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Fludrocortisone Acetate Tablets

DEFINITION

Fludrocortisone Acetate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of fludrocortisone acetate ($C_{23}H_{31}FO_6$).

IDENTIFICATION

Delete the following:

▲• **A. Thin-Layer Chromatography**

Standard solution: 100 µg/mL of USP Fludrocortisone Acetate RS in acetone

Sample solution: Nominally 0.1 mg/mL of fludrocortisone acetate from Tablets prepared as follows. Transfer a portion of powdered Tablets, equivalent to 1 mg of fludrocortisone acetate, to a glass stoppered centrifuge tube, add 10 mL of acetone, and shake by mechanical means for 3 min. Centrifuge the mixture. Use the clear solution.

Chromatographic system

(See *Chromatography ⟨621⟩*.)

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volumes

Standard solution: 20 µL

Sample solution: 20 µL, in 5-µL increments

Developing solvent system: Chloroform, methanol, and water (85:14:1)

Analysis

Samples: *Standard solution* and *Sample solution*

Apply the *Samples* in a line parallel to and about 2.5 cm from the bottom of the plate. Develop the plate in a chamber using the *Developing solvent system* until the solvent front has moved about 15 cm. Remove the plate, air-dry, and examine under short-wavelength UV light.

Acceptance criteria: The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*. ▲2S *(USP41)*

Add the following:

▲• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay*.▲2S *(USP41)*

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution,* as obtained in the *Assay*.▲2S *(USP41)*

ASSAY

Change to read:

• **Procedure**

▲Throughout the following procedures protect the solutions containing samples or Reference Standards from light.

Mobile phase: Acetonitrile, water, and phosphoric acid (40: 60: 0.1)

Standard stock solution: 0.2 mg/mL of USP Fludrocortisone Acetate RS in acetonitrile

Standard solution: 4 µg/mL of USP Fludrocortisone Acetate RS from *Standard stock solution* in *Mobile phase*

Sample solution: Nominally 4 µg/mL of fludrocortisone acetate from Tablets prepared as follows. Transfer NLT 10 Tablets to a suitable volumetric flask, and add 80% of the final flask volume of *Mobile phase.* Stir for 20 min, and dilute with *Mobile phase* to volume. Pass the resulting solution through a suitable filter, discarding the first 5 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 1.4 times the retention time of fludrocortisone acetate

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.7 for fludrocortisone acetate

Relative standard deviation: NMT 1.0% for fludrocortisone acetate

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fludrocortisone acetate ($C_{23}H_{31}FO_6$) in the portion of Tablets 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 Fludrocortisone Acetate RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of fludrocortisone acetate in the *Sample solution* (µg/mL)▲2S *(USP41)*

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲Throughout the following procedures protect the solutions containing samples or Reference Standards from light.▲2S *(USP41)*

Medium: ▲0.01 N hydrochloric acid TS;▲2S *(USP41)* 500 mL

Apparatus 2: 75 rpm

Time: 30 min

Mobile phase: Acetonitrile and water (45:55)

Standard stock solution: 0.025 mg/mL of USP Fludrocortisone Acetate RS prepared as follows. Transfer an appropriate amount of USP Fludrocortisone Acetate RS to a suitable volumetric flask. Add 5% of the flask volume of acetonitrile, sonicate for 5 min to promote dissolution, and dilute with *Medium* to volume.

Standard solution: ▲(*L*/500) mg/mL of USP Fludrocortisone Acetate RS from *Standard stock solution* in *Medium*, where *L* is the label claim in mg/Tablet▲2S *(USP41)*

Sample solution: Withdraw a portion of the solution under test with glass syringes, and pass through a membrane filter that has been checked for absorptive loss.

Chromatographic system

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

Mode: LC

Detector: ▲UV 254 nm▲2S *(USP41)*

Column: 4.6-mm × 15-cm; ▲5-µm▲2S *(USP41)* packing L1

Flow rate: 2 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

▲▲2S *(USP41)*

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fludrocortisone acetate ($C_{23}H_{31}FO_6$) dissolved:

$$\text{▲Result} = (r_U/r_S) \times C_S \times V \times (1/L) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)▲2S *(USP41)*

Tolerances: NLT 80% (Q) of the labeled amount of fludrocortisone acetate ($C_{23}H_{31}FO_6$) is dissolved.

Change to read:

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

▲▲2S *(USP41)*

IMPURITIES

Change to read:

• **▲Organic Impurities**

Throughout the following procedures protect the solutions containing samples or Reference Standards from light.

Mobile phase: Acetonitrile, water, and phosphoric acid (40: 60: 0.1)

Standard stock solution: 0.40 mg/mL of USP Fludrocortisone Acetate RS in acetonitrile

Standard solution: 0.4 µg/mL of USP Fludrocortisone Acetate RS from *Standard stock solution* in *Mobile phase*

Sensitivity solution: 0.04 µg/mL of USP Fludrocortisone Acetate RS from *Standard solution* in *Mobile phase*

Sample solution: Nominally 80 µg/mL of fludrocortisone acetate from Tablets prepared as follows. Transfer NLT 20 Tablets to a suitable volumetric flask, add 80% of the final volume of *Mobile phase,* and stir for 20 min. Dilute with *Mobile phase* to volume. Centrifuge a portion of the solution and use the supernatant. [Note—The use of a centrifuge speed of 4000 rpm for 10 min may be suitable.]

Chromatographic system: Proceed as directed in the *Assay*, except for the *Run time*.

Run time: NLT 2.7 times the retention time of fludrocortisone acetate

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Tailing factor: NMT 1.5, *Standard solution*

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

Signal-to-noise ratio: NLT 10.0, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each degradation product in the portion of Tablets taken:

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

r_U = peak response of each degradation product from the *Sample solution*

r_S = peak response of fludrocortisone acetate from the *Standard solution*

C_S = concentration of USP Fludrocortisone Acetate RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of fludrocortisone acetate in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Fludrocortisone[a]	0.41	1.5
Fludrocortisone acetate	1.0	—
Any other individual degradation product	—	0.5
Total degradation products	—	4.0▲2S *(USP41)*

▲a 9-Fluoro-11β,17,21-trihydroxypregn-4-ene-3,20-dione.▲ (ERR 1-Mar-2019)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** ▲Preserve in tight, light-resistant containers. Store at controlled room temperature.▲2S *(USP41)*

Change to read:

- **USP Reference Standards** ⟨11⟩

USP Fludrocortisone Acetate RS

▲▲2S *(USP41)*

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

Topic/Question	Contact	Expert Committee
FLUDROCORTISONE ACETATE TABLETS	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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