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Doxycycline for Oral Suspension

DEFINITION

Doxycycline for Oral Suspension contains the equivalent of NLT 90.0% and NMT 125.0% of the labeled amount of doxycycline ($C_{22}H_{24}N_2O_8$) when constituted as directed. It contains one or more suitable buffers, colors, diluents, flavors, and preservatives.

IDENTIFICATION

Change to read:

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197A

Standard: Transfer about 25 mg of [USP Doxycycline Monohydrate RS](#) to a suitable flask. Add 25 mL of [acetonitrile](#) and mix for approximately 10 min with a magnetic stir bar. Pass through suitable filter paper (Whatman #40 or equivalent), and remove the solvent by natural evaporation.

Sample: Place an amount of Doxycycline for Oral Suspension, nominally equivalent to about 25 mg of doxycycline, in a suitable flask. Add 25 mL of [acetonitrile](#) and mix for approximately 10 min with a magnetic stir bar. Pass through suitable filter paper (Whatman #40 or equivalent), and remove the solvent by natural evaporation.

Analysis: Examine the spectra of the *Standard* and the *Sample* in the range between 2000 and 650 cm^{-1} .

Acceptance criteria: The *Sample* exhibits bands at about 1644, 1577, 1518, 1452, 1396, 1167, 995, and 952 cm^{-1} , similar to the *Standard*.

▲[NOTE—Peak positions may vary slightly (within $\pm 10\text{ cm}^{-1}$). Other peaks may be present in the spectra that do not appear in this list.]▲ (USP 1-Aug-2023)

- **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

Change to read:

• **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 ± 0.2 .

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](#)

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. Constitute Doxycycline for Oral Suspension as directed in the labeling. Transfer an accurately measured portion of the constituted suspension, freshly mixed and free from air bubbles, equivalent to about 25 mg of doxycycline, to a suitable volumetric flask. Add 50% of the final volume of *Diluent*, shake by mechanical means 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**
 - Sample:** *Standard solution*
 - Suitability requirements**
 - Tailing factor:** NMT 1.5
 - Relative standard deviation:** NMT ▲1.0%▲ (USP 1-Aug-2023)

Analysis

Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of doxycycline (C₂₂H₂₄N₂O₈) in the portion of Doxycycline for Oral Suspension taken:

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

- r_U = peak response of doxycycline from the *Sample solution*
- r_S = peak response of doxycycline 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%–125.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#).

Protect solutions containing doxycycline from light.

- Medium:** [0.01 N hydrochloric acid](#); 900 mL
- Apparatus 2:** 25 rpm
- Time:** 10 min
- Solution A:** Transfer 1.36 g of [monobasic potassium phosphate](#), 0.37 g of [sodium hydroxide](#), 0.25 g of [tetrabutylammonium hydrogen sulfate](#), and 0.2 g of [edetate disodium](#) to a 1000-mL volumetric flask. Add about 850 mL of [water](#) and mix. Add 75 g of [tert-butyl alcohol](#) and dilute with [water](#) to volume. Adjust with [1 N sodium hydroxide](#) or [5 N hydrochloric acid](#) to a pH of 8.0 ± 0.05.
- Solution B:** [Acetonitrile](#) and [water](#) (80:20)
- Mobile phase:** See [Table 2](#).

Table 2

Time (min)	Solution A (%)	Solution B (%)
0.0	100	0
13.0	100	0
15.0	20	80
21.0	20	80
▲23.0	100	0
30.0	100	0▲ (USP 1-Aug-2023)

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Standard solution: 32 μg/mL of [USP Doxycycline Hyclate RS](#) in *Medium*