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Betamethasone Oral Solution

DEFINITION
Betamethasone Oral Solution contains NLT 90.0% and NMT 115.0% of the labeled amount of betamethasone ($C_{22}H_{29}FO_5$).

IDENTIFICATION

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

Diluent: Chloroform and methanol (1:1)

Standard solution: 1 mg/mL of USP Betamethasone RS in alcohol

Sample solution: Place a volume of Oral Solution, equivalent to about 1 mg of betamethasone, in a centrifuge tube. Add 15 mL of 0.1 N hydrochloric acid and 20 mL of ethyl acetate. Shake the tube for about 1 min. Centrifuge to separate the phases. Transfer the upper phase (ethyl acetate) to a suitable container. Evaporate to dryness on a steam bath under a gentle stream of nitrogen.

Allow to cool to room temperature. Dissolve the residue in about 0.5 mL of *Diluent* by using a vortex mixer. Transfer the solution to a 2-mL volumetric flask with small portions of *Diluent*. Dilute with *Diluent* to volume, and mix.

Evaporate 1 mL of the resulting solution on a steam bath just to dryness, and dissolve the residue in 0.5 mL of alcohol.

Chromatographic system

Application volume: 10 µL

Developing solvent system: Chloroform and diethylamine (2:1)

Spray reagent: Dilute sulfuric acid (1 in 2)

Analysis: Proceed as directed in the chapter. Locate the spots by lightly spraying with *Spray reagent*, and heat on a hot plate or under a lamp until spots appear.

Acceptance criteria: Meets the requirements

• **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**

Protect all standard and sample solutions from light.

Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 2.9.

Solution A: Acetonitrile and *Buffer* (25:75)

Solution B: Acetonitrile and *Buffer* (45:55)

Diluent: Dehydrated alcohol and water (2:3)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
25.0	0	100
25.1	100	0
35.0	100	0

Standard stock solution: 0.12 mg/mL of USP Betamethasone RS prepared as follows. Transfer a quantity of USP Betamethasone RS to a suitable container, and dilute, using sonication, with dehydrated alcohol to obtain a solution containing 0.3 mg/mL. Quantitatively dilute an aliquot of this solution with water to obtain a 0.12-mg/mL solution of betamethasone.

Standard solution: 0.048 mg/mL of USP Betamethasone RS in *Diluent* from *Standard stock solution*

Beclomethasone solution: 0.12 mg/mL of beclomethasone prepared as follows. Transfer a quantity of beclomethasone to a suitable container, and dilute, using sonication, with dehydrated alcohol to obtain a solution containing 0.3 mg/mL. Quantitatively dilute an aliquot of this solution with water to obtain a 0.12 mg/mL solution of beclomethasone.

System suitability solution: 0.048 mg/mL each of USP Betamethasone RS and beclomethasone in *Diluent*, prepared from the *Standard stock solution* and *Beclomethasone solution*

Sample solution: Nominally 0.048 mg/mL of betamethasone prepared as follows. Transfer a measured volume of Oral Solution, containing a known amount of betamethasone, to a suitable volumetric flask, and dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 4-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

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

[Note—The relative retention times for betamethasone and beclomethasone are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 4.0 between betamethasone and beclomethasone, *System suitability solution*

Tailing factor: NMT 1.5 for betamethasone, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of betamethasone ($C_{22}H_{29}FO_5$) in the portion of Oral Solution 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 Betamethasone RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–115.0%

IMPURITIES

• **Organic Impurities**

Protect all sample and standard solutions from light.

Buffer, Solution A, Solution B, Diluent, Mobile phase, Standard stock solution, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.48 µg/mL of USP Betamethasone RS in *Diluent* from the *Standard stock solution*

Sensitivity solution: 0.024 µg/mL of USP Betamethasone RS in *Diluent* from the *Standard solution*

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

[Note—The relative retention times for betamethasone and beclomethasone are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 4.0 between betamethasone and beclomethasone, *System suitability solution*

Relative standard deviation: NMT 10% for betamethasone, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each related compound in the portion of Oral Solution taken:

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

r_U = peak response for individual related compounds from the *Sample solution*

r_S = peak response for betamethasone from the *Standard solution*

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Betamethasone	1.0	—
9,11-Expoxy-17α,21-dihydroxy-16β-methylpregna-1,4 diene-3,20-dione	1.25	1.3
17α,21-Dihydroxy-16β-methylpregna-1,4,11-triene-3,20-dione	1.33	0.7

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** It meets the requirements of the test for the absence of *Escherichia coli*. The total aerobic microbial count is NMT 10^2 cfu/mL, and the total combined molds and yeasts count is NMT 10^1 cfu/mL.

• **pH ⟨791⟩:** 2.8–3.6

• **Deliverable Volume ⟨698⟩:** Meets the requirements for oral solution packaged in multiple-unit containers

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store at controlled room temperature, protected from light. Preserve in tight containers.

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

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

Topic/Question	Contact	Expert Committee
BETAMETHASONE ORAL SOLUTION	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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