98.5% of $C_{23}H_{28}N_2O_4$, calculated on the dehydrated basis.

Description Quinine Ethyl Carbonate occurs as white crystals. It is odorless, and tasteless at first but slowly develops a bitter taste.

It is very soluble in methanol, freely soluble in ethanol (95) and in ethanol (99.5), soluble in diethyl ether, and practically insoluble in water.

It dissolves in dilute hydrochloric acid.

Identification (1) Determine the absorption spectrum of a solution of Quinine Ethyl Carbonate in methanol (1 in 20,000) 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.

(2) Determine the infrared absorption spectrum of Quinine Ethyl Carbonate as directed in the potassium bromide 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.

Optical rotation $[\alpha]_D^{20}$: -42.2 – $-44.0°$ (0.5 g, calculated on the dehydrated basis, methanol, 50 mL, 100 mm).

Melting point 91 – 95°C

Purity (1) Chloride—Dissolve 0.30 g of Quinine Ethyl Carbonate in 10 mL of dilute nitric acid and 20 mL of water. To 5 mL of the solution add 2 to 3 drops of silver nitrate TS: no color develops.

(2) Sulfate—Dissolve 1.0 g of Quinine Ethyl Carbonate in 5 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 1.0 mL of 0.005 mol/L sulfuric acid VS, 5 mL of dilute hydrochloric acid and water to make 50 mL (not more than 0.048%).

(3) Heavy metals—Proceed with 2.0 g of Quinine Ethyl Carbonate 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).

(4) Related substances—Dissolve 0.020 g of Quinine Ethyl Carbonate in the mobile phase to make exactly 100 mL, and use this solution as the sample solution. Separately, dissolve 0.025 g of quinine sulfate in the mobile phase to make exactly 100 mL. Pipet 2 mL of this solution, add mobile phase to make exactly 100 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 these solutions by the automatic integration method, and calculate the amount of a main impurity in the sample solution which appears at about 1.2 times of the retention time of quinine ethyl carbonate by the area percentage method: it is not more than 10.0%. The total peak area other than the principal peak and above mentioned peak from the sample solution is not larger than the peak area of Quinine from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 235 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 (5 μm in particle diameter).

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

Mobile phase: Dissolve 1.2 g of sodium 1-octanesulfonate in 1000 mL of a mixture of water and methanol (1:1), and adjust to pH 3.5 with diluted phosphoric acid (1 in 20).

Flow rate: Adjust the flow rate so that the retention time of the peak of quinine ethyl carbonate is about 20 minutes.

Selection of column: Dissolve 5 mg each of Quinine Ethyl Carbonate and quinine sulfate in the mobile phase to make 50 mL. Proceed with 10 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of quinine, dihydroquinine, quinine ethyl carbonate and the main impurity of quinine ethyl carbonate in this order with the resolution between the peaks of quinine and dihydroquinine being not less than 2.7, and between the peaks of quinine and quinine ethyl carbonate being not less than 5.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of quinine obtained from 10 μL of the standard solution is between 5 mm and 10 mm.

Time span of measurement: About 2 times as long as the retention time of quinine ethyl carbonate.

Water Not more than 3.0% (0.5 g, direct titration).

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

Assay Weigh accurately about 0.3 g of Quinine Ethyl Carbonate, dissolve in 60 mL of acetic acid (100), add 2 mL of acetic anhydride, 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
= 19.824 mg of $C_{23}H_{28}N_2O_4$

Containers and storage Containers—Well-closed containers.

Quinine Hydrochloride

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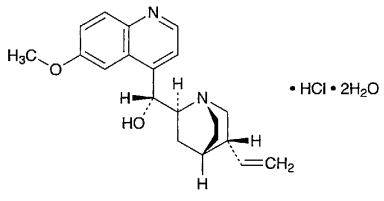

$C_{20}H_{24}N_2O_2.HCl.2H_2O$: 396.91
(8*S*,9*R*)-6′-Methoxycinchonan-9-ol monohydrochloride dihydrate [*6119-47-7*]

Quinine Hydrochloride, when dried, contains not less than 98.5% of $C_{20}H_{24}N_2O_2.HCl$ (mol. wt.: 360.88).

Description Quinine Hydrochloride occurs as white crys-

tals. It is odorless, and has a very bitter taste.

It is very soluble in ethanol (99.5), freely soluble in acetic acid (100), in acetic anhydride and in ethanol (95), soluble in water, and practically insoluble in diethyl ether. Quinine Hydrochloride, previously dried, is freely soluble in chloroform.

It gradually changes to brown by light.

Optical rotation $[\alpha]_D^{20}$: -245 – $-255°$ (after drying, 0.5 g, 0.1 mol/L hydrochloric acid VS, 25 mL, 100 mm).

Identification (1) A solution of Quinine Hydrochloride (1 in 50) shows no fluorescence. To 1 mL of the solution add 100 mL of water and 1 drop of dilute sulfuric acid: a blue fluorescence is produced.

(2) To 5 mL of a solution of Quinine Hydrochloride (1 in 1000) add 1 to 2 drops of bromine TS and 1 mL of ammonia TS: a green color develops.

(3) To 5 mL of a solution of Quinine Hydrochloride (1 in 50) add 1 mL of dilute nitric acid and 1 mL of silver nitrate TS: a white precipitate is produced. Collect the precipitate, and add an excess of ammonia TS: it dissolves.

pH Dissolve 1.0 g of Quinine Hydrochloride in 100 mL of freshly boiled and cooled water: the pH of this solution is between 6.0 and 7.0.

Purity (1) Sulfate—Perform the test with 1.0 g of Quinine Hydrochloride. Prepare the control solution with 1.0 mL of 0.005 mol/L sulfuric acid VS (not more than 0.048%).

(2) Barium—Dissolve 0.5 g of Quinine hydrochloride in 10 mL of water by warming, and add 1 mL of dilute sulfuric acid: no turbidity is produced.

(3) Chloroform-ethanol-insoluble substances—Warm 2.0 g of Quinine Hydrochloride with 15 mL of a mixture of chloroform and ethanol (99.5) (2:1) at 50°C for 10 minutes. After cooling, filter through a tared glass filter (G4) by gentle suction. Wash the residue with five 10-mL portions of a mixture of chloroform and ethanol (99.5) (2:1), dry at 105°C for 1 hour, and weigh: the mass of the residue so obtained is not more than 2.0 mg.

(4) Related substances—Dissolve 0.020 g of Quinine Hydrochloride in the mobile phase to make exactly 100 mL, and use this solution as the sample solution. Separately, dissolve 0.025 g of cinchonidine in the mobile phase to make exactly 100 mL. Pipet 2 mL of this solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 50 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 the sample solution by the automatic integration method, and calculate the amount of dihydroquinine hydrochloride by the area percentage method: it is not more than 10.0%. The total area of the peaks other than the main peak and the above peaks is not larger than the peak area of cinchonidine from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 235 nm).

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

Column temperature: Room temperature.

Mobile phase: A mixture of water, acetonitrile, methanesulfonic acid TS and a solution of diethylamine (1 in 10) (43:5:1:1).

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

Selection of column: Dissolve 10 mg each of Quinine Hydrochloride and quinidine sulfate in 5 mL of methanol, and add the mobile phase to make 50 mL. Proceed with 50 μL of this solution under the above operating conditions. Use a column giving elution of quinidine, quinine, dihydroquinidine and dihydroquinine in this order with the resolution between quinidine and quinine, and that between quinine and dihydroquinidine being not less than 1.2, respectively.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of cinchonidine from 50 μL of the standard solution is between 5 mm and 10 mm.

Time span of measurement: About twice as long as the retention time of quinine after the solvent peak.

(5) Readily carbonizable substances—Perform the test with 0.25 g of Quinine Hydrochloride. The solution has no more color than Matching Fluid M.

Loss on drying Not more than 10.0% (1 g, 105°C, 5 hours).

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

Assay Weigh accurately about 0.4 g of Quinine Hydrochloride, previously dried, dissolve in 100 mL of a mixture of acetic anhydride and acetic acid (100) (7:3) by warming, cool, 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
= 18.044 mg of $C_{20}H_{24}N_2O_2.HCl$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Quinine Sulfate

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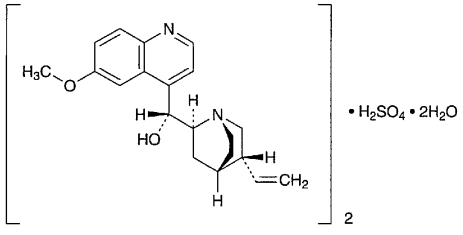

$(C_{20}H_{24}N_2O_2)_2.H_2SO_4.2H_2O$: 782.94

(8*S*,9*R*)-6′-Methoxycinchonan-9-ol hemisulfate monohydrate [*6119-70-6*]

Quinine Sulfate contains not less than 98.5% of $(C_{20}H_{24}N_2O_2)_2.H_2SO_4$ (mol. wt.: 746.91), calculated on the dried basis.

Description Quinine Sulfate occurs as white crystals or crystalline powder. It is odorless, and has a very bitter taste.