sample solution. Dissolve 0.01 g each of hydrocortisone acetate and diphenhydramine in 10 mL each of methanol, and use these solutions as standard solutions (1) and (2). Perform the test with the sample solution and standard solutions (1) and (2) as directed under the Thin-layer Chromatography. Spot 5 μL each of these solutions on a plate of silica gel with a complex fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of ethyl acetate and diethyl ether (4:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (broad spectrum wavelength): two spots from the sample solution show the same Rf value as the corresponding spots from standard solutions (1) and (2).

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Hydrogenated Oil

硬化油

Hydrogenated Oil is the fat obtained by hydrogenation of fish oil or of other oils originating from animal or vegetable.

Description Hydrogenated Oil occurs as a white mass or powder and has a characteristic odor and a mild taste.

It is freely soluble in diethyl ether, very slightly soluble in ethanol (95), and practically insoluble in water.

The oil obtained by hydrogenation of castor oil is slightly soluble in diethyl ether, very slightly soluble in ethanol (95), and practically insoluble in water.

Acid value Not more than 2.0.

Purity **(1)** Moisture and coloration—Hydrogenated Oil (5.0 g), melted by heating on a water bath, forms a clear liquid, from which no water separates. In a 10-mm thick layer of the liquid, it is colorless or slightly yellow.

(2) Alkali—To 2.0 g of Hydrogenated Oil add 10 mL of water, melt by heating on a water bath, and shake vigorously. After cooling, add 1 drop of phenolphthalein TS to the separated water layer: no color develops.

(3) Chloride—To 1.5 g of Hydrogenated Oil add 30 mL of ethanol (95), boil for 10 minutes under a reflux condenser, and filter after cooling. To 20 mL of the filtrate add 5 drops of a solution of silver nitrate in ethanol (95) (1 in 50): the turbidity of the solution does not exceed that of the following control solution.

Control solution: To 1.0 mL of 0.01 mol/L hydrochloric acid VS add ethanol (95) to make 20 mL, then add 5 drops of a solution of silver nitrate in ethanol (95) (1 in 50).

(4) Heavy metals—Heat 2.0 g of Hydrogenated Oil with 5 mL of dilute hydrochloric acid and 10 mL of water on a water bath for 5 minutes with occasional shaking. After cooling, filter, and make 5 mL of the filtrate weakly alkaline with ammonia TS, then add 3 drops of sodium sulfide TS: the solution remains unchanged.

(5) Nickel—Place 5.0 g of Hydrogenated Oil in a quartz or porcelain crucible, heat slightly with caution at the beginning, and, after carbonization, incinerate by strong heating (500 ± 20°C). Cool, add 1 mL of hydrochloric acid, evaporate on a water bath to dryness, dissolve the residue in 3 mL of dilute hydrochloric acid, and add 7 mL of water. Then add 1 mL of bromine TS and 1 mL of a solution of citric acid monohydrate (1 in 5), make alkaline with 5 mL of ammonia TS, and cool in running water. To this solution add 1 mL of dimethylglyoxime TS, add water to make 20 mL, and use this solution as the test solution. Allow to stand for 5 minutes: the solution has no more color than the following control solution.

Control solution: Evaporate 1 mL of hydrochloric acid on a water bath to dryness, add 1 mL of Standard Nickel Solution and 3 mL of dilute hydrochloric acid, and add 6 mL of water. Then proceed as directed in the test solution, add water to make 20 mL, and allow to stand for 5 minutes.

Residue on ignition Not more than 0.10% (5 g).

Containers and storage Containers—Well-closed containers.

Hydrophilic Ointment

親水軟膏

Method of preparation

White Petrolatum	250 g
Stearyl Alcohol	200 g
Propylene Glycol	120 g
Polyoxyethylene hydrogenated castor oil 60	40 g
Glycerin Monostearate	10 g
Methyl Parahydroxybenzoate	1 g
Propyl Parahydroxybenzoate	1 g
Purified Water	a sufficient quantity
To make	1000 g

Melt White Petrolatum, Stearyl Alcohol, polyoxyethylene hydrogenated castor oil 60 and Glycerin Monostearate by heating on a water bath, stir, and keep temperature of the mixture at about 75°C. To Propylene Glycol add Methyl Parahydroxybenzoate and Propyl Parahydroxybenzoate, melt by warming if necessary, dissolve in Purified Water, and warm to about 75°C. Add this solution to the above mixture, stir to form emulsion, cool, and stir thoroughly until it congeals.

Description Hydrophilic Ointment is white in color. It has a slight, characteristic odor.

Containers and storage Containers—Tight containers.

Hydroxypropylcellulose

ヒドロキシプロピルセルロース

Hydroxypropylcellulose is a hydroxypropyl ether of cellulose.

Hydroxypropylcellulose, when dried, contains not less than 53.4% and not more than 77.5% of hydroxypropoxyl group (-OC_3H_6OH: 75.09).

Description Hydroxypropylcellulose occurs as a white to yellowish white powder.

It is practically insoluble in diethyl ether.

It forms a viscous liquid upon addition of water or ethanol (95).

Identification **(1)** To 1 g of Hydroxypropylcellulose add 100 mL of water, heat in a water bath at 70°C for 5 minutes with stirring, and cool while shaking. Allow to stand at room temperature until it becomes more homogeneous and viscous, and use this solution as the sample solution. To 2 mL of the sample solution add 1 mL of anthrone TS gently: a blue to green color develops at the zone of contact.

(2) Heat the sample solution obtained in (1): a white turbidity or precipitate is produced, and the turbidity or precipitate disappears when cooled.

(3) To 1 g of Hydroxypropylcellulose add 100 mL of ethanol (95), and allow to stand after stirring: a homogeneous and viscous liquid is produced.

pH Dissolve 1.0 g of Hydroxypropylcellulose in 50 mL of freshly boiled and cooled water: the pH of the solution is between 5.0 and 7.5.

Purity **(1)** Clarity of solution—Use an outer glass cylinder, 250 mm in height, 25 mm in internal diameter, 2 mm in thickness, with a high-quality glass plate 2 mm thick at the bottom, and inner glass cylinder, 300 mm in height, 15 mm in internal diameter, 2 mm in thickness, with a high-quality glass plate 2 mm thick at the bottom. In the outer cylinder place a solution prepared by adding 1.0 g of Hydroxypropylcellulose to 100 mL of water, heat while stirring in a water bath at 70°C, and then cool to room temperature. Place this cylinder on a sheet of white paper on which 15 parallel, black, 1-mm width lines are drawn at 1-mm intervals. Place the inner cylinder, and move it up and down while viewing downward through the bottom of the inner cylinder, and measure the minimum height of the solution between the bottom of the outer cylinder and the lower end of the inner cylinder at the time when the lines on the paper cannot be differentiated. The average value obtained from three repeated procedures is greater than that obtained from the following control solution treated in the same manner.

Control solution: To 5.50 mL of 0.005 mol/L sulfuric acid VS add 1 mL of dilute hydrochloric acid, 5 mL of ethanol (95) and water to make 50 mL. To this solution add 2 mL of barium chloride TS, mix, allow to stand for 10 minutes, and shake well before use.

(2) Chloride—Add 1.0 g of Hydroxypropylcellulose to 30 mL of water, heat in a water bath with stirring for 30 minutes, and filter while being hot. Wash the residue with three 15-mL portions of hot water, combine the washings with the filtrate, and add water to make 100 mL after cooling. To 10 mL of the sample solution add 6 mL of dilute nitric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.40 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.142%).

(3) Sulfate—To 40 mL of the sample solution obtained in (2) add 1 mL of dilute hydrochloric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.048%).

(4) Heavy metals—Proceed with 1.0 g of Hydroxypropylcellulose according to Method 2 and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(5) Arsenic—Prepare the test solution with 1.0 g of Hydroxypropylcellulose according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

Loss on drying Not more than 5.0% (1 g, 105°C, 4 hours).

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

Assay (i) Apparatus—Reaction flask: A 5-mL screw-cap pressure-tight glass bottle, having an inverted conical bottom inside, 20 mm in outside diameter, 50 mm in height up to the neck, 2 mL in capacity up to a height of about 30 mm, equipped with a pressure-tight septum of heat-resisting resin and also with an inside stopper or sealer of fluoroplastic.

Heater: A square aluminum block 60 to 80 mm thick, having holes 20.6 mm in diameter and 32 mm in depth, capable of maintaining the inside temperature within ±1°C.

(ii) Procedure—Weigh accurately about 0.065 g of Hydroxypropylcellulose, previously dried, transfer to the reaction flask, add 0.065 g of adipic acid, 2.0 mL of the internal standard solution and 2.0 mL of hydroiodic acid, stopper the flask tightly, and weigh accurately. Shake the flask for 30 seconds, heat at 150°C on the heater for 30 minutes with repeated shaking at 5-minute intervals, and continue heating for an additional 30 minutes. Allow the flask to cool, and again weigh accurately. If the mass loss is less than 10 mg, use the upper layer of the mixture as the sample solution. Separately, take 0.065 g of adipic acid, 2.0 mL of the internal standard solution and 2.0 mL of hydroiodic acid in another reaction flask, stopper tightly, and weigh accurately. Add 50 μL of isopropyl iodide for assay, and again weigh accurately. Shake the reaction flask for 30 seconds, and use the upper layer of the content as the standard solution. Perform the test as directed under the Gas Chromatography with 1 μL each of the sample solution and the standard solution according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of isopropyl iodide to that of the internal standard.

$$\text{Amount (\%) of hydroxypropoxyl group } (C_3H_7O_2) = \frac{Q_T}{Q_S} \times \frac{W_S}{\text{amount (mg) of the sample}} \times 44.17$$

W_S: Amount (mg) of isopropyl iodide in the standard solution.

Internal standard solution—A solution of *n*-octane in *o*-xylene (4 in 100).

Operating conditions—

Detector: A thermal conductivity detector or hydrogen flame-ionization detector.

Column: A glass column about 3 mm in inside diameter and about 3 m in length, packed with siliceous earth for gas chromatography, 180 to 250 μm in particle diameter, coated with methyl silicone polymer for gas chromatography at the ratio of 20%.

Column temperature: A constant temperature of about 100°C.

Carrier gas: Helium (for thermal-conductivity detector); helium or nitrogen (for hydrogen flame-ionization detector).

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

Selection of column: Proceed with 1 μL of the standard solution under the above operating conditions. Use a column giving well-resolved peaks of isopropyl iodide and the internal standard in this order.

Containers and storage Containers—Well-closed containers.

Low Substituted Hydroxypropylcellulose

低置換度ヒドロキシプロピルセルロース

Low Substituted Hydroxypropylcellulose is a low substituted hydroxypropyl ether of cellulose.

Low Substituted Hydroxypropylcellulose, when dried, contains not less than 5.0% and not more than 16.0% of hydroxypropoxyl group ($-OC_3H_6OH$: 75.09).

Description Low Substituted Hydroxypropylcellulose occurs as a white to yellowish white powder or granules. It is odorless or has a slight, characteristic odor. It is tasteless.

It is practically insoluble in ethanol (95) and in diethyl ether.

It dissolves in a solution of sodium hydroxide (1 in 10), and produces a viscous solution.

It swells in water, in sodium carbonate TS and in 2 mol/L hydrochloric acid TS.

Identification **(1)** To 0.02 g of Low Substituted Hydroxypropylcellulose add 2 mL of water, shake, and produce a turbid solution. Add 1 mL of anthrone TS gently: a blue to blue-green color develops at the zone of contact.

(2) To 0.1 g of Low Substituted Hydroxypropylcellulose add 10 mL of water, stir and produce a turbid solution. Add 1 g of sodium hydroxide, shake until it becomes homogeneous, and use this solution as the sample solution. To 0.1 mL of the sample solution add 9 mL of diluted sulfuric acid (9 in 10), shake well, heat in a water bath for exactly 3 minutes, immediately cool in an ice bath, add carefully 0.6 mL of ninhydrin TS, shake well, and allow to stand at 25°C: a red color develops at first, and it changes to purple within 100 minutes.

(3) To 5 mL of the sample solution obtained in (2) add 10 mL of a mixture of acetone and methanol (4:1), and shake: a white, flocculent precipitate is produced.

pH To 1.0 g of Low Substituted Hydroxypropylcellulose add 100 mL of freshly boiled and cooled water, and shake: the pH of the solution is between 5.0 and 7.5.

Purity **(1)** Chloride—To 0.5 g of Low Substituted Hydroxypropylcellulose add 30 mL of hot water, stir well, heat on a water bath for 10 minutes, and filter the supernatant liquid by decantation while being hot. Wash the residue thoroughly with 50 mL of hot water, combine the washings with the filtrate, and add water to make 100 mL after cooling. To 5 mL of the sample solution add 6 mL of dilute nitric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.25 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.335%).

(2) Heavy metals—Proceed with 2.0 g of Low Substituted Hydroxypropylcellulose 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) Arsenic Prepare the test solution with 1.0 g of Low Substituted Hydroxypropylcellulose, according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

Loss on drying Not more than 6.0% (1 g, 105°C, 1 hour).

Residue on ignition Not more than 1.0% (1 g).

Assay (i) Apparatus—Reaction flask: A 5-mL screw-cap pressure-tight glass bottle, having an inverted conical bottom inside, 20 mm in outside diameter, 50 mm in height up to the neck, 2 mL in capacity up to a height of about 30 mm, equipped with a pressure-tight septum of heat-resisting resin and also with an inside stopper or sealer of fluoroplastic.

Heater: A square-shaped aluminum block 60 to 80 mm thick, having holes 20.6 mm in diameter and 32 mm in depth, capable of maintaining the inside temperature within ± 1°C.

(ii) Procedure—Weigh accurately about 0.065 g of Low Substituted Hydroxypropylcellulose, previously dried, transfer to the reaction flask, add 0.065 g of adipic acid, 2.0 mL of the internal standard solution and 2.0 mL of hydroiodic acid, stopper the flask tightly, and weigh accurately. Shake the flask for 30 seconds, heat at 150°C on the heater for 30 minutes with repeated shaking at 5-minute intervals, and continue heating for an additional 30 minutes. Allow the flask to cool, and again weigh accurately. If the mass loss is less than 10 mg, use the upper layer of the mixture as the sample solution. Separately, take 0.065 g of adipic acid, 2.0 mL of the internal standard solution and 2.0 mL of hydroiodic acid in another reaction flask, stopper tightly, and weigh accurately. Add 15 μL of isopropyl iodide for assay, and again weigh accurately. Shake the reaction flask for 30 seconds, and use the upper layer of the content as the standard solution. Perform the test as directed under the Gas Chromatography with 2 μL each of the sample solution and the standard solution according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of isopropyl iodide to that of the internal standard.

Amount (%) of hydroxypropoxyl group ($C_3H_7O_2$)

$$= \frac{Q_T}{Q_S} \times \frac{W_S}{\text{amount (mg) of the sample}} \times 44.17$$

W_S: Amount (mg) of isopropyl iodide in the standard solution.

Internal standard solution—A solution of *n*-octane in *o*-xylene (1 in 50).

Operating conditions—

Detector: A thermal conductivity detector or hydrogen flame-ionization detector.

Column: A glass column about 3 mm in inside diameter and about 3 m in length, packed with siliceous earth for gas chromatography, 180 to 250 μm in particle diameter, coated with methyl silicone polymer for gas chromatography at the ratio of 20%.

Column temperature: A constant temperature of about 100°C.

Carrier gas: Helium (for thermal-conductivity detector); helium or nitrogen (for hydrogen flame-ionization detector).