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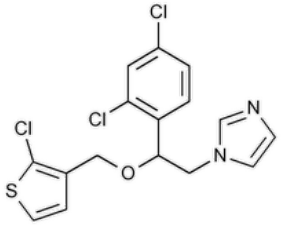
Tioconazole



$C_{16}H_{13}Cl_3N_2OS$ 387.71

1*H*-Imidazole, 1-[2-[(2-chloro-3-thienyl)methoxy]-2-(2,4-dichlorophenyl)ethyl]-;

1-[2,4-Dichloro-[β-(2-chloro-3-thenyl)-oxy]phen ethyl]imidazole CAS RN®: 65899-73-2; UNII: S57Y5X1117.

DEFINITION

Tioconazole contains NLT 97.0% and NMT 103.0% of $C_{16}H_{13}Cl_3N_2OS$.

IDENTIFICATION

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

• **B. Procedure**

Standard solution: 50 mg/mL of USP Tioconazole RS in methanol

Sample solution: 50 mg/mL of Tioconazole in methanol

Developing solvent system: Chloroform, methanol, and glacial acetic acid (40:5:1)

Visualizing solution: Dissolve 0.85 g of bismuth subnitrate in 10 mL of glacial acetic acid, and dilute with water to 50 mL. Mix 10 mL of this solution, 50 mL of potassium iodide solution (2 in 25), and 20 mL of glacial acetic acid, and dilute to 100 mL.

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography.*)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Analysis

Samples: *Standard solution* and *Sample solution*

Develop the chromatogram until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber and locate the spots on the plate by viewing under short- and long-wavelength UV light after drying the plate at 80° for 5 min. Spray the plate with *Visualizing solution*, air-dry for 2 min, and overspray with sodium nitrite solution (1 in 20). Air-dry the plate for 5 min, and examine it for brown spots on a pale yellow background.

Acceptance criteria: The R_F value of the principal spot from the *Sample solution* corresponds to that from the *Standard solution*.

• **C.** The retention time of the major peak for tioconazole of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Mobile phase: Acetonitrile, methanol, and water (44:40:28). Degas the solution, and add 2.0 mL of ammonium hydroxide to 1120 mL of *Mobile phase*. [Note—Prepare the *Mobile phase* fresh daily.]

Standard solution: 200 µg/mL of USP Tioconazole RS in methanol

Sample solution: 200 µg/mL of Tioconazole in methanol

Chromatographic system

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

Mode: LC

Detector: UV 219 nm

Column: 5-mm × 25-cm; packing L1 with a precolumn containing packing L4 installed between the pump and the injector. [NOTE—Replace the precolumn daily.]

Flow rate: Adjust to obtain a retention time of between 12 and 17 min for tioconazole.

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 1000 theoretical plates, determined from the analyte peak

Tailing factor: NMT 2.0 for the analyte peak

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{16}H_{13}Cl_3N_2OS$ in the Tioconazole 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 Tioconazole RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 97.0%–103.0%

IMPURITIES

Inorganic Impurities

- **Residue on Ignition ⟨281⟩:** NMT 0.2%
- **Chloride and Sulfate, *Chloride*⟨221⟩:** A 0.7-g portion dissolved in methanol shows no more chloride than corresponds to 0.50 mL of 0.020 N hydrochloric acid (0.05%).

Organic Impurities

- **Procedure**

Mobile phase and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: Dissolve 1 mg each of USP Tioconazole Related Compound A RS, USP Tioconazole Related Compound B RS, and USP Tioconazole Related Compound C RS in 15.0 mL of methanol, and shake until the contents are completely dissolved.

Sample solution: Dissolve 100 mg of Tioconazole in 15.0 mL of methanol, and shake until the substance is completely dissolved.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate, in turn, the percentages of 1-[2,4-dichloro-β-[(3-thenyl)-oxy]phenethyl]imidazole hydrochloride (tioconazole related compound A), 1-[2,4-dichloro-β-[(2,5-dichloro-3-thenyl)-oxy]phenethyl]imidazole hydrochloride (tioconazole related compound B), and 1-[2,4-dichloro-β-[(5-bromo-2-chloro-3-thenyl)-oxy]phenethyl]imidazole hydrochloride (tioconazole related compound C) in the portion of Tioconazole taken:

$$\text{Result} = (r_U/r_S) \times (W_I/W_U) \times 100$$

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

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

W_I = weight of the respective USP Reference Standard taken to prepare the *Standard solution* (mg)

W_U = weight of Tioconazole taken to prepare the *Sample solution* (mg)

Acceptance criteria: The limit of each related compound is NMT 1.0%.

SPECIFIC TESTS

• **Water Determination,** *Method I*⟨921⟩**:** NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Tioconazole RS

USP Tioconazole Related Compound A RS

1-[2,4-Dichloro-β-[(3-thenyl)-oxy]phenethyl]imidazole hydrochloride.

$C_{16}H_{14}Cl_2N_2OS \cdot HCl$ ▲389.72▲ (ERR 1-Jul-2023)

USP Tioconazole Related Compound B RS

1-[2,4-Dichloro-β-[(2,5-dichloro-3-thenyl)oxy]phenethyl]imidazole hydrochloride.

$C_{16}H_{12}Cl_4N_2OS \cdot HCl$ ▲458.60▲ (ERR 1-Jul-2023)

USP Tioconazole Related Compound C RS

1-[2,4-Dichloro-β-[(5-bromo-2-chloro-3-thenyl)-oxy]-phenethyl]imidazole hydrochloride.

▲$C_{16}H_{12}BrCl_3N_2OS \cdot HCl$ 503.06▲ (ERR 1-Jul-2023)

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

Topic/Question	Contact	Expert Committee
TIOCONAZOLE	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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