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Doxycycline Hyclate Delayed-Release Tablets

DEFINITION

Doxycycline Hyclate Delayed-Release Tablets contain an amount of Doxycycline Hyclate equivalent to NLT 90.0% and NMT 120.0% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$).

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 spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

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](#) to a pH of 8.5 ± 0.1 . Pass through a suitable filter of 0.22- μ m pore size.

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](#)

Standard solution: 0.12 mg/mL of [USP Doxycycline Hyclate RS](#) in *Diluent*. Sonicate as needed to dissolve.

Sample solution: Nominally 0.1 mg/mL of doxycycline from NLT 20 Tablets prepared as follows. Transfer a suitable portion of finely powdered Tablets to a suitable volumetric flask. Add 80% of the final volume of *Diluent*, sonicate for about 15 min, shake for about 15 min, and dilute with *Diluent* to volume. Pass through a suitable filter of 0.2- μ m pore size and use the filtrate for analysis.

Chromatographic system

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

Mode: LC

Detector: UV 270 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

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

Column temperature: 60°

Flow rate: 0.6 mL/min

Injection volume: 5 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

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 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 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 \(711\)](#)

Protect solutions containing doxycycline from light.

Test 1: Proceed as directed for [Dissolution \(711\), Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B Procedure](#).

Acid stage

Medium: 0.06 N hydrochloric acid; 900 mL, degassed with helium

Apparatus 1: 50 rpm

Time: 20 min

Standard solution: 0.128 mg/mL of [USP Doxycycline Hyclate RS](#) in *Medium*. Calculate the concentration, C_S , in mg/mL, of doxycycline using the designated potency, in µg/mg, of doxycycline in [USP Doxycycline Hyclate RS](#). [NOTE—Sonicate if necessary to dissolve.]

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

Detector: UV 346 nm

Cell: 0.1-cm quartz

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage 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/Tablet)

V = volume of *Medium*, 900 mL

Tolerances

Level 1 (6 Tablets tested): No individual value is more than 30% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) dissolved in 20 min.

Level 2 (6 Tablets tested): NMT 2 individual values of the 12 tested are greater than 30% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) in 20 min.

Buffer stage

Conduct this stage of testing on separate Tablets, selecting those that were not previously subjected to the *Acid stage* testing.

Medium: pH 5.5 neutralized phthalate buffer (see [Reagents, Indicators, and Solutions—Solutions, Buffer Solutions](#)); 900 mL, degassed

Apparatus 1: 50 rpm

Time: 30 min

Standard solution: 0.128 mg/mL of [USP Doxycycline Hyclate RS](#) in *Medium*. Calculate the concentration, C_S , in mg/mL, of doxycycline using the designated potency, in µg/mg, of doxycycline in [USP Doxycycline Hyclate RS](#). [NOTE—Sonicate if necessary to dissolve.]

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

Analysis: Determine the percentage of doxycycline ($C_{22}H_{24}N_2O_8$) dissolved by the procedure described for the *Acid stage*.

Tolerances: NLT 85% (Q) of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*. Proceed as directed for [Dissolution \(711\), Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B Procedure](#).

Acid stage

Medium, Apparatus 1, Time, Blank, and Analysis: Proceed as directed for *Acid stage* in *Test 1*.

Standard solution: ($L/900$) mg/mL of [USP Doxycycline Hyclate RS](#) in *Medium*. Calculate the concentration, C_s , in mg/mL, of doxycycline using the designated potency, in $\mu\text{g}/\text{mg}$, of doxycycline in [USP Doxycycline Hyclate RS](#). Sonicate if necessary to dissolve.

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

Detector: UV 345 nm

Cell: See [Table 2](#).

Table 2

Tablet Strength (mg/Tablet)	Cell Size (cm)
75	0.5
100	0.5
150	0.2

Tolerances

Level 1 (6 Tablets tested): No individual value is more than 50% of the labeled amount of doxycycline ($\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_8$) dissolved in 20 min.

Level 2 (6 Tablets tested): NMT 2 individual values of the 12 tested are greater than 50% of the labeled amount of doxycycline ($\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_8$) in 20 min.

Buffer stage

Conduct this stage of testing on separate Tablets, selecting those that were not previously subjected to the *Acid stage* testing.

Medium: pH 5.5 neutralized phthalate buffer (see [Reagents, Indicators, and Solutions—Solutions, Buffer Solutions](#)); 1000 mL, degassed

Apparatus 1 and Analysis: Proceed as directed for *Buffer stage* in *Test 1*.

Time: 45 min

Standard solution: ($L/1000$) mg/mL of [USP Doxycycline Hyclate RS](#) in *Medium*. Calculate the concentration, C_s , in mg/mL, of doxycycline using the designated potency, in $\mu\text{g}/\text{mg}$, of doxycycline in [USP Doxycycline Hyclate RS](#). Sonicate if necessary to dissolve.

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

Detector and Cell: Proceed as directed for *Acid stage* in *Test 2*.

Tolerances: NLT 70% (Q) of the labeled amount of doxycycline ($\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_8$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 3*. Proceed as directed for [Dissolution \(711\), Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B Procedure](#).

Acid stage

Apparatus 1 and Time: Proceed as directed for *Acid stage* in *Test 1*.

Medium: 0.06 N hydrochloric acid; 900 mL

Standard solution: Prepare the solutions from [USP Doxycycline Hyclate RS](#) in *Medium* as directed in [Table 3](#). Calculate the concentration, C_s , in mg/mL, of doxycycline using the designated potency, in $\mu\text{g}/\text{mg}$, of doxycycline in [USP Doxycycline Hyclate RS](#).

Table 3

Tablet Strength (mg/Tablet)	Concentration of Doxycycline (mg/mL)
75	0.1
100	0.1
150	0.17

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

Detector: UV 345 nm

Cell: 0.2 cm

Blank: *Medium*

Analysis

Samples: *Standard solution and Sample solution*