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

Dextran 1 for Injection

General Notices

(Ph. Eur. monograph 1506)

Action and use

Plasma substitute.

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DEFINITION

Low-molecular-weight fraction of dextran, consisting of a mixture of isomaltooligosaccharides.

Average relative molecular mass 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

Appearance

White or almost white hygroscopic powder.

Solubility

Very soluble in water, very slightly soluble in ethanol (96 per cent).

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. Infrared absorption spectrophotometry (2.2.24).

Preparation To 1-2 mg add 1 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 but 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 with the residue.

Comparison Repeat the operations using *dextran 1 CRS*.

C. 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)

Maximum 0.12, determined at 375 nm on solution S.

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

Maximum 110 ppm of N.

Carry out the determination of nitrogen by sulfuric 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.

Sodium chloride

Maximum 1.5 per cent.

Accurately weigh 3-5 g and dissolve in 100 mL of *water R*. Titrate with *0.1 M silver nitrate*, determining the end-point potentiometrically (*2.2.20*).

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

Molecular-mass distribution

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 contents of a vial 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.

Column 2 columns coupled in series:

— *size*: *l* = 0.30 m, *Ø* = 10 mm;

— *stationary phase*: dextran covalently bound to highly cross-linked porous agarose beads, allowing resolution of oligosaccharides in the molecular mass range of 180 to 3000;

— *temperature*: 20-25 °C.

Mobile phase 2.92 g/L solution of *sodium chloride R*.

Flow rate 0.07-0.08 mL/min maintained constant to ± 1 per cent.

Detection Differential refractometer.

Injection 100 µL.

Identification of peaks Use the chromatogram obtained with reference solution (b) to identify the peaks due to isomaltotriose, isomaltononaose and sodium chloride.

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, using the following expression:

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

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 m_i 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

System suitability The values obtained for *dextran 1 CRS* are within the values stated on the label.

Limits:

— *average molecular mass (M_w)*: 850 to 1150;

— *fraction with less than 3 glucose units*: less than 15 per cent;

— *fraction with more than 9 glucose units*: less than 20 per cent.

Loss on drying (*2.2.32*)

Maximum 5.0 per cent, determined on 5.000 g by drying in an oven at 105 °C for 5 h.

Bacterial endotoxins (*2.6.14*)

Less than 25 IU/g.

Microbial contamination

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

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