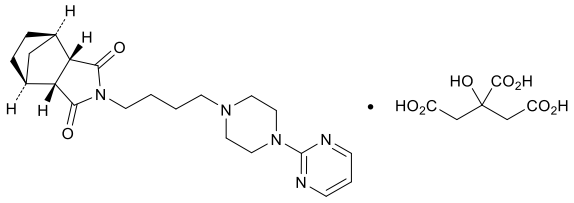
Tandospirone Citrate

タンドスピロンクエン酸塩



$C_{21}H_{29}N_5O_2.C_6H_8O_7$: 575.61

(3a*R*,4*S*,7*R*,7a*S*)-2-{4-[4-(Pyrimidin-2-yl)piperazin-1-yl]butyl}hexahydro-1*H*-4,7-methanoisoindole-1,3(2*H*)-dione monocitrate

［*112457-95-1*］

Tandospirone Citrate, when dried, contains not less than 99.0% and not more than 101.0% of tandospirone citrate ($C_{21}H_{29}N_5O_2.C_6H_8O_7$).

Description Tandospirone Citrate occurs as white, crystals or crystalline powder.

It is freely soluble in acetic acid (100), sparingly soluble in water and in methanol, and very slightly soluble in ethanol (99.5).

Identification **(1)** Determine the absorption spectrum of a solution of Tandospirone Citrate in methanol (3 in 200,000) as directed under Ultraviolet-visible Spectrophotometry *<2.24>*, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Tandospirone Citrate RS prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Tandospirone Citrate, previously dried, as directed in the potassium bromide disk method under Infrared Spectrophotometry *<2.25>*, and compare the spectrum with the Reference Spectrum or the spectrum of dried Tandospirone Citrate RS: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) A solution of Tandospirone Citrate (1 in 200) responds to Qualitative Tests *<1.09>* (1) for citrate.

Purity **(1)** Chloride *<1.03>*—Perform the test with 0.5 g of Tandospirone Citrate. Prepare the control solution with 0.45 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.032%).

(2) Related substances—Weigh accurately about 50 mg of Tandospirone Citrate, and dissolve in the mobile phase to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 50 mg of Tandospirone Citrate RS, previously dried, and dissolve in the mobile phase to make exactly 100 mL. Pipet 2 mL of this solution, add the mobile phase to make exactly 100 mL. Pipet 5 mL of this solution, add the mobile phase to make exactly 100 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 operating conditions described below. Determine the peak area, A_T, of each related substance from the sample solution, and the peak area, A_S, of tandospirone from the standard solution by the automatic integration method, and calculate the amount of the related substances by the equation described below: the amount of each related substance is not more than 0.10% and the total amount of the related substances is not more than 0.5%. For the areas of the peaks of related substances A, B, C and D, having the relative retention times of about 0.18, about 0.24, about 0.65 and about 1.47 to tandospirone, multiply their correction factors, 0.3, 0.4, 0.4 and 34.8, respectively.

$$\text{Amount (\%) of each related substance} = M_S / M_T \times A_T / A_S \times 1/10$$

M_S: Amount (g) of Tandospirone Citrate RS taken

M_T: Amount (g) of Tandospirone Citrate taken

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 243 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 (3 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Dissolve 1.36 g of potassium dihydrogen phosphate in 1000 mL of water, and adjust to pH 7.5 by adding a solution of sodium hydroxide (1 in 10). To 600 mL of this solution add 400 mL of acetonitrile for liquid chromatography.

Flow rate: 1.0 mL per minute.

Time span of measurement: About 2 times as long as the retention time of tandospirone, 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 10 mL. When the procedure is run with 20 μL of this solution under the above operating conditions, the SN ratio of the peak of tandospirone is not less than 10.

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 tandospirone are not less than 5000 and not more than 1.5, 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 tandospirone is not more than 2.0%.

Loss on drying *<2.41>* Not more than 1.0% (1 g, in vacuum, 105°C, 3 hours).

Residue on ignition *<2.44>* Not more than 0.1% (1 g).

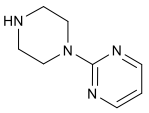
Assay Weigh accurately about 0.5 g of Tandospirone Citrate, previously dried, dissolve in 80 mL of acetic acid (100), and titrate *<2.50>* with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
＝28.78 mg of $C_{21}H_{29}N_5O_2.C_6H_8O_7$

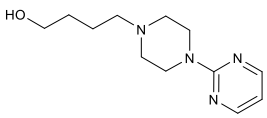
Containers and storage Containers—Tight containers.

Others

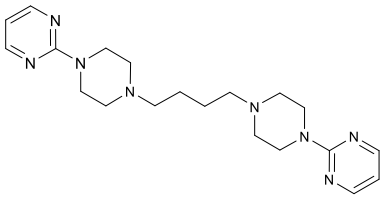
Related substance A:
2-(Piperazin-1-yl)pyrimidine



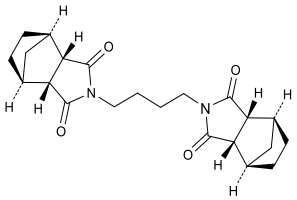
Related substance B:
4-[4-(Pyrimidin-2-yl)piperazin-1-yl]butan-1-ol



Related substance C:
1,1'-(Butane-1,4-diyl)bis[4-(pyrimidin-2-yl)piperazine]



Related substance D:
(3*aR*,3*a*'*R*,4*S*,4'*S*,7*R*,7*aS*,7'*R*,7*a*'*S*)-2,2'-(Butane-1,4-diyl)bis[hexahydro-1*H*-4,7-methanoisoindole-1,3(2*H*)-dione]



Add the following to 9.01 Reference Standards (1):

Tandospirone Citrate RS