DEFINITION

Dexpanthenol contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of (2*R*)-2,4-dihydroxy-*N*-(3-hydroxypropyl)-3,3-dimethylbutanamide, calculated with reference to the anhydrous substance.

CHARACTERS

A colourless or slightly yellowish, viscous hygroscopic liquid, or a white or almost white, crystalline powder, very soluble in water, freely soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. It complies with the test for specific optical rotation (see Tests).

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *dexpanthenol CRS*. Examine the substances using discs prepared as follows: dissolve the substance to be examined and the reference substance separately in 1.0 ml of *anhydrous ethanol R* to obtain a concentration of 5 mg/ml. Place dropwise 0.5 ml of this solution on a disc of *potassium bromide R*. Dry the disc at 100-105 °C for 15 min.

C. Examine the chromatograms obtained in the test for 3-aminopropanol. 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 1 ml of solution S (see Tests) add 1 ml of *dilute sodium hydroxide solution R* and 0.1 ml of *copper sulphate solution R*. A blue colour develops.

TESTS

Solution S. Dissolve 2.500 g in *carbon dioxide-free water R* and dilute to 50.0 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution B_6 (*2.2.2, Method II*).

pH (*2.2.3*). The pH of solution S is not greater than 10.5.

Specific optical rotation (*2.2.7*). The specific optical rotation is + 29.0 to + 32.0, determined on solution S and calculated with reference to the anhydrous substance.

3-Aminopropanol. Examine by thin-layer chromatography (*2.2.27*), using *silica gel G R* as the coating substance.

Test solution (a). Dissolve 0.25 g of the substance to be examined in *anhydrous ethanol R* and dilute to 5 ml with the same solvent.

Test solution (b). Dilute 1 ml of test solution (a) to 10 ml with *anhydrous ethanol R*.

Reference solution (a). Dissolve the contents of a vial of *dexpanthenol CRS* in 1.0 ml of *anhydrous ethanol R* to obtain a concentration of 5 mg/ml.

Reference solution (b). Dissolve 25 mg of *3-aminopropanol R* in *anhydrous ethanol R* and dilute to 100 ml with the same solvent.

Apply separately to the plate 10 µl of each solution. Develop over a path of 15 cm using a mixture of 20 volumes of *concentrated ammonia R*, 25 volumes of *methanol R* and 55 volumes of *butanol R*. Allow the plate to dry in air, spray with a 100 g/l solution of *trichloroacetic acid R* in *methanol R* and heat at 150 °C for 10 min. Spray with a 1 g/l solution of *ninhydrin R* in *methanol R* and heat at 120 °C until a colour appears. Any spot due to 3-aminopropanol in the chromatogram obtained with test solution (a) is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.5 per cent).

Heavy metals (*2.4.8*). 12 ml of solution S complies with limit test A for heavy metals (20 ppm). Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Water (*2.5.12*). Not more than 1.0 per cent, determined on 1.000 g.

Sulphated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

To 0.400 g add 50.0 ml of *0.1 M perchloric acid*. Boil under a reflux condenser for 5 h protected from humidity. Allow to cool. Add 50 ml of *dioxan R* by rinsing the condenser, protected from humidity. Add 0.2 ml of *naphtholbenzein solution R* and titrate with *0.1 M potassium hydrogen phthalate* until the colour changes from green to yellow. Carry out a blank titration.

1 ml of *0.1 M perchloric acid* is equivalent to 20.53 mg of $C_9H_{19}NO_4$.

STORAGE

In an airtight container.

01/2005:1506

DEXTRAN 1 FOR INJECTION

Dextranum 1 ad iniectabile

DEFINITION

Dextran 1 for injection is a low molecular weight fraction of dextran, consisting of a mixture of isomaltooligosaccharides.

The average relative molecular mass is about 1000.

PRODUCTION

It is obtained by hydrolysis and fractionation of dextrans produced by fermentation of sucrose using *Leuconostoc mesenteroides* strain NRRL B-512 = CIP 78.59 or substrains thereof (for example *L. mesenteroides* B-512 F = NCTC 10817).

It is prepared in conditions designed to minimise the risk of microbial contamination.

CHARACTERS

A white or almost white powder, hygroscopic, very soluble in water, very slightly soluble in alcohol.

IDENTIFICATION

A. Dissolve 3.000 g in *water R*, heat on a water-bath and dilute to 100.0 ml with the same solvent. The specific optical rotation (*2.2.7*) is + 148 to + 164, calculated with reference to the dried substance. Dry an aliquot of the solution first on a water-bath and then to constant weight *in vacuo* at 70 °C. Calculate the dextran content after correction for the content of sodium chloride.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *dextran 1 CRS*. Prepare the discs as follows: to 1-2 mg add one or a few drops of *water R*; grind in an agate mortar for 1-2 min; add about 300 mg of *potassium bromide R* and mix to a slurry (do not grind); dry *in vacuo* at 40 °C for 15 min, crush the residue (if it is not dry, dry for another 15 min). Prepare a disc using *potassium bromide R*. Run the infrared spectrum with a blank disc using *potassium bromide R* in the reference beam.

C. It complies with the test for molecular-mass distribution (see Tests).

TESTS

Solution S. Dissolve 7.5 g in *carbon dioxide-free water R*, heat on a water-bath and dilute to 50 ml with the same solvent.

Absorbance (*2.2.25*). Measure the absorbance of solution S at 375 nm. The absorbance is not more than 0.12.

Acidity or alkalinity. To 10 ml of solution S add 0.1 ml of *phenolphthalein solution R*. The solution is colourless. Add 0.2 ml of *0.01 M sodium hydroxide*. The solution is pink. Add 0.4 ml of *0.01 M hydrochloric acid*. The solution is colourless. Add 0.1 ml of *methyl red solution R*. The solution is red or orange.

Nitrogen-containing substances. Carry out the determination of nitrogen by sulphuric acid digestion (*2.5.9*), using 0.200 g and heating for 2 h. Collect the distillate in a mixture of 0.5 ml of *bromocresol green solution R*, 0.5 ml of *methyl red solution R* and 20 ml of *water R*. Titrate with *0.01 M hydrochloric acid*. Not more than 0.15 ml of *0.01 M hydrochloric acid* is required to change the colour of the indicator (110 ppm N).

Sodium chloride. Not more than 1.5 per cent. Accurately weigh 3-5 g and dissolve in 100 ml of *water R*. Add 0.3 ml of *potassium chromate solution R* and titrate with *0.1 M silver nitrate* until the yellowish-white colour changes to reddish-brown.

1 ml of *0.1 M silver nitrate* is equivalent to 5.844 mg of NaCl.

Molecular-mass distribution. The average molecular mass (M_w) is 850 to 1150. The fraction with less than 3 units of glucose is less than 15 per cent, the fraction with more than 9 units of glucose is less than 20 per cent.

Examine by size-exclusion chromatography (*2.2.30*).

Test solution. Dissolve 6.0-6.5 mg of the substance to be examined in 1.0 ml of the mobile phase.

Reference solution (a). Dissolve 6.0-6.5 mg of *dextran 1 CRS* in 1.0 ml of the mobile phase.

Reference solution (b). Dissolve the content of an ampoule of *isomaltooligosaccharide CRS* in 1 ml of the mobile phase, and mix. This corresponds to approximately 45 µg of isomaltotriose (3 glucose units), approximately 45 µg of isomaltononaose (9 glucose units), and approximately 60 µg of sodium chloride per 100 µl.

The chromatographic procedure may be carried out using:

- 2 columns, 30 cm long and 10 mm in internal diameter, in series, prepacked with a packing material of dextran covalently bound to highly cross-linked porous agarose beads, allowing resolution of oligosaccharides in the molecular mass range of 180 to 3000, kept at a temperature of 20-25 °C,
- as mobile phase at a flow rate of 0.07-0.08 ml/min maintained constant to ± 1 per cent, a 2.92 g/l solution of *sodium chloride R*,
- as detector a differential refractometer.

Inject 100 µl of reference solution (b) and record the chromatogram for definition of the positions of isomaltotriose, isomaltononaose and sodium chloride. Inject 100 µl of the test solution and 100 µl of reference solution (a) and record the chromatograms. Determine the peak areas. Disregard any peak due to sodium chloride.

Calculate the average relative molecular mass M_w and the amount of the fraction with less than 3 and more than 9 glucose units, of *dextran 1 CRS* and of the substance to be examined. The test is not valid unless the values obtained for *dextran 1 CRS* are within the values stated on the label.

$$M_w = \sum w_i \times m_i$$

M_w = average molecular mass of the dextran,
m_i = molecular mass of oligosaccharide *i*,
w_i = weight proportion of oligosaccharide *i*.

Use the following molecular mass values for the calculation:

Oligosaccharide *i*	m_i
glucose	180
isomaltose	342
isomaltotriose	504
isomaltotetraose	666
isomaltopentaose	828
isomaltohexaose	990
isomaltoheptaose	1152
isomaltooctaose	1314
isomaltononaose	1476
isomaltodecaose	1638
isomaltoundecaose	1800
isomaltododecaose	1962
isomaltotridecaose	2124
isomaltotetradecaose	2286
isomaltopentadecaose	2448
isomaltohexadecaose	2610
isomaltoheptadecaose	2772
isomaltooctadecaose	2934
isomaltononadecaose	3096

Heavy metals (*2.4.8*). Dilute 20 ml of solution S to 30 ml with *water R*. 12 ml of this solution complies with limit test A (10 ppm). Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*). Not more than 5.0 per cent, determined on 5.000 g by drying in an oven at 100-105 °C for 5 h.

Bacterial endotoxins (*2.6.14*): less than 25 IU/g.

Microbial contamination. Total viable aerobic count (*2.6.12*) not more than 10^2 micro-organisms per gram, determined by plate-count. It complies with the test for *Escherichia coli* (*2.6.13*).

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DEXTRAN 40 FOR INJECTION

Dextranum 40 ad iniectabile

DEFINITION

Dextran 40 for injection is a mixture of polysaccharides, principally of the α-1,6-glucan type.

The average relative molecular mass is about 40 000.