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Methylprednisolone Hemisuccinate

$C_{26}H_{34}O_8$ 474.54

Pregna-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-6-methyl-, (6α,11β)-;

11β,17,21-Trihydroxy-6α-methylpregna-1,4-diene-3,20-dione 21-(hydrogen succinate) CAS RN®: 2921-57-5; UNII: 5GMR90S4KN.

DEFINITION

Methylprednisolone Hemisuccinate contains NLT 97.0% and NMT 103.0% of methylprednisolone hemisuccinate ($C_{26}H_{34}O_8$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

Change to read:

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

Standard solution: 20 µg/mL of USP Methylprednisolone Hemisuccinate RS in alcohol

Sample solution: 20 µg/mL of methylprednisolone hemisuccinate in alcohol

Analytical wavelength: 243 nm

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

ASSAY

• **Procedure**

Solution A: Chloroform and glacial acetic acid (97:3)

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

Internal standard solution: 6 mg/mL of USP Fluorometholone RS in tetrahydrofuran

Standard solution: 0.4 mg/mL of USP Methylprednisolone Hemisuccinate RS prepared as follows. Transfer a suitable quantity of USP Methylprednisolone Hemisuccinate RS to a suitable volumetric flask, and add 5.0% of the flask volume of *Internal standard solution*. Dilute with *Solution A* to volume.

Sample solution: 0.4 mg/mL of Methylprednisolone Hemisuccinate prepared as follows. Transfer a suitable quantity of Methylprednisolone Hemisuccinate to a suitable volumetric flask, and add 5.0% of the flask volume of *Internal standard solution*. Dilute with *Solution A* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4-mm × 30-cm; packing L3

Injection volume: 4–8 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between methylprednisolone hemisuccinate and fluorometholone

Relative standard deviation: NMT 2.0% for six replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of methylprednisolone hemisuccinate ($C_{26}H_{34}O_8$) in the portion of Methylprednisolone Hemisuccinate taken:

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

R_U = peak area ratio of methylprednisolone hemisuccinate to fluorometholone from the *Sample solution*

R_S = peak area ratio of methylprednisolone hemisuccinate to fluorometholone from the *Standard solution*

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

C_U = concentration of Methylprednisolone Hemisuccinate in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.2%
- **Organic Impurities**

Mobile phase: Tetrahydrofuran, formic acid, and water (255:1:745)

Diluent: Tetrahydrofuran, acetonitrile, acetic acid, and water (25:25:3:47)

Standard solution: 0.02 mg/mL of USP Methylprednisolone Hemisuccinate RS in *Diluent*

Sample solution: 1 mg/mL of Methylprednisolone Hemisuccinate in *Diluent*. Shake or sonicate to aid in solubilization.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 20-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 5000 theoretical plates

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Methylprednisolone Hemisuccinate taken:

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

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

r_S = peak area of methylprednisolone hemisuccinate from the *Standard solution*

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

C_U = concentration of Methylprednisolone Hemisuccinate in the *Sample solution* (mg/mL)

Acceptance criteria

Any individual impurity: NMT 1.0%

Total impurities: NMT 2.0%

SPECIFIC TESTS

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

Sample solution: 10 mg/mL of Methylprednisolone Hemisuccinate in dioxane

Acceptance criteria: +87° to +95°

- **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

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

USP Fluorometholone RS

USP Methylprednisolone Hemisuccinate RS

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

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

Chromatographic Database Information: Chromatographic Database

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