# Ethylcellulose

エチルセルロース

[*9004-57-3*]

This monograph is harmonized with the European Pharmacopoeia and the U. S. Pharmacopeia.

The parts of the text that are not harmonized among the targeted texts for the harmonization are marked with symbols (◆ ◆), and the texts that are uniquely specified by the JP other than the targeted texts for the harmonization are marked with symbols (◇ ◇).

Ethylcellulose is a partly *O*-ethylated cellulose.

It contains not less than 44.0% and not more than 51.0% of ethoxy group ($-OC_2H_5$: 45.06), calculated on the dried basis.

It may contain a suitable antioxidant.

The viscosity is shown in millipascal second (mPa･s) on the label.

◆**Description** Ethylcellulose occurs as a white to yellowish white, amorphous powder or grains.

It is soluble in dichloromethane.

It forms a slightly white-turbid or white-turbid, viscous liquid upon addition of ethanol (95).

To 1 g of Ethylcellulose add 100 mL of hot water, shake to become turbid, cool to room temperature, and add freshly boiled and cooled water to make 100 mL: the solution is neutral. ◆

**Identification** Spread 2 drops of a solution of Ethylcellulose in dichloromethane (1 in 25) between sodium chloride plates, then remove one of the plates to evaporate the solvent, and determine the infrared absorption spectrum of the plate as directed in the film method under Infrared Spectrophotometry <*2.25*>, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

**Viscosity** <*2.53*> Weigh exactly a quantity of Ethylcellulose, equivalent to 5.00 g calculated on the dried basis, add 95 g of a mixture of 80 g of toluene and 20 g of ethanol (95), and shake to dissolve. Perform the test with this solution at 25℃ as directed in Method I: not less than 80.0% and not more than 120.0% of the labeled viscosity for a nominal viscosity more than 6 mPa･s, and not less than 75.0% and not more than 140.0% of the labeled viscosity for a nominal viscosity not more than 6 mPa･s.

**Purity** **(1)** Acidity or alkalinity — To 0.5 g of Ethylcellulose add 25 mL of freshly boiled and cooled water, shake for 15 minutes, filter through a glass filter (G3), and use the filtrate as the sample solution. To 10 mL of the sample solution add 0.1 mL of dilute phenolphthalein TS and 0.5 mL of 0.01 mol/L sodium hydroxide VS: a light red color develops. To 10 mL of the sample solution add 0.1 mL of methyl red-sodium hydroxide TS and 0.5 mL of 0.01 mol/L hydrochloric acid: a red color develops.

**(2)** Chloride — Disperse 0.250 g of Ethylcellulose in 50 mL of water, and boil with occasional shaking. Allow to cool, and filter. Discard the first 10 mL of the filtrate, to 10 mL of the subsequent filtrate add water to make 15 mL, and use this solution as the sample solution. Separately, to 10 mL of Standard Chloride Solution add 5 mL of water, and use this solution as the control solution. To 15 mL each of the sample solution and the control solution add 1 mL of 2 mol/L nitric acid TS, transfer to test tubes containing 1 mL of a solution of silver nitrate (17 in 1000), allow to stand for 5 minutes protecting from light, and compare the opalescence developed in the both solutions against a black background by viewing transversely: the opalescence developed in the sample solution is not more intense than that of the control solution (not more than 0.1%).

◇**(3)** Heavy metal <*1.07*> — Proceed with 1.0 g of Ethylcellulose according to Method 2, and perform the test. Prepare the control solution with 4.0 mL of Standard Lead Solution (not more than 40 ppm). ◇

**(4)** Acetaldehyde — Introduce 3.0 g of Ethylcellulose into a 250-mL glass-stoppered conical flask, add 10 mL of water, and stir for 1 hour. Allow to stand for 24 hours, filter, add water to the filtrate to make 100 mL, and use this solution as the sample solution. Separately, dissolve 1.0 g of acetaldehyde for assay in water to make 100 mL. To 5 mL of this solution add water to make 500 mL. To 3 mL of this solution add water to make 100 mL, and use this solution as the control solution. Transfer 5 mL each of the sample solution and the control solution to 25-mL volumetric flasks, add 5 mL of a solution of 3-methyl-2-benzothiazolonehydrazone hydrochloride monohydrate (1 in 2000), and heat in a water bath at 60℃ for 5 minutes. Add 2 mL of iron (III) chloride-amidosulfuric acid TS, and heat again at 60℃ for 5 minutes. After cooling, add water to make 25 mL, and compare the color of these solutions: the sample solution is not more intensely colored than the control solution (not more than 100 ppm).

**Loss on drying** <*2.41*> Not more than 3.0% (1 g, 105℃, 2 hours).

**Residue on Ignition** <*2.44*> Not more than 0.5% (1 g).

**Assay** Weigh accurately about 30 mg of Ethylcellulose, transfer to a 5-mL pressure-tight serum vial, add exactly 60 mg of adipic acid, 2 mL of the internal standard solution and 1 mL of hydroiodic acid, seal the vial immediately with a septum coated with fluororesin and an aluminum cap, and weigh accurately the vial. Place the vial in an oven or heat in a suitable heater with continuous stirring, maintaining an

internal temperature of about 115 ± 2℃ for 70 min. Allow to cool, and weigh accurately the vial. If the difference of the mass between before heating and after heating is more than 10 mg, prepare a new sample solution. If the difference of the mass between before heating and after heating is not more than 10 mg, after phase separation, pierce through the septum of the vial with a cooled syringe, and withdraw a sufficient volume of the upper phase as the sample solution. Separately, place exactly 60 mg of adipic acid, 2 mL of the internal standard solution and 1 mL of hydroiodic acid in another serum vial, and seal immediately. Weigh accurately the vial, inject 25 μL of iodoethane for assay through the septum in the vial, and weigh again accurately. Shake thoroughly, after phase separation, pierce through the septum of the vial with a cooled syringe, withdraw a sufficient volume of the upper phase, and use this solution as the standard solution. Perform the test as directed under Gas Chromatography *<2.02>* with 1 μL each of the sample solution and standard solution according to the following conditions, calculate the ratios, $Q_T$ and $Q_S$, of the peak area of iodoethane to that of the internal standard.

$$\text{Amount (\%) of ethoxy group } (C_2H_5O) = M_S / M_T \times Q_T / Q_S \times 28.89$$

$M_S$: Amount (mg) of iodoethane for assay taken
$M_T$: Amount (mg) of Ethylcellulose taken, calculated on the dried basis

*Internal standard solution*—A solution of *n*-octane in *o*-xylene (1 in 200).

*Operating conditions*—

Detector: A hydrogen flame-ionization detector.

Column: A fused silica column 0.53 mm in inside diameter and 30 m in length, coated with dimethylpolysiloxane for gas chromatography in 3 μm thickness.

Column temperature: Maintain the temperature at 50℃ for 3 minutes, raise to 100℃ at a rate of 10℃ per minute, then to 250℃ at a rate of 35℃ per minute, and maintain at 250℃ for 8 minutes.

Injection port temperature: A constant temperature of about 250℃.

Detector temperature: A constant temperature of about 280℃.

Carrier gas: Helium.

Flow rate: 4.2 mL per minute (the retention time of the internal standard is about 10 minutes).

Split ratio: 1:40.

*System suitability*—

System performance: When the procedure is run with 1 μL of the standard solution under the above operating conditions, iodoethane and the internal standard are eluted in this order with the relative retention time of iodoethane to that of the internal standard being about 0.6 and the resolution between these peaks being not less than 5.0.

System repeatability: When the test is repeated 6 times with 1 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratio of the peak area of iodoethane to that of the internal standard is not more than 2.0%.

◆**Containers and storage** Containers — Well-closed containers.◆

***Add the following to 9.22 Standard Solutions:***

**Standard Chloride Solution** Pipet 10 mL of Standard Chloride Stock Solution, add water to make exactly 1000 mL. Prepare before use. Each mL of this solution contains 5 μg of chloride (Cl).

**Standard Chloride Stock Solution** Weigh accurately 0.842 g of sodium chloride, previously dried at 130℃ for 2 hours, and dissolve in water to make exactly 1000 mL.

***Add the following to 9.41 Reagents, Test Solutions:***

**Iodoethane for assay** $C_2H_5I$ Colorless to slightly yellow liquid, turning brown on exposure to air and light. Miscible with ethanol (95). Boiling point: about 72℃; Specific gravity $d_{20}^{20}$: about 1.95.

*Refractive index <2.45>* $n_D^{20}$: about 1.513.

*Content*: not less than 99.0%. Assay—Proceed as directed in the Assay under isopropyl iodide for assay.

Each mL of 0.1 mol/L silver nitrate VS = 15.60 mg of $C_2H_5I$

*Storage*—Preserve in tight, light-resistant containers.

**Iron (III) chloride-amidosulfuric acid TS** Dissolve 10 g of iron (III) chloride hexahydrate and 16 g of amidosulfuric acid (standard reagent) in water to make 1000 mL.

**3-Methyl-2-benzothiazolonehydrazone hydrochloride monohydrate** $C_8H_{10}ClN_3S.H_2O$ A white to light yellow-white crystalline powder.

*Melting point <2.60>*: about 270℃ (with decomposition)

**Methyl red-sodium hydroxide TS** Dissolve 50 mg of methyl red in a mixture of 1.86 mL of 0.1 mol/L sodium hydroxide VS and 50 mL of ethanol (95), and add water to make 100 mL.

**Phenolphthalein TS, dilute** Dissolve 0.1 g of phenolphthalein in 80 mL of ethanol (95), and add water to make 100 mL.