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).

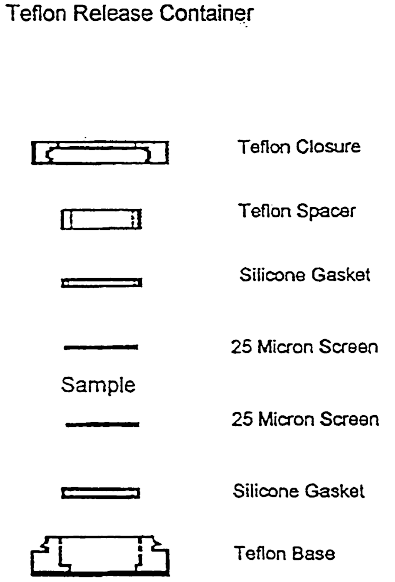


Figure 1. Sample Extraction Configuration

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:

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

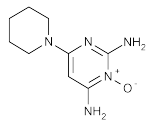
r_U = peak response of each impurity from the *Sample solution*
r_T = sum of the peak responses from the *Sample solution*. [Note—Exclude peaks eluting in the solvent front.]

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

Minoxidil



$C_9H_{15}N_5O$ 209.25

2,4-Pyrimidinediamine, 6-(1-piperidinyl)-, 3-oxide;
2,4-Diamino-6-piperidinopyrimidine 3-oxide [38304-91-5].

DEFINITION
Minoxidil contains NLT 97.0% and NMT 103.0% of minoxidil ($C_9H_{15}N_5O$), calculated on the dried basis.

IDENTIFICATION
• **A. Infrared Absorption ⟨197M⟩:** Do not dry specimens.

ASSAY
• **Procedure**
Mobile phase: Methanol, glacial acetic acid, and water (700:10:300). Add 3.0 g/L of docusate sodium. Adjust with perchloric acid to a pH of 3.0.
Internal standard solution: 0.2 mg/mL of medroxyprogesterone acetate in *Mobile phase*
Standard solution: 0.25 mg/mL of USP Minoxidil RS in *Internal standard solution*
Sample solution: 0.25 mg/mL of Minoxidil in *Internal standard solution*
Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: 4-mm × 25-cm; packing L1
Flow rate: 1 mL/min
Injection volume: 10 µL
System suitability
Sample: *Standard solution*
[NOTE—The relative retention times for the internal standard and minoxidil are 0.8 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 2.0 between the internal standard and minoxidil
Relative standard deviation: NMT 2.0% from NLT four replicate injections
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of minoxidil ($C_9H_{15}N_5O$) in the portion of Minoxidil taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of minoxidil to the internal standard from the *Sample solution*
R_S = peak response ratio of minoxidil to the internal standard from the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
C_U = concentration of the *Sample solution* (mg/mL)
Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES
• **Residue on Ignition ⟨281⟩:** NMT 0.5%

Delete the following:

•• **Heavy Metals,** *Method II* **⟨231⟩:** NMT 20 ppm• (Official 1-Jan-2018)
• **Organic Impurities**
Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.
Sample solution: 0.25 mg/mL of Minoxidil in *Mobile phase*
Analysis
Sample: *Sample solution*
Calculate the total percentage of impurities in the portion of Minoxidil taken:

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

r_U = sum of the peak responses of all impurities from the *Sample solution*
r_T = sum of all the peak responses from the *Sample solution*
Acceptance criteria: NMT 1.5%

SPECIFIC TESTS
• **Loss on Drying ⟨731⟩**
Analysis: Dry a sample at 50° and at a pressure not exceeding 5 mm of mercury for 3 h.
Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS
• **Packaging and Storage:** Preserve in well-closed containers.
• **USP Reference Standards ⟨11⟩**
USP Minoxidil RS

Minoxidil Tablets

DEFINITION
Minoxidil Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of minoxidil ($C_9H_{15}N_5O$).

IDENTIFICATION
• **Infrared Absorption**
Sample: Transfer a portion of finely powdered Tablets, equivalent to 10 mg of minoxidil, to a separator. Add 25 mL of water, and extract with three 15-mL portions of chloroform. Combine the chloroform extracts, and evaporate with the aid of a stream of nitrogen. Wash the inside of the container with 5 mL of alcohol, add 300 mg of potassium bromide, and evaporate under vacuum at 50° until dry.
Acceptance criteria: The IR absorption spectrum of the potassium bromide dispersion prepared from the *Sample* exhibits maxima at the same wavelengths as that of a similar preparation of USP Minoxidil RS.

ASSAY
• **Procedure**
Mobile phase: Methanol, glacial acetic acid, and water (70:1:30). Add 3.0 g/L of docusate sodium, and adjust with perchloric acid to a pH of 3.0.
Internal standard solution: 0.2 mg/mL of medroxyprogesterone acetate in *Mobile phase*
Standard solution: 0.25 mg/mL of USP Minoxidil RS in *Internal standard solution*
Sample solution: Nominally 0.25 mg/mL of minoxidil in *Internal standard solution*, prepared as follows. Dissolve the equivalent to 5 mg of minoxidil, from powdered Tablets (NLT 10), in 20.0 mL of *Internal standard solution*, and shake for 5 min.
Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: 4-mm × 25-cm; packing L1
Flow rate: 1 mL/min
Injection volume: 10 µL
System suitability
Sample: *Standard solution*
[NOTE—The relative retention times for the internal standard and minoxidil are 0.8 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 2.0 between the internal standard and minoxidil peaks
Relative standard deviation: NMT 2.0% from NLT four replicate injections