Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-6029F4B0-06AF-4AA4-A274-D77B6E2A4298_2_en-US
DOI: https://doi.org/10.31003/USPNF_M2753_02_01
DOI Ref: wsw9c

Minocycline Periodontal System

DEFINITION

Minocycline Periodontal System is an extended-release formulation of Minocycline Hydrochloride containing the equivalent of NLT 90.0% and NMT 120.0% of the labeled amount of minocycline ($C_{23}H_{27}N_3O_7$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**▲ (CN 1-May-2020)

Wavelength range: 250–450 nm

Standard stock solution: Transfer USP Minocycline Hydrochloride RS to a suitable volumetric flask. Dissolve first in dimethylformamide, using about 20% of the final volume, then dilute with water to volume, and mix to obtain a solution having a known concentration of about 0.48 mg/mL of minocycline.

Standard solution: 0.024 mg/mL minocycline hydrochloride from *Standard stock solution* in water

Sample stock solution: Transfer Minocycline Periodontal System equivalent to 12 mg of minocycline hydrochloride to a 25-mL volumetric flask. Add 5.0 mL of dimethylformamide, and mix to dissolve. Dilute with water to volume and filter.

Sample solution: 0.024 mg/mL minocycline hydrochloride from *Sample stock solution* in water

Acceptance criteria: The *Sample solution* exhibits maxima at the same wavelengths as the *Standard solution*, concomitantly measured.

• **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**

Mobile phase: Dimethylformamide, 0.2 M ammonium oxalate, and 0.1 M edetate disodium (25:55:20), adjusted with 0.4 M aqueous tetrabutylammonium hydroxide solution to a pH of 6.3 ± 0.2

Diluent: Dimethylformamide and methanol (1:1)

System suitability solution: Prepare a solution in water containing 2 mg/mL USP Minocycline Hydrochloride RS. Heat over a steam bath for 60 min. To one part of this solution add four parts of *Mobile phase* and mix. Refrigerate the solution immediately after preparation and during analysis, using a refrigerated autosampler.

Standard solution: 0.4 mg/mL of minocycline from USP Minocycline Hydrochloride RS in *Diluent*. Refrigerate the solution immediately after preparation and during analysis, using a refrigerated autosampler. [Note—Use low-actinic glassware.]

Sample solution: Mix the contents of NLT 10 dispensing units of Minocycline Periodontal System. Transfer a portion of the mixture, equivalent to 10 mg of minocycline, into a 25-mL volumetric flask. Add *Diluent* and sonicate for 2–5 min, or until the sample is dissolved. Dilute with *Diluent* to volume, and mix to obtain a solution having a nominal concentration of 0.4 mg/mL of minocycline, based on the label claim. Refrigerate the solution immediately after preparation and during analysis, using a refrigerated autosampler. [Note—Use low-actinic glassware.]

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Guard column: 4.6-mm × 3-cm; 10-µm packing L7

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

Flow rate: 2 mL/min

Autosampler temperature: 5°

Injection size: 10 µL

System suitability

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

[Note—The relative retention times of epiminocycline and minocycline are 0.81 and 1, respectively.]

Suitability requirements

Resolution: NLT 2.0 between epiminocycline and minocycline, *System suitability solution*

Tailing factor: NMT 2.0 for the minocycline peak, *System suitability solution*

Relative standard deviation: NMT 2.0% for the minocycline peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of minocycline ($C_{23}H_{27}N_3O_7$) in the portion of the Minocycline Periodontal System taken:

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

r_U = peak response of minocycline from the *Sample solution*

r_S = peak response of minocycline 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 (µg/mg)

F = conversion factor, 0.001 mg/µg

Acceptance criteria: 90.0%–120.0%

PERFORMANCE TESTS

• **Dissolution**

Medium: 6.9 g/L of monobasic sodium phosphate monohydrate in water, adjusted with phosphoric acid to a pH of 4.2. This solution is stable for 10 days.

Apparatus: Tube rotator. [Note—Suitable equipment is available as Labquake® tube rotator, catalog number 400110.]

0.1 M Edetate disodium: 37.2 g/L of edetate disodium in water

0.2 M Ammonium oxalate: 28.4 g/L of ammonium oxalate in water

Mobile phase: Mix 310 mL of *0.1 M Edetate disodium* and 500 mL of *0.2 M Ammonium oxalate*, adjust with 0.4 M aqueous tetrabutylammonium hydroxide to a pH of 6.2, and add 175 mL of dimethylformamide. The injector wash solution is a mixture of dimethylformamide and water (25:75).

Standard stock solution: 0.11 mg/mL of USP Minocycline Hydrochloride RS in *Medium*

Standard solutions: Dilute the *Standard stock solution* with *Medium* to obtain solutions with final concentrations of 0.088 mg/mL, 0.0528 mg/mL, 0.0352 mg/mL, 0.022 mg/mL, and 0.0176 mg/mL.

System suitability solution: Transfer 10 mg of USP Minocycline Hydrochloride RS to a 50-mL beaker. Add 5 mL of water and heat on a steam bath for 60 min. Add 20 mL of *Medium* or *Mobile phase*, and mix well. Store at 5°.

Sample solution: Use borosilicate glass tubes, 25 mm outside diameter and 15 cm long. Close the tubes with a snap type cell with a Teflon prong consisting of a Teflon closure and holder that snap together, two 25-µm stainless steel screens, two silicone gaskets, and a Teflon spacer (see *Figure 1*). Prepare six tubes as follows: partially assemble a release tube and tare its weight; dispense one dose of Minocycline Periodontal System into a partially assembled release cell (see *Figure 1*); record the sample weight in mg; assemble the cell so that the sample is enclosed between the two 25-µm screens; close the cells and place each one of them into separate glass tubes containing 10 mL of *Medium* previously equilibrated at 37°; add the Teflon prong, and cap the tube with Teflon faced rubber-lined caps; seal with Teflon tape. Place the tubes in the tube rotator. Place the tube rotator in a convection incubator that is maintained at 37°. Allow the tubes to rotate for 4 h. Remove the solution under test, and add 10 mL of *Medium* previously equilibrated at 37°. Replace the tubes in the apparatus and rotate

for 20 h (24 h total). Repeat the sampling procedure after 24 h (48 h total), and after another 24 h (72 h total).

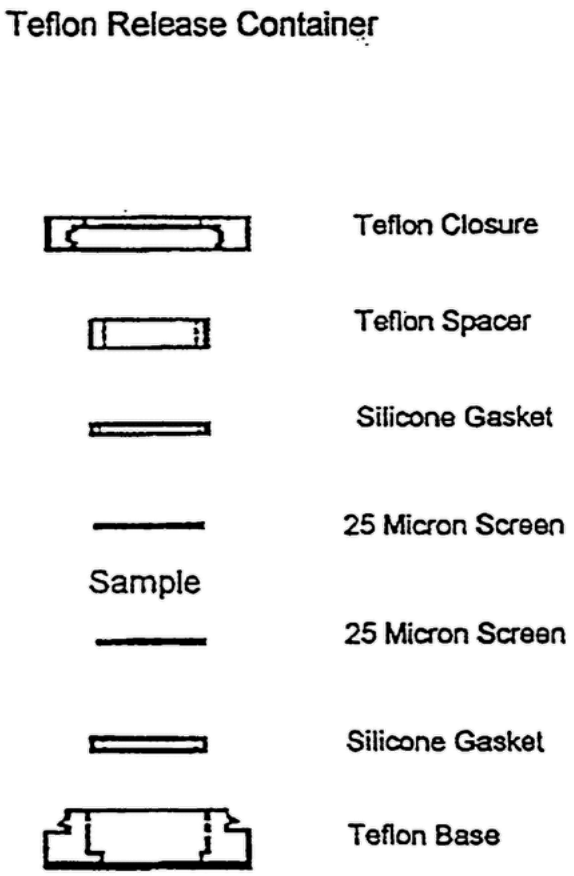

Figure 1. Sample Extraction Configuration

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Guard column: 4.6-mm × 3-cm; 10-µm packing L7

Column: 4.6-mm × 3.3-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Autosampler temperature: 5°

Injection size: 20 µL for the 4 and 24 h time points; 50 µL for the 48 and 72 h time points

Suitability requirements

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

Resolution: NLT 2.0 between epiminocycline and minocycline. Inject 20 µL of the *System suitability solution*.

Tailing factor: NMT 2.0. Inject 20 µL of the *System suitability solution*.

Relative standard deviation: NMT 2.0% for the minocycline peak, any of the *Standard solutions*

Analysis: Construct a calibration curve for each sampling interval by plotting the concentration of the *Standard solutions* versus peak area.

Calculate the slopes and y-intercepts using linear regression analysis.

Calculate the release rate of minocycline:

$$\text{Result}_i = [(r_{Ui} - y_i)/S_i] \times 10/(i \times W \times A)$$

i = sampling time, 4, 24, 48, 72 h

r_{Ui} = peak response from each of the *Standard solutions* at time i

y_i = y-intercept of the calibration curve at sampling time i

S_i = slope of the calibration curve at sampling time i

W = weight of the sample (mg)

A = amount of minocycline in the sample (mg/mg of sample) as determined in the *Assay*

Tolerances

Time (h)	Release Rate (µg/h) Average of 6 Measurements
0–4	NLT 25
4–24	NLT 1.0
24–48	NLT 0.2
48–72	NLT 0.05

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

IMPURITIES

Organic Impurities

• **Procedure**

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

Analysis

Sample: *Sample solution*

Calculate the percentage of each related compound in the portion of Minocycline Periodontal System taken:

$$\text{Result} = (r_U/r_T) \times 100$$

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

r_T = sum of the peak responses from the *Sample solution*. [Note—Exclude peaks eluting in the solvent front.]

Acceptance criteria

Individual impurities: NMT 6.0% of epiminocycline

Total impurities (excluding epiminocycline): NMT 3.5%

SPECIFIC TESTS

• **Water Determination, *Method I* ⟨921⟩:** NMT 5.0%

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Organisms ⟨62⟩:** The total aerobic microbial count does not exceed 1000 cfu/g; the total combined molds and yeasts count does not exceed 100 cfu/g; and the product meets the requirements of the test for the absence of *Escherichia coli*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in a tight, light-resistant container. Store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Minocycline Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
MINOCYCLINE PERIODONTAL SYSTEM	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 36(2)

Current DocID: GUID-6029F4B0-06AF-4AA4-A274-D77B6E2A4298_2_en-US

DOI: https://doi.org/10.31003/USPNF_M2753_02_01

DOI ref: wsw9c