

Separately, dissolve 0.010 g of Epitiostanol Reference Standard in a mixture of acetone and triethylamine (1000:1) to make exactly 10 mL. Pipet 1 mL and 3 mL of this solution, to each add a mixture of acetone and triethylamine (1000:1) to make exactly 25 mL, and use these solutions as the standard solution (1) and the standard solution (2), respectively. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μ L each of the sample solution and the standard solutions (1) and (2) on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of hexane and acetone (3:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly diluted sulfuric acid (1 in 5) on the plate, heat between 120°C and 130°C for 5 minutes, and examine under ultraviolet light (main wavelength: 365 nm): the spots other than the principal spot from the sample solution showing the same R_f value as the standard solutions are not more intense than the spot from the standard solution (2), and the remaining spots other than the principal spot are not more intense than the spot from the standard solution (1).

Water Not more than 0.7% (0.3 g, back titration).

Residue on ignition Not more than 0.1% (0.5 g).

Assay Weigh accurately about 0.3 g of Mepitiothane, and dissolve in cyclohexane to make exactly 10 mL. Pipet 2 mL of this solution, add 10 mL of ethanol (99.5), mix with exactly 2 mL each of 0.01 mol/L hydrochloric acid TS and the internal standard solution, add ethanol (99.5) to make 20 mL, allow to stand at ordinary temperature for 30 minutes, and use this solution as the sample solution. Separately, weigh accurately about 0.045 g of Epitiostanol Reference Standard, dissolve in exactly 2 mL of the internal standard solution, add ethanol (99.5) to make 20 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 calculate the ratios, Q_T and Q_S , of the peak area of epitiostanol to that of the internal standard, respectively.

$$\begin{aligned} & \text{Amount (mg) of } C_{25}H_{40}O_2S \\ &= \text{amount (mg) of Epitiostanol Reference Standard,} \\ & \quad \text{calculated on the anhydrous basis} \\ & \times \frac{Q_T}{Q_S} \times 5 \times 1.3202 \end{aligned}$$

Internal standard solution—A solution of *n*-octylbenzene in ethanol (99.5) (1 in 300).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 265 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μ m in particle diameter).

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

Mobile phase: A mixture of methanol and water (20:3).

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

Selection of column: Proceed with 10 μ L of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of

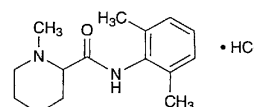
epitiostanol and the internal standard in this order with the resolution between these peaks being not less than 4.

Containers and storage Containers—Hermetic containers.

Storage—Light-resistant, under Nitrogen atmosphere, and in a cold place.

Mepivacaine Hydrochloride

塩酸メピバカイン



$C_{15}H_{22}N_2O \cdot HCl$: 282.81

N-(2,6-Dimethylphenyl)-1-methylpiperidine-2-carboxamide monohydrochloride [1722-62-9]

Mepivacaine Hydrochloride, when dried, contains not less than 98.5% of $C_{15}H_{22}N_2O \cdot HCl$.

Description Mepivacaine Hydrochloride occurs as white crystals or crystalline powder.

It is freely soluble in water and in methanol, soluble in acetic acid (100), sparingly soluble in ethanol (99.5), and practically insoluble in diethyl ether.

A solution of Mepivacaine Hydrochloride (1 in 10) shows no optical rotation.

Melting point: about 256°C (with decomposition).

Identification (1) Determine the absorption spectrum of a solution of Mepivacaine Hydrochloride (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) Determine the infrared absorption spectrum of Mepivacaine Hydrochloride 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 Mepivacaine Hydrochloride (1 in 50) responds to the Qualitative Tests for chloride.

pH Dissolve 0.2 g of Mepivacaine Hydrochloride in 10 mL of water: the pH of this solution is between 4.0 and 5.0.

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Mepivacaine Hydrochloride in 10 mL of water: the solution is clear and colorless.

(2) Sulfate—Perform the test with 0.5 g of Mepivacaine Hydrochloride. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.038%).

(3) Heavy metals—Proceed with 2.0 g of Mepivacaine Hydrochloride according to Method 1, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(4) Related substances—Dissolve 0.10 g of Mepivacaine Hydrochloride in 5 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and

add methanol to make exactly 20 mL. Pipet 4 mL of this solution, add methanol 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 10 μ L 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 diethyl ether, methanol and ammonia solution (28) (100:5:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly bismuth nitrate-potassium iodide TS on the plate: 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 1.0% (1 g, 105°C, 3 hours).

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

Assay Weigh accurately about 0.4 g of Mepivacaine Hydrochloride, previously dried, dissolve in 10 mL of acetic acid (100) and add 70 mL of acetic anhydride. 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
= 28.281 mg of $C_{15}H_{22}N_2O.HCl$

Containers and storage Containers—Tight containers.

Mepivacaine Hydrochloride Injection

塩酸メピバカイン注射液

Mepivacaine Hydrochloride Injection is an aqueous solution for injection. It contains not less than 95% and not more than 105% of the labeled amount of mepivacaine hydrochloride ($C_{15}H_{22}N_2O.HCl$: 282.81).

Method of preparation Prepare as directed under Injections, with Mepivacaine Hydrochloride.

Description Mepivacaine Hydrochloride Injection is a clear, colorless liquid.
pH: 4.5 – 6.8

Identification To a volume of Mepivacaine Hydrochloride Injection, equivalent to 0.02 g of Mepivacaine Hydrochloride according to the labeled amount, add 1 mL of sodium hydrochloride TS, and extract with 20 mL of hexane. To 8 mL of the hexane extract add 20 mL of 1 mol/L hydrochloric acid TS, shake vigorously, and determine the absorption spectrum of the water layer separated as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 261 nm and 265 nm, and between 270 nm and 273 nm.

Assay To an exactly measured volume of Mepivacaine Hydrochloride Injection, equivalent to about 0.04 g of Mepivacaine Hydrochloride according to the labeled amount, add exactly 4 mL of the internal standard solution and 0.001 mol/L hydrochloric acid TS to make 20 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.04 g of mepivacaine hydrochloride for assay, previously dried at 105°C for 3 hours, dissolve in 0.001

mol/L hydrochloric acid TS, add exactly 4 mL of the internal standard solution and 0.001 mol/L hydrochloric acid TS to make 20 mL, and use this solution as the standard solution. Perform the test with 5 μ L 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 mepivacaine to that of the internal standard.

Amount (mg) of $C_{15}H_{22}N_2O.HCl$
= amount (mg) of mepivacaine hydrochloride for assay
 $\times \frac{Q_T}{Q_S}$

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

Operating conditions—

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

Column: A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with octadecylsilylated silica gel for liquid chromatography (10 μ m in particle diameter).

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

Mobile phase: Dissolve 2.88 g of sodium lauryl sulfate in 1000 mL of a mixture of 0.02 mol/L phosphate buffer solution, pH 3.0 and acetonitrile (11:9).

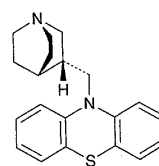
Flow rate: Adjust the flow rate so that the retention time of mepivacaine is about 6 minutes.

Selection of column: Proceed with 5 μ L of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of mepivacaine and benzophenone in this order with the resolution between these peaks being not less than 6.

Containers and storage Containers—Hermetic containers.

Mequitazine

メキタジン



and enantiomer

$C_{20}H_{22}N_2S$: 322.47

10-[(*RS*)-1-Azabicyclo[2.2.2]oct-3-ylmethyl]-10H-phenothiazine [29216-28-2]

Mequitazine, when dried, contains not less than 98.5% of $C_{20}H_{22}N_2S$.

Description Mequitazine occurs as white crystals or crystalline powder.

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

It is gradually colored by light.

A solution of Mequitazine in methanol (1 in 50) shows no