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Hydrocortisone Sodium Succinate for Injection

DEFINITION

Hydrocortisone Sodium Succinate for Injection is a sterile mixture of Hydrocortisone Sodium Succinate and suitable buffers. It may be prepared from Hydrocortisone Sodium Succinate, or from Hydrocortisone Hemisuccinate with the aid of Sodium Hydroxide or Sodium Carbonate. It contains the equivalent of NLT 90.0% and NMT 110.0% of the labeled amount of hydrocortisone ($C_{21}H_{30}O_5$) in single-compartment containers, or in the volume of solution designated on the label of containers that are constructed to hold, in separate compartments, the Hydrocortisone Sodium Succinate for Injection and a solvent.

IDENTIFICATION

• **A. Infrared Absorption**

Sample: Transfer a quantity of Hydrocortisone Sodium Succinate for Injection, equivalent to 100 mg of hydrocortisone sodium succinate, to a suitable container, and dissolve in 10 mL of water. In rapid succession, add 1 mL of 3 N hydrochloric acid, shake briefly, immediately decant the aqueous layer, and wash the precipitate with two additional 10-mL portions of water, each time removing the water by decanting. Remove as much of the water as possible, spread the precipitate in a suitable container, and dry under vacuum at 60° for 3 h.

Acceptance criteria: The IR spectrum of a mineral oil dispersion of the precipitate so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hydrocortisone Hemisuccinate RS.

ASSAY

• **Procedure**

Mobile phase: Butyl chloride, water-saturated butyl chloride, tetrahydrofuran, methanol, and glacial acetic acid (95:95:14:7:6)

Internal standard solution: 3 mg/mL of USP Fluorometholone RS in tetrahydrofuran

Diluent: Glacial acetic acid in chloroform (3 in 100)

Solution A: 0.30 mg/mL of USP Hydrocortisone RS in *Diluent*

Standard solution: 0.65 mg/mL of USP Hydrocortisone Hemisuccinate RS, prepared as follows. Transfer 32.5 mg of USP Hydrocortisone Hemisuccinate RS to a 50-mL volumetric flask. Add by pipet 5.0 mL of *Internal standard solution* and 5.0 mL of *Solution A*. Dilute with *Diluent* to volume.

Sample solution: Mix the constituted solutions prepared from the contents of 10 vials of Hydrocortisone Sodium Succinate for Injection. Transfer a volume, equivalent to 50 mg of hydrocortisone from the resulting constituted solution, to a suitable flask containing 10.0 mL of *Internal standard solution*, and dilute with *Diluent* to 100.0 mL. Shake thoroughly for 5 min, then allow the phases to separate, discarding the upper phase.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L3

Flow rate: 1.0 mL/min

Injection volume: 6 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between hydrocortisone hemisuccinate and the internal standard

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

[Note—The order of elution of peaks is that from the internal standard, hydrocortisone hemisuccinate, and successive smaller peaks representing free hydrocortisone and hydrocortisone 17-hemisuccinate, the relative retention times of which are about 1.0, 1.5, 2.0, and 2.5,

respectively.]

Calculate the percentage of the labeled amount of hydrocortisone ($C_{21}H_{30}O_5$) in the portion of Hydrocortisone Sodium Succinate for Injection taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

R_U = ratio of the summation of the peak areas of hydrocortisone hemisuccinate and hydrocortisone 17-hemisuccinate to the peak area of the internal standard from the *Sample solution*

R_S = ratio of the summation of the peak areas of hydrocortisone hemisuccinate and hydrocortisone 17-hemisuccinate to the peak area of the internal standard from the *Standard solution*

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

C_U = nominal concentration of the *Sample solution* (mg/mL)

M_{r1} = molecular weight of hydrocortisone, 362.46

M_{r2} = molecular weight of hydrocortisone hemisuccinate, 462.53

To this percentage add the percentage of free hydrocortisone found in the test for *Free Hydrocortisone*.

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

• **Free Hydrocortisone**

Analysis: Using the chromatograms obtained in the *Assay*, measure the areas of the peaks from the internal standard and free hydrocortisone.

Calculate the percentage of free hydrocortisone ($C_{21}H_{30}O_5$) in the portion of Hydrocortisone Sodium Succinate for Injection taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak area ratio of the free hydrocortisone to the internal standard from the *Sample solution*

R_S = peak area ratio of the free hydrocortisone to the internal standard from the *Standard solution*

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

C_U = nominal concentration of the *Sample solution* (mg/mL)

Acceptance criteria: NMT 6.7% of the labeled amount of hydrocortisone

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

SPECIFIC TESTS

• **pH ⟨791⟩**

Sample solution: A solution containing the equivalent of 50 mg/mL of hydrocortisone

Acceptance criteria: 7.0–8.0

• **Loss on Drying ⟨731⟩**

Sample: Dry at 105° for 3 h.

Acceptance criteria: NMT 2.0%

• **Bacterial Endotoxins Test ⟨85⟩:** Contains NMT 1.25 USP Endotoxin Units/mg of hydrocortisone

• **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections

• **Constituted Solution:** At the time of use, it meets the requirements in *Injections and Implanted Drug Products ⟨1⟩, Specific Tests, Completeness and clarity of solutions*.

• **Sterility Tests ⟨71⟩:** Meets the requirements

• **Other Requirements:** It meets the requirements in *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for constitution*.

• **Labeling:** Label it to indicate that the constituted solution prepared from Hydrocortisone Sodium Succinate for Injection is suitable for use only if it is clear, and that the solution is to be discarded after 3 days. Label it to indicate that it was prepared by freeze-drying, having been filled into its container in the form of a true solution.

• **USP Reference Standards** ⟨11⟩

USP Fluorometholone RS
USP Hydrocortisone RS
USP Hydrocortisone Hemisuccinate RS

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

Topic/Question	Contact	Expert Committee
HYDROCORTISONE SODIUM SUCCINATE FOR INJECTION	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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