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Minocycline Hydrochloride Extended-Release Tablets

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DEFINITION

Minocycline Hydrochloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of minocycline ($C_{23}H_{27}N_3O_7$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **B.** The UV absorption spectrum of the major peak of the *Sample solution* and that of the *Standard solution* exhibit maxima and minima at the same wavelengths, as obtained in the Assay.

ASSAY

PROCEDURE

Protect solutions containing minocycline from light.

Buffer: 3.5 g/L of [tetrabutylammonium hydrogen sulfate](#), 2 g/L of [anhydrous citric acid](#), and 6.8 g/L of [monobasic potassium phosphate](#).

Adjust with 10 N [sodium hydroxide](#) to a pH of 7.0.

Mobile phase: [Acetonitrile](#) and *Buffer* (24:76)

Diluent: [Acetonitrile](#) and [water](#) (20:80)

Standard solution: 0.045 mg/mL of minocycline from [USP Minocycline Hydrochloride RS](#) in *Diluent*. Store at 4° and use within 24 h.

Sample stock solution: Nominally about 0.9 mg/mL of minocycline from Tablets prepared as follows. Transfer a suitable portion of finely powdered Tablets (NLT 10) to a suitable volumetric flask. Add [acetonitrile](#), using 20% of the final volume, and mix vigorously for 15 min. Add [water](#), using 65% of the final volume, and mix vigorously for 30 min. Dilute with [water](#) to volume and mix.

Sample solution: Nominally 0.045 mg/mL of minocycline from *Sample stock solution* in *Diluent*. Centrifuge and use the clear supernatant. Store at 4° and use within 24 h.

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 277 nm. When this procedure is used for *Identification test B*, use a diode array detector set at 200–400 nm.

Column: 4.6-mm × 15-cm; 5-μm packing [L1](#)

Temperatures

Column: 35°

Autosampler: 4°

Flow rate: 1.3 mL/min

Injection volume: 10 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of minocycline ($C_{23}H_{27}N_3O_7$) in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Minocycline Hydrochloride RS](#) in the *Standard solution* (mg/mL)

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

P = potency of minocycline in [USP Minocycline Hydrochloride RS](#) ($\mu\text{g}/\text{mg}$)

F = conversion factor, 0.001 $\text{mg}/\mu\text{g}$

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#)

Test 1: Protect solutions containing minocycline from light.

Medium: pH 6.8 phosphate buffer (see [Reagents and Reference Tables, Solutions, Buffer Solutions](#)); 900 mL

Apparatus 2: 50 rpm

Times: 1, 2, and 5 h

Standard stock solution: 0.5 mg/mL of minocycline from [USP Minocycline Hydrochloride RS](#) in *Medium*

Standard solution: ($L/900$) mg/mL of minocycline from *Standard stock solution* in *Medium*, where L is the label claim of minocycline in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

Mode: UV

Analytical wavelength: 348 nm

Cell: See [Table 1](#).

Table 1

Tablet Strength (mg)	Cell Path Length (cm)
45	0.5
90	0.2
135	0.2

Blank: *Medium*

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Autozero the instrument using the *Blank*.

Calculate the concentration (C_i) of minocycline ($\text{C}_{23}\text{H}_{27}\text{N}_3\text{O}_7$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result} = (A_U/A_S) \times C_S \times P \times F$$

A_U = absorbance of the *Sample solution* at time point i

A_S = absorbance of the *Standard solution*

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

P = potency of minocycline in [USP Minocycline Hydrochloride RS](#) ($\mu\text{g}/\text{mg}$)

F = conversion factor, 0.001 $\text{mg}/\mu\text{g}$

Calculate the percentage of the labeled amount (Q_i) of minocycline ($\text{C}_{23}\text{H}_{27}\text{N}_3\text{O}_7$) dissolved at each time point (i):

$$\text{Result}_1 = C_i \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{[C_3 \times [V - (2 \times V_S)]] + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of minocycline in the portion of sample withdrawn at the specified time point (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See [Table 2](#).

Table 2

Time Point (i)	Time (h)	Amount Dissolved (%)
1	1	20–45
2	2	40–70
3	5	NLT 85

The percentages of the labeled amounts of minocycline ($C_{23}H_{27}N_3O_7$) dissolved at the times specified conform to [Dissolution <711>](#), [Acceptance Table 2](#).

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

Protect solutions containing minocycline from light.

Medium: 0.1 N [hydrochloric acid](#); 900 mL

Apparatus 1: 100 rpm

Times: 1, 2, and 4 h

Standard solution: 0.0225 mg/mL of minocycline from [USP Minocycline Hydrochloride RS](#) in *Medium*

Sample solution: At the times specified, withdraw 10 mL of the solution under test and replace with 10 mL of *Medium*. Pass through a suitable filter. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 348 nm

Cell: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Autozero the instrument using the *Blank*.

Calculate the concentration (C_i) of minocycline ($C_{23}H_{27}N_3O_7$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result} = (A_U/A_S) \times C_S \times D \times P \times F$$

A_U = absorbance of the *Sample solution* at time point i

A_S = absorbance of the *Standard solution*

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

D = dilution factor (mL/mL)

P = potency of minocycline in [USP Minocycline Hydrochloride RS](#) (μg/mg)

F = conversion factor, 0.001 mg/μg

Calculate the percentage of the labeled amount (Q_i) of minocycline ($C_{23}H_{27}N_3O_7$) dissolved at each time point (i):

$$\text{Result}_1 = C_i \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of minocycline in the portion of sample withdrawn at the specified time point (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See [Table 3](#).

Table 3

Time Point (i)	Time (h)	Amount Dissolved (%)	
		45 mg/Tablet	90 mg/Tablet and 135 mg/Tablet
1	1	40–60	40–60
2	2	70–95	70–90
3	4	NLT 85	NLT 85

The percentages of the labeled amounts of minocycline ($C_{23}H_{27}N_3O_7$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

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

Protect solutions containing minocycline from light.

Medium: 0.1 N [hydrochloric acid](#); 900 mL

Apparatus 1: 100 rpm

Times: 0.5, 1.5, and 4 h

Standard solution: 0.021 mg/mL of minocycline from [USP Minocycline Hydrochloride RS](#) in *Medium*

Sample solution: At the times specified, withdraw 10 mL of the solution under test and replace with 10 mL of *Medium*. Pass through a suitable filter. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 265 nm

Cell: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Autozero the instrument using the *Blank*.

Calculate the concentration (C_i) of minocycline ($C_{23}H_{27}N_3O_7$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result} = (A_U/A_S) \times C_S \times D \times P \times F$$

A_U = absorbance of the *Sample solution* at time point i

A_S = absorbance of the *Standard solution*

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

D = dilution factor (mL/mL)

P = potency of minocycline in [USP Minocycline Hydrochloride RS](#) (μg/mg)

F = conversion factor, 0.001 mg/μg

Calculate the percentage of the labeled amount (Q_i) of minocycline ($C_{23}H_{27}N_3O_7$) dissolved at each time point (i):

$$\text{Result}_1 = C_i \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of minocycline in the portion of sample withdrawn at the specified time point (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point and replaced with *Medium* (mL)

Tolerances: See [Table 4](#).

Table 4