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Dextran 1

DEFINITION

Dextran 1 is a low molecular weight fraction of dextran, consisting of a mixture of isomaltooligosaccharides. It is obtained by controlled hydrolysis and fractionation of dextrans produced by fermentation of *Leuconostoc mesenteroides* (strain NRRL B-512; CIP 78.59, or its sub-strains, for example *L. mesenteroides* B-512F; NCTC, 10817), in the presence of sucrose. It is a glucose polymer in which the linkages between glucose units are almost exclusively α-1,6. Its weight-average molecular weight is about 1000.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020) **:** To 1–2 mg each of USP Dextran 1 RS and the sample, add 1–2 drops of water, grind in an agate mortar for 1–2 min, add 300 mg of potassium bromide, and mix to a slurry. [Note—Do not grind.] Dry under vacuum at 40° for 15 min, and if it is not dry, continue drying for another 15 min. Crush the residue, prepare a disk, and run the IR spectrum with a blank potassium bromide disk in the reference beam.

• **B.** It meets the requirements of the test for *Molecular Weight Distribution* and *Average Molecular Weight*.

IMPURITIES

• **Limit of Sodium Chloride**

Sample: 5 g

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Direct titration

Titrant: 0.1 N silver nitrate VS

Endpoint detection: Visual

Analysis: Dissolve the *Sample* in 100 mL of water. Add 0.2 mL of potassium chromate TS, and titrate with *Titrant*. Each mL of *Titrant* is equivalent to 5.844 mg of sodium chloride.

Acceptance criteria: NMT 1.5%

• **Limit of Nitrogenous Impurities** (where it is labeled as intended for use in the preparation of injectables)

(See *Nitrogen Determination* ⟨461⟩.)

Sulfate solution: To 1000 mL of sulfuric acid add 5 g of anhydrous cupric sulfate and 500 g of potassium sulfate. Dissolve by heating, and store at 60°. [Note—If storage at 60° is not possible, prepare a smaller quantity of *Sulfate solution* on the day of use, adjusting proportions accordingly.]

Indicator: Dilute a mixture of 20 mL of a 0.1% solution of bromocresol green in alcohol and 4 mL of methyl red TS with water to 100 mL.

Sample solution: Transfer 0.2 g of Dextran 1, accurately weighed, to a micro-Kjeldahl flask. Add 4 mL of *Sulfate solution*.

Analysis

Sample: *Sample solution*

Heat the *Sample solution* until the solution exhibits a clear green color and the sides of the flask are free from carbonaceous material. Cool, cautiously add 30 mL of water, and transfer the solution to a steam distillation unit. Rinse the Kjeldahl flask with three 5-mL portions of water, adding the washings to the solution. Add 15 mL of 45% sodium hydroxide solution, immediately close the distillation apparatus, and commence steam distillation without delay. Receive the distillate in 1 mL of *Indicator* and sufficient water to cover the end of the condensing tube. Upon completion of the distillation, remove the receiving flask, and rinse the end of the condensing tube with a small quantity of water, adding the rinse to the distillate. Titrate the distillate with 0.010 N hydrochloric acid until the color changes from blue to reddish violet. Perform a blank determination, and make any necessary correction.

Acceptance criteria: The corrected volume of 0.010 N hydrochloric acid required to change the color does not exceed 0.15 mL (110 ppm of nitrogen).

• **Limit of Alcohol and Related Impurities**

Standard solution: To 25.0 mL of the *Sample solution* add 0.5 mL of a 2.5% (w/v) solution of *n*-propyl alcohol.

Sample solution: Dissolve without heating 5.0 g of Dextran 1 in 100 mL of water, and distill the solution, collecting the first 45 mL of the distillate. Dilute the distillate with water to 50.0 mL, and mix.

Chromatographic system

Mode: GC

Detector: Flame ionization

Column: 2-mm × 1.8-m; packed with S3

Temperatures

Column: 160°

Injection port: 240°

Detector: 210°

Carrier gas: Nitrogen

Flow rate: 25 mL/min. [NOTE—Injector seals may deteriorate after multiple injections of the *Standard solution* and *Sample solution*. Inspect the seals before making a series of injections.]

Injection volume: 1 µL

Analysis

Samples: *Standard solution*, *Sample solution*, and a 0.05% (w/v) solution of *n*-propyl alcohol and water

Acceptance criteria: After corrections for any impurities in the *n*-propyl alcohol solution and water, the total area of peaks from impurities in the *Sample solution* does not exceed the area of the *n*-propyl alcohol solution peak.

SPECIFIC TESTS

• **ULTRAVIOLET-VISIBLE SPECTROSCOPY** ⟨857⟩

Sample solution: 15%

Instrumental conditions

Mode: UV

Analytical wavelength: 375 nm

Blank: Water

Acceptance criteria: NMT 0.12

• **OPTICAL ROTATION,** *Specific Rotation*⟨781S⟩

Sample solution: A solution in water at 20°, on the dried basis (dried at 70° under vacuum to constant weight), corrected for sodium chloride content

Acceptance criteria: +148° to +164°

• **MICROBIAL ENUMERATION TESTS** ⟨61⟩and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨62⟩**:** The total aerobic microbial count does not exceed 10^2 cfu/g, determined by plate-count, and the total combined molds and yeasts count does not exceed 10 cfu/g.

• **pH** ⟨791⟩

Sample solution: A 15% solution in water

Acceptance criteria: 4.5–7.0

• **LOSS ON DRYING** ⟨731⟩

Analysis: Dry at 100°–105° for 5 h.

Acceptance criteria: NMT 5.0%

• **BACTERIAL ENDOTOXINS TEST** ⟨85⟩(where it is labeled as intended for use in the preparation of injectables)**:** NMT 25.0 USP Endotoxin Units/g

• **MOLECULAR WEIGHT DISTRIBUTION** and **AVERAGE MOLECULAR WEIGHT**

Mobile phase: 2.9 mg/mL of sodium chloride, filtered and degassed

Calibration solution: 0.45 mg of isomaltotriose (3 glucose units) and 0.60 mg of sodium chloride per mL

Standard solution: 6.0–6.5 mg/mL of USP Dextran 1 RS in *Mobile phase*

Sample solution: 6.0–6.5 mg/mL solution of Dextran 1 in *Mobile phase*

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: Differential refractive index

Column: Two 10-mm × 30-cm columns in series; packing L54

Column temperature: 20°–25°

Flow rate: 0.07–0.08 mL/min, maintained constant to ±1%

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements: The M_w and the amounts of the fractions obtained for the *Standard solution* are within the values stated in the data sheet that accompanies USP Dextran 1 RS.

Analysis

Samples: *Calibration solution* and *Sample solution*

Using the retention times in the chromatogram of the *Calibration solution*, identify the peaks due to isomaltotriose and sodium chloride in the chromatograms of the *Standard solution* and the *Sample solution*. Disregard the peak due to sodium chloride in the *Standard solution* and the *Sample solution*.

Calculate the weight-average molecular weight, M_W:

$$\text{Result} = \Sigma W_i M_i$$

W_i = weight proportion of oligosaccharide i

M_i = molecular weight of oligosaccharide i

Use the molecular weight values for calculation from *Table 1*.

Table 1

Oligosaccharide	Molecular Weight
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

Calculate the amounts of the fractions with fewer than 3 and with more than 9 glucose units for the *Standard solution* and the *Sample solution*.

Acceptance criteria: The M_w of Dextran 1 is 850–1150. The fraction with fewer than 3 units of glucose is less than 15%, and the fraction with more than 9 units of glucose is less than 20%.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store in well-closed containers at a temperature between 4° and 30°.

• **Labeling:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

• **USP Reference Standards** (11)
USP Dextran 1 RS

Topic/Question	Contact	Expert Committee
DEXTRAN 1	Kishan Chandra Senior Scientist I, Documentary Standards	BIO32020 Biologics Monographs 3 - Complex Biologics and Vaccines

Chromatographic Database Information: Chromatographic Database

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