Doxazosin Mesilate Tablets

Dissolution <6.10> Perform the test with 1 tablet of Doxazosin Mesilate Tablets at 75 revolutions per minute according to the Paddle method, using 900 mL of 0.05 mol/L acetic acid-sodium acetate buffer solution, pH 4.0 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 0.05 mol/L acetic acid-sodium acetate buffer solution, pH 4.0 to make exactly V' mL so that each mL contains about 0.56 μg of doxazosin ($C_{23}H_{25}N_5O_5$) according to the labeled amount. Pipet 5 mL of this solution, add exactly 5 mL of methanol, and use this solution as the sample solution. Separately, weigh accurately about 21 mg of Doxazosin Mesilate RS, previously dried at 105ºC for 4 hours, and dissolve in methanol to make exactly 50 mL. To exactly 2 mL of this solution add methanol to make exactly 50 mL. Further, to exactly 2 mL of this solution add methanol to make exactly 50 mL. Pipet 5 mL of this solution, add exactly 5 mL of 0.05 mol/L acetic acid-sodium acetate buffer solution, pH4.0, 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 A_S, of doxazosin in each solution.

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

Dissolution rate (%) with respect to the labeled amount of doxazosin ($C_{23}H_{25}N_5O_5$)

$= M_S \times A_T/A_S \times V'/V \times 1/C \times 72/25 \times 0.824$

M_S: Amount (mg) of Doxazosin Mesilate RS

C: Labeled amount (mg) of doxazosin ($C_{23}H_{25}N_5O_5$) in 1 tablet

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 246 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 35ºC.

Mobile phase: Dissolve 3.4 g of potassium dihydrogenphosphate in 500 mL of water, and adjust to pH 3.0 with diluted phosphoric acid (1 in 10). To 450 mL of this solution add 550 mL of methanol.

Flow rate: Adjust the flow rate so that the retention time of doxazosin 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 doxazosin are not less than 2000 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 doxazosin is not more than 2.0%.

Dissolution Requirements

Labeled amount*	Specified minute	Dissolution rate
0.5 mg	15 minutes	Not less than 70%
1 mg	15 minutes	Not less than 75%
2 mg	15 minutes	Not less than 75%
4 mg	15 minutes	Not less than 75%

*as Doxazosin

Doxazosin Mesilate RS $C_{23}H_{25}N_5O_5.CH_4O_3S$

(±)-1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(1,4-benzodioxan-2-ylcarbonyl)piperazine methanesulfonate. It meets the following requirements:

Description—Doxazosin Mesilate RS occurs as a white to yellowish white crystalline powder.

Identification—Determine the infrared absorption spectrum of Doxazosin Mesilate RS as directed in the paste method under Infrared Spectrophotometry <*2.25*>: it exhibits absorption at the wave numbers of about 3180 cm^{-1}, 1662 cm^{-1}, 1598 cm^{-1}, 1271 cm^{-1}, 1118 cm^{-1} and 1043 cm^{-1}.

Related substances—Dissolve 20 mg of Doxazosin Mesilate RS in 5 mL of a mixture of methanol and acetic acid (100) (1:1), and use this solution as the sample solution. Pipet 1 mL of this solution, add a mixture of methanol and acetic acid (100) (1:1) to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under Thin-layer Chromatography <*2.03*>. Spot 5 μL each of the sample solution and standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with the upper layer of a mixture of 4-methyl-2-pentanone, acetic acid (100) and water (2:1:1) to a distance of about 10 cm, and air-dry the plate. Examine the plate under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying <*2.41*>: not more than 1.0% (1g, 105ºC, 4 hours).

Content: not less than 99.0%. Assay—Weigh accurately about 0.4 g of Doxazosin Mesilate RS, previously dried, add 20 mL of water, shake well, add 5 mL of sodium hydroxide TS, and extract with three 20-mL portions of chloroform. Filter each extract through anhydrous sodium sulfate on a pledget of absorbent cotton. Combine the chloroform extracts, add 50 mL of acetic anhydride, and titrate <*2.50*> with 0.1 mol/L perchloric acid VS (indicator: 2 drops of methylrosaniline chloride TS). Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 54.76 mg of $C_{23}H_{25}N_5O_5.CH_4O_3S$