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Fluticasone Propionate Ointment

DEFINITION
Fluticasone Propionate Ointment contains NLT 90.0% and NMT 110.0% of the labeled amount of fluticasone propionate ($C_{25}H_{31}F_3O_5S$).

IDENTIFICATION

• **A. Thin-Layer Chromatographic Identification Test ⟨201⟩**

Standard solution: 0.17 mg/mL of USP Fluticasone Propionate RS in acetonitrile

Test solution: Transfer a quantity of Ointment, equivalent to 100 µg of fluticasone propionate, to a 125-mL separatory funnel. Add 50 mL of hexane and 10 mL of acetonitrile to the separatory funnel. Stopper and shake the funnel until the Ointment is completely dispersed. Shake the separatory funnel for an additional min, and allow the phases to separate. Filter the lower layer through a 10-mL syringe containing a cotton plug into a 25-mL volumetric flask. Repeat the extraction with one 10-mL aliquot of acetonitrile, and filter the lower layer into the volumetric flask. Wash the cotton plug with 2 mL of acetonitrile, and collect the washings into the volumetric flask. Dilute the sample extract with acetonitrile to volume. Transfer one-half of the sample extract to a glass tube suitable for evaporation, and evaporate to dryness at about 40°. Transfer the remainder of the sample extract into the same tube, and continue evaporating to dryness. Dissolve the residue in 0.6 mL of acetonitrile. [Note—The *Test solution* may be cloudy because of the presence of undissolved excipients.]

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography.*)

Adsorbent: 0.2-mm layer of chromatographic silica gel mixture on a high-performance thin-layer chromatographic plate, 5-µm particle size

Application volume: 40 µL

Developing solvent system: Dichloromethane, ethyl acetate, and glacial acetic acid (30:8:1)

Analysis

Samples: *Standard solution* and *Test solution*

Separately apply the *Standard solution* and the *Test solution* to the plate. On the same plate, apply 20 µL of the *Standard solution*, allow the application to dry, and apply 20 µL of the *Test solution* on top of the dried 20-µL *Standard solution* spot. Allow each of the applications to dry thoroughly. Place the plate in a tank equilibrated with the developing solvent, and allow the developing solvent to travel 8 cm from the point of application. Remove the plate and allow to air-dry. Examine the plate under ultraviolet light at 254 nm.

Acceptance criteria: The R_F value of the principal spot from the *Test solution* corresponds to that of the *Standard solution*. [Note—If the excipients in the Ointment interfere with the appearance of the principal spot obtained for the *Test solution*, use the *Standard solution* and the *Test solution* overspot to confirm identity.]

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

[Note—Protect the *Standard solution* and the *Sample solution* from direct light by using a light-protective volumetric flask and autosampler vials.]

Buffer: 1.20 g/L of monobasic ammonium phosphate. Adjust with phosphoric acid to a pH of 3.50 ± 0.03.

Mobile phase: Methanol, acetonitrile, and *Buffer* (46:14:40)

Diluent: Methanol and water (80:20)

System suitability stock solution: 0.5 mg/mL of USP Fluticasone Propionate Nasal Spray Resolution Mixture RS in methanol. [Note—USP Fluticasone Propionate Nasal Spray Resolution Mixture RS is a mixture of fluticasone propionate and fluticasone propionate related compound D.]

System suitability solution: 5 µg/mL of USP Fluticasone Propionate Nasal Spray Resolution Mixture RS in *Diluent* from *System suitability stock solution*

Standard stock solution: 0.25 mg/mL USP Fluticasone Propionate RS. Dissolve the standard first in a volume of methanol, equivalent to 80% of the final volume, and dilute with water to volume.

Standard solution: 4 µg/mL USP Fluticasone Propionate RS in *Diluent,* from *Standard stock solution*

Sample solution: Equivalent to 4 µg/mL of fluticasone propionate. Transfer a quantity of Ointment, equivalent to about 100 µg of fluticasone propionate, to a 125-mL separatory funnel. Add to the separatory funnel 45 mL of hexane previously heated to about 60° in a water bath. [NOTE—Hexane is highly flammable.] Stopper and shake vigorously until the Ointment is completely dispersed. Wash the stopper and neck of the separatory funnel with 5 mL of hexane heated to 60°, and allow the funnel to cool to room temperature. Transfer 10 mL of *Diluent* into the separatory funnel, and shake the contents for 1 min. Allow the phases to separate, and filter the lower aqueous layer via a cotton wool plug, previously washed with *Diluent,* into a 25-mL volumetric flask. Repeat the extraction with two 5-mL aliquots of *Diluent,* filtering the lower layers into the volumetric flask. Wash the cotton plug with 2 mL of *Diluent,* and collect the washings into the volumetric flask. Dilute the sample with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: 240 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 1.5 mL/min

Injection size: 50 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.4 between fluticasone propionate and fluticasone propionate related compound D, *System suitability solution*

Tailing factor: NMT 1.4, *Standard solution* (calculated using the width of the peak at 10% of the height)

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fluticasone propionate ($C_{25}H_{31}F_3O_5S$) in the portion of Ointment taken:

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

r_U = peak response of fluticasone propionate from the *Sample solution*

r_S = peak response of fluticasone propionate from the *Standard solution*

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

C_U = nominal concentration of fluticasone propionate in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

• **MICROBIAL ENUMERATION TESTS ⟨61⟩** and **TESTS FOR SPECIFIED MICROORGANISMS ⟨62⟩:** Meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The total aerobic microbial count is NMT 100 cfu/g, and the total combined molds and yeasts count is NMT 10 cfu/g.

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in collapsible tubes or tight containers, protected from light. Store between 2° and 30°.

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Fluticasone Propionate RS

USP Fluticasone Propionate Nasal Spray Resolution Mixture RS

This Reference Standard is a mixture of fluticasone propionate and fluticasone propionate related compound D, and the chemical names for both are given below:

Fluticasone propionate: S-Fluoromethyl 6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxyandrosta-1,4-diene-17β-carbothioate.

Fluticasone propionate related compound D: S-Methyl- 6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxy-androsta-1,4-diene-17β-carbothioate.

Chromatographic Database Information: Chromatographic Database

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