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Fluconazole Tablets

DEFINITION
Fluconazole Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$).

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 absorption spectrum of the major peak of the *Sample solution* exhibits maxima and minima at the same wavelengths as those of the corresponding peak of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **Procedure**

Buffer: 2.89 g of tetramethyl ammonium bromide and 0.51 g of sodium acetate trihydrate in 750 mL of water. Adjust with glacial acetic acid to a pH of 5.0. Pass through a suitable filter of 0.45-µm pore size.

Mobile phase: Acetonitrile, water, and *Buffer* (22:15:75)

Diluent: Methanol and water (30:70)

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

Sample stock solution: Nominally 2–4 mg/mL of fluconazole prepared as follows. Transfer NLT 10 Tablets to a suitable volumetric flask, add water up to 10% of the flask volume and swirl to disperse the tablets. Add an additional 60% of the flask volume of *Diluent* and sonicate for 45 min with intermittent shaking. Dilute with *Diluent* to volume. Centrifuge a suitable portion of this solution for 15 min.

Sample solution: Nominally 0.4 mg/mL of fluconazole in *Diluent* from *Sample stock solution*. Pass through a suitable filter of 0.45-µm pore size.

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

Mode: LC

Detector: UV 261 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 40 µL

Run time: NLT 1.5 times the retention time of the fluconazole peak

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS
• **Dissolution ⟨711⟩**

Test 1

Medium: Water; 500 mL (900 mL for Tablets labeled to contain more than 100 mg)

Apparatus 2: 50 rpm

Time: 45 min

Buffer: 0.01 M anhydrous sodium acetate solution. Adjust with glacial acetic acid to a pH of 5.0.

Mobile phase: Methanol, acetonitrile, and *Buffer* (20:10:70)

Standard solution: 2 mg/mL of USP Fluconazole RS in *Medium*. Sonicate the solution to facilitate dissolution, if necessary. Quantitatively dilute a portion of this solution with *Medium* to obtain a final concentration similar to the one expected in the *Sample solution*.

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

Chromatographic system

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

Mode: LC

Detector: UV 261 nm

Column: 3.9-mm × 15-cm; 4-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 1100 theoretical plates

Tailing factor: NMT 3.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$) dissolved:

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

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

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

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 or 900 mL

Tolerances: NLT 75% (*Q*) of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that it meets *Dissolution Test 2*.

Medium: Water; 900 mL (for all Tablet strengths)

Apparatus 2: 50 rpm

Time: 45 min

Mobile phase: Water and acetonitrile (4:1)

Standard stock solution: 1.1 mg/mL of USP Fluconazole RS in methanol

Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of (*L*/900) mg/mL, where *L* is the label claim in mg/Tablet.

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

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 1000 theoretical plates

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 fluconazole ($C_{13}H_{12}F_2N_6O$) dissolved:

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

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

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

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 75% (*Q*) of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$) is dissolved.

Test 3: If the product complies with this test, the labeling indicates that it meets *Dissolution Test 3*.

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Buffer: 3.9 g/L of sodium dihydrogen phosphate in water

Mobile phase: Methanol and *Buffer* (45:55). Adjust the pH of the solution to 7.0 with 0.1 N sodium hydroxide solution.

Standard stock solution: 1.0 mg/mL of USP Fluconazole RS in *Mobile phase*

Standard solution: (*L*/900) mg/mL of USP Fluconazole RS in *Medium* from the *Standard stock solution*, where *L* is the Tablet label claim in milligrams

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

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: At least 2 times the retention time of fluconazole

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of fluconazole ($C_{13}H_{12}F_2N_6O$) dissolved:

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

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

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

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

Tolerances: NLT 80% (*Q*) of the labeled amount of fluconazole is dissolved.

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

IMPURITIES

• **Organic Impurities**

Solution A: Acetonitrile and water (15:85)

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
16	100	0
50	90	10
55	100	0
65	100	0

Peak identification solution: 0.01 mg/mL of USP Fluconazole RS and 6.0 µg/mL each of USP Fluconazole Related Compound A RS, USP Fluconazole Related Compound B RS, and USP Fluconazole Related Compound C RS in *Solution A*. Sonicate, if necessary, to dissolve.

Standard solution: 0.01 mg/mL of USP Fluconazole RS in *Solution A*. Sonicate, if necessary, to dissolve.

Sample solution: Nominally 3 mg/mL of fluconazole from NLT 20 finely powdered Tablets in *Solution A*. Sonicate for 30 min with occasional swirling, prior to final dilution. Pass through a suitable filter of 0.45-µm pore size.

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 25 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 5.0% for the fluconazole peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual unspecified impurity in the portion of Tablets taken:

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

r_U = peak response of any individual unspecified impurity from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Fluconazole related compound A[a]	0.43	—
Fluconazole related compound B[a]	0.72	—
Fluconazole related compound C[a]	0.83	—
Fluconazole	1.0	—
Any individual unspecified impurity	—	0.20
Total impurities	—	1.0

[a] This is a process-related impurity, and monitored in the drug substance.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Fluconazole RS

USP Fluconazole Related Compound A RS

2-[2-Fluoro-4-(1*H*-1,2,4-triazol-1-yl)phenyl]-1,3-bis(1*H*-1,2,4-triazol-1-yl)-propan-2-ol.

$C_{15}H_{14}FN_9O$ 355.33

USP Fluconazole Related Compound B RS

2-(4-Fluorophenyl)-1,3-bis(1*H*-1,2,4-triazol-1-yl)-propan-2-ol.

▲$C_{13}H_{13}FN_6O$▲ (ERR 1-Oct-2024) 288.28

USP Fluconazole Related Compound C RS

1,1'-(1,3-Phenylene)di(1*H*-1,2,4-triazole).

$C_{10}H_8N_6$ 212.21

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

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

Chromatographic Database Information: Chromatographic Database

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