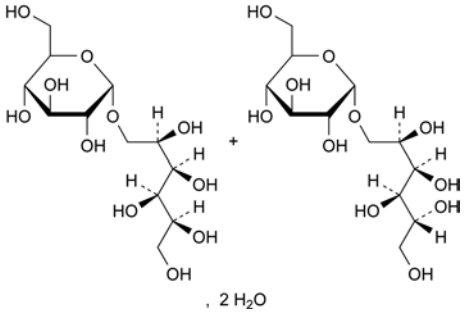
01/2008:1531

ISOMALT

Isomaltum



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

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

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 a path of 10 cm.

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* prepared from *distilled water R* 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 the aid of gentle heat. Cool and add 20 mL of *cupri-citric solution R* and a few glass beads. Heat so that the 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 1.00 g of the substance to be examined in 20 mL of *water R* and dilute to 50.0 mL with the same solvent.

Reference solution (a). Dissolve 1.00 g of *isomalt CRS* in 20 mL of *water R* and dilute to 50.0 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 ± 1 °C.

Column:

- *size*: *l* = 0.3 m, Ø = 7.8 mm;
- *stationary phase*: *strong cation-exchange resin (calcium form) R* (9 µm);
- *temperature*: 80 ± 1 °C.

Mobile phase: degassed *water R*.

Flow rate: 0.5 mL/min.

Detection: differential refractometer maintained at a constant temperature.

Injection: 20 µL of the test solution and reference solution (b).

Run time: until impurity C is completely eluted (about 25 min).

Relative retention with reference to 1,1-GPM (retention time = about 12.3 min): impurity A = about 0.8; 1,6-GPS = about 1.2; impurity B = about 1.6; impurity C = about 2.0.

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);
- *any other impurity*: 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 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).

Lead (*2.4.10*): maximum 0.5 ppm.

Nickel (*2.4.15*): maximum 1 ppm.

Water (*2.5.12*): maximum 7.0 per cent, determined on 0.3 g. As solvent, use a mixture of 20 mL of *anhydrous methanol R* and 20 mL of *formamide R* 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) from the declared content of 1,1-GPM and 1,6-GPS in *isomalt CRS*.

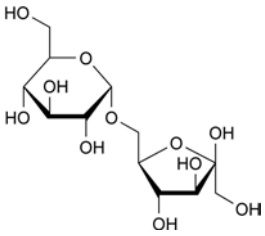
LABELLING

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

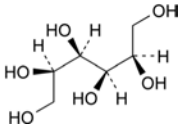
IMPURITIES

Specified impurities: *B, C.*

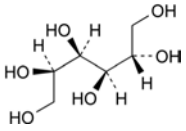
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical use (2034)*. 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.*



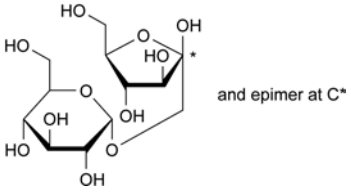
A. 6-*O*-α-D-glucopyranosyl-β-D-*arabino*-hex-2-ulofuranose (isomaltulose),



B. D-mannitol,



C. D-glucitol (D-sorbitol),

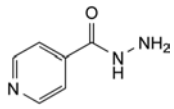


D. 1-*O*-α-D-glucopyranosyl-D-*arabino*-hex-2-ulofuranose (trehalulose).

01/2008:0146
corrected 6.0

ISONIAZID

Isoniazidum



$C_6H_7N_3O$ M_r 137.1
[54-85-3]

DEFINITION

Isoniazid contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of pyridine-4-carbohydrazide, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder or colourless crystals, freely soluble in water, sparingly soluble in alcohol.

IDENTIFICATION

First identification: A, B.

Second identification: A, C.

A. Melting point (*2.2.14*): 170 °C to 174 °C.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *isoniazid CRS*.

C. Dissolve 0.1 g in 2 mL of *water R* and add 10 mL of a warm 10 g/L solution of *vanillin R*. Allow to stand and scratch the wall of the test tube with a glass rod. A yellow precipitate is formed, which, after recrystallisation from 5 mL of *alcohol (70 per cent V/V) R* and drying at 100 °C to 105 °C, melts (*2.2.14*) at 226 °C to 231 °C.

TESTS

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 50 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution BY_7 (*2.2.2, Method II*).

pH (*2.2.3*). The pH of solution S is 6.0 to 8.0.

Hydrazine and related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance.

Test solution. Dissolve 1.0 g of the substance to be examined in a mixture of equal volumes of *acetone R* and *water R* and dilute to 10.0 mL with the same mixture of solvents.

Reference solution. Dissolve 50.0 mg of *hydrazine sulfate R* in 50 mL of *water R* and dilute to 100.0 mL with *acetone R*. To 10.0 mL of this solution add 0.2 mL of the test solution and dilute to 100.0 mL with a mixture of equal volumes of *acetone R* and *water R*.

Apply separately to the plate 5 µL of each solution and develop over a path of 15 cm using a mixture of 10 volumes of *water R*, 20 volumes of *acetone R*, 20 volumes of *methanol R* and 50 volumes of *ethyl acetate R*. Allow the plate to dry in air and examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with the test solution, apart from the principal spot, is not more intense than the spot in the chromatogram obtained with the reference solution (0.2 per cent). Spray the plate with *dimethylaminobenzaldehyde solution R1*. Examine in daylight. An additional spot, corresponding to hydrazine, appears in the chromatogram obtained with the reference solution. Any corresponding spot in the chromatogram obtained with the test solution is not more intense than the spot corresponding to hydrazine in the chromatogram obtained with the reference solution (0.05 per cent).