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Metronidazole Capsules

DEFINITION

Metronidazole Capsules 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⟩, *Infrared Spectroscopy*: 197K**

Wavelength range: Between 1600 and 1000 cm^{-1}

Acceptance criteria: Capsule contents show maxima only at the same wavelengths as those of similarly prepared USP Metronidazole RS.

• **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 (1:4)

Standard solution: 0.03 mg/mL of USP Metronidazole RS in *Mobile phase*

Sample stock solution: Nominally 1 mg/mL of metronidazole prepared as follows. Mix the contents of Capsules (NLT 20). Transfer an amount equivalent to 100 mg of metronidazole to a 100-mL volumetric flask, add 80 mL of *Mobile phase*, and sonicate with intermittent shaking for 10 min. Shake for 30 min, and dilute with *Mobile phase* to volume. Centrifuge a portion of the solution.

Sample solution: 0.03 mg/mL of metronidazole in *Mobile phase*, from the *Sample stock solution*. Pass a portion of the solution through a nylon membrane filter of 0.45-µm or finer pore size. Discard the first 10 mL of the filtrate, and use the remainder.

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

Run time: 2 times the retention time of the metronidazole peak

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0% for five replicate injections

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 Capsules taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response 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: 30 min

Standard solution: 0.4 mg/mL of USP Metronidazole RS in *Medium*. Sonicate to dissolve if necessary.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, and discard the first few mL.

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum at about 278 nm

Cell: 0.05 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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)

L = label claim (mg/Capsule)

V = volume of *Medium*, 900 mL

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

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

Change to read:

• **Organic Impurities**

▲**Mobile phase** and **Chromatographic system:**▲ (ERR 1-Jun-2024) Proceed as directed in the *Assay*.

Standard solution: 1 µg/mL of metronidazole from USP Metronidazole RS and 2 µg/mL of tinidazole related compound A from USP Tinidazole Related Compound A RS in *Mobile phase*

▲**Sample solution:** Nominally 1 mg/mL of metronidazole prepared as follows. Mix the contents of Capsules (NLT 20). Transfer an amount equivalent to 100 mg of metronidazole to a 100-mL volumetric flask, add 80 mL of *Mobile phase*, and sonicate with intermittent shaking for 10 min. Shake for 30 min, and dilute with *Mobile phase* to volume. Centrifuge a portion of the solution.▲ (ERR 1-Jun-2024)

System suitability

Sample: *Standard solution*

[Note—The relative retention times for tinidazole related compound A and metronidazole are 0.75 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between tinidazole related compound A and metronidazole

Tailing factor: NMT 2.0 for metronidazole

Relative standard deviation: NMT 6.0% for both tinidazole related compound A and metronidazole

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of tinidazole related compound A in the portion of Capsules 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* (mg/mL)

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

Calculate the percentage of any unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of any unspecified degradation product 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: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tinidazole related compound A	0.75	0.1
Metronidazole	1.0	—
Each unspecified degradation product	—	0.1
Total impurities	—	0.5

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed, light-resistant containers, and 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 CAPSULES	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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