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Hydrocortisone Butyrate

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

Pregn-4-ene-3,20-dione, 11,21-dihydroxy-17- (1-oxobutoxy)-, (11β)-;

Cortisol 17-butyrate;

11β,17,21-Trihydroxypregn-4-ene-3,20-dione 17-butyrate CAS RN®: 13609-67-1; UNII: 05RMF7YPWN.

DEFINITION

Hydrocortisone Butyrate contains NLT 97.0% and NMT 102.0% of hydrocortisone butyrate ($C_{25}H_{36}O_6$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

Change to read:

• **B.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**▲ (CN 1-May-2020)

Sample solution: 10 µg/mL in methanol

Analytical wavelength: 242 nm

Acceptance criteria: Absorptivities, calculated on the dried basis, do not differ by more than 3.0%.

ASSAY

• **Procedure**

Mobile phase: Acetonitrile, glacial acetic acid, and water (76:1:124)

Diluent A: Tetrahydrofuran and glacial acetic acid (1000:1)

Diluent B: Methanol, water, and glacial acetic acid (500:500:1)

System suitability stock solution: 0.1 mg/mL each of USP Hydrocortisone Butyrate RS and propyl 4-hydroxybenzoate in *Diluent A*

System suitability solution: 0.02 mg/mL each of USP Hydrocortisone Butyrate RS and propyl 4-hydroxybenzoate in *Diluent B*, from *System suitability stock solution*

Standard stock solution: 0.1 mg/mL of USP Hydrocortisone Butyrate RS in *Diluent A*

Standard solution: 0.02 mg/mL of USP Hydrocortisone Butyrate RS in *Diluent B*, from *Standard stock solution*

Sample stock solution: 0.1 mg/mL of Hydrocortisone Butyrate in *Diluent A*

Sample solution: 0.02 mg/mL of Hydrocortisone Butyrate in *Diluent B*, from *Sample stock solution*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 3.0-mm × 10-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 5 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for propyl 4-hydroxybenzoate and hydrocortisone butyrate are 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 4.0 between propyl 4-hydroxybenzoate and hydrocortisone butyrate, *System suitability solution*

Column efficiency: NLT 4000 theoretical plates, *Standard solution*

Tailing factor: NMT 1.6, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of hydrocortisone butyrate ($C_{25}H_{36}O_6$) in the portion of Hydrocortisone Butyrate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Hydrocortisone Butyrate RS in the *Standard solution* (mg/mL)

C_U = concentration of Hydrocortisone Butyrate in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–102.0% on the dried basis

IMPURITIES

• **Organic Impurities**

Solution A: 1 g of monobasic potassium phosphate in 1000 mL of water, adjusted with 45% potassium hydroxide to a pH of 5.5

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	80	20
12.5	35	65
15.5	35	65
20.5	80	20
22.5	80	20

Diluent: Acetonitrile and *Solution A* (80:20)

Standard solution: 0.5 mg/mL of USP Hydrocortisone Butyrate RS in *Diluent*

Sample solution: 1 mg/mL of Hydrocortisone Butyrate in *Diluent*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 10-cm; 3-µm packing L1

Flow rate: 2 mL/min

Injection volume: 5 µL

System suitability

Samples: *Standard solution* and *Sample solution*

Suitability requirements

Resolution: NLT 1.0 between hydrocortisone butyrate and any impurity

Column efficiency: NLT 10,000 theoretical plates

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Hydrocortisone Butyrate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of hydrocortisone butyrate from the *Standard solution*

C_S = concentration of USP Hydrocortisone Butyrate RS in the *Standard solution* (mg/mL)

C_U = concentration of Hydrocortisone Butyrate in the *Sample solution* (mg/mL)

Acceptance criteria

Disregard any peak having a percentage of 0.05% or less.

Any individual impurity: NMT 1.0%

Total impurities: NMT 2.0%

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation*⟨781S⟩

Sample solution: 10 mg/mL, in chloroform

Acceptance criteria: +47° to +54° at 20°

- **Loss on Drying** ⟨731⟩

Sample: Dry Hydrocortisone Butyrate under vacuum at 78° for 3 h.

Acceptance criteria: NMT 1.0%

- **Completeness of Solution** ⟨641⟩

Sample solution: 1 g in 10 mL of dichloromethane

Acceptance criteria: The *Sample solution* is clear.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨11⟩

USP Hydrocortisone Butyrate RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
HYDROCORTISONE BUTYRATE	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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