expressed as mass (potency) of ampicillin ($C_{16}H_{19}N_3O_4S$: 349.40).

Description Bacampicillin Hydrochloride occurs as a white to pale yellow crystalline powder. It has a characteristic odor.

It is freely soluble in methanol and in ethanol (95), and soluble in water.

Identification **(1)** Determine the absorption spectrum of a solution of Bacampicillin Hydrochloride in methanol (1 in 1000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Bacampicillin Hydrochloride Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

(2) Determine the infrared absorption spectrum of Bacampicillin Hydrochloride as directed in the potassium chloride disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Bacampicillin Hydrochloride Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) A solution of Bacampicillin Hydrochloride (1 in 50) responds to the Qualitative Tests for chloride.

Purity Ampicillin—Weigh accurately about 0.1 g of Bacampicillin Hydrochloride, transfer into a 100-mL separater, add exactly 15 mL of ice-cold water to dissolve, add and mix with exactly 10 mL of ice-cold 0.05 mol/L phosphate buffer solution, pH 7.0, then add 25 mL of ice-cold chloroform, shake, and abandon the chloroform layer. Repeat the procedure twice with two 25-mL portions of ice-cold chloroform. Centrifuge the water layer, filter the supernatant, and use the filtrate as the sample solution. Separately, weigh accurately an amount of Ampicillin Reference Standard, equivalent to about 0.02 g, and dissolve in water to make exactly 100 mL. Pipet 5 mL of this solution, add 10 mL of 0.05 mol/L phosphate buffer solution, pH 7.0 and water to make exactly 25 mL, and use this solution as the standard solution. To exactly 10 mL each of the sample solution and the standard solution add exactly 2 mL of sodium hydroxide TS, allow to stand for exactly 15 minutes, add exactly 2 mL of 1 mol/L hydrochloric acid TS, exactly 10 mL of 0.3 mol/L potassium hydrogen phthalate buffer solution, pH 4.6, and exactly 10 mL of 0.005 mol/L iodine VS, allow to stand for exactly 20 minutes without exposure to light. Titrate these solutions with 0.01 mol/L sodium thiosulfate VS until the color of the solution changes to colorless. Separately, to exactly 10 mL each of the sample solution and the standard solution add exactly 10 mL of 0.3 mol/L potassium hydrogen phthalate buffer solution, pH 4.6 and exactly 10 mL of 0.005 mol/L iodine VS, and perform a blank determination with the same manner. Determine the consumed amounts (mL) of 0.005 mol/L iodine VS, V_T and V_S, of the sample solution and the standard solution: the amount of ampicillin is not more than 1.0%.

Amount (mg) of ampicillin ($C_{16}H_{19}N_3O_4S$)
= amount (mg) of Ampicillin Reference Standard
$\times \frac{V_T}{V_S} \times \frac{1}{20}$

Water Not more than 1.0% (0.5 g, volumetric titration, direct titration).

Residue on ignition Not more than 1.5% (1 g).

Assay Weigh accurately an amount of Bacampicillin Hydrochloride and Bacampicillin Hydrochloride Reference Standard, equivalent to about 0.04 g (potency), dissolve each in water to make exactly 100 mL, and use these solutions as the sample solution and the standard solution. Perform the test with exactly 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the peak areas, A_T and A_S, of bacampicillin of these solutions.

Amount [μg (potency)] of bacampicillin ($C_{21}H_{27}N_3O_7S$)
= amount [mg (potency)] of Bacampicillin Hydrochloride Reference Standard $\times \frac{A_T}{A_S} \times 1000$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 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: To 500 mL of diluted 2 mol/L sodium dihydrogenphosphate TS (1 in 100), add diluted 0.05 mol/L disodium hydrogenphosphate TS (2 in 5) to adjust the pH to 6.8. To 500 mL of this solution add 500 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of bacampicillin is about 6.5 minutes.

System suitability—

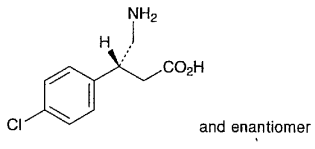
System performance: When the procedure is run with 20 μL of this solution under the above operating conditions, the number of theoretical plates and the symmetry constant of the peak of bacampicillin are not less than 10,000 and not more than 2, respectively.

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 peak areas of bacampicillin is not more than 2.0%.

Containers and storage Containers—Tight containers.

Baclofen

バクロフェン



$C_{10}H_{12}ClNO_2$: 213.66
(*RS*)-4-Amino-3-(4-chlorophenyl)butanoic acid
[*1134-47-0*]

Baclofen contains not less than 98.5% of $C_{10}H_{12}ClNO_2$, calculated on the anhydrous basis.

Description Baclofen occurs as a white to pale yellowish white, crystalline powder.

It is freely soluble in acetic acid (100), slightly soluble in water, very slightly soluble in methanol and in ethanol (95), and practically insoluble in diethyl ether.

It dissolves in dilute hydrochloric acid.

Identification (1) To 5 mL of a solution of Baclofen (1 in 1000) add 1 mL of ninhydrin TS, and heat on a water bath for 3 minutes: a blue-purple color develops.

(2) Determine the absorption spectrum of a solution of Baclofen in 0.1 mol/L hydrochloric acid TS (1 in 2000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Baclofen Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Perform the test with Baclofen as directed under the Flame Coloration Test (2): a green color appears.

Purity (1) Chloride—Dissolve 0.5 g of Baclofen in 50 mL of acetic acid (100), and add water to make 100 mL. To 10 mL of this solution add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.30 mL of 0.01 mol/L hydrochloric acid VS add 5 mL of acetic acid (100), 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.21%).

(2) Heavy metals—Proceed with 2.0 g of Baclofen 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 Baclofen according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.050 g of Baclofen in 50 mL of the mobile phase, and use this solution as the sample solution. Pipet 1.0 mL and 1.5 mL of the sample solution, to each add the mobile phase to make exactly 100 mL, and use these solutions as the standard solution (1) and the standard solution (2), respectively. Perform the test with 25 μL each of the sample solution and the standard solutions (1) and (2) as directed under the Liquid Chromatography according to the following conditions. Determine each peak height of these solutions: each height of the peaks other than the peak of baclofen from the sample solution is not larger than the peak height of baclofen from the standard solution (1), and the total height of these peaks is not larger than the peak height of baclofen from the standard solution (2).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 268 nm).

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

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

Mobile phase: A mixture of methanol and diluted acetic acid (100) (1 in 900) (3:2).

Flow rate: Adjust the flow rate so that the retention time of baclofen is about 4 minutes.

Time span of measurement: About 3 times as long as the retention time of baclofen after the solvent peak.

System suitability—

Test for required detection: Adjust the sensitivity so that the peak height of baclofen obtained from 25 μL of the standard solution (1) is between 5 and 10 mm.

System performance: Dissolve 0.40 g of Baclofen and 5 mg of methyl parahydroxybenzoate in 200 mL of the mobile phase. To 10 mL of this solution add the mobile phase to make 100 mL. When the procedure is run with 25 μL of this solution under the above operating conditions, baclofen and methyl parahydroxybenzoate are eluted in this order with the resolution between these peaks being not less than 5.

System repeatability: When the test is repeated 6 times with 25 μL of the standard solution (1) under the above operating conditions, the relative standard deviation of the peak heights of baclofen is not more than 3.0%.

Water Not more than 1.0% (1 g, direct titration).

Residue on ignition Not more than 0.30% (1 g).

Assay Weigh accurately about 0.5 g of Baclofen, dissolve in 80 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue to greenish blue (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 21.366 mg of $C_{10}H_{12}ClNO_2$

Containers and storage Containers—Well-closed containers.

Baclofen Tablets

バクロフェン錠

Baclofen Tablets contain not less than 93% and not more than 107% of the labeled amount of baclofen ($C_{10}H_{12}ClNO_2$: 213.66).

Method of preparation Prepare as directed under Tablets, with Baclofen.

Identification (1) To a portion of powdered Baclofen Tablets, equivalent to 0.01 g of Baclofen according to the labeled amount, add 10 mL of water, shake well, and filter. To 5 mL of the filtrate add 1 mL of ninhydrin TS, and proceed as directed in the Identification (1) under Baclofen.

(2) To a portion of powdered Baclofen Tablets, equivalent to 0.025 g of Baclofen according to the labeled amount, add 50 mL of 0.1 mol/L hydrochloric acid TS, shake for 15 minutes, and filter. Determine the absorption spectrum of the filtrate as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 257 nm and 261 nm, between 264 nm and 268 nm, and between 272 nm and 276 nm.

(3) To a portion of powdered Baclofen Tablets, equivalent to 0.01 g of Baclofen according to the labeled amount, add 2 mL of a mixture of methanol and acetic acid (100) (4:1), shake well, centrifuge, and use the supernatant liquid as the sample solution. Separately, dissolve 0.01 g of