CHARACTERS

Appearance: white or almost white, slightly hygroscopic powder or granules.

Solubility: freely soluble in water.

IDENTIFICATION

A. Dissolve 0.1 g in 2.5 mL of *water R* and heat with 2.5 mL of *cupri-tartaric solution R*. A red precipitate is formed.

B. Dip, for 1 s, a suitable stick with a reactive pad containing glucose-oxidase, peroxidase and a hydrogen-donating substance, such as tetramethylbenzidine, in a 5 g/L solution of the substance to be examined. Observe the colour of the reactive pad; within 60 s the colour changes from yellow to green or blue.

C. It is a powder or granules.

D. Dextrose equivalent (see Tests).

TESTS

Solution S. Dissolve 12.5 g in *carbon dioxide-free water R* and dilute to 50.0 mL with the same solvent.

pH (*2.2.3*): 4.0 to 7.0.

Mix 1 mL of a 223.6 g/L solution of *potassium chloride R* and 30 mL of solution S.

Sulfur dioxide (*2.5.29*): maximum 20 ppm.

Heavy metals (*2.4.8*): maximum 10 ppm.

Dilute 4 mL of solution S to 30 mL with *water R*. The solution complies with test E. Prepare the reference solution using 10 mL of *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 6.0 per cent, determined on 10.00 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*): maximum 0.5 per cent, determined on 1.0 g.

Dextrose equivalent (DE): within 10 per cent of the nominal value.

Weigh an amount of the substance to be examined equivalent to 2.85-3.15 g of reducing carbohydrates, calculated as dextrose equivalent, into a 500 mL volumetric flask. Dissolve in *water R* and dilute to 500.0 mL with the same solvent. Transfer the solution to a 50 mL burette.

Pipette 25.0 mL of *cupri-tartaric solution R* into a 250 mL flask and add 18.5 mL of the test solution from the burette, mix and add a few glass beads. Place the flask on a hot plate, previously adjusted so that the solution begins to boil after 2 min ± 15 s. Allow to boil for exactly 120 s, add 1 mL of a 1 g/L solution of *methylene blue R* and titrate with the test solution (V_1) until the blue colour disappears. Maintain the solution at boiling throughout the titration.

Standardise the cupri-tartaric solution using a 6.00 g/L solution of *glucose R* (V_0).

Calculate the dextrose equivalent using the following expression:

$$\frac{300 \times V_0 \times 100}{V_1 \times M \times D}$$

V_0 = total volume of glucose standard solution, in millilitres;

V_1 = total volume of test solution, in millilitres;

M = mass of the sample, in grams;

D = percentage content of dry matter in the substance.

Microbial contamination

TAMC: acceptance criterion 10^3 CFU/g (*2.6.12*).

TYMC: acceptance criterion 10^2 CFU/g (*2.6.12*).

Absence of *Escherichia coli* (*2.6.13*).

Absence of *Salmonella* (*2.6.13*).

LABELLING

The label states the dextrose equivalent (DE) (= nominal value).

FUNCTIONALITY-RELATED CHARACTERISTICS

This section provides information on characteristics that are recognised as being relevant control parameters for one or more functions of the substance when used as an excipient (see chapter 5.15). This section is a non-mandatory part of the monograph and it is not necessary to verify the characteristics to demonstrate compliance. Control of these characteristics can however contribute to the quality of a medicinal product by improving the consistency of the manufacturing process and the performance of the medicinal product during use. Where control methods are cited, they are recognised as being suitable for the purpose, but other methods can also be used. Wherever results for a particular characteristic are reported, the control method must be indicated.

The following characteristics may be relevant for spray-dried liquid glucose used as filler or binder for wet granulation.

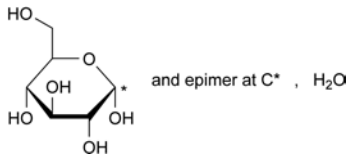
Dextrose equivalent (see Tests).

Particle-size distribution (*2.9.31* or *2.9.38*).

01/2008:0178
corrected 6.3

GLUCOSE MONOHYDRATE

Glucosum monohydricum



$C_6H_{12}O_6,H_2O$ M_r 198.2
[5996-10-1]

DEFINITION

(+)-D-Glucopyranose monohydrate.

CHARACTERS

Appearance: white or almost white, crystalline powder.

It has a sweet taste.

Solubility: freely soluble in water, sparingly soluble in ethanol (96 per cent).

IDENTIFICATION

A. Specific optical rotation (see Tests).

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

Solvent mixture: *water R, methanol R* (2:3 *V/V*).

Test solution. Dissolve 10 mg of the substance to be examined in the solvent mixture and dilute to 20 mL with the solvent mixture.

Reference solution (a). Dissolve 10 mg of *glucose CRS* in the solvent mixture and dilute to 20 mL with the solvent mixture.

Reference solution (b). Dissolve 10 mg each of *fructose CRS, glucose CRS, lactose CRS* and *sucrose CRS* in the solvent mixture and dilute to 20 mL with the solvent mixture.

Plate: *TLC silica gel G plate R*.

Mobile phase: *water R, methanol R, anhydrous acetic acid R, ethylene chloride R* (10:15:25:50 *V/V/V/V*); measure the volumes accurately since a slight excess of water produces cloudiness.

Application: 2 µL; thoroughly dry the points of application.

Development A: over a path of 15 cm.

Drying A: in a current of warm air.

Development B: immediately, over a path of 15 cm, after renewing the mobile phase.

Drying B: in a current of warm air.

Detection: spray with a solution of 0.5 g of *thymol R* in a mixture of 5 mL of *sulfuric acid R* and 95 mL of *ethanol (96 per cent) R*; heat at 130 °C for 10 min.

System suitability: reference solution (b):

– the chromatogram shows 4 clearly separated spots.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a).

C. Dissolve 0.1 g in 10 mL of *water R*. Add 3 mL of *cupri-tartaric solution R* and heat. A red precipitate is formed.

TESTS

Solution S. Dissolve 10.0 g in *distilled water R* and dilute to 100 mL with the same solvent.

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

Dissolve 10.0 g in 15 mL of *water R*.

Acidity or alkalinity. Dissolve 6.0 g in 25 mL of *carbon dioxide-free water R* and add 0.3 mL of *phenolphthalein solution R*. The solution is colourless. Not more than 0.15 mL of *0.1 M sodium hydroxide* is required to change the colour of the indicator to pink.

Specific optical rotation (*2.2.7*): + 52.5 to + 53.3 (anhydrous substance).

Dissolve 10.0 g in 80 mL of *water R*, add 0.2 mL of *dilute ammonia R1*, allow to stand for 30 min and dilute to 100.0 mL with *water R*.

Foreign sugars, soluble starch, dextrins. Dissolve 1.0 g by boiling in 30 mL of *ethanol (90 per cent V/V) R*. Cool; the appearance of the solution shows no change.

Sulfites: maximum 15 ppm, expressed as SO_2.

Test solution. Dissolve 5.0 g in 40 mL of *water R*, add 2.0 mL of *0.1 M sodium hydroxide* and dilute to 50.0 mL with *water R*. To 10.0 mL of the solution, add 1 mL of a 310 g/L solution of *hydrochloric acid R*, 2.0 mL of *decolorised fuchsin solution R1* and 2.0 mL of a 0.5 per cent *V/V* solution of *formaldehyde R*. Allow to stand for 30 min.

Reference solution. Dissolve 76 mg of *sodium metabisulfite R* in *water R* and dilute to 50.0 mL with the same solvent. Dilute 5.0 mL of this solution to 100.0 mL with *water R*. To 3.0 mL of this solution add 4.0 mL of *0.1 M sodium hydroxide* and dilute to 100.0 mL with *water R*. Immediately add to 10.0 mL of this solution 1 mL of a 310 g/L solution of *hydrochloric acid R*, 2.0 mL of *decolorised fuchsin solution R1* and 2.0 mL of a 0.5 per cent *V/V* solution of *formaldehyde R*. Allow to stand for 30 min.

Measure the absorbance (*2.2.25*) of the 2 solutions at the absorption maximum at 583 nm using for both measurements a solution prepared in the same manner using 10.0 mL of *water R* as the compensation liquid. The absorbance of the test solution is not greater than that of the reference solution.

Chlorides (*2.4.4*): maximum 125 ppm.

Dilute 4 mL of solution S to 15 mL with *water R*.

Sulfates (*2.4.13*): maximum 200 ppm.

Dilute 7.5 mL of solution S to 15 mL with *distilled water R*.

Arsenic (*2.4.2, Method A*): maximum 1 ppm, determined on 1.0 g.

Barium. To 10 mL of solution S add 1 mL of *dilute sulfuric acid R*. When examined immediately and after 1 h, any opalescence in the solution is not more intense than that in a mixture of 1 mL of *distilled water R* and 10 mL of solution S.

Calcium (*2.4.3*): maximum 200 ppm.

Dilute 5 mL of solution S to 15 mL with *distilled water R*.

Lead (*2.4.10*): maximum 0.5 ppm.

Water (*2.5.12*): 7.0 per cent to 9.5 per cent, determined on 0.50 g.

Sulfated ash: maximum 0.1 per cent.

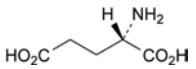
Dissolve 5.0 g in 5 mL of *water R*, add 2 mL of *sulfuric acid R*, evaporate to dryness on a water-bath and ignite to constant mass. If necessary, repeat the heating with *sulfuric acid R*.

Pyrogens (*2.6.8*). If intended for use in the manufacture of large-volume parenteral preparations without a further appropriate procedure for the removal of pyrogens, the competent authority may require that it comply with the test for pyrogens. Inject per kilogram of the rabbit's mass 10 mL of a solution in *water for injections R* containing 55 mg of the substance to be examined per millilitre.

01/2008:0750
corrected 6.0

GLUTAMIC ACID

Acidum glutamicum



$C_5H_9NO_4$ M_r 147.1
[56-86-0]

DEFINITION

Glutamic acid contains not less than 98.5 per cent and not more than the equivalent of 100.5 per cent of (2*S*)-2-aminopentanedioic acid, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder or colourless crystals, freely soluble in boiling water, slightly soluble in cold water, practically insoluble in acetic acid, in acetone and in alcohol.

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. Specific optical rotation (see Tests).

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *glutamic acid CRS*. Examine the substances prepared as discs. If the spectra obtained show differences, dissolve the substance to be examined and the reference substance separately in the minimum quantity of *water R*, evaporate to dryness at 60 °C and record new spectra using the residues.

C. Examine the chromatograms obtained in the test for ninhydrin-positive substances. The principal spot in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a).

D. To 2.0 mL of solution S (see Tests) add 0.1 mL of *phenolphthalein solution R* and 3.0 mL to 3.5 mL of *1 M sodium hydroxide* to change the colour of the indicator to red. Add a mixture of 3 mL of *formaldehyde solution R*, 3 mL of *carbon dioxide-free water R* and 0.1 mL of *phenolphthalein solution R*, to which sufficient *1 M sodium hydroxide* has been added to produce a pink colour. The solution is decolourised. Add *1 M sodium hydroxide* until a red colour is produced. The total volume of *1 M sodium hydroxide* used is 4.0 mL to 4.7 mL.

TESTS

Solution S. Dissolve 5.00 g in *1 M hydrochloric acid* with gentle heating, and dilute to 50.0 mL with the same acid.