

It is freely soluble in acetic acid (100), slightly soluble in water, in ethanol (95), in ethanol (99.5) and in chloroform, and practically insoluble in diethyl ether.

It gradually changes to brown by light.

Identification (1) Determine the absorption spectrum of a solution of Quinine Sulfate (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 Sulfate, previously dried, 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.

(3) To 0.4 g of Quinine Sulfate add 20 mL of water and 1 mL of dilute hydrochloric acid: the solution responds to the Qualitative Tests for sulfate.

Optical rotation $[\alpha]_D^{20}$: -235 – -245° (after drying, 0.5 g, 0.1 mol/L hydrochloric acid VS, 25 mL, 100 mm).

pH Shake 2.0 g of Quinine Sulfate in 20 mL of freshly boiled and cooled water, and filter: the pH of this filtrate is between 5.5 and 7.0.

Purity (1) Heavy metals—Proceed with 2.0 g of Quinine Sulfate 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) Chloroform-ethanol-insoluble substances—Warm 2.0 g of Quinine Sulfate 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 is not more than 2.0 mg.

(3) Related substances—Dissolve 0.020 g of Quinine Sulfate 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 μ L each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area from the sample solution by the automatic integration method, and calculate the amount of dihydroquinine sulfate by the area percentage method: it is not more than 5%. The total area of the peaks other than the main peak and the above peak 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 column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilanized silica gel (10 μ m in particle diameter).

Temperature: Room temperature

Mobile phase: A mixture of water, acetonitrile, methane sulfonic 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 0.01 g each of Quinine Sulfate and quinidine sulfate in 5 mL of methanol, and add the mobile phase to make 50 mL. Proceed with 50 μ L of this solution under the above operating conditions, and calculate the resolution. 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.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of cinchonidine obtained from 50 μ L 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.

Loss on drying 3.0% – 5.0% (1 g, 105°C, 3 hours).

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

Assay Weigh accurately about 0.5 g of Quinine Sulfate, dissolve in 20 mL of acetic acid (100), add 80 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue to blue-green (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

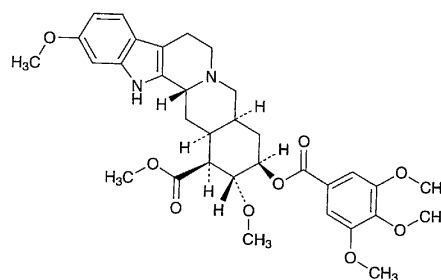
Each mL of 0.1 mol/L perchloric acid VS
= 24.898 mg of $(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Reserpine

レセルピン



$C_{33}H_{40}N_2O_9$: 608.68

Methyl(3*S*,16*S*,17*R*,18*R*,20*R*)-11,17-dimethoxy-18-(3,4,5-trimethoxybenzoyloxy)yoimban-16-carboxylate
[50-55-5]

Reserpine, when dried, contains not less than 96.0% of $C_{33}H_{40}N_2O_9$.

Description Reserpine occurs as white to pale yellow crystals or crystalline powder.

It is freely soluble in acetic acid (100) and in chloroform, slightly soluble in acetonitrile, very slightly soluble in ethanol (95), and practically insoluble in water and in

diethyl ether.

It is affected by light.

Identification (1) To 1 mg of Reserpine add 1 mL of vanillin-hydrochloric acid TS, and warm: a vivid red-purple color develops.

(2) Determine the absorption spectrum of a solution of Reserpine in acetonitrile (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Reserpine Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

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

Optical rotation $[\alpha]_D^{20}$: $-114 - -127^\circ$ (after drying, 0.25 g, chloroform, 25 mL, 100 mm).

Purity Related substances—Conduct this procedure without exposure to daylight, using light-resistant vessels. Dissolve 0.050 g of Reserpine in 50 mL of acetonitrile, and use this solution as the sample solution. Pipet 3 mL of the sample solution, add acetonitrile to make exactly 100 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. Determine each peak area from these solutions by the automatic integration method: the total area of all peaks other than reserpine peak from the sample solution is not larger than the peak area of reserpine from the standard solution.

Operating conditions—

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

Column: A stainless steel column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μ m in particle diameter).

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

Mobile phase: A mixture of 0.05 mol/L potassium dihydrogenphosphate, pH 3.0 and acetonitrile (13:7).

Flow rate: Adjust the flow rate so that the retention time of reserpine is about 20 minutes.

Selection of column: Dissolve 0.01 g of Reserpine and 4 mg of butyl parahydroxybenzoate in 100 mL of acetonitrile. To 5 mL of this solution add acetonitrile to make 50 mL. Proceed with 20 μ L of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of reserpine and butyl parahydroxybenzoate in this order with the resolution between these peaks being not less than 2.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of reserpine from 10 μ L of the standard solution is about 20 mm.

Time span of measurement: About twice as long as the retention time of reserpine.

Loss on drying Not more than 0.5% (0.2 g, in vacuum,

60°C, 3 hours).

Residue on ignition Not more than 0.25% (0.2 g).

Assay Conduct this procedure without exposure to daylight, using light-resistant vessels. Weigh accurately about 0.01 g each of Reserpine and Reserpine Reference Standard, previously dried, and dissolve each in acetonitrile to make exactly 100 mL. Pipet 5 mL each of these solutions, add exactly 10 mL of the internal standard solution, 5 mL of acetonitrile and water to make 50 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 20 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 reserpine to that of the internal standard.

$$\begin{aligned} & \text{Amount (mg) of } C_{33}H_{40}N_2O_9 \\ &= \text{amount (mg) of Reserpine Reference Standard} \\ & \quad \times \frac{Q_T}{Q_S} \end{aligned}$$

Internal standard solution—A solution of butyl parahydroxybenzoate in acetonitrile (1 in 50,000).

Operating conditions—

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

Column: A stainless steel column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μ m in particle diameter).

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

Mobile phase: A mixture of 0.05 mol/L potassium dihydrogenphosphate, pH 3.0 and acetonitrile (11:9).

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

Selection of column: Proceed with 20 μ L of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of reserpine and the internal standard in this order with the resolution between these peaks being not less than 2.

Containers and Storage Containers—Well-closed containers.

Storage—Light-resistant.

Reserpine Injection

レセルピン注射液

Reserpine Injection is an aqueous solution for injection. It contains not less than 90% and not more than 110% of the labeled amount of reserpine ($C_{33}H_{40}N_2O_9$: 608.68).

Method of preparation Prepare as directed under Injections with Reserpine.

Description Reserpine Injection is a clear, colorless or pale yellow liquid.

pH: 2.5 - 4.0