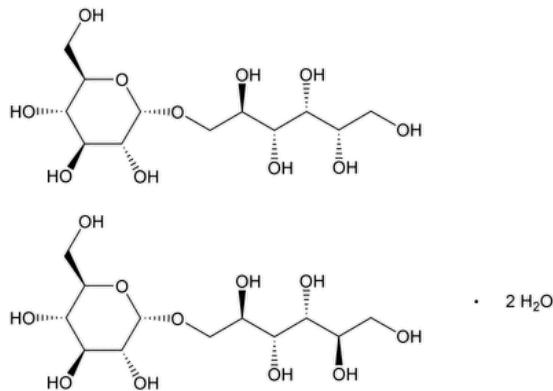


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Isomalt

Portions of this monograph that are national *USP* text, and are not part of the harmonized text, are marked with symbols (♦) to specify this fact.



$C_{12}H_{24}O_{11}$ 344.31
 $C_{12}H_{24}O_{11} \cdot 2H_2O$ 380.32

6-O- α -Glucopyranosyl- β -sorbitol and 1-O- α - β -glucopyranosyl- β -mannitol dihydrate;

6-O- α - β -Glucopyranosyl- β -glucitol and 1-O- α - β -glucopyranosyl- β -mannitol dihydrate CAS RN®: 64519-82-0.

DEFINITION

Isomalt contains NLT 98.0% and NMT 102.0% of a mixture of 6-O- α - β -glucopyranosyl- β -sorbitol (1,6-GPS) and 1-O- α - β -glucopyranosyl- β -mannitol (1,1-GPM), and neither of the two components is less than 3.0% of the mixture, calculated on the anhydrous basis.

IDENTIFICATION

• A. [THIN-LAYER CHROMATOGRAPHIC IDENTIFICATION TEST \(201\)](#)

Standard solution: 5 mg/mL of [USP Isomalt RS](#)

Sample solution: 5 mg/mL

Chromatographic system

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture containing a fluorescent indicator having optimal intensity at 254 nm

Application volume: 1 μ L

Developing solvent system: [Ethyl acetate](#), [pyridine](#), water, [acetic acid](#), and [propionic acid](#) (10:10:2:1:1)

Analysis

Samples: Standard solution and Sample solution

Proceed as directed in the chapter. Thoroughly dry the starting points in warm air. Develop over 10 cm using the *Developing solvent system*, dry the plate in a current of hot air, and dip for 3 s in a 1-mg/mL solution of [sodium periodate](#). Dip the plate for 3 s in a mixture of [dehydrated alcohol](#), [sulfuric acid](#), [acetic acid](#), and [anisaldehyde](#) (90:5:1:1). Dry the plate in a current of hot air until colored spots become visible. The background color may be brightened by exposure to warm steam. Examine in daylight.

Acceptance criteria: The principal spots of the *Sample solution* are similar in position and color to those of the *Standard solution*.

• B. The retention times of the two principal peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

• **PROCEDURE**

Mobile phase: Water

Standard solution: 20 mg/mL of [USP Isomalt RS](#)

Sample solution: 20 mg/mL of Isomalt

Chromatographic system

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

Mode: LC

Detector: Refractive index, maintained at a constant temperature (40° for example)

Columns

Guard: 4.6-mm × 3-cm; packing L19

Analytical: 7.8-mm × 30-cm; packing L19

Column temperature: 80 ± 3°

Flow rate: 0.5 mL/min

Injection volume: 20 µL

System suitability

Sample: Standard solution

[NOTE—The relative retention times for 1,1-GPM and 1,6-GPS are about 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 2.0 between 1,1-GPM and 1,6-GPS

Relative standard deviation: NMT 2.0% for the 1,6-GPS and 1,1-GPM peaks

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of 1,6-GPS in the portion of Isomalt taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times 100$$

r_u = peak response of 1,6-GPS from the Sample solution

r_s = peak response of 1,6-GPS from the Standard solution

C_s = concentration of 1,6-GPS in the Standard solution, with calculation based on the declared 1,6-GPS content of [USP Isomalt RS](#) (mg/mL)

C_u = concentration of Isomalt in the Sample solution (mg/mL)

Calculate the percentage of 1,1-GPM in the portion of Isomalt taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times 100$$

r_u = peak response of 1,1-GPM from the Sample solution

r_s = peak response of 1,1-GPM from the Standard solution

C_s = concentration of 1,1-GPM in the Standard solution, with calculation based on the declared 1,1-GPM content of [USP Isomalt RS](#) (mg/mL)

C_u = concentration of Isomalt in the Sample solution (mg/mL)

Acceptance criteria: 98.0%–102.0% of a mixture of 6-O- α -D-glucopyranosyl-D-sorbitol (1,6-GPS) and 1-O- α -D-glucopyranosyl-D-mannitol (1,1-GPM), and neither of the two components is less than 3.0% of the mixture, calculated on the anhydrous basis

IMPURITIES

• LIMIT OF NICKEL

[NOTE—The purity of the reagents and the water used must be suitable for trace analysis, and the reagents and water must be free of nickel.]

Sample solution: Dissolve 10.0 g of Isomalt in 30 mL of dilute acetic acid (115–125 g/L), add water, and shake to dissolve. Dilute with water to 100.0 mL. Add 2.0 mL of [saturated ammonium pyrrolidinedithiocarbamate TS](#) and 10.0 mL of water-saturated [methyl isobutyl ketone](#) ($C_6H_{12}O$, 4-methyl-2-pentanone), and then shake for 30 s, protected from bright light. Allow the layers to separate and use the methyl isobutyl ketone layer.

Standard solutions: Prepare three reference solutions in the same manner as the Sample solution except add 0.5 mL, 1.0 mL, and 1.5 mL, respectively, of [nickel standard solution TS](#) (10 ppm Ni) in addition to the 10.0 g of the substance to be examined.

Blank solution: Treat water-saturated [methyl isobutyl ketone](#) as described for preparation of the Sample solution omitting the Isomalt.

Instrumental conditions

(See [Atomic Absorption Spectroscopy \(852\)](#).)

Mode: Atomic absorption spectrophotometry**Analytical wavelength:** 232.0 nm**Lamp:** Nickel hollow-cathode**Flame:** Air-acetylene**Analysis****Samples:** Sample solution, Standard solutions, and Blank solution

Set the zero of the instrument using the *Blank solution*. Record the average of the steady readings for each of the *Standard solutions* and the *Sample solution*. Between each measurement, rinse with water and ascertain that the reading returns to zero with the *Blank solution*. Plot the absorbances of the *Standard solutions* and the *Sample solution* versus the added quantity of nickel. Extrapolate the line joining the points on the graph until it meets the concentration axis. The distance between this point and the intersection of the axes represents the concentration of nickel in the *Sample solution*.

Acceptance criteria: NMT 1 µg/g, calculated on the anhydrous basis• **ORGANIC IMPURITIES****Mobile phase, Sample solution, and Chromatographic system:** Proceed as directed in the Assay.**System suitability solution:** 20 mg/mL of [USP Isomalt RS](#) and 0.1 mg/mL each of [USP Mannitol RS](#) and [USP Sorbitol RS](#) in water**Standard solution:** 0.1 mg/mL each of [USP Sorbitol RS](#) and [USP Mannitol RS](#)**System suitability****Sample:** System suitability solution

[NOTE—The relative retention times for 1,1-GPM, 1,6-GPS, mannitol, and sorbitol are about 1.0, 1.2, 1.6, and 2.0, respectively. The typical retention time for 1,1-GPM is about 12.3 min.]

Suitability requirements**Resolution:** NLT 2.0 between 1,1-GPM and 1,6-GPS**Analysis****Samples:** Sample solution and Standard solution

Calculate the percentage of mannitol or sorbitol in the portion of Isomalt taken:

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

r_U = peak response of mannitol or sorbitol from the *Sample solution*

r_S = peak response of mannitol or sorbitol from the *Standard solution*

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

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

Calculate the percentage of any unknown impurity in the portion of Isomalt taken:

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

r_U = peak response of each unknown impurity from the *Sample solution*

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

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

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

Acceptance criteria: See [Table 1](#). [NOTE—Disregard any impurity peak that is less than 0.1%.]**Table 1**

Name	Acceptance Criteria, NMT (%)
Mannitol	0.5
Sorbitol	0.5

Name	Acceptance Criteria, NMT (%)
Any unknown impurity	0.5
Total impurities	2.0

• REDUCING SUGARS

Sample solution: Dissolve 3.3 g in 10 mL of Purified Water with the aid of gentle heat. Cool and add 20 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 100 mL of a 2.4% (v/v) solution of glacial acetic acid and 20 mL of 0.025 M iodine VS. With continuous shaking, add 25 mL of a mixture of hydrochloric acid and water (6:94).

Analysis: After the precipitate has dissolved, titrate the excess iodine with 0.05 N sodium thiosulfate VS, using 1 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, determined on the anhydrous basis as glucose.

SPECIFIC TESTS**• [WATER DETERMINATION \(921\), Method I](#)**

Sample: 0.3 g

Analysis: Add the *Sample* to a mixture of [anhydrous methanol](#) and [formamide](#) (1:1) at 50 ± 5°.

Acceptance criteria: NMT 7.0%

• CONDUCTIVITY

Sample solution: Dissolve 20 g in carbon dioxide-free water with gentle heating (40°–50°), cool, and dilute with the same solvent to 100 mL.

Analysis: Using an appropriate conductivity meter that has been standardized with a potassium chloride conductivity calibration standard, measure the conductivity of the *Sample solution* while gently stirring with a magnetic stirrer.

Acceptance criteria: NMT 20 µS/cm

ADDITIONAL REQUIREMENTS

• [PACKAGING AND STORAGE:](#) Preserve in well-closed containers. No storage requirements are specified.

• [LABELING:](#) Label it to indicate the percentage content of 1,6-GPS and 1,1-GPM.

• [USP REFERENCE STANDARDS \(11\)](#)

[USP Isomalt RS](#)

[USP Mannitol RS](#)

[USP Sorbitol RS](#)

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
ISOMALT	Documentary Standards Support	SE2020 Simple Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SE2020 Simple Excipients

Chromatographic Database Information: [Chromatographic Database](#)

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