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Maltitol Solution

DEFINITION

Maltitol Solution is a water solution containing NLT 50.0% of D-maltitol ($C_{12}H_{24}O_{11}$) (w/w) and NMT 8.0% of D-sorbitol ($C_6H_{14}O_6$) (w/w), calculated on the anhydrous basis. The amounts of total sugars, other polyhydric alcohols, and any polyol anhydrides, if detected, are not included in the requirements nor in the calculated amount as stated in *General Notices, 5.60.10 Other Impurities in USP and NF Articles*.

IDENTIFICATION

- **A.**

Sample solution: Dissolve 1.4 g of Maltitol Solution in 75 mL of water

Analysis: Transfer 3 mL of the *Sample solution* to a 15-cm test tube, add 3 mL of a freshly prepared solution of catechol (1 in 10), and mix. Add 6 mL of sulfuric acid, and mix. Gently heat the tube in a flame for about 30 s.

Acceptance criteria: A deep pink or wine-red color appears.

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

- **C. Limit of Diethylene Glycol and Ethylene Glycol**

Diluent: Acetone and water (96:4)

Internal standard solution: 0.5 mg/mL of 1,3-butanediol (internal standard) in *Diluent*

Standard stock solution: 0.5 mg/mL of USP Diethylene Glycol RS and 0.5 mg/mL of USP Ethylene Glycol RS in *Diluent*

Standard solution: 0.04 mg/mL of USP Diethylene Glycol RS, 0.04 mg/mL of USP Ethylene Glycol RS, and 0.04 mg/mL of 1,3-butanediol, in *Diluent*, prepared from the *Standard stock solution* and *Internal standard solution*

Sample solution: Transfer 1.0 g of Maltitol Solution to a 25-mL volumetric flask. Add 1.0 mL of water to the flask, and mix on a vortex mixer for 3 min. Add 2.0 mL of the *Internal standard solution* and 5 mL of *Diluent*, and mix on a vortex mixer for 3 min. Add the remaining *Diluent* to the flask to volume in 2 equal portions. Mix the contents for about 3 min after each addition of *Diluent*. Pass a portion of the supernatant layer through a nylon filter of 0.45-µm pore size. Discard the first 2 mL of the filtrate, and collect the rest of the filtrate for analysis. [Note—Acetone is used to precipitate maltitol.]

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 15-m fused-silica capillary column; 0.25-µm layer of phase G46

Temperatures

Detector: 300°

Injection port: 240°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
70	—	70	2
70	50	300	5

Carrier gas: Helium

Flow rate: 3.0 mL/min

Injection volume: 1.0 µL

Injection type: Split, split ratio 10:1. [Note—A general purpose split/splitless, taper, glass wool, and deactivated liner is used.]

System suitability

Sample: *Standard solution*

[NOTE—See *Table 2* for relative retention times. Relative retention times are provided for information only, and the standards should be used to ensure appropriate peak identification.]

Suitability requirements

Resolution: NLT 15 between ethylene glycol and 1,3-butanediol

Table 2

Name	Relative Retention Time
Ethylene glycol	1.0
1,3-Butanediol (internal standard)	2.2
Diethylene glycol	2.8

Analysis

Samples: *Standard solution* and *Sample solution*

Based on the *Standard solution*, identify the peaks of ethylene glycol, 1,3-butanediol (internal standard), and diethylene glycol. Compare peak area ratios of ethylene glycol to the internal standard and of diethylene glycol to the internal standard in the *Standard solution* and *Sample solution*, respectively.

Acceptance criteria

Diethylene glycol: The peak area ratio of diethylene glycol to the internal standard in the *Sample solution* is NMT the peak area ratio of diethylene glycol to the internal standard in the *Standard solution*, corresponding to NMT 0.10% of diethylene glycol in Maltitol Solution.

Ethylene glycol: The peak area ratio of ethylene glycol to the internal standard in the *Sample solution* is NMT the peak area ratio of ethylene glycol to the internal standard in the *Standard solution*, corresponding to NMT 0.10% of ethylene glycol in Maltitol Solution.

ASSAY

• **PROCEDURE**

Mobile phase: Water

Standard solution: 10 mg/g of USP Maltitol RS and 1.6 mg/g of USP Sorbitol RS

Sample solution: 20 mg/g of Maltitol Solution in water

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: Refractive index

Column: 7.8-mm × 10-cm; packing L34

Temperatures

Column: 60 ± 2°

Detector: 35°

Flow rate: 0.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[NOTE—The relative retention times for maltotriitol, maltitol, and sorbitol are 0.38, 0.48, and 1.0, respectively.]

Suitability requirements

Tailing factor: NMT 1.2 for maltitol and sorbitol

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage, on the anhydrous basis, of D-maltitol ($C_{12}H_{24}O_{11}$) and D-sorbitol ($C_6H_{14}O_6$) in the portion of Maltitol Solution taken:

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

r_U = peak response of D-maltitol or D-sorbitol from the *Sample solution*

r_S = peak response of D-maltitol or D-sorbitol from the *Standard solution*

C_S = concentration of the appropriate USP Reference Standard in the *Standard solution* (mg/g)

C_U = concentration of Maltitol Solution in the *Sample solution* (mg/g)

W = percentage in the test for *Water Determination* (%)

Acceptance criteria: NLT 50.0% of D-maltitol (w/w) and NMT 8.0% of D-sorbitol (w/w), on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%, calculated on the anhydrous basis, determined on a 2-g portion

Change to read:

• **Limit of Nickel**

▲[Note—When water is specified as the diluent, use deionized ultra-filtered water. Use of glass volumetric flasks is discouraged.]

Digest solution: Add 360 mL of hydrochloric acid, ultratrace and 240 mL of nitric acid, ultratrace to 1200 mL of water.

Blank solution: Add 40 mL of nitric acid, ultratrace to a 2000-mL volumetric flask, dilute with water to volume, and mix well.

Internal standard solution: Transfer 2.0 mL of solution containing 1000 mg/L of yttrium[1] to a 1000-mL volumetric flask, dilute with *Blank solution* to volume, and mix well. The *Internal standard solution* contains 2 µg/mL of yttrium. [Note—The concentration of the *Internal standard solution* can be adjusted if a high number of signal counts from the *Internal standard solution* causes an artifact.]

Standard stock solution: [Note—Prepare this solution fresh every 2 months.] Quantitatively dilute an accurately measured volume of the solution containing 1000 mg/L of nickel[2] with *Blank solution* to obtain a solution containing 10 µg/mL of nickel.

▲Standard nickel▲ (ERR 1-May-2021) solution A: [Note—Prepare this solution fresh weekly.] Separately pipet 1.0 mL of *Standard stock solution* into a 200-mL volumetric flask. Dilute the contents in the flask with *Blank solution* to volume, and mix well. This solution contains 50 ng/mL of nickel.

Standard nickel solution B: [Note—Prepare this solution fresh weekly.] Separately pipet 2.0 mL of *Standard stock solution* into a 200-mL volumetric flask. Dilute the contents in the flask with *Blank solution* to volume, and mix well. This solution contains 100 ng/mL of nickel.

Standard nickel solution C: [Note—Prepare this solution fresh weekly.] Separately pipet 4.0 mL of *Standard stock solution* into a 200-mL volumetric flask. Dilute the contents in the flask with *Blank solution* to volume, and mix well. This solution contains 200 ng/mL of nickel.

Sample solution: Transfer a quantity of Maltitol Solution, equivalent to 10.0 g on the anhydrous basis, into a 125-mL conical flask. Add 40 mL of *Digest solution*, and place on a hot plate. Heat the solution for about 20 min, being careful to prevent the solution from boiling over. Pull the sample off the hot plate just before it turns a dark caramel color. [Note—Do not overburn the sample.] Transfer the flask's contents into a clean, dry, 50-mL volumetric flask with washings of *Blank solution*. Dilute with *Blank solution* to volume. Filter the sample into a 15-mL centrifuge tube, using a 10-mL disposable syringe fitted with a syringe filter of 0.45-µm pore size.

Instrumental conditions

(See *Plasma Spectrochemistry ⟨730⟩*.)

Mode: ICP–OES

Emission wavelengths: 232.005 nm for nickel and 371.029 nm for yttrium. Set the sample read time and other instrument parameters as appropriate or as recommended by the instrument manufacturer.

System suitability

Samples: *Blank solution*, *Standard nickel solution A*, *Standard nickel solution B*, and *Standard nickel solution C*

Suitability requirements

[Note—Instrument performance must be verified to conform to the manufacturer's specifications for resolution and sensitivity. Before analyzing samples, the instrument must pass a suitable performance check.]

Correlation coefficient: NLT 0.999, determined from the *Calibration curve* constructed in the *Analysis*

Analysis

Samples: *Blank solution*, *Standard nickel solution A*, *Standard nickel solution B*, *Standard nickel solution C*, and *Sample solution*

[Note—The following analysis is described for one type of ICP–OES instruments. If a different ICP–OES instrument is used, follow the instrument manufacturer's recommendations for operation.]

Take 3 replicate scans with the integration set as recommended by the instrument manufacturer. Follow the instrument manufacturer's recommendations for delivering the sample. Add the *Internal standard solution* in-line via a mixing block between the sample probe and the spray chamber. Flush the samples through the system before analysis. Program a read delay into the sampling routine to allow for fluid flow equilibration after the high-speed flush, before the first analytical read of the sample. Between samples, wash the pumping system by flushing the *Blank solution*.

Calibration curve: Generate the calibration curve using the *Blank solution*, *Standard nickel solution A*, *Standard nickel solution B*, and *Standard nickel solution C* as follows. Scan the *Internal standard solution* while running the *Blank solution* to measure the intensity of the yttrium emission. Hold this value constant throughout the remainder of the test. Separately scan the *Blank solution*, *Standard nickel solution A*, *Standard nickel solution B*, and *Standard nickel solution C* for nickel and yttrium. [Note—Add the *Internal standard solution* via an in-line mixing chamber.] Normalize the yttrium intensity to the value of the *Internal standard solution*. Apply this normalization factor to the nickel intensity, which is then referred to as the corrected nickel intensity. Construct a calibration curve by plotting the corrected nickel intensity versus the known concentrations, in ng/mL, of the nickel.

Similarly, analyze the *Sample solution*. Plot the intensity of the emission of the *Sample solution* on the calibration curve. Determine the concentration of nickel, *C*, in ng/mL, in the *Sample solution* through the calibration curve.

Calculate the content, in µg/g, of nickel in the solid portion of Maltitol Solution taken:

$$\text{Result} = (F \times V \times C)/W$$

F = conversion factor, 10^{-3} µg/ng (ng to µg)

V = volume of the *Sample solution*, 50 mL

C = concentration of nickel in the *Sample solution* (ng/mL)

W = weight of Maltitol Solution calculated on the anhydrous basis (g)

Acceptance criteria: NMT 1 µg/g▲ (NF 1-May-2021)

• **Reducing Sugars**

[Note—The amount determined in this test is not included in the calculated amount as requested in *General Notices, 5.60.10 Other Impurities in USP and NF Articles*.]

Sample: An amount of Maltitol Solution equivalent to 3.3 g on the anhydrous basis

Analysis: To the *Sample* add 3 mL of water, 20.0 mL of cupric citrate TS, and a few glass beads. Heat so that boiling begins after 4 min, and maintain boiling for 3 min. Cool rapidly and add 40 mL of diluted acetic acid, 60 mL of water, and 20.0 mL of 0.05 N iodine VS. With continuous shaking, add 25 mL of a mixture of 6 mL of hydrochloric acid and 94 mL of water. When the precipitate has dissolved, titrate the excess of iodine with 0.05 N sodium thiosulfate VS using 2 mL of starch TS, added toward the end of the titration, as an indicator.

Acceptance criteria: NLT 12.8 mL of 0.05 N sodium thiosulfate VS is required, corresponding to NMT 0.3% of reducing sugars, on the anhydrous basis, as glucose.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specific Microorganisms ⟨62⟩:** The total aerobic microbial count using the *Plate Method* is NMT 10^3 cfu/mL, and the total combined molds and yeasts count is NMT 10^2 cfu/mL.

• **pH ⟨791⟩:** 5.0–7.5, in a 14% (w/w) solution of Maltitol Solution in carbon dioxide-free water

• **Water Determination ⟨921⟩, *Method I*:** NMT 31.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. No storage requirements are specified.

• **USP Reference Standards ⟨11⟩**

USP Diethylene Glycol RS
USP Ethylene Glycol RS
USP Maltitol RS
USP Sorbitol RS

[1] Yttrium ICP standard solutions are commercially available. A suitable yttrium ICP standard is available from LGC (www.lgcstandards.com) or Millipore Sigma (www.sigmaaldrich.com).

[2] Nickel ICP standard solutions are commercially available. A suitable nickel ICP standard is available from LGC (www.lgcstandards.com) or Millipore Sigma (www.sigmaaldrich.com).

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
MALTITOL SOLUTION	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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