Hydroxypropyl Cellulose, Low Substituted

(Stage 4)

DEFINITION

Cellulose, 2-hydroxypropyl ether *[9004-64-21.*

Hydroxypropyl Cellulose, Low substituted, is a low- substituted *O*-(2-hydroxypropylated) cellulose. It contains not less than 5.0 percent and not more than 16.0 percent of hydroxypropoxy groups, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

Identification—

A: Infrared absorption spectrophotometry.

B: Shake thoroughly 0.1 g with 10 mL of water. It does not dissolve.

C: To the suspension obtained in Identification B, add 1 g of sodium hydroxide, and shake until it becomes homogeneous. Transfer 5 mL to a suitable container, add 10 mL of a mixture of acetone and methanol (4:1), and shake: a white, flocculent precipitate is formed.

pH between 5.0 and 7.5, in a suspension of 1.0 g prepared by evenly distributing the powder with 100 mL of carbon dioxide free water stirring the mixture with a magnetic stirrer.

Loss on drying : Dry it at 105º for 1 hour: it loses not more than 5.0% of its weight.

Residue on ignition : not more than 0.8%

Assay for hydroxypropoxy groups—Gas Chromatography

(i) Apparatus – Reaction vial: A 5 mL pressure-tight serum vial, 20 mm in outside diameter, 50 mm in height, and 20 mm in outside diameter and 13 mm in inside diameter at the mouth, equipped with a pressure-tight septum having a polytetrafluoroethylene-faced butyl rubber, and air-tight sealing by an aluminum crimp or another sealing system providing a sufficient air-tightness.
Heater: A heating module with a square-shape aluminum block having holes in 20 mm diameter and 32 mm in depth, so that the reaction vials fits, capable of mixing the

contents of the vial using a magnetic stirrer equipped in the heating module or using a reciprocal shaker which performs reciprocating motion of approximately 100 times per minute.

(ii) Procedure – Weigh accurately about 0.065 g of Hydroxypropyl Cellulose, Low Substituted, place in a reaction vial, add 0.06 to 0.10 g of adipic acid, 2.0 mL of the internal standard solution and 2.0 mL of hydroiodic acid (typically the concentration is 57 %), immediately cap and seal the vial, and weigh accurately. Using a magnetic stirrer equipped in the heating module, or using a reciprocal shaker, mix the contents of the vial continuously for 60 minutes while heating the block so that the temperature of the contents is maintained at 130±2℃. If a reciprocal shaker or magnetic stirrer cannot be used, shake the vial well by hand at 5-minute intervals during the initial 30 minutes of the heating time. Allow the vial to cool, and again weigh accurately. If the weight loss is less than 0.50% of the contents and there is no evidence of a leak, use the upper layer of the mixture as the sample solution. Separately, take 0.06 to 0.10 g of adipic acid, 2.0 mL of the internal standard solution and 2.0 mL of hydroiodic acid in another reaction vial, cap and seal the vial, and weigh accurately. Add 15 to 22 μL of isopropyl iodide for assay through the septum with a syringe, weigh accurately. Shake the reaction vial well, and use the upper layer of the contents as the standard solution. Perform the test with 1 to 2 μL each of the sample solution and the standard solution as directed under the Gas Chromatography according to the following conditions.

Internal standard solution – A solution of *n*-octane in *o*-xylene (3 in 100).

Operating conditions -

Detector: A thermal conductivity detector or hydrogen flame- ionization detector.

Column: Fused silica, 0.53 mm inside diameter and 30 m in length, coated with 3 μm 100% dimethyl polysiloxane for gas chromatography. Use a guard column if necessary.

Carrier gas: Helium

Flow Rate: Adjust the flow rate so the retention time of the internal standard is about 10 minutes (4.3 mL/min).

Split ratio: 1:40.

Temperature:

— *temperature program a*s follows:

	Time (min)	**Temperature (C)**
Column	0-3	50
	3-8	50 → 100
	8-12.3	100 → 250
	12.3-20.3	250
Injection port		250
Detector		280

System Suitability:

System performance: When the procedure is run with 1 - 2 μLof the standard solution under the above operating conditions, isopropyl iodide and the internal standard are eluted in this order with the resolution between these peaks being not less than 5.

System repeatability: When the test is repeated 6 times with 1 - 2 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area ratio between isopropyl iodide and the internal standard is not more than 2.0%.

Calculate the ratios, Q_T of the peak area of isopropyl iodide from the sample solution to that of the internal standard, and Q_S of the peak area of isopropyl iodide from the standard solution to that of the internal standard.

Content (%) of hydroxypropoxyl group = $Q_T/Q_S \times W_S/W \times (M_1/M_2) \times 100$

W_S: Amount (mg) of isopropyl iodide in the standard solution.
W: Amount (mg) of the sample, calculated on the dried basis.
M_1:Molar mass of hydroxypropoxy group:75.1
M_2:Molar mass of isopropyl iodide group:170.0

Note: The following items will be added as local requirements in the Japanese Pharmacopoeia.

- Description
- Purity: Heavy metals