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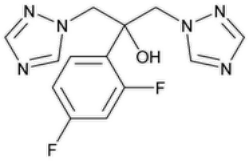
Fluconazole



$C_{13}H_{12}F_2N_6O$ 306.27

1*H*-1,2,4-Triazole-1-ethanol, 1-(2,4-difluorophenyl)-1-(1*H*-1,2,4-triazol-1-ylmethyl)-;

2,4-Difluoro-1',1'-bis(1*H*-1,2,4-triazol-1-ylmethyl)benzyl alcohol CAS RN®: 86386-73-4.

DEFINITION

Fluconazole contains NLT 98.0% and NMT 102.0% of fluconazole ($C_{13}H_{12}F_2N_6O$), calculated on the dried basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**

• **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: Acetonitrile and water (20:80)

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

Sample solution: 0.5 mg/mL of Fluconazole in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Column temperature: 40°

Flow rate: 0.5 mL/min

Injection volume: 20 µL

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 fluconazole ($C_{13}H_{12}F_2N_6O$) in the portion of Fluconazole 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 = concentration of Fluconazole in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

Change to read:

• **Organic Impurities**

Mobile phase: Acetonitrile and water (20:80)

Standard solution: 10 µg/mL each of USP Fluconazole RS, USP Fluconazole Related Compound A RS, USP Fluconazole Related Compound B RS, and USP Fluconazole Related Compound C RS, dissolved in acetonitrile, and then diluted in *Mobile phase*

Sample solution: 3 mg/mL of Fluconazole in *Mobile phase*

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: 40°

Flow rate: 0.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

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

Suitability requirements

Resolution: NLT 1.5 between fluconazole related compound B and fluconazole related compound C

Relative standard deviation: NMT 5.0% for each peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of fluconazole related compound A, fluconazole related compound B, and fluconazole related compound C in the portion of Fluconazole taken:

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

r_U = peak response of fluconazole related compound A, fluconazole related compound B, or fluconazole related compound C from the *Sample solution*

r_S = peak response of fluconazole related compound A, fluconazole related compound B, and fluconazole related compound C from the *Standard solution*

C_S = concentration of USP Fluconazole Related Compound A RS, USP Fluconazole Related Compound B RS, and USP Fluconazole Related Compound C RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any ▲other specified and▲ (ERR 1-Nov-2024) unspecified impurity in the portion of Fluconazole taken:

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

r_U = peak response of any▲other specified and unspecified▲ (ERR 1-Nov-2024) 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 = concentration of Fluconazole in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Fluconazole related compound A	0.5	0.2
Specified impurity	0.6	1.0
Fluconazole related compound B	0.81	0.1
Fluconazole related compound C	0.86	0.2
Fluconazole	1.0	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any individual unspecified impurity	—	0.1
Total unknown impurities	—	0.3
Total impurities	—	1.5

• **Residue on Ignition ⟨281⟩**

Sample: 0.5 g

Acceptance criteria: NMT 0.1%

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store below 30°.

• **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-di(1*H*-1,2,4-triazol-1-yl)-propan-2-ol.

$C_{13}H_{13}FN_6O$ 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	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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