tion using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.050 g of Bromazepam in 5 mL of a mixture of chloroform and methanol (4:1), and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add a mixture of chloroform and methanol (4:1) to make exactly 50 mL. Pipet 5 mL of this solution, add a mixture of chloroform and methanol (4:1) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 20 μL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of ethyl acetate, ammonia solution (28) and ethanol (99.5) (38:1:1) to a distance of about 12 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution and the spot of the starting point are not more than 2, and not more intense than the spot from the standard solution.

Loss on drying Not more than 0.20% (1 g, 105°C, 4 hours).

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

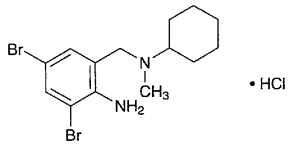
Assay Weigh accurately about 0.4 g of Bromazepam, previously dried, dissolve in 80 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 31.616 mg of $C_{14}H_{10}BrN_3O$

Containers and storage Containers—Well-closed containers.

Bromhexine Hydrochloride

塩酸ブロムヘキシン



$C_{14}H_{20}Br_2N_2.HCl$: 412.59
N-(2-Amino-3,5-dibromophenylmethyl)-*N*-cyclohexyl-*N*-methylamine monohydrochloride [*611-75-6*]

Bromhexine Hydrochloride, when dried, contains not less than 98.5% of $C_{14}H_{20}Br_2N_2.HCl$.

Description Bromhexine Hydrochloride occurs as white crystals or crystalline powder.

It is freely soluble in formic acid, sparingly soluble in methanol, and slightly soluble in water and in ethanol (95).

The pH of its saturated solution is between 3.0 and 5.0.

Melting point: about 239°C (with decomposition).

Identification (1) Dissolve 3 mg of Bromhexine Hydrochloride in 0.01 mol/L hydrochloric acid TS to make 100 mL. Determine the absorption spectrum of the solution 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) Determine the infrared absorption spectrum of Bromhexine Hydrochloride as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Infrared Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Add 20 mL of water to 1 g of Bromhexine Hydrochloride. After thorough shaking, add 3 mL of sodium hydroxide TS, and extract with four 20-mL portions of diethyl ether. Neutralize the water layer with dilute nitric acid: the solution responds to the Qualitative Tests (2) for chloride.

Purity (1) Heavy metals—Proceed with 2.0 g of Bromhexine 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) Related substances—Conduct this procedure without exposure to daylight, using light-resistant vessels. Dissolve 0.050 g of Bromhexine Hydrochloride in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add the mobile phase to make exactly 20 mL. Pipet 1 mL of this solution, add the mobile phase to make exactly 25 mL, and use this solution as the standard solution. Perform the test with 5 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and determine each peak area by the automatic integration method: each peak area other than bromhexine is not larger than the peak area of bromhexine of the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 245 nm).

Column: A stainless steel column about 5 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: Dissolve 1.0 g of potassium dihydrogen phosphate in 900 mL of water, adjust the pH to 7.0 with 0.5 mol/L sodium hydroxide TS, and add water to make 1000 mL. To 200 mL of this solution add 800 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of bromhexine is about 6 minutes.

Selection of column: To 0.05 g of bamethane sulfate add 0.5 mL of the sample solution, and add the mobile phase to make 10 mL. Proceed with 5 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of bamethane and bromhexine in this order with the resolution between these peaks being not less than 7.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of bromhexine from 5 μL of the standard solution is between 5 mm and 15 mm.

Time span of measurement: About 2 times as long as the retention time of bromhexine after the solvent peak.

Loss on drying Not more than 0.5% (1 g, 105°C, 4 hours).

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

Assay Weigh accurately about 0.5 g of Bromhexine Hydrochloride, previously dried, dissolve in 2 mL of formic acid, add 60 mL of acetic anhydride, and warm in a water bath at 50°C for 15 minutes. After cooling, titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue-green to yellow-green (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

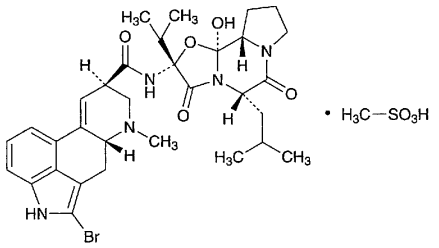
Each mL of 0.1 mol/L perchloric acid VS
= 41.26 mg of $C_{14}H_{20}Br_2N_2.HCl$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Bromocriptine Mesilate

メシル酸ブロモクリプチン



$C_{32}H_{40}BrN_5O_5.CH_4O_3S$: 750.70

(5′*S*)-2-Bromo-12′-hydroxy-5′-isobutyl-2′-isopropylergotaman-3′,6′,18-trione monomethanesulfonate [*22260-51-1*]

Bromocriptine Mesilate contains not less than 98.0% of $C_{32}H_{40}BrN_5O_5.CH_4O_3S$, calculated on the dried basis.

Description Bromocriptine Mesilate occurs as a white to pale yellowish white or pale brownish white, crystalline powder. It is odorless, or has a faint characteristic odor.

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

It is gradually colored by light.

Identification **(1)** Dissolve 2 mg of Bromocriptine Mesilate in 1 mL of methanol, add 2 mL of 4-dimethylaminobenzaldehyde-ferric chloride TS, and shake: a purplish blue color develops.

(2) Determine the absorption spectrum of a solution of Bromocriptine Mesilate in methanol (3 in 100,000) 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.

(3) Determine the infrared absorption spectrum of Bromocriptine Mesilate as directed in the paste 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.

(4) Perform the test with Bromocriptine Mesilate as directed under the Flame Coloration Test (2): a green color appears.

Optical rotation $[\alpha]_D^{20}$: +95 – +105° [0.1 g, calculated on the dried basis, a mixture of methanol and dichloromethane (1:1), 10 mL, 100 mm].

Purity **(1)** Clarity and color of solution—Dissolve 0.10 g of Bromocriptine Mesilate in 10 mL of methanol: the solution is clear, and has no more color than the following control solution.

Control solution: To 2.5 mL of Cobaltous Chloride Stock CS, 6.0 mL of Ferric Chloride Stock CS and 1.0 mL of Cupric Sulfate Stock CS add diluted hydrochloric acid (1 in 40) to make exactly 100 mL.

(2) Heavy metals—Proceed with 1.0 g of Bromocriptine Mesilate 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).

(3) Related substances—Conduct this procedure without exposure to daylight, using light-resistant vessels. Dissolve 0.10 g of Bromocriptine Mesilate in 10 mL of a mixture of methanol and chloroform (1:1), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of methanol and chloroform (1:1) to make exactly 200 mL, and use this solution as the standard solution (1). Pipet 10 mL of the standard solution (1), add a mixture of methanol and chloroform (1:1) to make exactly 20 mL, and use this solution as the standard solution (2). Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL each of the sample solution and the standard solutions (1) and (2), as a band with 1 cm in width, on a plate of silica gel for thin-layer chromatography. Develop the plate immediately with a mixture of dichloromethane, 1,4-dioxane, ethanol (95) and ammonia solution (28) (1800:150:50:1) to a distance of about 10 cm, and dry the plate under reduced pressure for 30 minutes. Spray evenly Dragendorff's TS for spraying on the plate, then spray evenly hydrogen peroxide TS, cover the plate with a glass plate, and examine: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution (1), and the spot other than the principal spot, which is more intense than the spot from the standard solution (2), is not more than one.

Loss on drying Not more than 3.0% (1 g, in vacuum at a pressure not exceeding 0.67 kPa, 80°C, 5 hours).

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

Assay Weigh accurately about 0.6 g of Bromocriptine Mesilate, dissolve in 80 mL of a mixture of acetic anhydride and acetic acid (100) (7:1), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 75.07 mg of $C_{32}H_{40}BrN_5O_5.CH_4O_3S$

Containers and storage Containers—Tight containers.

Storage—Light-resistant, and not exceeding −18°C.