HYDROXYETHYLCELLULOSE

(Stage 4)

DEFINITION

Partly *O*-(2-hydroxyethylated) cellulose. It may contain suitable pH-stabilisers such as phosphates.

Content: 30.0 per cent to 70.0 per cent of hydroxyethoxy (-OC_2H_4OH) groups (dried substance).

IDENTIFICATION

A. Infrared spectrophotometry.
Record the infrared absorption spectrum of hydroxyethylcellulose and compare with the Reference Spectrum or the spectrum obtained with the Reference Standard: the transmission minima correspond in position and relative size.

B. Heat 10 mL of solution S (see Tests) to boiling. The solution remains clear.

TESTS

Solution S. Disperse 1.0 g (dried substance) in 50 mL of *carbon dioxide-free water*. After 10 min, dilute to 100 mL with *carbon dioxide-free water* and stir until dissolution is complete.

pH: 5.5 to 8.5 for solution S.

Chlorides: maximum 1.0 per cent.

Dilute 1 mL of solution S to 30 mL with *water*. To 15 mL of the solution add 1 mL of a 200 g/l solution of *nitric acid* and pour the mixture as a single addition into a test tube containing 1 mL of a 17 g/l solution of *silver nitrate*. Prepare a standard in the same manner using 10 mL of *chloride standard solution (5 ppm Cl)* and 5 mL of *water*. Examine the tubes laterally against a black background.

After standing for 5 min protected from light, any opalescence in the test solution is not more intense than that in the standard.

Nitrates: maximum 3.0 per cent (dried substance), if hydroxyethylcellulose has a viscosity of 1000 mPa·s or less and maximum 0.2 per cent (dried substance), if hydroxyethylcellulose has a viscosity of more than 1000 mPa·s.

> ***Viscosity***. In order to determine the applicable limit, determine the viscosity using the following procedure. While stirring, introduce a quantity of the substance to be examined equivalent to 2.00 g of the dried substance into 50 g of *water*. Dilute to 100.0 g with *water* and stir until dissolution is complete. Determine the viscosity using a rotating viscometer at 25 °C and at a shear rate of 100 s^{-1} for substances with an expected viscosity up to 100 mPa·s, at a shear

rate of 10 s^{-1} for substances with an expected viscosity between 100 mPa·s and 20,000 mPa·s and at a shear rate of 1 s^{-1} for substances with an expected viscosity above 20,000 mPa·s. If it is impossible to obtain a shear rate of exactly 10 s^{-1} or 100 s^{-1} respectively, use a rate slightly higher and a rate slightly lower and interpolate.

Determination of nitrates. Determine potentiometrically using as indicator a nitrate selective electrode and a silver-silver chloride electrode with *0.1 M ammonium sulfate* as reference electrolyte.

Prepare the solutions immediately before use.

Buffer solution. To a mixture of 50 mL of *1 M sulfuric acid* and 800 mL of *water*, add 135 g of *potassium dihydrogen phosphate* and dilute to 1000 mL with *water*.

Buffered water. Dilute 80 mL of buffer solution to 2000 mL with *water*.

Nitrate standard solution (500 ppm NO_3). Dissolve 0.8154 g of *potassium nitrate* in 500 mL of buffered water and dilute to 1000.0 mL with the same solvent.

Test solution. Dissolve 0.50 g of the substance to be examined in buffered water and dilute to 100.0 mL with the same solvent.

Reference solutions. If hydroxyethylcellulose has a viscosity of 1000 mPa·s or less, dilute 10.0 mL, 20.0 mL and 40.0 mL of *nitrate standard solution (500 ppm NO_3)* to 100.0 mL with buffered water and mix.

If hydroxyethylcellulose has a viscosity of more than 1000 mPa·s, dilute 1.0 mL, 2.0 mL and 4.0 mL of *nitrate standard solution (500 ppm NO_3)* to 100.0 mL with buffered water and mix.

Carry out the measurements for each solution. Calculate the concentration of nitrates using the calibration curve.

Aldehydes: maximum 20 ppm, expressed as glyoxal.

Introduce 1.0 g into a test tube with a ground-glass stopper and add 10.0 mL of *anhydrous ethanol*. Stopper the tube and stir mechanically for 30 min. Centrifuge. To 2.0 mL of the supernatant liquid add 5.0 mL of a 4 g/l solution of *methylbenzothiazolone hydrazone hydrochloride* in an 80 per cent *V/V* solution of *glacial acetic acid* in *water*. Shake to homogenise. After 2 h, the solution is not more intensely coloured than a standard prepared at the same time and in the same manner using 2.0 mL of g*lyoxal standard solution (2 ppm $C_2H_2O_2$)* instead of the 2.0 mL of supernatant liquid.

Loss on drying: maximum 10.0 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

Sulfated ash: maximum 4.0 per cent if hydroxyethylcellulose has a viscosity of 1000 mPa·s or less and maximum 1.0 per cent if hydroxyethylcellulose has a viscosity

of more than 1000 mPa·s, determined on 1.0 g. In order to determine the applicable limit, determine the viscosity using the method described under the test for nitrates.

ASSAY

Gas chromatography. *Prepare the solutions immediately before use*.

Internal standard solution. To 10 mL of o-*xylene* add 0.5 mL of n-*octane* and dilute to 100.0 mL with o-*xylene*.

Test solution. To 30.0 mg, add 60 mg of *adipic acid* in a reaction vial. Add 2.00 mL of internal standard solution and 1.0 mL of hydroiodic acid and close immediately with the valve. Accurately weigh the reaction vial (total mass before heating). Place the vial in an oven or heat in a suitable heater with continuous stirring, maintaining an internal temperature of about 165 ± 2 °C for 2.5 h. Allow to cool and weigh accurately the reaction vial (total mass after heating). If the difference of the total mass before heating to the total mass after heating is more than 10 mg, prepare a new test solution. After phase separation, pierce through the septum of the vial with a cooled syringe and withdraw a sufficient volume of the upper phase as test solution.

Reference solution. Place 60 mg of *adipic acid* and 2.00 mL of internal standard solution in a reaction vial, add 1.0 mL of *hydroiodic acid* and close immediately with a septum. Weigh accurately the vial then inject 55 µl of *iodoethane* through the septum in the vial, weigh again accurately and mix. After phase separation, pierce through the septum of the vial with a cooled syringe and withdraw a sufficient volume of the upper layer as reference solution.

Column:

— *material*: fused silica,

— *size*: *l* = 30 m, Ø = 0.53 mm,

— *stationary phase*: *poly(dimethyl)siloxane* (3 µm).[1]

Carrier gas: *helium for chromatography*.

Flow rate: 4.2 mL/min.

Split ratio: 1:40.

Temperature:

— *temperature programme* as follows:

[1] RTX-1 Restek, DB-1 or HP-1 are suitable.

	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

Detection: flame ionisation.

Injection: 1µl.

Relative retention with reference to *n*-octane (retention time = about 10 min): iodoethane = about 0.6.

System suitability: reference solution:

— *resolution*: minimum of 5.0 between the peaks due to *n*-octane and iodoethane;

— relative standard deviation of the response factor of the principal peak: maximum 2.0 per cent after 6 injections.

Calculate the response factor (R) from the following expression:

$$(A_1 \times W_1 \times C) / (A_2 \times 100)$$

A_1	=	area of the peak due to the internal standard in the chromatogram obtained with the reference solution;
A_2	=	area of the peak due to iodoethane in the chromatogram obtained with the reference solution;
W_1	=	mass of iodoethane in the reference solution, in milligrams;
C	=	percentage content of *iodoethane*;

Calculate the percentage content *m/m* of the hydroxyethoxy groups from the following expression:

$$(A_4 \times R \times M_1 \times 100) / (A_3 \times W_2 \times M_2)$$

A_3 = area of the peak due to the internal standard in the chromatogram obtained with the test solution;

A_4 = area of the peak due to iodoethane in the chromatogram obtained with the test solution;

R = response factor;

M_1 = molar mass of hydroxyethoxy group (61.1);

M_2 = molar mass of iodoethane (156.0);

W_2 = mass of the sample (dried substance) in the test solution, in milligrams.

LABELLING

The label states:

- the name and concentration of any added pH-stabiliser.

Reagents

Chloride standard solution (5 ppm Cl).

Immediately before use, dilute with *water* to 100 times its volume a solution containing *sodium chloride* equivalent to 0.824 g of NaCl in 1000.0 mL.

Glyoxal standard solution (20 ppm $C_2H_2O_2$).

In a 100 mL graduated flask weigh a quantity of a 40 per cent *m/m* solution of *glyoxal* corresponding to 0.200 g of $C_2H_2O_2$ and make up to volume with *anhydrous ethanol*. Immediately before use dilute the solution to 100 times its volume with the same solvent.

Glyoxal standard solution (2 ppm $C_2H_2O_2$).

Immediately before use, dilute *glyoxal standard solution (20 ppm $C_2H_2O_2$) R* to 10 times its volume with *anhydrous ethanol*.

Iodoethane. C_2H_5I. (M_r 155.9). [75-03-6].
Colourless or slightly yellowish liquid, darkening on exposure to air and light, miscible with ethanol (96 per cent) and most organic solvents.
d_{20}^{20}: about 1.95.
n_D^{20}: about 1.513.
bp: about 72 °C.
Storage: in an airtight container.
Content: minimum 99.0 per cent.

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

- Description
- Purity: Heavy metals
- Containers and storage
- Apparent Viscosity