$C_{21}H_{30}O_5$: 362.46
11β,17,21-Trihydroxypregn-4-ene-3,20-dione [*50-23-7*]

Hydrocortisone, when dried, contains not less than 97.0% and not more than 102.0% of $C_{21}H_{30}O_5$.

Description Hydrocortisone occurs as a white, crystalline powder. It is odorless.

It is sparingly soluble in methanol, in ethanol (95) and in 1,4-dioxane, slightly soluble in chloroform, and very slightly soluble in diethyl ether and in water.

Melting point: 212 - 220°C (with decomposition).

Identification (1) Add 2 mL of sulfuric acid to 2 mg of Hydrocortisone: the solution shows a yellow-green fluorescence immediately, and the color of the solution changes gradually from orange to dark red. Dilute carefully the solution with 10 mL of water: the color changes through yellow to orange-yellow with green fluorescence, and a small amount of a flocculent precipitate is formed.

(2) Dissolve 0.01 g of Hydrocortisone in 1 mL of methanol, add 1 mL of Fehling's TS, and heat: a red precipitate is formed.

(3) Determine the infrared absorption spectrum of Hydrocortisone, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of previously dried Hydrocortisone Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers. If any difference appears between the spectra, dissolve Hydrocortisone and Hydrocortisone Reference Standard in ethanol (95), respectively, then evaporate the ethanol to dryness, and repeat the test on the residues.

Optical rotation $[\alpha]_D^{20}$: +150 - +156° (after drying, 0.1 g, 1,4-dioxane, 10 mL, 100 mm).

Purity Other steroids—Dissolve 0.020 g of Hydrocortisone in 10 mL of a mixture of chloroform and methanol (9:1), and use this solution as the sample solution. Pipet 1 mL of this solution, add a mixture of chloroform and methanol (9:1) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL 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 ethanol (95) (17:3) 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 1.0% (0.5 g, 105°C, 3 hours).

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

Assay Dissolve about 0.02 g each of Hydrocortisone and Hydrocortisone Reference Standard, previously dried and accurately weighed, in 20 mL each of a mixture of chloroform and methanol (9:1), add 10 mL each of the internal standard solution, then add a mixture of chloroform and methanol (9:1) to make 50 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 5 μL 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 hydrocortisone to that of the internal standard, respectively.

Amount (mg) of $C_{21}H_{30}O_5$
= amount (mg) of Hydrocortisone Reference Standard

$$\times \frac{Q_T}{Q_S}$$

Internal standard solution—A solution of prednisone in a mixture of chloroform and methanol (9:1) (9 in 10,000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 20°C.

Mobile phase: A mixture of chloroform, methanol and acetic acid (100) (1000:20:1).

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

System suitability—

System performance: When the procedure is run with 5 μL of the standard solution under the above operating conditions, the internal standard and hydrocortisone are eluted in this order with the resolution between these peaks being not less than 7.

System repeatability: When the test is repeated 6 times with 5 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of hydrocortisone to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Hydrocortisone Acetate

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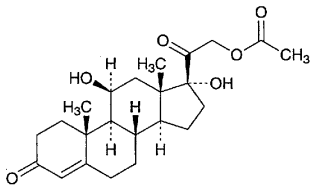

$C_{23}H_{32}O_6$: 404.50
11β,17,21-Trihydroxypregn-4-ene-3,20-dione 21-acetate
[*50-03-3*]

Hydrocortisone Acetate, when dried, contains not less than 97.0% and not more than 102.0% of $C_{23}H_{32}O_6$.

Description Hydrocortisone Acetate occurs as white crystals or crystalline powder. It is odorless.

It is sparingly soluble in 1,4-dioxane, slightly soluble in methanol, in ethanol (95) and in chloroform, very slightly soluble in diethyl ether, and practically insoluble in water.

Melting point: about 220°C (with decomposition).

Identification (1) Add 2 mL of sulfuric acid to 2 mg of Hydrocortisone Acetate: the solution shows a yellowish green fluorescence immediately, and the color of the solution gradually changes through orange-yellow to dark red. This solution shows a strong light green fluorescence under ultraviolet light. Add carefully 10 mL of water to this solution: the color changes from yellow to orange-yellow with a light green fluorescence, and a yellow-brown, flocculent precipitate is formed.

(2) Dissolve 0.01 g of Hydrocortisone Acetate in 1 mL of methanol by warming, add 1 mL of Fehling's TS, and heat: an orange to red precipitate is formed.

(3) To 0.05 g of Hydrocortisone Acetate add 2 mL of potassium hydroxide-ethanol TS, and heat on a water bath for 5 minutes. Cool, add 2 mL of diluted sulfuric acid (2 in 7), and boil gently for 1 minute: the odor of ethyl acetate is perceptible.

(4) Determine the infrared absorption spectra of Hydrocortisone Acetate and Hydrocortisone Acetate Reference Standard, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry: both the sample and the Reference Standard exhibit similar intensities of absorption at the same wave numbers. If any difference appears, dissolve the sample and Reference Standard in ethanol (95), respectively, evaporate to dryness, and repeat the test on the residues.

Optical rotation $[\alpha]_D^{20}$: +158 – +165° (after drying, 0.05 g, 1,4-dioxane, 10 mL, 100 mm).

Purity Other steroids—Dissolve 0.040 g of Hydrocortisone Acetate in 25 mL of a mixture of chloroform and methanol (9:1), and use this solution as the sample solution. Pipet 2 mL of the sample solution, add a mixture of chloroform and methanol (9:1) to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of dichloromethane, diethyl ether, methanol and water (160:30:8:1) to a distance of about 12 cm, and air-dry the plate. Spray evenly alkaline blue tetrazolium TS on the 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 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 0.02 g each of Hydrocortisone Acetate and Hydrocortisone Acetate Reference Standard, previously dried and accurately weighed, in methanol, add exactly 10 mL each of the internal standard solution, then add methanol to make 100 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following operating conditions, and calculate the ratios, Q_T and Q_S, of the peak area of hydrocortisone acetate to that of the internal standard, respectively.

$$\text{Amount (mg) of } C_{23}H_{32}O_6 = \text{amount (mg) of Hydrocortisone Acetate Reference Standard} \times \frac{Q_T}{Q_S}$$

Internal standard solution—A solution of benzyl parahydroxy benzoate in methanol (1 in 1000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 30 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

Column temperature: Room temperature.

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

Flow rate: Adjust the flow rate so that the retention time of hydrocortisone acetate is about 8 minutes.

Selection of column: Proceed with 20 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of hydrocortisone acetate and the internal standard in this order with the resolution between these peaks being not less than 4.

Containers and storage Containers—Tight containers.

Hydrocortisone Butyrate

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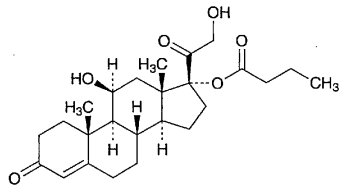

$C_{25}H_{36}O_6$: 432.55

11β,17,21-Trihydroxypregn-4-ene-3,20-dione 17-butyrate

[*13609-67-1*]

Hydrocortisone Butyrate, when dried, contains not less than 96.0% and not more than 104.0% of $C_{25}H_{36}O_6$.

Description Hydrocortisone Butyrate occurs as a white powder. It is odorless.

It is freely soluble in tetrahydrofuran, in chloroform and in 1,2-dichloroethane, soluble in methanol, sparingly soluble in ethanol (99.5), slightly soluble in diethyl ether, and practically insoluble in water.

Melting point: about 200°C (with decomposition).

Identification (1) Add 2 mL of sulfuric acid to 2 mg of Hydrocortisone Butyrate: the solution shows a yellowish green fluorescence immediately, and the color of the solution gradually changes through orange-yellow to dark red. This solution shows a strong light green fluorescence under ultraviolet light (main wavelength: 254 nm). Add carefully 10 mL of water to this solution: the color changes from yellow to orange-yellow with a light green fluorescence, and a yellow-brown, flocculent precipitate is formed.

(2) Dissolve 0.01 g of Hydrocortisone Butyrate in 1 mL