Mosapramine Hydrochloride Tablets

Dissolution <*6.10*> Perform the test with 1 tablet of Mosapramin Hydrochloride Tablets at 50 revolutions per minute according to the Paddle method, using 900 mL of water 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, and add a mixture of mobile phase and water (4:1) to make exactly *V*′ mL so that each mL contains about 11.2 μg of mosapramine hydrochloride ($C_{28}H_{35}ClN_4O \cdot 2HCl$) according to the labeled amount. Then, pipet 2 mL of this solution, add the mobile phase to make exactly 10 mL, and use this solution as the sample solution. Separately, weigh accurately about 28 mg of Mosapramine Hydrochloride RS, previously dried at 105ºC for 2 hours, and dissolve in water to make exactly 50 mL. Pipet 2 mL of this solution, add a mixture of the mobile phase and water (4:1) to make exactly 100 mL. Then, pipet 2 mL of this solution, add a mixture of the mobile phase and water (4:1) to make exactly 10 mL, and use this solution as the standard solution. Perform the test with exactly 10 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 mosapramine of both solutions.

The requirements are met if Mosapramine Hydrochloride Tablets conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of mosapramine hydrochloride ($C_{28}H_{35}ClN_4O \cdot 2HCl$)

$= M_S \times A_T/A_S \times V'/V \times 1/C \times 36$

M_S: Amount (mg) of Mosapramine Hydrochloride RS

C: Labeled amount (mg) of mosapramine hydrochloride ($C_{28}H_{35}ClN_4O \cdot 2HCl$) in 1 tablet

Dissolution Requirements

Labeled amount	Specified minute	Dissolution rate
10 mg	30 minutes	Not less than 80%
25 mg	30 minutes	Not less than 80%
50 mg	30 minutes	Not less than 80%

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 253 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 400 mL of acetonitrile and 1 mL of perchloric acid.

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

System suitability−

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of mosapramine are not less than 5000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of mosapramine is not more than 2.0%.

Mosapramine Hydrochloride RS $C_{28}H_{35}ClN_4O \cdot 2HCl$: 551.98 (±)-3-chloro-5-[3-(2-oxo-1,2,3,5,6,7,8,8a-octahydroimidazo [1,2-a]pyridine-3-spiro-4'-piperidino)propyl]-10,11-dihydro-5*H*-dibenz [b,f]azepine dihydrochloride. It meets the following reuirements. Purify according to the following method if needed.

Purification method−Conduct this procedure without exposure to light. Shake 30 g of mosapramine hydrochloride with 100 mL of water for 5 minutes, and then shake with 50 mL of ammonia TS for further 5 minutes. Shake with 700 mL of diethyl ether, and separate diethyl ether layer. To the diethyl ether layer add 30 g of anhydrous sodium sulfate, and immediately filter by suction. Evaporate the filtrate at 30ºC under reduced pressure, lightly crush the residue, and dry with a desiccator (reduced pressure, phosphorus (V) oxide) for 1 hour. To 25 g of the residue add 280 mL of ethanol (99.5), dissolve in a water bath by warming at 80ºC, and filter by suction while hot. Cool the filtrate with ice for 1 hour, and allow to stand in a refrigerator for further 40 hours. Filter the crystals separated, and dry with a desiccator (reduced pressure, phosphorus (V) oxide) for 1 hour. To 14 g of the crystals add 120 mL of 0.5 mol/L hydrochloric acid TS, shake vigorously to dissolve, and filter. Allow to stand the filtrate at room temperature overnight, filter the crystals separated, and dry with a desiccator (reduced pressure, phosphorus (V) oxide) for 5 hours.

Description−Mosapramine Hydrochloride RS occurs as a white, crystalline powder.

Identification−Determine the infrared absorption spectrum of Mosapramine Hydrochloride RS as directed in the potassium bromide disk method under Infrared Spectrophotometry <*2.25*>: it exhibits absorption at the wave numbers of about 2950cm^{-1}, 1721cm^{-1}, 1589cm^{-1}, 1474cm^{-1} and 756cm^{-1}.

Related substances−Dissolve 0.15 g of Mosaparamine Hydrochloride RS in 10 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 exactly 10 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, A_{Ta} and A_{Tb}, of 3-chloro-5-[3-(2-oxo-2,3,5,6,7,8-hexahydroimidazo[1,2-a]pyridine-3-spiro-4'-piperidino)propyl]-10,11-dihydro-5*H*-dibenz [b,f]azepine, having the retention time of about 0.7 with respect to mosapramine obtained from the sample solution, and 5-[3-(2-oxo-1,2,3,5,6,7,8,8a-octahydroimidazo [1,2-a]pyridine-3-spiro-4'-piperidino)propyl]-10,11-dihydro-5*H*-dibenz[b,f]azepine, having the retention time of about 0.8 with respect to mosapramine, is not larger than 3/5 times the peak area, *A*s, of mosapriamine from the standard solution, the 1/6 times the peak area, A_{Tc}, of chloroiminodibenzyl, having the retention time of about 4 with respect to mosapramine from the sample solution, is not larger than 1/5 times of *A*s, each peak area of related substances other than the above substances from the sample solution is not larger than 1/5 times of *A*s, and the total amount of the peaks of 1/6 times of A_{Ta}, A_{Tb}, A_{Tc}, and other related substances is not larger than *A*s.

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 (10 μm in particle diameter).

Column temperature: A constant temperature of about 25ºC.

Mobile phase: Dissolve 7.0 g of sodium perchlorate in 1000 mL of water, and adjust the pH to 2.5 with perchloric acid. To 900 mL of this solution add 1100 mL of acetonitrile.

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

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

System suitability

Test for required detectability: Pipet 1 mL of the standard solution, and add the mobile phase to make exactly 10 mL. Confirm that the peak area of mosapramine obtained from 10 μL of this solution is equivalent to 7 to 13% of that from 10 μL of the standard solution.

System performance: Dissolve 0.1 g of Mosapramine Hydrochloride RS and 30 mg of benzophenone in the mobile phase to make 100 mL. When the procedure is run with 5 μL of this solution under the above operating conditions, mosapramine and benzophenone are eluted in this order with the resolution between these peaks being not less than 4.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of mosapramine is not more than 2.0%.

Loss on drying <2.41>: not more than 0.5% (1 g, 105ºC, 2 hours).

Content: not less than 99.0%. Assay−Weigh accurately about 0.4 g of Mosapramine Hydrochloride RS, previously dried, dissolve in 3.0 mL of formic acid, add 60 mL of acetic anhydride, 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
= 27.60 mg of $C_{28}H_{35}ClN_4O \cdot 2HCl$