Perphenazine Fendizoate Powder

Dissolution <*6.10*> Conduct this procedure without exposure to light. Weigh accurately an amount of Perphenazine Fendizoate Powder, equivalent to about 10 mg of perphenazine fendizoate ($C_{21}H_{26}ClN_3OS \cdot 2C_{20}H_{14}O_4$) according to the labeled amount, and perform the test at 75 revolutions per minute according to the Paddle method, using 900 mL of 2nd fluid for dissolution test as the dissolution medium. Start the test, 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 4 mL of the subsequent filtrate, add the mobile phase to make exactly 10 mL, and use this solution as the sample solution. Separately, weigh accurately about 38 mg of Perphenazine Fendizoate RS, previously dried at 105ºC for 3 hours, and dissolve in methanol to make exactly 200 mL. Pipet 2 mL of this solution, add the mobile phase to make exactly 50 mL. Then, pipet 6 mL of this solution, add 2nd fluid for dissolution test to make exactly 10 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, and determine the peak areas, A_T and As, of perphenazine of both solutions.

The requirements are met if Perphenazine Fendizoate Powder conforms to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of perphenazine fendizoate ($C_{21}H_{26}ClN_3OS \cdot 2C_{20}H_{14}O_4$)

$= M_S/M_T \times A_T/A_S \times 1/C \times 27$

M_S: Amount (mg) of Perphenazine Fendizoate RS

M_T: Amount (g) of sample

C: Labeled amount (mg) of perphenazine fendizoate ($C_{21}H_{26}ClN_3OS \cdot 2C_{20}H_{14}O_4$) in 1 g

Operating conditions−

Detector: An ultraviolet absorption photometer (wavelength: 256 nm).

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

Column temperature: A constant temperature of about 30ºC.

Mobile phase: Dissolve 13.61 g of potassium dihydrogen phosphate in water to make 1000 mL. To 400 mL of this solution add 300 mL of acetonitrile and 1 mL of perchloric acid.

Flow rate: Adjust the flow rate so that the retention time of perphenazine is about 5 minutes.

System suitability−

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of perphenazine are not less than 5000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of perphenazine is not more than 2.0%.

Dissolution Requirements

Labeled amount	Specified minute	Dissolution rate
25.76 mg/g	60 minutes	Not less than 70%

Perphenazine Fendizoate RS $C_{21}H_{26}ClN_3OS \cdot 2C_{20}H_{14}O_4$:1040.61 4-[3-(2-chlorophenothiazin-10-yl)propyl]-1-piperazineethanol di-2-[(6-hydroxy-(1,1'biphenyl)-3-yl)carbonyl]benzoate. It meets the following requirements.

Description−Perphenazine Fendizoate RS occurs as white to pale yellow powder. It is affected by light.

Melting point <*2.60*>: about 210ºC (with decomposition).

Identification (1) Determine the UV spectrum of a solution Perphenazine Fendizoate RS in methanol (1 in 100000) as directed under Ultraviolet-visible Spectrophotometry <*2.24*>: it exhibits maxima between 253 nm and 257 nm, and between 285 nm and 291 nm.

(2) Determine the infrared absorption spectrum of Perphenazine Fendizoate 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 1649 cm^{-1}, 1583 cm^{-1}, 1458 cm^{-1}, 1393 cm^{-1} and 1129 cm^{-1}.

Related substances−Conduct this procedure without exposure to light, using light-resistant containers. Dissolve 10 mg of Perphenazine Fendizoate RS in the mobile phase to make 20 mL, and use this solution as the sample solution. Pipet 1 mL of this solution, add the mobile phase to make exactly 200 mL, and use this solution as the standard solution. Perform the test with exactly 7 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 of both solutions by the automatic integration method: the peak area other than perphenazine obtained from the sample solution is not larger than the peak area of perphenazine from the standard solution, and the total area of these peaks is not larger than 2 times the peak area of perphenazine from the standard solution.

Operating conditions

Detector: An ultraviolet absorption photometer (wavelength: 254 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: Dissolve 1.361 g of potassium dihydrogen phosphate in water to make 1000 mL, and adjust the pH to 6.5 with a solution prepared by dissolving 1 g of potassium hydroxide in water to make 10 mL. To 300 mL of this solution add 700 mL of acetonitrile.

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

Time span of measurement: About 5 times as long as the retention time of perphenazine beginning after the peak of fendizoate.

System suitability

Test for required detectability: Pipet 2 mL of the standard solution, and add the mobile phase to make exactly 10 mL. Confirm that the peak area of perphenazine obtained from 7 μL of this solution is equivalent to 14 to 26% of that from 7 μL of the standard solution.

System performance: To 10 mg each of Perphenazine Fendizoate RS and propyl parahydroxybenzoate add the mobile phase to make 200 mL. When the procedure is run with 7 μL of this solution under the above operating conditions, fendizoate, propyl parahydroxybenzoate, and perphenazine are eluted in this order with the resolutions between the peaks of propyl parahydroxybenzoate and perphenazine being not less than 10.

System repeatability: When the test is repeated 6 times with 7 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of perphenazine is not more than 2.0%.

Loss on drying <2.41>: not more than 1.0% (0.5 g, 105ºC, 3 hours).

Content: not less than 99.0%. Assay−Weigh accurately about 1.0 g of Perphenazine Fendizoate RS, previously dried, add 30 mL of acetone to dissolve, add 30 mL of acetic acid (100), and titrate <2.50> with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 52.03 mg of $C_{21}H_{26}ClN_3OS \cdot 2\ C_{20}H_{14}O$