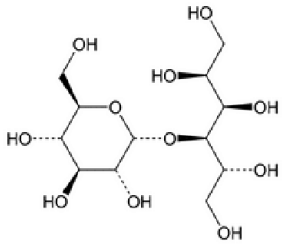
Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2021
Document Type: NF Monographs
DocId: GUID-66320AF0-558F-45F9-BBFF-1F8EB3B242EB_3_en-US
DOI: https://doi.org/10.31003/USPNF_M47119_03_01
DOI Ref: pl4lj

Maltitol



$C_{12}H_{24}O_{11}$ 344.31

D-Glucopyranosyl-D-glucitol CAS RN®: 585-88-6.

DEFINITION

Maltitol contains NLT 92.0% and NMT 100.5% of D-maltitol ($C_{12}H_{24}O_{11}$), 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. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K
- **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**

Mobile phase: Water. [Note—Degas the *Mobile phase* before use.]

System suitability solution: 4.8 mg/g of USP Maltitol RS and 4.8 mg/g of sorbitol

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

Sample solution: Dissolve 0.20 g of Maltitol in water and dilute with water to 20 g. Record the final solution weight, and mix thoroughly. The solution is 10 mg/g of Maltitol.

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

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

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

Suitability requirements

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

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of D-maltitol ($C_{12}H_{24}O_{11}$) in the portion of Maltitol taken:

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

r_U = peak response of maltitol from the *Sample solution*

r_S = peak response of maltitol from the *Standard solution*

C_S = concentration of USP Maltitol RS in the *Standard solution* (mg/g)

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

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

Acceptance criteria: 92.0%–100.5% on the anhydrous basis

IMPURITIES

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 solution A: [Note—Prepare this solution fresh weekly.] Pipet 1.0 mL of *Standard stock solution* into a 200-mL volumetric flask. Dilute the content 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.] Pipet 2.0 mL of *Standard stock solution* into a 200-mL volumetric flask. Dilute the content 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.] Pipet 4.0 mL of *Standard stock solution* into a 200-mL volumetric flask. Dilute the content in the flask with *Blank solution* to volume, and mix well. This solution contains 200 ng/mL of nickel.

Sample solution: Transfer 10.0 g of Maltitol 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 of 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 and 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 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 portion of Maltitol 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 (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 required in *General Notices, 5.60.10 Other Impurities in USP and NF Articles*.]

Sample: 3.3 g

Titrimetric system

Mode: Residual titration

Titrant: 0.05 N sodium thiosulfate VS

Endpoint detection: Visual

Analysis: Dissolve the *Sample* in 3 mL of water with the aid of gentle heat. Cool and add 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 solution of hydrochloric acid in water (6:94). When the precipitate has dissolved, titrate the excess of iodine with *Titrant* using 2 mL of starch TS, added toward the end of the titration, as an indicator.

Acceptance criteria: NLT 12.8 mL of *Titrant* is required, corresponding to NMT 0.3% of reducing sugars, as glucose.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count using the *Plate Method* does not exceed 10^3 cfu/g, and the total combined molds and yeasts count does not exceed 10^2 cfu/g.

• **Conductivity**

Sample solution: 200 mg/mL

Analysis: Using an appropriate conductivity meter, choose a conductivity cell that is appropriate for the properties and conductivity of the solution to be examined. Use a certified reference material, for example a solution of potassium chloride, that is appropriate for the measurement.[3]

The conductivity value of the certified reference material should be near the expected conductivity value of the solution to be examined. After calibrating the apparatus with a certified reference material solution, rinse the conductivity cell several times with water and at least twice with the aqueous solution to be examined. Measure the conductivity of the *Sample solution* at a temperature of 20°, while gently stirring with a magnetic stirrer.

Acceptance criteria: NMT 20 µS/cm

• **Water Determination ⟨921⟩, *Method I*:** NMT 1.0%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Maltitol 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).

[3] Commercially available conductivity calibration solutions for conductivity meter standardization, standardized by methods traceable to the National Institute of Standards and Technology (NIST), may be used. Solutions prepared according to the instructions given in ASTM Standard D1125 may be used, provided the conductivity of the resultant solution is the same as that of the solution prepared from the NIST-certified material.

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 50(2)

Current DocID: GUID-66320AF0-558F-45F9-BBFF-1F8EB3B242EB_3_en-US
DOI: https://doi.org/10.31003/USPNF_M47119_03_01
DOI ref: pi4lj