

Flow rate: Adjust the flow rate so that the retention time of the internal standard is about 10 minutes.

Selection of column: Proceed with 2 μ L of the standard solution under the above operating conditions. Use a column giving well-resolved peaks of iodomethane, isopropyl iodide and the internal standard in this order.

Containers and storage Containers—Well-closed containers.

Hydroxypropylmethylcellulose Phthalate

ヒドロキシプロピルメチルセルロースフタレート

Hydroxypropyl methylcellulose benzene-1,2-dicarboxylate
[9050-31-1]

Hydroxypropylmethylcellulose Phthalate is a monophthalic acid ester of hydroxypropyl methylcellulose.

It contains methoxyl group ($-\text{OCH}_3$: 31.03), hydroxypropoxyl group ($-\text{OC}_3\text{H}_6\text{OH}$: 75.09), and carboxybenzoyl group ($-\text{COC}_6\text{H}_4\text{COOH}$: 149.12).

There are two substitution types, 200731 and 220824, and each type contains indicated amount of carboxybenzoyl group in the accompanying table, calculated on the anhydrous basis.

Substitution Type	Carboxybenzoyl group (%)	
	Min.	Max.
200731	27.0	35.0
220824	21.0	27.0

Its substitution type and its viscosity are shown in square mm per second (mm^2/s) on the label.

Description Hydroxypropylmethylcellulose Phthalate occurs as white powder or granules. It is odorless and tasteless.

It is practically insoluble in acetonitrile, in ethanol (99.5), and hexane.

It becomes a viscous liquid when a mixture of methanol and dichloromethane (1:1) or a mixture of ethanol (99.5) and acetone (1:1).

It dissolves in sodium hydroxide TS.

Identification Determine the infrared absorption spectrum of Hydroxypropylmethylcellulose Phthalate as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or spectrum of Hydroxypropylmethylcellulose Phthalate Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

Viscosity To 10 g of Hydroxypropylmethylcellulose Phthalate, previously dried at 105°C for 1 hour, add 90 g of a mixture of methanol and dichloromethane in equal mass ratio, and shake to dissolve. Determine the viscosity at $20 \pm 0.1^\circ\text{C}$ as directed in the Capillary-Type Viscosimeter under the Viscosity Determination: the viscosity is not less than 80% and not more than 120% of the labeled unit.

Purity (1) Chloride—Dissolve 1.0 g of Hydroxypropylmethylcellulose Phthalate in 40 mL of 0.2 mol/L sodium hydroxide VS, add 1 drop of phenolphthalein TS, and add dilute nitric acid dropwise with vigorous stirring until the red color is discharged. Further add 20 mL of dilute nitric acid with stirring. Heat on a water bath with stirring until the gelatinous precipitate formed turns to granular particles. After cooling, centrifuge, and take off the supernatant liquid. Wash the precipitate with three 20-mL portions of water by centrifuging each time, combine the supernatant liquid and the washings, add water to make 200 mL, and filter. Perform the test with 50 mL of the filtrate. Control solution: To 0.50 mL of 0.01 mol/L hydrochloric acid VS add 10 mL of 0.2 mol/L sodium hydroxide VS, 7 mL of dilute nitric acid and water to make 50 mL (not more than 0.07%).

(2) Heavy metals—Proceed with 2.0 g of Hydroxypropylmethylcellulose Phthalate according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) Phthalic acid—Weigh accurately about 200 mg of Hydroxypropylmethylcellulose Phthalate, add about 50 mL of acetonitrile to dissolve partially with the aid of ultrasonicator, add 10 mL of water, and dissolve further with the ultrasonicator. After cooling, add acetonitrile to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 12.5 mg of phthalic acid, dissolve in about 125 mL of acetonitrile by mixing, add 25 mL of water and acetonitrile to make exactly 250 mL, and use this solution as the standard solution. Perform the test with 10 μ L each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and determine the peak areas of phthalic acid, A_T and A_S , of both solutions: amount of phthalic acid ($\text{C}_8\text{H}_6\text{O}_4$: 166.13) is not more than 1.0%.

Amount (%) of phthalic acid

$$= \frac{C}{W} \times \frac{A_T}{A_S} \times 10$$

C: concentration of phthalic acid in the standard solution ($\mu\text{g}/\text{mL}$)

W: amount (mg) of the sample, calculated on the anhydrous basis

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 235 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (3 to 10 μm in particle diameter).

Column temperature: A constant temperature of about 20°C.

Mobile phase: A mixture of 0.1 mol/L cyanoacetic acid and acetonitrile (17:3).

Flow rate: About 2.0 mL per minute.

System repeatability: Repeat the test six times with the standard solution under the above operating conditions: the relative standard deviation of the peak area of phthalic acid is not more than 1.0%.

Water Not more than 5.0% (1 g, direct titration, using a mixture of ethanol (99.5) and dichloromethane (3:2) instead of methanol for Karl Fischer method).

Residue on ignition Not more than 0.20% (1 g).

Assay Weigh accurately about 1 g of Hydroxypropylmethylcellulose Phthalate, dissolve in 50 mL of a mixture of ethanol (95), acetone and water (2:2:1), and titrate with 0.1 mol/L sodium hydroxide VS (indicator: 2 drops of phenolphthalein TS). Perform a blank determination, and make any necessary correction.

$$\begin{aligned} & \text{Amount (\% of carboxybenzoyl group (C}_8\text{H}_5\text{O}_3\text{))} \\ &= \frac{0.01 \times 149.1 \times V}{W} - \frac{2 \times 149.1 \times P}{166.1} \end{aligned}$$

P: amount (%) of phthalic acid obtained in the Purity (3)

V: amount (mL) of 0.1 mol/L sodium hydroxide VS consumed

W: amount (g) of the sample, calculated on the anhydrous basis

Containers and storage Containers—Tight containers.

Ichthammol

イクタモール

Ichthammol, calculated on the dried basis, contains not less than 2.5% of ammonia (NH₃: 17.030), not more than 8.0% of ammonium sulfate [(NH₄)₂SO₄: 132.14], and not less than 10.0% of total sulfur (as S: 32.07).

Description Ichthammol is a red-brown to blackish brown, viscous fluid. It has a characteristic odor.

It is miscible with water, and is partially soluble in ethanol (95) and in diethyl ether.

Identification (1) To 4 mL of a solution of Ichthammol (3 in 10) add 8 mL of hydrochloric acid: a yellow-brown to blackish brown, oily or resinous mass is produced. Cool the mass with ice to solidify, and discard the water layer. Wash the residue with diethyl ether: a part of the mass dissolves but it does not dissolve completely even when it is washed until almost no color develops in the washing. Perform the following tests with this residue.

(i) To 0.1 g of the residue add 1 mL of a mixture of diethyl ether and ethanol (95) (1:1): it dissolves.

(ii) To 0.1 g of the residue add 2 mL of water: it dissolves. To 1 mL of this solution add 0.4 mL of hydrochloric acid: a yellow-brown to blackish brown oily or resinous substance is produced.

(iii) To 1 mL of the solution obtained in (ii) add 0.3 g of sodium chloride: a yellow-brown or blackish brown oily or resinous substance is produced.

(2) Boil 2 mL of a solution of Ichthammol (1 in 10) with 2 mL of sodium hydroxide TS: the gas evolved changes moistened red litmus paper to blue.

Loss on drying Not more than 50% (0.5 g, 105°C, 6 hours).

Residue on ignition Not more than 0.5% (1 g).

Assay (1) Ammonia—Weigh accurately about 5 g of Ichthammol, transfer to a Kjeldahl flask, and add 60 mL of water, 1 mL of 1-octanol and 4.5 mL of a solution of sodium hydroxide (2 in 5). Connect the flask to a distilling tube with a spray trap and a condenser, and immerse the lower outlet

of the condenser in the receiver containing exactly 30 mL of 0.25 mol/L sulfuric acid VS. Distil slowly, collect about 50 mL of the distillate, and titrate the excess sulfuric acid with 0.5 mol/L sodium hydroxide VS (indicator: 3 drops of methyl red TS). Perform a blank determination, and make any necessary correction.

$$\begin{aligned} & \text{Each mL of 0.25 mol/L sulfuric acid VS} \\ &= 8.515 \text{ mg of NH}_3 \end{aligned}$$

(2) Ammonium sulfate—Weigh accurately about 1 g of Ichthammol, add 25 mL of ethanol (95), stir thoroughly, and filter. Wash with a mixture of diethyl ether and ethanol (95) (1:1) until the washings are clear and colorless. Dry the filter paper and the residue in air, dissolve the residue in 200 mL of hot water acidified slightly with hydrochloric acid, and filter. Boil the filtrate, add 30 mL of barium chloride TS slowly, heat for 30 minutes on a water bath, and filter. Wash the precipitate with water, dry, and ignite to constant mass. Weigh the residue as barium sulfate (BaSO₄: 233.39).

$$\begin{aligned} & \text{Amount (mg) of ammonium sulfate [(NH}_4\text{)}_2\text{SO}_4\text{]} \\ &= \text{amount (mg) of barium sulfate (BaSO}_4\text{)} \times 0.5662 \end{aligned}$$

(3) Total sulfur—Weigh accurately about 0.6 g of Ichthammol, transfer to a 200-mL Kjeldahl flask, and add 30 mL of water and 5 g of potassium chlorate, then add slowly 30 mL of nitric acid, and evaporate the mixture to about 5 mL. Transfer the residue to a 300-mL beaker with the aid of 25 mL of hydrochloric acid, and evaporate again to 5 mL. Add 100 mL of water, boil, filter, and wash with water. Heat the combined filtrate and washings to boil, add gradually 30 mL of barium chloride TS, heat the mixture on a water bath for 30 minutes, and filter. Wash the precipitate with water, dry, and ignite to constant mass. Weigh the residue as barium sulfate (BaSO₄).

$$\begin{aligned} & \text{Amount (mg) of total sulfur (S)} \\ &= \text{amount (mg) of barium sulfate (BaSO}_4\text{)} \times 0.13739 \end{aligned}$$

Containers and storage Containers—Tight containers.

Immature Orange

Aurantii Fructus Immaturus

キシッ

Immature Orange is the immature fruit or the fruit cut crosswise of *Citrus aurantium* Linné var. *daidai* Makino, *Citrus aurantium* Linné or *Citrus natsuda-daidai* Hayata (*Rutaceae*).

Description Nearly spherical fruit, 1–2 cm in diameter, or semispherical, 1.5–4.5 cm in diameter; external surface, deep green-brown to brown, and without luster, with numerous small dents associated with oil sacs; the outer portion of transverse section exhibits pericarp and mesocarp about 0.4 cm in thickness, yellow-brown in color in the region contacting epidermis, and light grayish brown color in the other parts; the central portion is radially divided into 8 to 16 small loculi; each loculus is brown and indented, often containing immature seeds. Odor, characteristic; taste, bitter.

Identification To 0.5 g of pulverized Immature Orange add