

bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of previously dried Prednisolone Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears between the spectra, dissolve Prednisolone and Prednisolone Reference Standard in ethyl acetate, respectively, then evaporate the ethyl acetate to dryness, and repeat the test on the residues.

Optical rotation $[\alpha]_D^{20}$: +113 – +119° (after drying, 0.2 g, ethanol (95), 20 mL, 100 mm).

Purity (1) Selenium—To 0.10 g of Prednisolone add 0.5 mL of a mixture of perchloric acid and sulfuric acid (1:1) and 2 mL of nitric acid, and heat on a water bath until no more brown gas evolves and the solution becomes to be a light yellow clear solution. After cooling, add 4 mL of nitric acid to this solution, then add water to make exactly 50 mL, and use this solution as the sample solution. Separately, pipet 3 mL of Standard Selenium Solution, add 0.5 mL of a mixture of perchloric acid and sulfuric acid (1:1) and 6 mL of nitric acid, then add water to make exactly 50 mL, and use this solution as the standard solution. Perform the test with the sample solution and the standard solution as directed under the Atomic Absorption Spectrophotometry according to the following conditions, and determine constant absorbances, A_T and A_S , obtained on a recorder after rapid increasing of the absorption: A_T is smaller than A_S (not more than 30 ppm).

Perform the test by using a hydride generating system and a thermal absorption cell.

Lamp: An selenium hollow cathode lamp

Wavelength: 196.0 nm

Temperature of sample atomizer: When an electric furnace is used, about 1000°C.

Carrier gas: Nitrogen or Argon

(2) Other steroids—Dissolve 0.020 g of Prednisolone in exactly 2 mL of a mixture of methanol and chloroform (1:1), and use this solution as the sample solution. Separately, dissolve 0.020 g of hydrocortisone and 0.010 g of prednisolone acetate each in a mixture of methanol and chloroform (1:1) to make exactly 100 mL, and use these solutions as the standard solution (1) and the standard solution (2). Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μ L each of the sample solution, the standard solutions (1) and (2) on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of acetone, toluene and diethylamine (55:45:2) to a distance of about 15 cm, and air-dry the plate (do not dip the filter paper in the developing vessel). Spray evenly alkaline blue tetrazolium TS on the plate: the spots from the sample solution corresponding to those from the standard solutions (1) and (2) are not more intense than the spots from the standard solutions (1) and (2), and no spots other than the principal spot, hydrocortisone and prednisolone acetate appear from the sample solution.

Loss on drying Not more than 1.0% (0.5 g, 105°C, 3 hours).

Residue on ignition Not more than 0.1% (0.5 g).

Assay Dissolve about 0.025 g each of Prednisolone and Prednisolone Reference Standard, previously dried and accurately weighed, in 50 mL of methanol, add exactly 25 mL

of the internal standard solution to each, and add methanol to make 100 mL. To 1 mL each of these solutions add the mobile phase to make 10 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 20 μ L each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S , of the peak area of prednisolone to that of the internal standard.

$$\begin{aligned} & \text{Amount (mg) of } C_{21}H_{28}O_5 \\ &= \text{amount (mg) of Prednisolone Reference Standard} \\ & \quad \times \frac{Q_T}{Q_S} \end{aligned}$$

Internal standard solution—A solution of methyl parahydroxybenzoate in methanol (1 in 2000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 247 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with fluorosilanized silica gel for liquid chromatography (5 μ m in particle diameter).

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

Mobile phase: A mixture of water and methanol (13:7).

Flow rate: Adjust the flow rate so that the retention time of prednisolone is about 15 minutes.

System suitability—

System performance: Dissolve 0.025 g of Prednisolone and 0.025 g of hydrocortisone in 100 mL of methanol. To 1 mL of this solution add the mobile phase to make 10 mL. When the procedure is run with 20 μ L of this solution under the above operating conditions, hydrocortisone and prednisolone are eluted in this order with the resolution between these peaks being not less than 1.5.

System repeatability: When the test is repeated 6 times with 20 μ L of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of prednisolone to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Prednisolone Tablets

プレドニゾロン錠

Prednisolone Tablets contain not less than 90% and not more than 110% of the labeled amount of prednisolone ($C_{21}H_{28}O_5$: 360.44).

Method of preparation Prepare as directed under Tablets, with Prednisolone.

Identification (1) Weigh a quantity of powdered Prednisolone Tablets, equivalent to 0.05 g of Prednisolone according to the labeled amount, add 10 mL of chloroform, shake for 15 minutes, and filter. Evaporate the filtrate on a water bath to dryness. Dry the residue at 105°C for 1 hour, and proceed as directed in the Identification (1) under Prednisolone.

(2) Determine the infrared absorption spectra of the residue obtained in (1) and Prednisolone Reference Stan-

dard, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears, dissolve the sample and the Reference Standard in ethyl acetate, evaporate to dryness, and repeat the test on the residues.

Content uniformity Transfer 1 tablet of Prednisolone Tablets to a volumetric flask, and shake with 10 mL of water until the tablet is disintegrated. Add 50 mL of methanol, shake for 30 minutes, and add methanol to make exactly 100 mL. Centrifuge this solution, pipet x mL of the supernatant liquid, and add methanol to make exactly V mL to provide a solution that contains about 10 μg of prednisolone ($\text{C}_{21}\text{H}_{28}\text{O}_5$) per ml, and use this solution as the sample solution. Separately, weigh accurately about 0.010 g of Prednisolone Reference Standard, previously dried at 105°C for 3 hours, dissolve in 10 mL of water and 50 mL of methanol, and add methanol to make exactly 100 mL. Pipet 5 mL of this solution, add methanol to make exactly 50 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S , of the sample solution and the standard solution at 242 nm as directed under the Ultraviolet-visible Spectrophotometry.

$$\begin{aligned} \text{Amount (mg) of prednisolone (C}_{21}\text{H}_{28}\text{O}_5) \\ = \text{amount (mg) of Prednisolone Reference Standard} \\ \times \frac{A_T}{A_S} \times \frac{V}{10} \times \frac{1}{x} \end{aligned}$$

Dissolution test Take 1 tablet of Prednisolone Tablets, perform the test as directed in Method 2 under the Dissolution Test at 100 revolutions per minute using 900 mL of water as the test solution. Twenty minutes after the start of the test, take 20 mL or more of the dissolved solution, and filter through a membrane filter with pore size of 0.8 μm or less. Discard the first 10 mL of the filtrate, and use the subsequent filtrate as the sample solution. Weigh accurately about 0.010 g of Prednisolone Reference Standard, previously dried at 105°C for 3 hours, and dissolve in ethanol (95) to make exactly 100 mL. Pipet 5 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S , of the sample solution and the standard solution at the maximum wavelength at about 242 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Prednisolone Tablets after 20 minutes should be not less than 70%.

$$\begin{aligned} \text{Dissolution rate (\%)} \text{ with respect to} \\ \text{the labeled amount of prednisolone (C}_{21}\text{H}_{28}\text{O}_5) \\ = W_S \times \frac{A_T}{A_S} \times \frac{45}{C} \end{aligned}$$

W_S : Amount (mg) of Prednisolone Reference Standard.

C : Labeled amount (mg) of prednisolone ($\text{C}_{21}\text{H}_{28}\text{O}_5$) in 1 tablet.

Assay Weigh accurately and powder not less than 20 Prednisolone Tablets using an agate mortar. Weigh accurately a portion of the powder, equivalent to about 5 mg of prednisolone ($\text{C}_{21}\text{H}_{28}\text{O}_5$), add 1 mL of water, and shake gently. Add exactly 5 mL of the internal standard solution and 15 mL of methanol, and shake vigorously for 20 minutes. To 1 mL of this solution add the mobile phase to make 10 mL, and filter through a membrane filter with pore size of 0.45 μm . Dis-

card the first 3 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.025 g of Prednisolone Reference Standard, previously dried at 105°C for 3 hours, dissolve in 50 mL of methanol, add exactly 25 mL of the internal standard solution, and add methanol to make 100 mL. To 1 mL of this solution add the mobile phase to make 10 mL, and use this solution as the standard solution. Proceed as directed in the Assay under Prednisolone with these solutions.

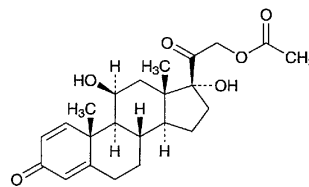
$$\begin{aligned} \text{Amount (mg) of prednisolone (C}_{21}\text{H}_{28}\text{O}_5) \\ = \text{amount (mg) of Prednisolone Reference Standard} \\ \times \frac{Q_T}{Q_S} \times \frac{1}{5} \end{aligned}$$

Internal standard solution—A solution of methyl parahydroxybenzoate in methanol (1 in 2000).

Containers and storage Containers—Tight containers.

Prednisolone Acetate

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$\text{C}_{23}\text{H}_{30}\text{O}_6$: 402.48

11 β ,17,21-Trihydroxypregna-1,4-diene-3,20-dione
21-acetate [52-21-1]

Prednisolone Acetate, when dried, contains not less than 96.0% and not more than 102.0% of $\text{C}_{23}\text{H}_{30}\text{O}_6$.

Description Prednisolone Acetate occurs as a white, crystalline powder.

It is slightly soluble in methanol, in ethanol (95), in ethanol (99.5), and in chloroform, and practically insoluble in water.

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

Identification (1) To 2 mg of Prednisolone Acetate 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 spectra of Prednisolone Acetate, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum in a range between 4000 cm^{-1} and 650 cm^{-1} with the Infrared Reference Spectrum or the spectrum of previously dried Prednisolone Acetate Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears, dissolve the sample and the Reference Standard in ethanol (99.5), respectively, evaporate to dryness, and repeat the test on the residues.

Optical rotation $[\alpha]_D^{20}$: +128 – +137° (after drying, 0.07