Hydroxypropyl 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.

Document History and Schedule for the Adoption Process

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Further follow-up action as required.	

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Change to: **Hydroxypropyl Cellulose**

Cellulose, 2-Hydroxypropyl Ether; Hyprolose

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 (♦♦).

Hydroxypropyl cellulose is a partly O-(2-hydroxypropylated) cellulose. It may contain suitable anti-caking agents such as silica, SiO_2.

Hydroxypropyl cellulose contains not less than 53.4 per cent and not more than 80.5 per cent of hydroxpropoxy groups, calculated on the dried basis.

♦**Category**. Pharmaceutical aid.

Description. A white or yellowish white powder or granules, hygroscopic after drying.♦

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *hydroxypropyl cellulose IPRS* or with the reference spectrum of hydroxypropyl cellulose. [*NOTE – Disregard any peak at about 1719 cm^{-1}*].

B. Dissolve 1 g in 100 ml of *water* (Solution A). Transfer 1 ml of solution A to a glass plate, and allow the *water* to evaporate; a thin film is produced.

Tests

♦**Appearance of solution**. Solution A is not more opalescent than opalescence standard OS3 (2.4.1), and not more intensely coloured than reference solution YS6 (2.4.1).♦

pH (2.4.24). 5.0 to 8.0, determined on 1 per cent w/v solution prepared by evenly distributing the substance under examination into boiling *carbon dioxide-free water* and stirring the mixture with a magnetic stirrer.

Viscosity (2.4.28). 50 to 150 per cent of the stated value, determined by the following method. Weigh a quantity equivalent to 2.0 g of the dried substance and add, with constant stirring, to 50 ml of *water* previously heated to 90°. Allow to cool, dilute to 100.0 ml with *water* and continue stirring until solution is complete. Adjust the weight of the solution to 100 g and centrifuge the solution to expel any trapped air. Determine the viscosity, Method C, at 20° using a shear rate of 10 s^{-1} (2.4.28). For a product of low viscosity, use a quantity of the substance under examination sufficient to prepare a solution of the concentration stated on the label.

♦**Chlorides** (2.3.12). Dilute 5.0 ml of solution A to 15 ml with *water*. The resulting solution complies with the limit test for chlorides (0.5 per cent).♦

Silica. Not more than 0.6 per cent, determined by the following method. If the addition of silica is stated on the label and if more than 0.2 per cent residue is found from the Sulphated ash test, add sufficient *water* to moisten the residue completely. Add 5 ml of *hydrofluoric acid* in small portions. Evaporate to dryness on a steam bath and cool. Add 5 ml of *hydrofluoric* acid and 0.5 ml of *sulphuric acid* and evaporate to dryness. Progressively increase the temperature until all the acids have been volatized, and ignite at 1000° ± 25°, allow to cool in a desicator and weigh. The difference between the weight of the residue obtained in the test for Sulphated ash and the weight of the final residue is equal to the amount of silica in the substance under examination.

Sulphated ash (2.3.18). Not more than 0.8 per cent, determined on 1.0 g in a platinum crucible.

Loss on drying (2.4.19). Not more than 5.0 per cent, determined on 1.0 g by drying in an oven at 105° for 4 hours.

Assay. Determine by gas chromatography (2.4.13).

Internal standard solution. A 2.0 per cent v/v solution of *methylcyclohexane* in *o-xylene*.

Test solution. To 30 mg (dried substance), add 60 mg of *adipic acid* in a reaction vial. Add 2.0 ml of the internal standard solution and 1.0 ml of *hydriodic acid* and close immediately and weigh accurately the vial (total weight before heating).

Place the vial in an oven or heat in a suitable heater, with continuous stirring, maintaining the internal temperature of the vial at 115 ± 2° for 70 minutes. Allow to cool and weigh accurately the 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. Weigh accurately 60 mg of *adipic acid* in a reaction vial, add 2.0 ml of the internal standard solution and 1.0 ml of *hydriodic acid* and close immediately, weigh accurately the reaction vial. Inject 25 µl of *isopropyl iodide* through the septum into the vial, again weigh 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 siloxane (film thickness 3 µm), (Such as DB-1)
- temperature:
  column 40º for 3 minutes, 40º to 100º @ 10º per minute, 100º to 250º @ 50º per minute and hold at 250º for 3 minutes,
- inlet port at 180° and detector at 280°,
- flame ionization detector,
- split ratio: 50:1,
- linear velocity: 52 cm per second using helium as carrier gas,
- injection volume: 2 µl.

The relative retention time with reference to methylcyclohexane (retention time: about 8 minutes) for isopropyl iodide is about 0.8.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to isopropyl iodide and methylcyclohexane is not less than 2 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 isopropyl iodide in the chromatogram obtained with the reference solution,
W_1 = weight of isopropyl iodide in the reference solution (mg),
C = percentage content of isopropyl iodide.

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

$$\frac{1.15 \times A_4 \times R \times M_1}{A_3 \times W_2 \times M_2} \times 100$$

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 isopropyl iodide in the chromatogram obtained with the test solution,
R = response factor,
M_1 = molar mass of the hydroxypropoxy groups 75.1,
M_2 = molar mass of isopropyl iodide 170.0,
W_2 = weight of the sample (dried substance) in the test solution (mg),
1.15 = correction factor.

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

Labelling. The label states the 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.