Felodipine Tablets

Dissolution <*6.10*> Perform the test with 1 tablet of Felodipine Tablets at 50 revolutions per minute according to the Paddle method, using 900 mL of a solution, prepared by adding water to 1 g of polysorbate 80 to make 5000 mL, 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 *V* mL of the subsequent filtrate, add a solution, prepared by adding water to 1 g of polysorbate 80 to make 5000 mL, to make exactly *V′* mL so that each mL contains about 2.8 μg of felodipine ($C_{18}H_{19}Cl_2NO_4$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 28 mg of Felodipine RS, and dissolve in methanol to make exactly 200 mL. Pipet 2 mL of this solution, add a solution, prepared by adding water to 1 g of polysorbate 80 to make 5000 mL, to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 50 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 *A*s, of felodipine of both solutions.

The requirements are met if Felodipine Tablets conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of felodipine ($C_{18}H_{19}Cl_2NO_4$)

$= M_S \times A_T/A_S \times V'/V \times 1/C \times 9$

M_S: Amount (mg) of Felodipine RS

C: Labeled amount (mg) of felodipine ($C_{18}H_{19}Cl_2NO_4$) in 1 tablet

Operating conditions−

Detector: An ultraviolet absorption photometer (wavelength: 238 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 25ºC.

Mobile phase: A mixture of a solution of methanol, water and sodium perchlorate (281 in 2000) and diluted perchloric acid (17 in 200) (65:25:8:2).

Flow rate: Adjust the flow rate so that the retention time of felodipine is about 12 minutes.

System suitability−

System performance: When the procedure is run with 50 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of felodipine are not less than 3000 and not more than 1.5, respectively.

System repeatability: When the test is repeated 6 times with 50 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of felodipine is not more than 2.0%.

Dissolution Requirements

Labeled amount	Specified minute	Dissolution rate
2.5 mg	45 minutes	Not less than 80%
5 mg	45 minutes	Not less than 75%

Felodipine RS $C_{18}H_{19}Cl_2NO_4$:384.25 (±)-4-(2,3-dichlorophenyl)-1,4-dihydro-2,6-dimethyl-3,5-pyridinecarboxylic acid ethyl ester methyl ester. It meets the following requirements. Purify according to the following method if needed.

Purification method−Recrystallize Felodipine RS in a mixture of 2-propanol and water.

Description−Felodipine RS occurs as a pale yellowish white to light yellowish white crystals or crystalline powder.

Identification−Determine the infrared absorption spectrum of Felodipine RS as directed in the potassium bromide disk method under Infrared Spectrophotometry <*2.25*>: it exhibits absorption at the wave numbers of about 3370 cm^{-1}, 1698 cm^{-1}, 1278 cm^{-1}, 1205 cm^{-1}, and 1100 cm^{-1}.

Related substances−Dissolve 12 mg of Felodipine RS in 5 mL of the mobile phase, 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 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 of both solutions by the automatic integration method: the total area of the peaks other than felodipine obtained from the sample solution is not larger than the peak area of felodipine from the standard solution.

Operating conditions

Detector: An ultraviolet absorption photometer (wavelength: 264 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 25ºC.

Mobile phase: A mixture of a solution of methanol, water and sodium perchlorate (281 in 2000) and diluted perchloric acid (17 in 200) (65:25:8:2).

Flow rate: Adjust the flow rate so that the retention time of felodipine is about 12 minutes.

Time span of measurement: About 2.5 times as long as the retention time of felodipine beginning after the solvent peak.

System suitability

Test for required detectability: Pipet 5 mL of the standard solution, and add the mobile phase to make exactly 50 mL. Confirm that the peak area of felodipine obtained from 20 μL of this solution is equivalent to 7 to 13% of that from 20 μL of the standard solution.

System performance: To 25 mg of Felodipine RS add 5 mL of a solution of butyl parahydroxybenzoate in methanol (1 in 3000), and add methanol to make exactly 100 mL. When the procedure is run with 20 μL of this solution under the above operating conditions, butyl parahydroxybenzoate and felodipine are eluted in this order with the resolution between these peaks being not less than 5.

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 felodipine is not more than 2.0%.

Content: not less than 99.5%. Assay−Weigh accurately about 0.25 g of Felodipine RS, dissolve in 25 mL of ethanol (95) and 25 mL of diluted perchloric acid (17 in 200) with thorough shaking, and titrate <*2.50*> with 0.1 mol/L cerium (IV) tetraammonium sulfate VS (indicator: 5 drops of 1,10-phenanthroline TS) until the color of the solution changes from orange to colorless. Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 0.1 mol/L cerium (IV) tetraammonium sulfate VS
= 19.21 mg of $C_{18}H_{19}Cl_2NO4$