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Captopril Tablets

DEFINITION

Captopril Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of captopril ($C_9H_{15}NO_3S$).

IDENTIFICATION

Delete the following:

▲• **A.** **Thin-Layer Chromatographic Identification Test** ⟨201⟩

Standard solution: 4 mg/mL in methanol

Sample solution: 4 mg/mL of captopril in methanol prepared as follows. Dissolve the equivalent to 100 mg of captopril from a portion of powdered Tablets, taken in a conical flask, in 25 mL of methanol. Stir for 30 min using a magnetic stirrer, and centrifuge. Use the clear supernatant.

Chromatographic system

Application volume: 50 µL as streaks

Developing solvent system: Toluene, methanol, and glacial acetic acid (75:1:25)

Spray reagent: Freshly prepared mixture of 1 volume of ammonium hydroxide and 6 volumes of a solution of 0.04% 5,5'-dithiobis(2-nitrobenzoic acid) in methanol

Analysis: Proceed as directed in the chapter. Locate the spots on the plate by lightly spraying with *Spray reagent*.

Acceptance criteria: Meet the requirements▲2S *(USP41)*

Add the following:

▲• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲2S *(USP41)*

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲2S *(USP41)*

ASSAY

Change to read:

• **Procedure**

Protect solutions from exposure to air and use within 8 h of preparation.

Mobile phase: 550 mL of methanol and 450 mL of water containing 0.50 mL of phosphoric acid

Standard solution: 1 mg/mL of USP Captopril RS and 0.05 mg/mL of USP Captopril Disulfide RS in *Mobile phase*

Sample solution: Nominally equivalent to 1 mg/mL of captopril prepared as follows. Transfer NLT 20 Tablets into a suitable volumetric flask and add *Mobile phase* to fill about 50% of the volume of the flask. Sonicate for 15 min. Dilute with *Mobile phase* to volume, shake by mechanical means for 15 min, and filter.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm. ▲For *Identification B*, use a diode array detector in the range of 190–400 nm.▲2S *(USP41)*

Column: 4.6-mm × 25-cm; ▲5-µm▲2S *(USP41)* packing L1▲▲2S *(USP41)*

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for captopril and captopril disulfide are 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between captopril and captopril disulfide

Relative standard deviation: NMT 2.0% ▲for both the captopril and captopril disulfide peaks▲2S *(USP41)*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of captopril ($C_9H_{15}NO_3S$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

[Note—Completely deaerate the *Medium* to minimize exposure of captopril to air, and analyze the samples immediately.]

Medium: 0.01 N hydrochloric acid; 900 mL

Apparatus 1: 50 rpm

Time: 20 min

Standard solution: USP Captopril RS at a known concentration in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary, to a concentration similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 205 nm

▲**Analysis**

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of captopril ($C_9H_{15}NO_3S$) dissolved:

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

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 900 mL

D = dilution factor for the *Sample solution*▲2S *(USP41)*

Tolerances: NLT 80% (Q) of the labeled amount of captopril ($C_9H_{15}NO_3S$) is dissolved.

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

IMPURITIES

• **Limit of Captopril Disulfide**

Protect solutions from exposure to air and use within 8 h of preparation.

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

System suitability solution: Use the *Standard solution* prepared as directed in the *Assay*.

Standard solution: 0.05 mg/mL of USP Captopril Disulfide RS in *Mobile phase*

Sample solution: Nominally 1 mg/mL of captopril in *Mobile phase* prepared as follows. Transfer 25 mg of captopril from NLT 20 finely powdered Tablets into a suitable centrifuge tube. Add 25 mL of *Mobile phase*, sonicate for 15 min, and centrifuge. Use the clear supernatant.

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for captopril and captopril disulfide are 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between captopril and captopril disulfide, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of captopril disulfide in the portion of Tablets 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* (mg/mL)

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

Acceptance criteria: NMT 3.0%

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight containers. ▲Store at controlled room temperature.▲2S *(USP41)*

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.▲2S *(USP41)*

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

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

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

Chromatographic Database Information: Chromatographic Database

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