Tropisetoron Hydrochloride Capsules

Dissolution *<6.10>* Perform the test with 1 capsule of Tropisetoron Hydrochloride Capsules at 50 revolutions per minute according to the Paddle method, using the sinker, using 900 mL of water 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 water to make exactly V' mL so that each mL contains about 5.6 μg of tropisetoron ($C_{17}H_{20}N_2O_2$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 16 mg of Tropisetoron Hydrochloride RS, previously dried at 105ºC for 4 hours, and dissolve in water to make exactly 100 mL. Pipet 4 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with the sample solution and standard solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*, and determine the absorbances, A_{T1}, A_{T2}, and A_{S1}, at 285 nm, and the absorbance, A_{S2}, at 330 nm, respectively.

The requirements are met if Tropisetoron Hydrochloride Capsules conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of tropisetoron ($C_{17}H_{20}N_2O_2$)

$= M_S \times A_{T1} - A_{T2}/A_{S1} - A_{S2} \times V'/V \times 1/C \times 36 \times 0.886$

M_S: Amount (mg) of Tropisetoron Hydrochloride RS

C: Labeled amount (mg) of tropisetoron ($C_{17}H_{20}N_2O_2$) in 1 capsule

Dissolution Requirements

Labeled amount*	Specified minute	Dissolution rate
5 mg	15 minutes	Not less than 75%

* as Tropisetoron

Tropisetoron Hydrochloride RS $C_{17}H_{20}N_2O_2.HCl$: 320.81

(1*R*,3*r*,5*S*)-1*H*-indole-3-carboxylic acid 8-methyl-8-azabicyclo[3.2.1]oct-3-yl ester monohydrochloride. It meets the following requirements. Purify by the following method if needed.

Purification method —To Tropisetoron Hydrochloride add ethanol (99.5), dissolve by heating, and immediately filter. After cooling, separate the crystals produced, and wash with ethanol (99.5). Repeat the recrystallization, and dry the crystals so obtained in vacuum by warming.

Description —Tropisetoron Hydrochloride RS occurs as a while crystalline powder.

Identification —Determine the infrared absorption spectrum of Tropisetoron Hydrochloride 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 3230 cm^{-1}, 1692 cm^{-1}, 1526 cm^{-1}, 1455 cm^{-1} and 1185 cm^{-1}.

Related substances —

(1) Dissolve 50 mg of Tropisetoron Hydrochloride RS in 20 mL of the mobile phase A, and use this solution as the sample solution. To exactly 1 mL of this solution add the mobile phase A to make exactly 100 mL. Pipet 2 mL of this solution, add the mobile phase A to make exactly 20 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 by the automatic integration method: the peak area other than tropisetoron from the sample solution is not larger than the peak area of tropisetoron from the standard solution except the peak of 20 μL of the mobile phase A.

Operating conditions

Detector: An ultraviolet absorption photometer (wavelength: 281 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 22 cm in length, packed with octylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25ºC.

Mobile phase A: A mixture of methanol, water, acetonitrile and triethylamine (5650:4000:350:3).

Mobile phase B: A mixture of methanol, water, acetonitrile and triethylamine (8000:1000:1000:3).

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 - 14	100	0
14 – 32	100→0	100→0
32 – 35	0	100

Flow rate: 1.5 mL per minute.

Time span of measurement: About 1.4 times as long as the retention time of tropisetoron beginning after the solvent peak.

System suitability

System performance: Dissolve 10 mg of Tropisetoron Hydrochloride RS and 40 mg of naphazoline hydrochloride in 100 mL of the mobile phase A. When the procedure is run with 20 μL of this solution under the above operating conditions, tropisetoron and naphazoline 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 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of tropisetoron is not more than 2.0%.

(2) Dissolve 0.2 g of Tropisetoron Hydrochloride RS in 10 mL of methanol, and use this solution as the sample solution. To exactly 1 mL of this solution add methanol to make exactly 100 mL. Pipet 2 mL of this solution, add methanol to make exactly 20 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under Thin-layer Chromatography <*2.03*>. Spot 10 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 a mixture of dichloromethane, methanol and ammonia water (28) (12:8:1) to a distance of about 15 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. Furthermore, after spraying evenly Dragendorff's TS on the plate, spray evenly hydrogen peroxide TS, while covering the plate with a glass plate: 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 0.3% (1g, 105ºC, 4 hours).

Content: not less than 99.0%. Assay ─ Weigh accurately about 0.25 g of Tropisetoron Hydrochloride RS, previously dried, dissolve in 80 mL of a mixture of acetic anhydride and acetic acid (100) (7:1), 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
= 32.08 mg of $C_{17}H_{20}N_2O_2$.HCl