Pergolide Mesilate Tablets

Dissolution <*6.10*> Perform the test with 1 tablet of Pergolide Mesilate Tablets at 50 revolutions per minute according to the Paddle method, using 900 mL of 2nd fluid for dissolution test as the dissolution medium. Withdraw not less than 20 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 10 mL of the filtrate, pipet V mL of the subsequent filtrate, add 2nd fluid for dissolution test to make exactly V' mL so that each mL contains about 56 ng of pergolide ($C_{19}H_{26}N_2S$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 18 mg of Pergolide Mesilate RS, dissolve in 10 mL of methanol, and add water to make exactly 250 mL. To exactly 5 mL of this solution add 2nd fluid for dissolution test to make exactly 100 mL. Pipet 2 mL of this solution, add 2nd fluid for dissolution test to make exactly 100 mL, and use this solution as the standard solution. Pipet 5 mL of the sample solution and the standard solution, and add exactly 2 mL each of triethylamine-phosphoric acid-acetonitrile TS. Perform the test with 200 μL each of these solutions as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine the peak areas, A_T and A_S, of pergolide in each solution.

The requirements are met if Pergolide Mesilate Tablets conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of pergolide ($C_{19}H_{26}N_2S$)

$= M_S \times A_T/A_S \times V'/V \times 1/C \times 360 \times 0.766$

M_S: Amount (mg) of Pergolide Mesilate RS

C: Labeled amount (mg) of pergolide ($C_{19}H_{26}N_2S$) in 1 tablet

Operating conditions —

Detector: A fluorophotometer (excitation wavelength: 280 nm, fluorescence wavelength: 335 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with cyanopropylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25ºC.

Mobile phase: To 1000 mL of a mixture of acetonitrile and water (21:19) add 2 mL of triethylamine, and adjust to pH 5.0 with phosphoric acid.

Flow rate: Adjust the flow rate so that the retention time of pergolide is about 2 minutes.

System suitability —

System performance: When the procedure is run with 200 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of pergolide is not less than 1000 and not more than 2.0, respectively.

System repeatability: Pipet 5 mL of the standard solution, and when the test is repeated 6 times with 200 μL of a solution, prepared by adding exactly 2 mL of triethylamine-phosphoric acid-acetonitrile TS, under the above operating conditions, the relative standard deviation of the peak areas of pergolide is not more than 2.0%.

Dissolution Requirements

Labeled amount	Specified minute	Dissolution rate
50 μg	15 minutes	Not less than 85%
250 μg	15 minutes	Not less than 85%

Pergolide Mesilate RS $C_{19}H_{26}N_2S.CH_4O_3S$: 410.60

(-)-8*β*-[(methylthio)methyl]-6-propylergolin-methanesulfonate mesilate. It meets the following requirements. Purify by the following method if needed.

Purification method—To 100 g of pergolide mesilate add 1600 mL of methanol. Add 20 g of active carbon while stirring, and heat for 30 minutes to boil. Filter this solution while boiling, and wash the residue on the glass filter with 400 mL of boiled methanol. Concentrate 400 to 500 mL of methanol from the filtrate, maintain at 55 to 60ºC for 30 minutes, gradually cool at the rate of 5ºC per 30 minutes to about 40ºC by stirring, and slowly allow the crystals to separate. After the temperature of the solution reaches 40ºC, cool to room temperature for 1 to 4 hours, and then allow to stand at 0 to 5ºC for 30 minutes while stirring. Dry the separated crystals of pergolide mesilate in vacuum at 65 to 70ºC overnight. Repeat this procedure twice.

Description—Pergolide Mesilate RS occurs as while crystals or crystalline powder.

Identification—Determine the infrared absorption spectrum of Pergolide Mesilate RS, previously dried, as directed in the potassium bromide disk method under Infrared Spectrophotometry <*2.25*>: it exhibits absorption at the wave numbers of about 3190 cm^{-1}, 1456 cm^{-1}, 1160 cm^{-1}, 1038 cm^{-1}, 776 cm^{-1}, 552 cm^{-1} and 534 cm^{-1}.

Related substances—Weigh about 15 mg of Pergolide Mesilate RS, add 5 mL of methanol to dissolve, and use this solution as the sample solution. Pipet 1 mL of this solution, add methanol to make exactly 200 mL, and use this solution as the standard solution. Perform the test with exactly 20 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions. Determine each peak area by the automatic integration method: the total area of the peaks other than the peak of pergolide from the sample solution is not larger than the peak area of pergolide from the standard solution (not more than 0.5%).

Operating conditions

Detector: An ultraviolet absorption photometer (wavelength: 280 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 40ºC.

Mobile phase A: Adjust to pH 7.0 of a mixture of water and morpholine (199:1) with phosphoric acid.

Mobile phase B: A mixture of acetonitrile, methanol and tetrahydrofuran (1:1:1).

Flowing of the mobile phase: Control the gradient by mixing the mobile phases A and B as directed in the following table.

Time after injection of sample (min)	Mobile phase A (vol%)	Mobile phase B (vol%)
0 - 35	70→0	30→100

Flow rate: 1.0 mL per minute.

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

System suitability

Test for required detectability: To exactly 4 mL of the standard solution add methanol to make exactly 20 mL. Confirm that the peak area of pergolide obtained from 20 μL of this solution is equivalent to 15 to 25% of that from 20 μL of the standard solution.

System performance: To exactly 1 mL of the sample solution add methanol to make exactly 100 mL. When the procedure is run with 20 μL of this solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of pergolide are not less than 10,000 and not more than 1.5, respectively.

System repeatability: When the test is repeated 5 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of pergolide is not more than 2.0%.

Content: not less than 99.0%. Assay－Weigh accurately about 60 mg of Pergolide Mesilate RS, dissolve in 50 mL of methanol, and titrate <*2.50*> with 0.02 mol/L sodium methoxide VS (potentiometric titration).

Each mL of 0.02 mol/L sodium methoxide VS
= 8.212 mg of $C_{19}H_{26}N_2S.CH_4O_3S$

Triethylamine-Phosphoric Acid-Acetonitrile TS Triethylamine-phosphoric acid-acetonitrile TS: To 1 mL of triethylamine add 500 mL of acetonitrile, mix, and adjust to pH 5.0 with phosphoric acid. It is

white suspension and is used with constant stirring.

Morpholine

Morpholine C_4H_9ON A colorless or light yellow liquid.

Melting point <2.60>: about −5ºC

Boiling point <2.57>: about 129ºC

0.02 mol/L Sodium Methoxide VS 1000 mL of this solution contains 1.0804 g of sodium methoxide (CH_3ONa: 54.02).

Preparation—Before use, dilute 0.1 mol/L sodium methoxide VS with icecold methanol to make exactly 5 times the internal volume.