requirements

Resolution: NLT 2.0 between sorbitol and mannitol, *System suitability solution A*

Analysis

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

Calculate the percentage of mannitol ($C_6H_{14}O_6$) in the portion of Mannitol taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from *Standard solution A*

C_S = concentration of [USP Mannitol RS](#) in *Standard solution A* (mg/mL)

C_U = concentration of the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–102.0% on the dried basis

IMPURITIES

• RELATED SUBSTANCES

Mobile phase, System suitability solution A, System suitability solution B, Standard solution B, Standard solution C, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.

Analysis

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

Acceptance criteria: See [Table 1](#) for the relative retention times.

Table 1

Name	Relative Retention Time
Isomalt (1st peak)	0.60
Maltitol	0.69
Isomalt (2nd peak)	0.73
Mannitol	1.0
Sorbitol	1.2

[NOTE—Impurity A—Sorbitol; Impurity B—Maltitol; Impurity C—Isomalt.]

[NOTE—Isomalt elutes in two peaks.]

[NOTE—Coelution of impurity B and the second peak of impurity C may be observed.]

Disregard limit: NMT 0.05%; any peak NMT the area of the principal peak obtained with *Standard solution C*

Sorbitol: NMT 2.0%; NMT the area of the principal peak obtained with *Standard solution B*

Sum of isomalt and maltitol: NMT 2.0%; NMT the area of the principal peak obtained with *Standard solution B*

Unspecified impurities: NMT 0.10% for each impurity; NMT twice the area of the principal peak obtained with *Standard solution C*

Total impurities: NMT 2.0%; NMT the area of the principal peak obtained with *Standard solution B*

• REDUCING SUGARS

Ferric sulfate solution: Dissolve 50 g of [ferric sulfate](#) in an excess of water, add 200 mL of [sulfuric acid](#), and dilute with water to 1000 mL.

Copper sulfate solution: 69.2 mg/mL of [copper sulfate](#) ($CuSO_4 \cdot 5H_2O$) in water

Sodium potassium tartrate solution: Dissolve 173 g of [sodium potassium tartrate](#) ($C_4H_4KNaO_6 \cdot 4H_2O$) and 50 g of [sodium hydroxide](#) in 400 mL of water. Heat to boiling, allow to cool, and dilute with carbon dioxide-free water to 500 mL.

Cupri-tartaric solution: Mix equal volumes of *Copper sulfate solution* and *Sodium potassium tartrate solution* immediately before use.

Sample: 7.0 g

Analysis: To the *Sample* add 13 mL of water. Boil gently with 40 mL of *Cupri-tartaric solution* for 3 min, and allow to stand for about 2 min. A precipitate is formed. Pass through a sintered-glass filter (10–16 μm) coated with diatomaceous earth or a sintered-glass filter (5–10 μm). Wash the precipitate with hot water (at about 50°–60°) until the washing is no longer alkaline, and pass the washings through the filter described above. Discard all the filtrate at this step. Immediately dissolve the precipitate in 20 mL of *Ferric sulfate solution*, pass through the filter described above in a clean flask, and wash the filter with 15–20 mL of water. Combine the washings and the filtrate, heat to 80°, and titrate with [0.02 M potassium permanganate VS](#).

Acceptance criteria: NMT 0.1%, expressed as glucose; NMT 3.2 mL of [0.02 M potassium permanganate VS](#) is required to change the color of the solution. The green color turns to pink, and the color persists at least 10 s.

• NICKEL