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Megestrol Acetate Oral Suspension

DEFINITION

Megestrol Acetate Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of megestrol acetate ($C_{24}H_{32}O_4$).

IDENTIFICATION

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

Standard solution: 4.0 mg/mL of USP Megestrol Acetate RS in chloroform

Sample solution: Transfer Oral Suspension, equivalent to 160 mg of megestrol acetate, to a separatory funnel, add 50 mL of water and 40 mL of chloroform, and shake. Allow the phases to separate, and discard the aqueous layer.

Developing solvent system: Chloroform and ethyl acetate (4:1)

ASSAY

• **Procedure**

Mobile phase: Acetonitrile and water (11:9)

Standard solution: 80 µg/mL of USP Megestrol Acetate RS in *Mobile phase*

Sample solution: A volume of Oral Suspension diluted with *Mobile phase* to obtain nominally 80 µg/mL of megestrol acetate

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1.5 mL/min

Injection size: 25 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2500 theoretical plates

Tailing factor: NMT 1.4

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{24}H_{32}O_4$ in the portion of Oral Suspension 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 Megestrol Acetate RS in the *Standard solution* (µg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Medium: 0.5% sodium lauryl sulfate in water; 900 mL

Apparatus 2: 25 rpm

Time: 30 min

Detector: UV 292 nm

Standard solution: 45 mg of USP Megestrol Acetate RS in a 250-mL volumetric flask. Add 12 mL of methanol, and place the flask in a warm water bath until the solid is dissolved. Dilute with *Medium* to volume. The final concentration is 180 µg/mL of megestrol acetate. Dilute with *Medium*, if necessary.

Sample solution: Transfer to the surface of the *Medium* in the dissolution vessel an accurately measured volume of Oral Suspension, freshly mixed and free from air bubbles, equivalent to 160 mg of megestrol acetate. At the sampling time, withdraw a volume of the solution under test and pass through a suitable filter with 0.45-µm pore size. Dilute with *Medium*, if necessary.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{24}H_{32}O_4$ released:

$$\text{Result} = (A_U/A_S) \times (C_S/V) \times V_D \times (100/L)$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

V = volume of Oral Suspension taken

V_D = volume of *Medium*, 900 mL

L = label claim (mg/mL)

Tolerances: NLT 80% (Q) of the labeled amount of $C_{24}H_{32}O_4$ is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: 0.5% sodium lauryl sulfate in water; 900 mL

Apparatus 2: 25 rpm

Time: 30 min

Detector: UV 292 nm, using 0.5-cm pathlength cuvettes

Standard solution: 45 mg of USP Megestrol Acetate RS in a 250-mL volumetric flask. Add 5 mL of methanol. Dilute with *Medium* to volume. Transfer 10 mL of this solution to a 100-mL volumetric flask, and dilute with *Medium* to volume. The final concentration is 18 µg/mL.

Sample solution: [NOTE—Use a separate syringe for each vessel.] Withdraw more than 10 mL of the Oral Suspension, using a 10-mL syringe with a long cannula. Remove air bubbles from the syringe. Adjust the volume to the 10-mL mark on the syringe, and remove the needle. Wipe the tip of the syringe, and weigh (gross weight). Operate the apparatus, and rapidly dispense the Oral Suspension to the side of the vessel at about halfway from the bottom. Similarly dispense the Oral Suspension into other vessels. Weigh each syringe after dispensing the sample (tare weight). Record sample weights. After completion of the dissolution, pass an aliquot through a suitable nylon filter with 0.45-µm pore size, and dilute 2.0 mL of the filtrate with *Medium* to 50.0 mL to obtain a solution having a theoretical concentration of about 18 µg/mL.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{24}H_{32}O_4$ released:

$$\text{Result} = (A_U/A_S) \times (C_S/W) \times V_D \times d \times (100/L)$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

W = weight of the Oral Suspension taken (mg)

V_D = volume of the *Medium* in the dissolution vessel, 900 mL

d = density of the Oral Suspension (mg/mL), obtained by dividing the weight of Oral Suspension taken by 10 mL

L = label claim (mg/mL)

Tolerances: NLT 80% (Q) of the labeled amount of $C_{24}H_{32}O_4$ is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: 0.5% sodium lauryl sulfate in degassed water; 900 mL. [NOTE—Use ultrapure sodium lauryl sulfate with an *Assay* content of NLT 99.0%.]

Apparatus 2: 50 rpm

Time: 30 min

Determine the amount of $C_{24}H_{32}O_4$ dissolved by using the following method.

Mobile phase: Proceed as directed in the *Assay*.

Standard solution: 0.46 mg/mL of USP Megestrol Acetate RS in *Mobile phase*

Sample solution: Proceed as directed for *Test 2*, introducing the sample into the vessel over a 10- to 15-s period (about 1 mL/s).

Chromatographic system: Proceed as directed in the *Assay*.

Injection size: 10 µL

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{24}H_{32}O_4$ released:

$$\text{Result} = (r_U/r_S) \times (C_S/W) \times V_D \times d \times (100/L)$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

W = weight of the Oral Suspension taken (mg)

V_D = volume of the *Medium* in the dissolution vessel, 900 mL

d = density of the Oral Suspension (mg/mL), obtained by dividing the weight of Oral Suspension taken by 10 mL

L = label claim (mg/mL)

Tolerances: NLT 80% (Q) of the labeled amount of $C_{24}H_{32}O_4$ is dissolved.

• **DELIVERABLE VOLUME ⟨698⟩:** Meets the requirements

SPECIFIC TESTS

• **PH ⟨791⟩:** 3.0–4.7

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers.

• **LABELING:** When more than one test for *Dissolution* is given, the labeling states the test used only if *Test 1* is not used.

• **USP REFERENCE STANDARDS ⟨11⟩**

USP Megestrol Acetate RS

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

Topic/Question	Contact	Expert Committee
MEGESTROL ACETATE ORAL SUSPENSION	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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