Hydroxyethyl Cellulose

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Draft for Comments

Document History and Schedule for the Adoption Process

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Further follow-up action as required.	

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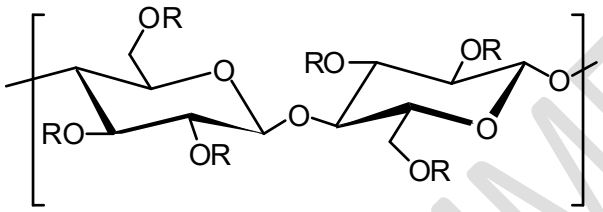
Change to:

Hydroxyethyl Cellulose

Cellulose, 2-Hydroxyethyl Ether

This monograph has been harmonized with corresponding texts of the European Pharmacopoeia, the Japanese Pharmacopoeia and the United States Pharmacopeia. Portions of the IP text that and are not part of the PDG harmonized text, are marked with symbols (♦♦).



R = -H or —CH_2CH_2OH

Hydroxyethyl Cellulose is a partly O-(2-hydroxyethylated) cellulose. It may contain suitable pH-stabilizers such as phosphates.

Hydroxyethyl Cellulose contains not less than 30.0 per cent and not more than 70.0 per cent of hydroxyethoxy (-OC_2H_4OH) groups, calculated on the dried basis.

♦**Category**. Pharmaceutical aid.

Description. A white to yellowish-white or grayish white hygroscopic powder or granules.♦

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *hydroxyethyl cellulose IPRS* or with the reference spectrum of hydroxyethyl cellulose.

B. Disperse 1 g in 50 ml of *carbon dioxide-free water*. After 10 minutes, dilute to 100 ml with *carbon dioxide-free water* and stir until dissolved completely (Solution A). Heat 10 ml of the solution to boiling; the solution remains clear.

Tests

pH (2.4.24). 5.5 to 8.5, determined in Solution A.

Viscosity (2.4.28). 75 per cent to 140 per cent of the value stated on the label.

While stirring, introduce a quantity of the substance under examination equivalent to 2.0 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 the rotating viscometer, Method C at 25° 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 substance with an expected viscosity between 100 mPa.s and 20,000 mPa.s, and at a shear rate of 10 s^{-1} for substance with an expected viscosity above 20,000 mPa.s. If it is impossible to obtain a shear 1 s^{-1}, 10 s^{-1} or 100 s^{-1} respectively, use a rate slightly higher and a rate slightly lower and interpolate.

Aldehydes. Not more than 20 ppm, expressed as glyoxal.

NOTE – Prepare solutions immediately before use.

Test solution. Transfer 1.0 g of the substance under examination to a test tube with a ground-glass stopper and add 10.0 ml of *ethanol*. Stopper the tube and stir by mechanical means for 30 minutes. Centrifuge and retain the supernatant.

Reference solution. Dissolve a quantity of glyxol solution (40 per cent w/w) equivalent to 0.2 g of glyoxal, $C_2H_2O_2$ in *ethanol* and dilute to 100.0 ml with *ethanol*. Dilute 1.0 ml of the solution to 100.0 ml with *ethanol*. Further dilute 1.0 ml of the solution to 10.0 ml with *ethanol*.

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To 2.0 ml of the test solution, add 5.0 ml of a 0.4 per cent w/v solution of *methylbenzothiazolone hydrazone hydrochloride* in 80 per cent v/v solution of *glacial acetic acid* in *water*. Shake to homogenize. After 2 hours the solution is not more intensely coloured than a reference solution prepared at the same time and in the same manner, using 2.0 ml of reference solution instead of 2.0 ml of the test solution.

Chlorides (2.3.12). Not more than 1.0 per cent.

Test solution. Dilute 1 ml of solution A to 30 ml with *water*.

Reference solution. Dissolve 0.824 g of *sodium chloride IPRS* in *water* and dilute to 1000 ml with *water*. Dilute 1.0 ml of the solution to 100.0 ml with *water*. Mix 10 ml of the solution with 5 ml of *water* in a test tube, immediately before use.

Transfer 15 ml of the test solution to a test tube, add 1 ml of *dilute nitric acid* to, each of, the test solution and the reference solution and pour the mixture into two separate test tubes containing 1 ml of *0.1 M silver nitrate*. Examine the tubes laterally against a black background. After standing for 5 minutes protected from light, any opalescence in the test solution is not more intense than that in the reference solution.

Nitrates. Not more than 3.0 per cent, on the dried basis, if hydroxyethyl cellulose has a viscosity of 100 mPa.s or less; and not more than 0.2 per cent, on the dried basis, if hydroxyethyl cellulose has a viscosity of more than 100 mPa.s.

NOTE – Prepare the test solution and the reference solution immediately before use.

Buffered water. To a mixture of 50 ml of *1 M sulphuric acid* and 800 ml of *water*, add 135 g of *potassium dihydrogen phosphate* and dilute to 1000 ml with *water*. Dilute 80 ml of the solution to 2000 ml with *water*.

Test solution. Dissolve 0.5 g of the substance under examination in the *buffered water* and dilute to 100.0 ml with the *buffered water*.

Reference solution. Dissolve 0.8154 g of *potassium nitrate* in 500.0 ml of the *buffered water* and dilute to 1000.0 ml with the *buffered water*.If hydroxyethyl cellulose has a viscosity of 1000 mPa.s or less, dilute 10.0 ml, 20.0 ml and 40.0 ml of reference solution (a) to 100.0 ml with the *buffered water*. If hydroxyethyl cellulose has a viscosity greater than 1000 mPa.s, dilute 1.0 ml, 2.0 ml and 4.0 ml of reference solution (a) to 100.0 ml with the *buffered water*.

Carry out the measurements for each solution potentiometrically (2.5.25) using a nitrate selective electrode as an indicator and a silver-silver chloride electrode with *0.1 M ammonium Sulphate* electrolyte.

Calculate the concentration of nitrates using a calibration curve.

♦**Lead** (2.3.15). Not more than 0.001 per cent.♦

Sulphated ash (2.3.18). Not more than 4.0 per cent, if the viscosity of hydroxyethyl cellulose is not more than 1000 mPa.s and not more than 1.0 per cent, if the viscosity of hydroxyethyl cellulose is not less than 1000 mPa.s, determined on 1.0 g.

Loss on drying (2.4.19). Not more than 10.0 per cent, determined on 1.0 g by drying in an oven at 105° for 3 hours.

Assay. Determine by gas chromatography (2.4.13).

Apparatus:

Reaction vial: a 5 ml pressure-tight vial, equipped with a pressure-tight butyl rubber membrane stopper coated with polytetrafluoroethylene and secured with an aluminium crimp cap or another sealing system providing sufficient air tightness.

Heater: a heating module with a square aluminium block having holes into which the reaction vials fit; mixing of content of the vial is affected using a magnetic stirrer equipped in the heating module or using a reciprocal shaker that performs approximately 100 cycles per minute.

Hydriodic acid: use a reagent with a typical concentrates of hydrogen iodide (HI), about 57 per cent.

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 mg of the dried substance under examination, add 60 mg of *adipic acid* in a 5 ml pressure–tight reaction vial equipped with a pressure-tight membrane stopper coated with *polytetrafluoroethylene* and secured with an aluminium crimped cap or another sealing system providing a sufficient air-tightness. Add 2.0 ml of the internal standard solution and 1.0 ml of hydriodic acid and close immediately. Accurately weigh the vial (total weight before heating). Do not mix the contents of the vial by hand before heating. Place the vial in an oven or heat in a suitable heater, with continuous mechanical agitation, maintaining the internal temperature of the vial at 165± 2° for 150 minutes. Allow to cool and accurately weigh the

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vial (total weight after heating). If the difference between the total weight before heating and the total weight 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 layer as the test solution.

Reference solution. Transfer 60 mg of *adipic acid* and 2.0 ml of the internal standard solution to a 5 ml reaction vial, add 1.0 ml of hydriodic acid and close immediately. Accurately weigh the vial then inject 55 µl of iodoethane through the septum into 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 the reference solution.

Chromatographic system

- a fused silica column 30 m × 0.53 mm, packed with dimethyl polysiloxane (film thickness 3 µm), (Such as DB-1),
- temperature:
  column 50° for 3 minutes, 50° to 100° @ 10° per minute, 100° to 250° @ 34.9° per minute and hold at 250° for 8 minutes,
- inlet port at 250° and detector at 280°,
- flame ionization detector,
- split ratio: 40:1,
- flow rate: 4.2 ml per minute using helium as carrier gas,
- Injection volume: 1 µl.

The relative retention time with reference to n-octane (retention time: about 10 minutes), for iodoethane is about 0.6.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to iodoethane and n-octane is not less than 5.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the response factor using the following expression.

$$\frac{A_1 \times W_1 \times C}{A_2 \times 100}$$

where, 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 = weight of iodoethane in the reference solution (in mg),
C = percentage content of iodoethane.

Calculate the percentage content w/w of hydroxyethoxy groups using the following expression.

$$\frac{A_4 \times R \times M_1 \times 100}{A_3 \times W_2 \times M_2}$$

where, 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 the hydroxyethoxy groups, 61.1,
M_2 = molar mass of iodoethane, 156.0,
W_2 = weight of the sample (dried substance) in the test solution (in mg).

♦**Storage**. Store protected from moisture.

Labelling. The label indicates its viscosity, under specified conditions, in aqueous solution. The indicated viscosity may be in the form of a range encompassing 50 per cent to 150 per cent of the average value. The label states the name and concentration of any added pH-stabilizers.♦

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