

Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Jul-2022
Document Type: USP Monographs
DocId: GUID-794186AC-B34B-4349-820B-3A0D47917416_6_en-US
DOI: https://doi.org/10.31003/USPNF_M28350_06_01
DOI Ref: 9jw8s

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Doxycycline Hyclate Capsules

DEFINITION

Doxycycline Hyclate Capsules contain the equivalent of NLT 90.0% and NMT 120.0% of the labeled amount of doxycycline (C₂₂H₂₄N₂O₈).

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. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy: 197A](#)**
Standard solution: Transfer about 25 mg of [USP Doxycycline Hyclate RS](#) to a suitable flask. Add 25 mL of [acetonitrile](#) and mix for approximately 5 min with a magnetic stir bar. Pass the solution through a suitable filter, and remove the solvent by natural evaporation or by using a rotary evaporator under vacuum.
Sample solution: Transfer the contents of NLT 10 Capsules, equivalent to 25 mg of doxycycline hyclate, to a suitable flask. Add 25 mL of [acetonitrile](#) and mix for approximately 5 min with a magnetic stir bar. Pass the solution through a suitable filter, and remove the solvent by natural evaporation or by using a rotary evaporator under vacuum.
Analysis: Examine the spectra of the *Standard solution* and the *Sample solution* in the range between 2000 and 650 cm⁻¹.
Acceptance criteria: The *Sample solution* exhibits bands at about 1663, 1611, 1576, 1453, 1213, 1037, 1002, 935, and 659 cm⁻¹, similar to the *Standard solution*.

ASSAY

- PROCEDURE**
Protect solutions containing doxycycline from light.
Solution A: Transfer 3.1 g of [monobasic potassium phosphate](#), 0.5 g of [edetate disodium](#), and 0.5 mL of [triethylamine](#) to a 1000-mL volumetric flask. Add about 850 mL of water and mix. Dilute with water to volume and adjust with [1 N sodium hydroxide VS](#) to a pH of 8.5 ± 0.2.
Solution B: Methanol
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	90	10
2.0	90	10
4.0	60	40
6.0	90	10
9.0	90	10

Diluent: 0.01 N hydrochloric acid
System suitability stock solution 1: 1 mg/mL each of [USP Doxycycline Related Compound A RS](#) and [USP Methacycline Hydrochloride RS](#) in *Diluent*
System suitability stock solution 2: 1.2 mg/mL of [USP Doxycycline Hyclate RS](#) in *Diluent*
System suitability solution: Transfer 5 mL of *System suitability stock solution 2* to a 25-mL volumetric flask, heat on a steam bath for 60 min, and evaporate to dryness on a hot plate, taking care not to char the residue. Dissolve the residue in *Diluent*, add 0.5 mL of *System suitability stock solution 1*, and dilute with *Diluent* to volume. Pass the solution through a suitable filter and use the filtrate.
This solution contains a mixture of 4-epidoxycycline, doxycycline related compound A, methacycline, and doxycycline. When stored in a refrigerator, this solution may be used for 14 days.
Standard solution: 0.3 mg/mL of [USP Doxycycline Hyclate RS](#) in *Diluent*. Sonicate as needed to dissolve.

Sample solution: Nominally 0.25 mg/mL of doxycycline in *Diluent*, prepared as follows. Empty as completely as possible the contents of NLT 20 Capsules. Mix the combined contents and transfer a suitable portion of the powder to a suitable volumetric flask. Add 75% of the final volume of *Diluent*, sonicate for about 5 min, shake for about 15 min, and dilute with *Diluent* to volume. Pass a portion of this solution through a suitable filter of 0.2-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 350 nm

Column: 2.1-mm × 5-cm; 1.7-µm packing [L7](#). [NOTE—A 1.7-µm guard column with packing [L7](#) was used during method validation.]

Column temperature: 60°

Flow rate: 0.6 mL/min

Injection volume: 5 µL

System suitability

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

[NOTE—See [Table 2](#) for relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between methacycline and 4-epidoxycycline; NLT 1.5 between 4-epidoxycycline and doxycycline related compound A; NLT 1.5 between doxycycline related compound A and doxycycline, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) in the portion of Capsules 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 Doxycycline Hyclate RS](#) in the *Standard solution* (mg/mL)

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

P = potency of doxycycline in [USP Doxycycline Hyclate RS](#) (µg/mg)

F = conversion factor, 0.001 mg/µg

Acceptance criteria: 90.0%–120.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Medium: Water; 900 mL

Apparatus 2: 75 rpm, the distance between the blade and the inside bottom of the vessel being maintained at 4.5 ± 0.5 cm during the test

Time: 30 min

Standard solution: [USP Doxycycline Hyclate RS](#) in *Medium*

Sample solution: Dilute with *Medium* to a concentration that is similar to the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 276 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage (Q) of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL