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Hydrocortisone Hemisuccinate

$C_{25}H_{34}O_8 \cdot H_2O$ 480.55

Pregn-4-ene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11, 17-dihydroxy-, (11β)-, monohydrate.

Cortisol 21-(hydrogen succinate) monohydrate CAS RN®: 83784-20-7; UNII: LIU00Z1Z84.

Anhydrous 462.54 CAS RN®: 2203-97-6; UNII: IHV1VP592V.

» Hydrocortisone Hemisuccinate contains not less than 97.0 percent and not more than 103.0 percent of $C_{25}H_{34}O_8$, calculated on the dried basis. It contains one molecule of water of hydration or is anhydrous.

Packaging and storage—Preserve in tight containers.

Labeling—Label it to indicate whether it is hydrous or anhydrous.

USP Reference standards ⟨11⟩—

USP Hydrocortisone Hemisuccinate RS
USP Fluorometholone RS

Identification—

Change to read:

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

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

Solution: 20 µg per mL.

Medium: alcohol.

Absorptivities at 242 nm, calculated on the dried basis, do not differ by more than 3.0%.

Specific rotation ⟨781S⟩**:** between +124° and +134°.

Test solution: 10 mg per mL, in acetone.

Loss on drying ⟨731⟩—Dry it at 105° for 3 hours: the anhydrous form loses not more than 1.0% of its weight, and the hydrous form loses not more than 4.0% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Chromatographic purity—

Mobile phase—Prepare a filtered and degassed mixture of water, acetonitrile, and methanol (700:285:15). Add 3.0 mL of glacial acetic acid per Liter of this solution. Mix thoroughly. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluting solution—Prepare a mixture of water, acetonitrile, tetrahydrofuran, and glacial acetic acid (500:250:250:1). Mix thoroughly.

Standard solution—Dissolve an accurately weighed quantity of USP Hydrocortisone Hemisuccinate RS in *Diluting solution*, and dilute quantitatively, and stepwise if necessary, with *Diluting solution* to obtain a solution having a known concentration of about 6.6 µg per mL.

Test solution—Transfer about 6.6 mg of Hydrocortisone Hemisuccinate, accurately weighed, to a 10-mL volumetric flask, dissolve in and dilute with *Diluting solution* to volume, and mix. [Note—Samples should be maintained at 5° or colder during analysis.]

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 15-cm column that contains packing L1. The flow rate is about 0.8 mL per minute. Chromatograph the *Standard solution*, and record the peak responses as directed for *Procedure:* the column efficiency is not less than 5000 theoretical plates; and the relative standard deviation for replicate injections is not more than 5.0%.

Procedure—Inject a volume (about 15 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure the peak responses. Calculate the percentage of each impurity in the portion of Hydrocortisone Hemisuccinate taken by the formula:

$$100(r_i/r_s)$$

in which r_i is the peak response for each impurity; and r_s is the sum of the responses of all the peaks: not more than 1.0% of any individual impurity is found; and not more than 2.0% of total impurities is found. Disregard any peak representing less than 0.05%.

Assay—

Internal standard solution—Prepare a solution of USP Fluorometholone RS in tetrahydrofuran containing about 3 mg per mL.

Mobile phase—Prepare a filtered mixture of butyl chloride, water-saturated butyl chloride, tetrahydrofuran, methanol, and glacial acetic acid (95:95:14:7:6). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Transfer an accurately weighed amount of USP Hydrocortisone Hemisuccinate RS to a suitable container to obtain a solution containing 0.6 mg per mL. Add an accurately measured volume of *Internal standard solution* so that the *Standard preparation* contains 10% *Internal standard solution.* Dilute with chloroform containing 3% glacial acetic acid to volume.

Assay preparation—Transfer about 30 mg of Hydrocortisone Hemisuccinate, accurately weighed, to a 50-mL volumetric flask, add 5.0 mL of *Internal standard solution*, and dilute with chloroform containing 3% glacial acetic acid to volume.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L3. The flow rate is about 1.0 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between hydrocortisone hemisuccinate and the internal standard is not less than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 6 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{25}H_{34}O_8$ in the portion of Hydrocortisone Hemisuccinate taken by the formula:

$$50C(R_U/R_S)$$

in which C is the concentration, in mg per mL, of USP Hydrocortisone Hemisuccinate RS in the *Standard preparation;* and R_U and R_S are the peak area ratios of hydrocortisone hemisuccinate to the internal standard obtained from the *Assay preparation* and the *Standard preparation*, respectively.

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

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