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Norethindrone Tablets

DEFINITION

Norethindrone Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of norethindrone ($C_{20}H_{26}O_2$).

IDENTIFICATION

• **A. Infrared Absorption**

Analysis: Mix an amount of powdered Tablets equivalent to 50 mg of norethindrone with 15 mL of solvent hexane. Stir the solution occasionally for 15 min. Centrifuge the mixture, then decant and discard the solvent hexane. Extract the residue with two 10-mL portions of solvent hexane, centrifuging and decanting as before, and discard the solvent hexane. Add 25 mL of chloroform to the residue, mix by shaking for 1–2 min, and filter. Evaporate the filtrate to about 3 mL, add a few mL of solvent hexane to induce crystallization, and evaporate to dryness.

Acceptance criteria: The IR absorption spectrum of a potassium bromide dispersion prepared from the residue so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Norethindrone RS.

ASSAY

• **Procedure**

Solution A: Dissolve 1.0 g of isoniazid in 1000 mL of anhydrous methanol, and add 1.3 mL of hydrochloric acid.

Standard stock solution: 14 µg/mL of USP Norethindrone RS in methanol

Standard solution: Transfer 10.0 mL of the *Standard stock solution* to a suitable container, add 2.0 mL of *Solution A*, mix, seal, and allow to stand for 30 min.

Sample stock solution: Transfer an amount of finely powdered Tablets equivalent to 0.7 mg of norethindrone (powder NLT 20 Tablets) to a 50-mL volumetric flask, and add anhydrous methanol to volume. Mix, and allow to stand for 10 min, with occasional mixing. Filter a portion of the mixture to clarify the solution. Use the filtrate.

Sample solution: Transfer 10.0 mL of the *Sample stock solution* to a suitable container. Add 2.0 mL of *Solution A*, mix, seal, and allow to stand for 30 min.

Sample blank solution: Transfer 10.0 mL of the *Sample stock solution* to a suitable container, add 2.0 mL of methanol, and mix.

Reagent blank solution: Transfer 10.0 mL of methanol to a suitable container, add 2.0 mL of *Solution A*, mix, seal, and allow to stand for 30 min.

Instrumental conditions

Mode: UV

Analytical wavelength: 380 nm

Analysis

Samples: *Standard solution*, *Sample solution*, *Sample blank solution*, and *Reagent blank solution*

Concomitantly determine the absorbances of these solutions, using methanol as the reference for the *Sample blank solution*, and using the *Reagent blank solution* as the reference for the *Sample solution* and the *Standard solution*.

Calculate the precentage of the labeled amount of norethindrone ($C_{20}H_{26}O_2$) in the portion of Tablets taken:

$$\text{Result} = (A_U - A_{UB})/A_S \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*

A_{UB} = absorbance of the *Sample blank solution*

A_S = absorbance of the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Test 1

Medium: 0.09% Sodium lauryl sulfate in 0.1 N hydrochloric acid; 500 mL, deaerated

Apparatus 2: 75 rpm

Time: 30 min

Mobile phase: Acetonitrile and water (2:3)

Standard stock solution: 0.07 mg/mL of USP Norethindrone RS in methanol. Sonication may be used to aid dissolution.

Standard solution: (*L*/500) mg/mL of USP Norethindrone RS in *Medium* from the *Standard stock solution*, where *L* is the claim in mg/Tablet of norethindrone

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of norethindrone ($C_{20}H_{26}O_2$) 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 norethindrone in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of norethindrone ($C_{20}H_{26}O_2$) is dissolved.

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

Medium: 0.09% Sodium lauryl sulfate in 0.1 N hydrochloric acid; 500 mL, deaerated

Apparatus 2: 75 rpm

Time: 45 min

Mobile phase: Acetonitrile and 0.02 M phosphate buffer pH 6.0 (35:65)

Standard stock solution: 0.028 mg/mL of USP Norethindrone RS in methanol

Standard solution: (*L*/500) mg/mL of USP Norethindrone RS in *Medium* from the *Standard stock solution*, where *L* is the claim in mg/Tablet of norethindrone

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size or centrifuge at least 10 mL of the solution under test and use the supernatant.

Use one of the following two chromatographic systems. (See *Chromatography ⟨621⟩, System Suitability*.)

Chromatographic system 1

Mode: LC

Detector: UV 200 nm

Column: 4.6-mm × 10-cm; 3-µm packing L1

Flow rate: 1 mL/min

Injection volume: 100 µL

Chromatographic system 2

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 10-cm; 3- or 3.5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 100 µL

System suitability

Use this *System suitability* for either *Chromatographic system 1* or *Chromatographic system 2*.

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of norethindrone ($C_{20}H_{26}O_2$) 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 norethindrone in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of norethindrone ($C_{20}H_{26}O_2$) 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 0.1 N hydrochloric acid; 500 mL, deaerated

Apparatus 2: 75 rpm

Time: 20 min

Mobile phase: Acetonitrile and water (50:50)

Standard stock solution: 0.028 mg/mL of USP Norethindrone RS in methanol. Sonication may be used to aid dissolution.

Standard solution: (L/500) mg/mL of USP Norethindrone RS in *Medium* from the *Standard stock solution*, where L is the claim in mg/Tablet of norethindrone

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size or centrifuge and use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

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

Column temperature: 30°

Flow rate: 1.3 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of norethindrone ($C_{20}H_{26}O_2$) 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 norethindrone in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of norethindrone ($C_{20}H_{26}O_2$) is dissolved.

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

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

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

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

Topic/Question	Contact	Expert Committee
NORETHINDRONE TABLETS	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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