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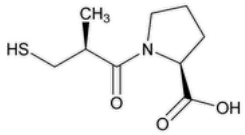
Captopril



$C_9H_{15}NO_3S$ 217.29

L-Proline, 1-[(2*S*)-3-mercapto-2-methyl-1-oxopropyl]-;

1-[(2*S*)-3-Mercapto-2-methylpropionyl]-L-proline CAS RN®: 62571-86-2; UNII: 9G64RSX1XD.

DEFINITION

Captopril contains NLT 97.5% and NMT 102.0% of captopril ($C_9H_{15}NO_3S$), calculated on the dried basis.

IDENTIFICATION

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

ASSAY

• **Procedure**

Sample solution: Dissolve about 300 mg of Captopril in 100 mL of water in a suitable glass-stoppered flask. Add 10 mL of 3.6 N sulfuric acid, 1 g of potassium iodide, and 2 mL of starch TS.

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Titrant: Dissolve 3.567 g of potassium iodate, previously dried at 110° to constant weight, in water to make 1.0 L.

Endpoint detection: Visual

Analysis: Titrate with *Titrant* to a faint blue endpoint that persists for NLT 30 s. Perform a blank determination, and make any necessary correction. Each mL of *Titrant* is equivalent to 21.73 mg of captopril ($C_9H_{15}NO_3S$).

Acceptance criteria: 97.5%–102.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

• **Organic Impurities**

Use low-actinic glassware to prepare the *Standard solution* and *Sample solution*.

Mobile phase: 9-in-100 solution of tetrahydrofuran in methanol and 1-in-2000 solution of phosphoric acid (33:67)

System suitability stock solution: 0.1 mg/mL each of USP Captopril RS, USP Captopril Disulfide RS, and 3-acetylthio-2-methylpropanoic acid in methanol

System suitability solution: 10 µg/mL each of USP Captopril RS, USP Captopril Disulfide RS, and 3-acetylthio-2-methylpropanoic acid in methanol from *System suitability stock solution*

Standard solution: 10 µg/mL of USP Captopril Disulfide RS in methanol

Sample solution: 2 mg/mL of Captopril in methanol. Use the solution promptly.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for captopril, 3-acetylthio-2-methylpropanoic acid, and captopril disulfide are 0.32, 0.42, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 3.0 between captopril and 3-acetylthio-2-methylpropanoic acid

Analysis

Samples: *Standard solution* and *Sample solution*

Compare the peak responses from the *Sample solution*, excluding those of the solvent, captopril, and captopril disulfide, with the main peak response from the *Standard solution*.

Calculate the percentage of captopril disulfide in the portion of Captopril taken:

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

r_U = peak response of captopril disulfide from the *Sample solution*

r_S = peak response of captopril disulfide from the *Standard solution*

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

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

Acceptance criteria: NMT 1.0% of captopril disulfide. The peak response of each impurity does not exceed 40% of the main peak response from the *Standard solution* (0.2%), and the sum of the impurity peak responses does not exceed the main peak response from the *Standard solution* (0.5%).

SPECIFIC TESTS

• **Optical Rotation,** *Specific Rotation* ⟨781S⟩

Sample solution: 10 mg/mL in dehydrated alcohol

Acceptance criteria: −125° to −134°

• **Loss on Drying** ⟨731⟩

Analysis: Dry a sample under vacuum at 60° for 3 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

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

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Captopril RS

USP Captopril Disulfide RS

▲(2′*S*)-[(2*S*,2′*S*)-3,3′-Disulfanediylbis(2-methylpropanoyl)]di-L-proline.▲ (ERR 1-Dec-2021)

$C_{18}H_{28}N_2O_6S_2$ 432.55

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

Topic/Question	Contact	Expert Committee
CAPTOPRIL	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

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