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Metronidazole Tablets

DEFINITION

Metronidazole Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of metronidazole ($C_6H_9N_3O_3$).

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*: 197U**

Sample stock solution: Equivalent to 15 mg/mL of metronidazole from powdered Tablets in dilute hydrochloric acid (1 in 100). Shake for several min, and filter.

Medium: Sulfuric acid in methanol (1 in 350)

Sample solution: 20 µg/mL of metronidazole in *Medium* from the *Sample stock solution*

Acceptance criteria: Meet the requirements

• **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: Methanol and water (20:80)

Standard solution: 0.5 mg/mL of USP Metronidazole RS in *Mobile phase*

Sample stock solution: Nominally 10 mg/mL of metronidazole in methanol from Tablets prepared as follows. Transfer 10 Tablets, whole or ground, to a suitable size volumetric flask. Add methanol, and shake by mechanical means for 30 min or until the Tablets are disintegrated. Dilute with methanol to volume, and allow the solution to stand until the insoluble material has settled.

Sample solution: Nominally 0.5 mg/mL of metronidazole in *Mobile phase* prepared from the clear supernatant of the *Sample stock solution*. Filter.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; packing L7

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of metronidazole ($C_6H_9N_3O_3$) in the portion of Tablets taken:

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

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

r_S = peak response of metronidazole from the *Standard solution*

C_S = concentration of USP Metronidazole RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 1: 100 rpm

Time: 60 min

Standard solution: USP Metronidazole RS in *Medium*

Sample solution: Filter a portion of the solution under test, and dilute with *Medium* to a concentration similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 278 nm

Blank: *Medium*

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Calculate the percentage of the labeled amount of metronidazole ($C_6H_9N_3O_3$) dissolved.

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times D \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Metronidazole RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

D = dilution factor to prepare the *Sample solution*

Tolerances: NLT 85% (Q) of the labeled amount of metronidazole ($C_6H_9N_3O_3$) is dissolved.

Change to read:

• **Uniformity of Dosage Units ⟨905⟩:** ▲Meet the requirements▲ (CN 1-Aug-2023)

Procedure for content uniformity

Diluent: Diluted hydrochloric acid (1 in 100)

Standard solution: 20 µg/mL of USP Metronidazole RS in *Diluent*

Sample stock solution: Transfer 1 Tablet to a 250-mL volumetric flask. Add about 100 mL of *Diluent*, and shake for 30 min. Dilute with *Diluent* to volume. Filter, discarding the first 15 mL of the filtrate. Nominally 200 µg/mL of metronidazole is prepared by transferring the filtrate quantitatively with the *Diluent*.

Sample solution: 20 µg/mL of metronidazole in *Diluent* from *Sample stock solution*

Instrumental conditions

Mode: UV

Analytical wavelength: 278 nm

Cell: 1 cm

Blank: *Diluent*

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Calculate the quantity, in mg, of metronidazole ($C_6H_9N_3O_3$) in each Tablet taken:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of USP Metronidazole RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of metronidazole in the *Sample solution* (µg/mL)

L = label claim (mg/Tablet)

▲▲ (CN 1-Aug-2023)

IMPURITIES

• **Organic Impurities**

Mobile phase: Methanol and water (20:80)

Standard solution: 0.5 µg/mL of USP Metronidazole RS and 2.5 µg/mL of USP Tinidazole Related Compound A RS in *Mobile phase*

Sample solution: Nominally 500 µg/mL of metronidazole prepared as follows. Transfer a suitable amount of powdered Tablets (NLT 20) to a suitable volumetric flask. Add *Mobile phase* equivalent to 80% of the flask size. Sonicate for 10 min. Dilute with *Mobile phase* to volume, and pass a portion of the solution through a suitable filter. Use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 319 nm

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

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 30 µL

System suitability

Sample: *Standard solution*

[NOTE—See *Table 1* for relative retention times.]

Suitability requirements

Resolution: NLT 4.0 between metronidazole and tinidazole related compound A

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of tinidazole related compound A in the portion of Tablets taken:

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

r_U = peak response of tinidazole related compound A from the *Sample solution*

r_S = peak response of tinidazole related compound A from the *Standard solution*

C_S = concentration of USP Tinidazole Related Compound A RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of metronidazole in the *Sample solution* (µg/mL)

Calculate the percentage of each impurity in the portion of Tablets taken:

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

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

r_S = peak response of metronidazole from the *Standard solution*

C_S = concentration of USP Metronidazole RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of metronidazole in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tinidazole related compound A	0.7	0.5
Metronidazole	1.0	—
Any individual unspecified degradation product	—	0.10
Total impurities	—	2.0

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed, light-resistant containers. Store at controlled room temperature.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Metronidazole RS

USP Tinidazole Related Compound A RS

2-Methyl-5-nitroimidazole.

$C_4H_5N_3O_2$ 127.10

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

Topic/Question	Contact	Expert Committee
METRONIDAZOLE TABLETS	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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