Ethylcellulose

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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:**

Ethylcellulose

Cellulose ethyl 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 (♦ ♦).

Ethylcellulose is a partly O-ethylated cellulose.

Ethylcellulose contains not less than 44.0 per cent and not more than 51.0 per cent of ethoxy ($-OC_2H_5$) groups, calculated on the dried basis. It may contain suitable antioxidants.

♦**Category**. Pharmaceutical aid.

Description. A white to yellowish-white, powder or granules.♦

Identification

Dissolve 40 mg in 1 ml of *dichloromethane*, and spread two drops of the solution between two sodium chloride plates, then remove one plate to evaporate the solvent. The residue complies with the following test.

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

Tests

♦**pH** (2.4.24). 5.5 to 8.0, determined in a solution prepared in the following manner. Stir 1.0 g with 50 ml of *carbon dioxide-free water* previously heated to 90°, then cool and dilute with sufficient *carbon dioxide-free water* to produce 100 ml.♦

Acidity or Alkalinity. To 0.5 g add 25 ml with *carbon dioxide-free water* and shake for 15 minutes. Filter using a sintered-glass filter. To 10 ml of the solution add 0.1 ml of *phenolphthalein solution* and 0.5 ml of *0.01M sodium hydroxide*; the solution turns pink. To 10 ml of the solution add 0.1 ml of *methyl red solution* and 0.5 ml of *0.01M hydrochloric acid*; the solution turns red.

Acetaldehyde. Not more than 100 ppm.

NOTE – Prepare the test solution and the reference solution at the same time and use immediately.

Solution A. A 0.05 per cent w/v solution of *methylbenzothiazolone hydrazone hydrochloride* in *water*.

Solution B. A solution containing 1 per cent w/v of *ferric chloride* and 1.6 per cent w/v of *sulphamic acid* in *water*.

Test solution. Dissolve 3.0 g of substance under examination in 10 ml of *water*. Stir by mechanical means for 1 hour and allow to stand for 24 hours, filter. Dilute the filtrate to 100.0 ml with *water*.

Reference solution. A 0.0003 per cent w/v solution of *acetaldehyde* in *water*.

Transfer 5.0 ml, each of, the test solution and the reference solution to separate flask. To each flask add 5 ml of solution A and heat in a water bath at 60° for 5 minutes, add 2 ml of solution B and heat again at 60° for 5 minutes. Cool and dilute to 25.0 ml with *water*. The test solution is not more intensely coloured than the reference solution.

♦**Arsenic** (2.3.10). Not more than 3 ppm.

Mix 3.30 g with 5 ml of *sulphuric acid AsT*, add a few glass beads and digest in a fume hood, preferably on a hot plate at a temperature not exceeding 120°, until charring begins. (Additional acid may be necessary to wet some samples completely but the total volume added should not exceed 10 ml). Cautiously add, drop wise, *hydrogen peroxide solution (30 per cent)* allowing the reaction to subside and again heating between additions of drops. Add the first few drops very slowly with sufficient mixing to prevent a rapid reaction. Discontinue heating if foaming becomes excessive. When the reaction has abated, heat cautiously, rotating the flask occasionally to prevent the sample from caking on glass exposed to the heating unit. *(NOTE - Maintain oxidising conditions at all times during the digestion by adding small quantities of the hydrogen peroxide solution whenever the mixture turns brown or darkens)*. Continue the digestion until the organic matter is destroyed, gradually raising the temperature of the heating unit until fumes of sulphur trioxide are copiously evolved and the solution

becomes colourless or retains only a light straw colour. Cool, add cautiously 10 ml of *water*, mix, and again evaporate till strong fuming, repeating this procedure to remove any trace of hydrogen peroxide. Cool, add cautiously 10 ml of *water*, wash the sides of the flask with a few ml of *water*, and dilute with *water* to 35 ml. The resulting solution complies with the limit test for arsenic.♦

Chlorides (2.3.12). Not more than 0.1 per cent.

Dissolve 0.25 g in 50 ml of water, heat to boil, cool and shake occasionally. Filter and discard the first 10 ml of the filtrate. Dilute 10 ml of the filtrate to 15 ml with *water*. The solution complies with the limit test for chlorides.

Sulphated ash (2.3.18). Not more than 0.5 per cent, determined on 1.0 g.

Viscosity (2.4.28). 80.0 per cent to 120.0 per cent of that stated on the label for a nominal viscosity greater than 6 mPa.s; 75.0 per cent to 140.0 per cent of that stated on the label for a nominal viscosity less than 6 mPa.s, determined by the following method. Weigh accurately about 5.0 g, of the dried substance and dissolve in 95.0 g of a mixture of 80 parts of *toluene* and 20 parts of *ethanol (95 per cent)*. Determine the viscosity at 25° by Method A (2.4.28).

♦**Loss on drying** (2.4.19). Not more than 3.0 per cent, determined on 1.0 g by drying in an oven at 105° for 2 hours.♦

♦**Assay**. Determine by gas chromatography (2.4.13).

CAUTION – Hydroic acid and its byproducts are highly toxic. Perform all steps of the reference solution and the test solution in a properly functioning hood. Specific safety practices to be followed.

NOTE – Prepare the solutions immediately before use.

Internal standard solution. To 10 ml of *o-xylene* add 0.5 ml of *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 mass 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 115 ± 2° for 70 minutes. Allow to cool and accurately weigh the vial (total mass after heating). If the difference between the total mass before heating and 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 layer as the test solution.

Reference solution. Place 60 mg of *adipic acid* and 2.0 ml of the internal standard solution in another 5 ml reaction vial, add 1.0 ml of *hydriodic acid* and close immediately. Accurately weigh the vial then inject 25 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 poly (dimethyl) siloxane (film thickness 3 µm),
- temperature:
  column 50° for 3 minutes, 50° to 100° @10° per minutes, 100° to 250° @ 34.9 per minutes and hold at 250° for 8 minutes,
- inlet port at 250° and detector at 280°,
- flow rate: 4.2 ml per minute using helium as carrier gas,
- flame ionization detector,
- split ratio: 40:1,
- injection volume: 1 µl.

The relative retention time with reference to 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 octane is not less than 5 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 of iodoethane 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 = mass of iodoethane in the reference solution in mg,
C = percentage content of iodoethane.

Calculate the percentage content w/w of ethoxy group 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 ethoxy group, 45.1,
M_2 = molar mass of iodoethane,156.0,
W_2 = mass of the sample (dried substance) in the test solution, in mg.♦

Storage. Store protected from moisture.

Labelling. The label states (a) the viscosity in mPa.s of a 5.0 per cent w/w solution and the name and amount of any added antioxidant.