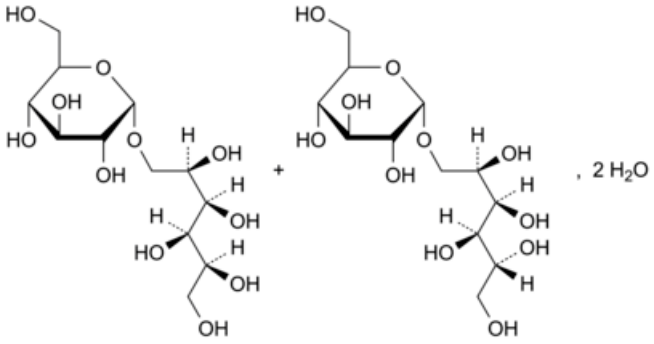
Edition: BP 2025 (Ph. Eur. 11.6 update)

Isomalt[1]

General Notices

(Ph. Eur. monograph 1531)



$C_{12}H_{24}O_{11}$ 344.3

$C_{12}H_{24}O_{11},2H_2O$ 380.3

Anhydrous isomalt *64519-82-0*

Action and use

Sweetening agent.

Ph Eur

DEFINITION

Mixture of 6-*O*-α-D-glucopyranosyl-D-glucitol (6-*O*-α-D-glucopyranosyl-D-sorbitol; 1,6-GPS) and 1-*O*-α-D-glucopyranosyl-D-mannitol (1,1-GPM).

Content

98.0 per cent to 102.0 per cent for the mixture of 1,6-GPS and 1,1-GPM and neither of the 2 components is less than 3.0 per cent (anhydrous substance).

♦ CHARACTERS

Appearance

White or almost white powder or granules.

Solubility

Freely soluble in water, practically insoluble in anhydrous ethanol.♦

IDENTIFICATION

First identification: A.

◊ *Second identification: B, C.*◊

A. Examine the chromatograms obtained in the assay.

Results The 2 principal peaks in the chromatogram obtained with the test solution are similar in retention time to the 2 principal peaks in the chromatogram obtained with reference solution (a).

◊ B. Thin-layer chromatography (*2.2.27*).

Test solution Dissolve 50 mg of the substance to be examined in *water R* and dilute to 10 mL with the same solvent.

Reference solution Dissolve 50 mg of *isomalt CRS* in *water R* and dilute to 10 mL with the same solvent.

Plate *TLC silica gel F_{254} plate R*.

Mobile phase *acetic acid R*, *propionic acid R*, *water R*, *ethyl acetate R*, *pyridine R* (5:5:10:50:50 *V/V/V/V/V*).

Application 1 µL; thoroughly dry the points of application in warm air.

Development Over 1/2 of the plate.

Drying In a current of warm air.

Detection Dip for 3 s in a 1 g/L solution of *sodium periodate R* and dry in a current of hot air; dip for 3 s in a mixture of 1 volume of *acetic acid R*, 1 volume of *anisaldehyde R*, 5 volumes of *sulfuric acid R* and 90 volumes of *anhydrous ethanol R*; dry in a current of hot air until coloured spots become visible; the background colour may be brightened in warm steam; examine in daylight.

Results The chromatogram obtained with the reference solution shows 2 blue-grey spots with R_F values of about 0.13 (1,6-GPS) and 0.16 (1,1-GPM). The chromatogram obtained with the test solution shows principal spots similar in position and colour to the principal spots in the chromatogram obtained with the reference solution.

C. To 3 mL of a freshly prepared 100 g/L solution of *pyrocatechol R* add 6 mL of *sulfuric acid R* while cooling in iced water. To 3 mL of the cooled mixture add 0.3 mL of a 100 g/L solution of the substance to be examined. Heat gently over a naked flame for about 30 s. A pink colour develops.◊

TESTS

Conductivity (*2.2.38*)

Maximum 20 µS·cm^{-1}.

Dissolve 20.0 g in *carbon dioxide-free water R* with gentle heating (40-50 °C) and dilute to 100.0 mL with the same solvent. Measure the conductivity of the solution while gently stirring with a magnetic stirrer.

Reducing sugars

Maximum 0.3 per cent, expressed as glucose equivalent.

Dissolve 3.3 g in 10 mL of *water R* with gentle heating. Cool and add 20 mL of *cupri-citric solution R* 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 per cent *V/V* solution of *glacial acetic acid R* and 20.0 mL of *0.025 M iodine*. With continuous shaking, add 25 mL of a mixture of 6 volumes of *hydrochloric acid R* and 94 volumes of *water R*. When the precipitate has dissolved, titrate the excess of iodine with *0.05 M sodium thiosulfate* using 1 mL of *starch solution R* as indicator, added towards the end of the titration. Not less than 12.8 mL of *0.05 M sodium thiosulfate* is required.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 0.200 g of the substance to be examined in 4 mL of water R and dilute to 10.0 mL with the same solvent.

Reference solution (a) Dissolve 0.200 g of isomalt CRS in 4 mL of water R and dilute to 10.0 mL with the same solvent.

Reference solution (b) Dissolve 10.0 mg of sorbitol CRS (impurity C) and 10.0 mg of mannitol CRS (impurity B) in 20 mL of water R and dilute to 100.0 mL with the same solvent.

Precolumn:

— *size*: *l* = 30 mm, *Ø* = 4.6 mm;

— *stationary phase*: strong cation-exchange resin (calcium form) R (9 µm);

— *temperature*: 80 ± 3 °C.

Column:

— *size*: *l* = 0.3 m, *Ø* = 7.8 mm;

— *stationary phase*: strong cation-exchange resin (calcium form) R (9 µm);

— *temperature*: 80 ± 3 °C.

Mobile phase Degassed water for chromatography R.

Flow rate 0.5 mL/min.

Detection Differential refractometer maintained at a constant temperature (e.g. 40 °C).

Injection 20 µL.

Run time 2.5 times the retention time of 1,1-GPM.

Relative retention With reference to 1,1-GPM (retention time = about 14 min): 1,6-GPS = about 1.2; impurity B = about 1.6; impurity C = about 2.0.

System suitability Reference solution (a):

— resolution: minimum 2.0 between the peaks due to 1,1-GPM and 1,6-GPS.

Limits:

— *impurities B, C*: for each impurity, not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the peak due to impurity C in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *total*: not more than 4 times the area of the peak due to impurity C in the chromatogram obtained with reference solution (b) (2.0 per cent);

— *disregard limit*: 0.2 times the area of the peak due to impurity C in the chromatogram obtained with reference solution (b) (0.1 per cent).

Water (2.5.12)

Maximum 7.0 per cent, determined on 0.300 g. As solvent, use a mixture of 20 mL of anhydrous methanol R and 20 mL of formamide R1 at 50 ± 5 °C.

ASSAY

Liquid chromatography (2.2.29) as described in the test for related substances with the following modification.

Injection Test solution and reference solution (a).

Calculate the percentage content of isomalt (1,1-GPM and 1,6-GPS) taking into account the assigned contents of 1,1-GPM and 1,6-GPS in *isomalt CRS*.

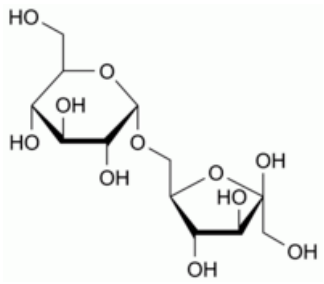
LABELLING

The label states the percentage contents of 1,1-GPM and 1,6-GPS.

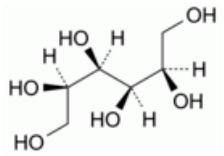
IMPURITIES

Specified impurities *B, C.*

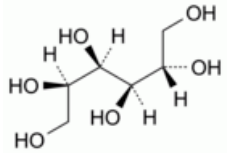
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities. It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) *A, D.*



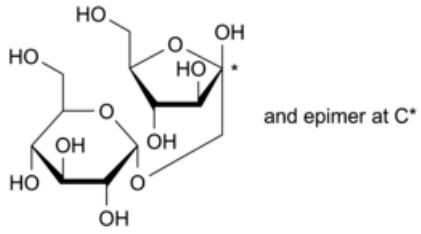
A. 6-*O*-α-D-glucopyranosyl-β-D-*arabino*-hex-2-ulofuranose (isomaltulose),



B. D-mannitol,



C. D-glucitol (D-sorbitol),



D. 1-*O*-α-D-glucopyranosyl-D-*arabino*-hex-2-ulofuranose (trehalulose).

I This monograph has undergone pharmacopoeial harmonisation. See chapter *5.8 Pharmacopoeial harmonisation*.