

pranoprofen from the standard solution, and the total peak area of them is not larger than twice of the peak area of pranoprofen from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 275 nm).

Column: A stainless steel column about 6 mm in inside diameter and about 15 cm in length, packed with octadecylsilylated silica gel for liquid chromatography (5 μ m in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: Dissolve 7.02 g of sodium perchlorate monohydrate in 1000 mL of water, and adjust the pH to 2.5 with perchloric acid. To 2 volumes of this solution add 1 volume of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of pranoprofen is about 10 minutes.

Selection of column: Dissolve 4 mg each of Pranoprofen and ethyl parahydroxybenzoate in 200 mL of the mobile phase. Proceed with 10 μ L of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of pranoprofen and ethyl parahydroxybenzoate in this order with the resolution between these peaks being not less than 2.1.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of pranoprofen from 10 μ L of the standard solution is between 10 mm and 20 mm.

Time span of measurement: About three times as long as the retention time of pranoprofen.

Loss on drying Not more than 0.5% (1 g, in vacuum, phosphorus (V) oxide, 4 hours).

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately about 0.4 g of Pranoprofen, previously dried, dissolve in 70 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

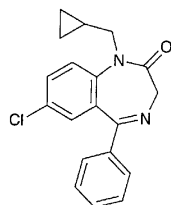
Each mL of 0.1 mol/L perchloric acid VS
= 25.527 mg of C₁₅H₁₃NO₃

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Prazepam

プラゼパム



C₁₉H₁₇ClN₂O: 324.80
7-Chloro-1-(cyclopropylmethyl)-1,3-dihydro-5-phenyl-2H-1,4-benzodiazepin-2-one [2955-38-6]

Prazepam, when dried, contains not less than 98.5% of C₁₉H₁₇ClN₂O.

Description Prazepam occurs as white to light yellow crystals or crystalline powder. It is odorless.

It is freely soluble in acetone, soluble in acetic anhydride, sparingly soluble in ethanol (99.5) and in diethyl ether, and practically insoluble in water.

Identification (1) Dissolve 0.01 g of Prazepam in 3 mL of sulfuric acid, and observe under ultraviolet light (main wavelength: 365 nm): the solution shows a grayish blue fluorescence.

(2) Dissolve 0.01 g of Prazepam in 1000 mL of a solution of sulfuric acid in ethanol (99.5) (3 in 1000). Determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Determine the infrared absorption spectrum of Prazepam, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(4) Perform the Flame Coloration Test (2) with Prazepam: a green color appears.

Melting point 145 – 148°C

Purity (1) Chloride—To 1.0 g of Prazepam add 50 mL of water, allow to stand for 1 hour with occasional shaking, and filter. To 20 mL of the filtrate add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.40 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.036%).

(2) Sulfate—To 20 mL of the filtrate obtained in (1) add 1 mL of dilute hydrochloric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.048%).

(3) Heavy metals—Proceed with 2.0 g of Prazepam according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(4) Arsenic—Prepare the test solution with 1.0 g of Prazepam according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(5) Related substances—Dissolve 0.40 g of Prazepam in 10 mL of acetone, and use this solution as the sample solution. Pipet 1 mL of the sample solution, and add acetone to make exactly 20 mL. Pipet 1 mL of this solution, add acetone to make exactly 25 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μ L each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of chloroform and acetone (9:1) to a distance of about 10 cm, and air-dry the plate. Examine 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 Not more than 0.20% (1 g, 105°C, 2 hours).

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately about 0.4 g of Prazepam, previously dried, dissolve in 60 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 32.481 mg of C₁₉H₁₇ClN₂O

Containers and storage Containers—Tight containers.

Prazepam Tablets

プラゼパム錠

Prazepam Tablets contain not less than 93% and not more than 107% of the labeled amount of prazepam (C₁₉H₁₇ClN₂O: 324.80).

Method of preparation Prepare as directed under the Tablets, with Prazepam.

Identification (1) To a quantity of powdered Prazepam Tablets, equivalent to 0.05 g of Prazepam according to the labeled amount, add 25 mL of acetone, shake well, and filter. Take 5 mL of the filtrate, evaporate on a water bath to dryness, and dissolve the residue in 3 mL of sulfuric acid. With this solution, proceed as directed in the Identification (1) under Prazepam.

(2) To a quantity of powdered Prazepam Tablets, equivalent to 0.02 g of Prazepam according to the labeled amount, add 200 mL of a solution of sulfuric acid in ethanol (99.5) (3 in 1000), shake well, and filter. To 5 mL of the filtrate add a solution of sulfuric acid in ethanol (99.5) (3 in 1000) to make 50 mL, and determine the absorption spectrum as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 241 nm and 245 nm, between 283 nm and 287 nm and between 363 nm and 367 nm, and minima between 263 nm and 267 nm and between 334 nm and 338 nm.

Dissolution test Proceed with 1 tablet of Prazepam Tablets according to Method (1) in the Dissolution Test, and perform the test, using 900 mL of 0.1 mol/L hydrochloric acid TS as the test solution at 100 rotations per minute. 30 minutes after starting the test, separate 20 mL or more of the dissolved solution, and filter with a membrane filter with pore size not more than 0.8 μm. Discard the first 10 mL of the filtrate, measure exactly the subsequent *V* mL of the filtrate, add 0.1 mol/L hydrochloric acid TS to make exactly *V'* mL so that each mL of this solution might contain about 5 μg of prazepam (C₁₉H₁₇ClN₂O) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 5 mg of prazepam for assay, previously dried at 105°C for 2 hours, add 200 mL of 0.1 mol/L hydrochloric acid TS and dissolve with shaking, or by ultrasonication if necessary, add 0.1 mol/L hydrochloric acid TS to make exactly 1000 mL and use this solution as the standard solution. Determine the ab-

sorbances, *A_T* and *A_S*, of the sample solution and the standard solution at 240 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Prazepam Tablets during 30 minutes is not less than 80%: it meets the Dissolution Test.

$$\begin{aligned} & \text{Dissolution rate (\%)} \text{ of prazepam} \\ & \text{(C}_{19}\text{H}_{17}\text{ClN}_2\text{O)} \text{ to the labeled amount} \\ & = W_S \times \frac{A_T}{A_S} \times \frac{V'}{V} \times \frac{90}{C} \end{aligned}$$

W_S: Amount (mg) of prazepam for assay.

C: Labeled amount (mg) of prazepam (C₁₉H₁₇ClN₂O) in each tablet.

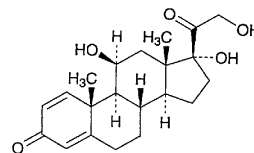
Assay Weigh accurately not less than 20 Prazepam Tablets, and powder. Weigh accurately a quantity of the powder, equivalent to about 0.05 g of prazepam (C₁₉H₁₇ClN₂O), add 30 mL of acetone, shake well, centrifuge, and separate the supernatant. Repeat the same procedure twice with 30 mL each of acetone, combine all the supernatants, and evaporate on a water bath to dryness. Dissolve the residue in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.02 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.02 mol/L perchloric acid VS
= 6.496 mg of C₁₉H₁₇ClN₂O

Containers and storage Containers—Tight containers.

Prednisolone

プレドニゾロン



C₂₁H₂₈O₅: 360.44
11β,17,21-Trihydroxypregna-1,4-diene-3,20-dione
[50-24-8]

Prednisolone, when dried, contains not less than 97.0% and not more than 102.0% of C₂₁H₂₈O₅.

Description Prednisolone occurs as a white, crystalline powder.

It is soluble in methanol and in ethanol (95), slightly soluble in ethyl acetate and in chloroform, and very slightly soluble in water.

Melting point: about 235°C (with decomposition).

Identification (1) To 2 mg of Prednisolone add 2 mL of sulfuric acid, and allow to stand for 2 to 3 minutes: a deep red color, without fluorescence, develops. To this solution add 10 mL of water cautiously: the color disappears and a gray, flocculent precipitate is formed.

(2) Determine the infrared absorption spectrum of Prednisolone, previously dried, as directed in the potassium