Column temperature: A constant temperature of about 25°C.

Mobile phase: Dissolve 0.68 g of sodium acetate trihydrate in 900 mL of water, adjust to pH 3.4 with acetic acid (100), and add water to make 1000 mL. To 990 mL of this solution add 10 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of cefuroxime is about 8 minutes.

System suitability—

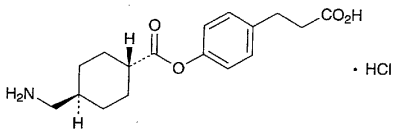
System performance: Allow the sample solution to stand at 60°C for 10 minutes. When the procedure is run with 20 μL of this solution soon after cooling under the above operating conditions, the resolution between the peak of cefuroxime and the peak corresponding to the retention time of about 0.7 to the peak of cefuroxime is being not less than 2.0.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of cefuroxime is not more than 1.0%.

Containers and storage Containers—Tight containers.

Cetraxate Hydrochloride

塩酸セトラキサート



$C_{17}H_{23}NO_4$.HCl: 341.83

trans-3-{4-[4-(Aminomethyl)cyclohexylcarbonyloxy]-phenyl}propanoic acid monohydrochloride [*27724-96-5*]

Cetraxate Hydrochloride, when dried, contains not less than 98.5% of $C_{17}H_{23}NO_4$.HCl.

Description Cetraxate Hydrochloride occurs as white crystals or crystalline powder.

It is soluble in methanol, sparingly soluble in water and in ethanol (95), and practically insoluble in diethyl ether.

Melting point: about 236°C (with decomposition).

Identification **(1)** Determine the absorption spectrum of a solution of Cetraxate Hydrochloride in methanol (1 in 2500) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Dissolve 0.5 g of Cetraxate Hydrochloride in 5 mL of a mixture of water and 2-propanol (1:1) by warming, cool to below 25°C. Filter, dry the formed crystals in vacuum for 4 hours, and further dry at 105°C for 1 hour. Determine the infrared absorption spectrum of the dried matter as directed in the potassium chloride disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) A solution of Cetraxate Hydrochloride (1 in 100) responds to the Qualitative Tests (2) for chloride.

Purity **(1)** Heavy metals—Proceed with 2.0 g of Cetraxate Hydrochloride 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).

(2) Arsenic—Prepare the test solution with 1.0 g of Cetraxate Hydrochloride according to Method 3, and perform the test with a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 5) using Apparatus B (not more than 2 ppm).

(3) *cis* Isomer—Dissolve 0.10 g of Cetraxate Hydrochloride in 10 mL of water, and use this solution as the sample solution. To exactly 5 mL of the sample solution add water to make exactly 100 mL. To exactly 2 mL of this solution add water to make exactly 50 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of both solutions by the automatic integration method: the area of the peak which has a retention time 1.3 to 1.6 times that of cetraxate from the sample solution is not larger than the peak area of cetraxate from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 220 nm).

Column: A stainless steel column about 6 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: Adjust the pH of a mixture of water, methanol and 0.5 mol/L ammonium acetate TS (15:10:4) to 6.0 with acetic acid (31).

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

Selection of column: Dissolve 0.02 g of Cetraxate Hydrochloride and 0.01 g of phenol in 100 mL of water. To 2 mL of this solution add water to make 20 mL. Proceed with 10 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of cetraxate and phenol in this order with the resolution between these peaks being not less than 5.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of cetraxate obtained from 10 μL of the standard solution is not less than 20 mm.

(4) 3-(*p*-Hydroxyphenyl)propionic acid—To 0.10 g of Cetraxate Hydrochloride add exactly 2 mL of the internal standard solution and methanol to make 10 mL, and use this solution as the sample solution. Separately, dissolve 0.025 g of 3-(*p*-hydroxyphenyl)propionic acid in methanol to make exactly 100 mL. To exactly 2 mL of this solution add exactly 2 mL of the internal standard solution and methanol to make 10 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of 3-(*p*-hydroxyphenyl)propionic acid to that of the internal standard: Q_T is not larger than Q_S.

Internal standard solution—A solution of caffeine in methanol (1 in 4000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 230 nm).

Column: A stainless steel column about 6 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Adjust the pH of a mixture of water, methanol and 0.5 mol/L ammonium acetate TS (15:5:2) to 5.5 with acetic acid (31).

Flow rate: Adjust the flow rate so that the retention time of 3-(*p*-hydroxyphenyl)propionic acid is about 7 minutes.

Selection of column: Proceed with 10 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of 3-(*p*-hydroxyphenyl)propionic acid and the internal standard in this order with the resolution between these peaks being not less than 5.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of 3-(*p*-hydroxyphenyl)propionic acid obtained from 10 μL of the standard solution is not less than 30 mm.

(5) Related substances—Dissolve 0.10 g of Cetraxate Hydrochloride in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of chloroform, methanol and acetic acid (100) (20:4:3) to a distance of about 10 cm, and air-dry the plate. Spray evenly ninhydrin TS on the plate, and heat at 90°C for 10 minutes: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying Not more than 0.5% (0.5 g, 105°C, 3 hours).

Residue on ignition Not more than 0.10% (1 g).

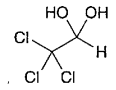
Assay Weigh accurately about 0.5 g of Cetraxate Hydrochloride, previously dried, dissolve in 100 mL of water, and adjust the pH of this solution to between 7.0 and 7.5 with dilute sodium hydroxide TS. To this solution add 10 mL of formaldehyde solution, stir for about 5 minutes, and titrate with 0.1 mol/L sodium hydroxide VS by taking over about 20 minutes (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L sodium hydroxide VS
= 34.183 mg of $C_{17}H_{23}NO_4.HCl$

Containers and storage Containers—Tight containers.

Chloral Hydrate

抱水クロラール



$C_2H_3Cl_3O_2$: 165.40
2,2,2-Trichloroethane-1,1-diol [*302-17-0*]

Chloral Hydrate contains not less than 99.5% of $C_2H_3Cl_3O_2$.

Description Chloral Hydrate occurs as colorless crystals. It has a pungent odor and an acrid, slightly bitter taste.

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

It slowly volatilizes in air.

Identification **(1)** Dissolve 0.2 g of Chloral Hydrate in 2 mL of water, and add 2 mL of sodium hydroxide TS: the turbidity is produced, and it separates into two clear layers by warming.

(2) Heat 0.2 g of Chloral Hydrate with 3 drops of aniline and 3 drops of sodium hydroxide TS: the disagreeable odor of phenylisocyanide (poisonous) is perceptible.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Chloral Hydrate in 2 mL of water: the solution is clear and colorless.

(2) Acid—Dissolve 0.20 g of Chloral Hydrate in 2 mL of water, and add 1 drop of methyl orange TS: a yellow color develops.

(3) Chloride—Perform the test with 1.0 g of Chloral Hydrate. Prepare the control solution with 0.30 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.011%).

(4) Chloral alcoholate—Warm 1.0 g of Chloral Hydrate with 10 mL of sodium hydroxide TS, filter the upper layer, add iodine TS to the filtrate until a yellow color develops, and allow the solution to stand for 1 hour: no yellow precipitate is produced.

(5) Benzene—Warm the solution obtained in (1) with 3 mL of water: no odor of benzene is perceptible.

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately about 4 g of Chloral Hydrate in a glass-stoppered flask, add 10 mL of water and exactly 40 mL of 1 mol/L sodium hydroxide VS, and allow the mixture to stand for exactly 2 minutes. Titrate the excess sodium hydroxide immediately with 0.5 mol/L sulfuric acid VS (indicator: 2 drops of phenolphthalein TS). Perform a blank determination, and make any necessary correction.

Each mL of 1 mol/L sodium hydroxide VS
= 165.40 mg of $C_2H_3Cl_3O_2$

Containers and storage Containers—Tight containers.