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Halcinonide Ointment

DEFINITION

Halcinonide Ointment is Halcinonide in a suitable ointment base. It contains NLT 90.0% and NMT 110.0% of the labeled amount of halcinonide ($C_{24}H_{32}ClFO_5$).

IDENTIFICATION

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

• **B.** The UV spectrum of the halcinonide peak of the *Sample solution* corresponds to that of the *Diluted standard stock solution*, as obtained in the test for *Organic Impurities*.

ASSAY

• **Procedure**

Mobile phase: Acetonitrile and water (50:50)

Internal standard solution: 6 µg/mL of butylparaben in acetonitrile

Standard stock solution: 0.04 mg/mL of USP Halcinonide RS in *Internal standard solution*

Standard solution: 0.02 mg/mL of USP Halcinonide RS from *Standard stock solution* prepared as follows. Mix equal volumes of *Mobile phase* and *Standard stock solution*.

Sample solution: Nominally 0.02 mg/mL of halcinonide in *Mobile phase* prepared as follows. Transfer an equivalent to 1 mg of halcinonide from a quantity of Ointment to a glass-stoppered, 50-mL centrifuge tube, and add 25.0 mL of *Internal standard solution* and 5.0 mL of hexane. Place in a water bath at 58 ± 2° for 3 min, then mix in a vortex mixer for 1 min until the sample is well dispersed. Repeat the above-specified heating and mixing step once. Cool in an ice–methanol bath for 15 min, or until the two phases separate, centrifuging if necessary. Transfer 5.0 mL of the lower layer to a 15-mL centrifuge tube, and add 5.0 mL of *Mobile phase*.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for butylparaben and halcinonide are 0.6 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between halcinonide and butylparaben

Relative standard deviation: NMT 3.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of halcinonide ($C_{24}H_{32}ClFO_5$) in the portion of Ointment taken:

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

R_U = peak response ratio of halcinonide to butylparaben from the *Sample solution*

R_S = peak response ratio of halcinonide to butylparaben from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Minimum Fill ⟨755⟩:** Meets the requirements

IMPURITIES

• **Organic Impurities**

Solution A: 10 mM ammonium acetate in water

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
20.0	10	90
22.0	10	90
22.1	90	10
25.0	90	10

Diluent 1: Acetonitrile and water (60:30), saturated with hexane

Diluent 2: Acetonitrile and water (10:90)

Standard stock solution: 0.2 mg/mL of USP Halcinonide RS in *Diluent 1*

Diluted standard stock solution: 0.1 mg/mL of USP Halcinonide RS in *Diluent 2* from the *Standard stock solution*

Standard solution: 0.2 µg/mL each of USP Halcinonide RS in *Diluent 2* from the *Standard stock solution*

Sample stock solution: Nominally 0.2 mg/mL of halcinonide in *Diluent 1* prepared as follows. Transfer a portion of Ointment equivalent to 4 mg of halcinonide to a 50-mL centrifuge tube. Add 10 mL of *Diluent 1* and 20 mL of hexane heated at 58 ± 2° for 20 min. Shake for NLT 1 min initially to ensure dispersion and at 5-min intervals thereafter. Cool, centrifuge at 3000 rpm for 10 min, and transfer the lower layer to a 20-mL volumetric flask. Repeat the extraction with an additional 5 mL of *Diluent 1* and 20 mL of hexane each time. Dilute with *Diluent 1* to volume.

Sample solution: 0.1 mg/mL of halcinonide from the *Sample stock solution* in *Diluent 2*

Chromatographic system

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

Mode: LC

Detector: UV 240 nm. For *Identification* test *B*, use a diode array detector in the range of 200–450 nm.

Column: 2.1-mm × 15-cm; 1.8-µm packing L1

Flow rate: 0.3 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Relative standard deviation: NMT 2.4%

Signal-to-noise ratio: NLT 50

Analysis

Samples: *Diluted standard stock solution*, *Standard solution*, and *Sample solution*

[Note—The *Diluted standard stock solution* is used for *Identification* test *B*.]

Calculate the percentage of any individual unspecified impurity in the portion of Ointment taken:

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

r_U = peak response of each unspecified impurity from the *Sample solution*

r_S = peak response of halcinonide from the *Standard solution*

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Dihydrotriamcinolone[a]	0.5	—
Halcinonide	1.0	—
Any individual unspecified impurity	—	0.2
Total impurities	—	3.0

[a] Drug substance process impurity included in the table for identification only.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** Meets the requirements for the absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature. Avoid excessive heat.

• **USP Reference Standards ⟨11⟩**
USP Halcinonide RS

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

Topic/Question	Contact	Expert Committee
HALCINONIDE OINTMENT	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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