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Cyclobenzaprine Hydrochloride Extended-Release Capsules

DEFINITION

Cyclobenzaprine Hydrochloride Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197A**▲ (CN 1-May-2020)

Standard: Transfer 90 mg of USP Cyclobenzaprine Hydrochloride RS to a 25-mL volumetric flask. Add 10 mL of water and sonicate for 30 s. Transfer the solution to a 40-mL vial. Add 10 mL of methylene chloride. Cap the vial and shake. Centrifuge, if necessary, and transfer the lower methylene chloride layer to a watch glass. Evaporate the solvent, and use the residue. [Note—The use of a glass vial and a centrifuge speed of NMT 2000 rpm may be suitable. An infrared heat lamp may be used to evaporate the solvent.]

Sample: Transfer a portion of the contents of NLT 10 Capsules containing nominally 90 mg of cyclobenzaprine hydrochloride to a 25-mL volumetric flask. Add 10 mL of water and sonicate for 30 s. Transfer the solution to a 40-mL vial. Add 10 mL of methylene chloride. Cap the vial and shake. Centrifuge, and transfer the lower methylene chloride layer to a watch glass. Evaporate the solvent, and use the residue. [Note—The use of a glass vial and a centrifuge speed of NMT 2000 rpm may be suitable. An infrared heat lamp may be used to evaporate the solvent.]

Analysis

Samples: *Standard* and *Sample*

Acceptance criteria: The maxima of the IR spectrum from the *Sample* correspond to those from the *Standard*.

• **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**

Buffer: Add 3.7 mL of methanesulfonic acid per 1 L of water and adjust with diethylamine to a pH of 3.6.

Mobile phase: Acetonitrile, methanol, and *Buffer* (25.5:21.0:53.5)

Diluent: Acetonitrile and water (50:50)

Standard solution: 0.12 mg/mL of USP Cyclobenzaprine Hydrochloride RS in *Diluent*

Sample solution: Nominally 0.12 mg/mL of cyclobenzaprine hydrochloride from Capsules prepared as follows. Remove the contents of NLT 20 Capsules, and transfer a suitable portion of the contents to a volumetric flask. Add 80% of the final flask volume of *Diluent.* Stir and sonicate, if necessary. Dilute with *Diluent* to volume, and centrifuge. Use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 290 nm

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

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$) in the portion of Capsules 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 Cyclobenzaprine Hydrochloride RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **Dissolution** ⟨711⟩

Medium: 0.1 N hydrochloric acid; 900 mL

Apparatus 2: 50 rpm, wire helix sinkers

Times: 2, 4, 8, and 16 h

Solution A: Transfer 10 empty Capsule shells to a 1-L volumetric flask. Add 80% of the final flask volume of *Medium*, which has been warmed to 37°, and stir until the Capsule shells have dissolved. Allow to cool, and dilute with *Medium* to volume.

Standard solution: (L/900) mg/mL of USP Cyclobenzaprine Hydrochloride RS in *Medium*, where L is the label claim of cyclobenzaprine hydrochloride in mg/Capsule

Sample solution: Centrifuge a portion of the solution under test. Use the supernatant.

Instrumental conditions

Mode: UV

Analytical wavelength: 290 nm

Cell: 1 cm

Blank: A mixture of *Solution A* and *Medium* prepared as follows. Transfer 10% of the final flask volume of *Solution A* to a suitable volumetric flask. Dilute with *Medium* to volume, centrifuge, and use the supernatant.

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Correct the instrument by using the *Blank*.

Calculate the concentration (C_i) of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$) dissolved at each time point (i):

$$\text{Result}_i = (A_U/A_S) \times C_S$$

A_U = absorbance from the *Sample solution* at time point i

A_S = absorbance from the *Standard solution*

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

Calculate the percentage of the labeled amount of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = (\{C_3 \times [V - (2 \times V_S)]\} + [(C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

$$\text{Result}_4 = (\{C_4 \times [V - (3 \times V_S)]\} + [(C_3 + C_2 + C_1) \times V_S]) \times (1/L) \times 100$$

C_i = concentration of cyclobenzaprine hydrochloride in the portion of sample withdrawn at the specified time point (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See *Table 1*.

Table 1

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	2	NMT 40
2	4	43–63
3	8	66–86
4	16	NLT 80

The percentage of the labeled amount of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$) dissolved at the times specified conform to *Acceptance Table 2* in ⟨711⟩.

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

IMPURITIES

- **Organic Impurities**

Buffer: Dissolve 10 mL of *n*-butylamine in 900 mL of water, and adjust with acetic acid to a pH of 6.0. Dilute to 1 L.

Mobile phase: Acetonitrile, methanol, and *Buffer* (15:29:56)

Sensitivity solution: 0.001 mg/mL of USP Cyclobenzaprine Hydrochloride RS in *Mobile phase*

Standard solution: 0.02 mg/mL of USP Cyclobenzaprine Hydrochloride RS and 0.01 mg/mL of USP Amitriptyline Hydrochloride RS in *Mobile phase*

Sample solution: Nominally 2 mg/mL of cyclobenzaprine hydrochloride from Capsules prepared as follows. Remove the contents of NLT 20 Capsules, and transfer a suitable portion of the contents to a volumetric flask. Add 70% of the final flask volume of *Mobile phase*. Stir and sonicate, if necessary. Dilute with *Mobile phase* to volume, and centrifuge. Use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 239 nm

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

Flow rate: 1.2 mL/min

Injection volume: 20 µL

Run time: NLT 3.5 times the retention time of cyclobenzaprine

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[Note—The relative retention times for cyclobenzaprine and amitriptyline are 1.0 and 1.3, respectively. For other relative retention times, see *Table 2*.]

Suitability requirements

Resolution: NLT 2.5 between cyclobenzaprine and amitriptyline, *Standard solution*

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of each unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 2*. Disregard peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Cyclobenzaprine related compound A[a,b]	0.5	—
Cyclobenzaprine	1.0	—
Cyproheptadine related compound B[b,c]	2.9	—
Any individual unspecified degradation product	—	0.2
Total degradation products	—	0.5

[a] 5-[3-(Dimethylamino)propyl]-5*H* -dibenzo[a,d]-cycloheptene-5-ol.

[b] This is a process impurity that is included in the table for identification purposes only. It is controlled in the drug substance and is not to be reported or included in the total impurities for the drug product.

[c] Dibenzo[*a,d*]cycloheptene-5-one (also known as dibenzocycloheptenone).

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩
  USP Amitriptyline Hydrochloride RS
  USP Cyclobenzaprine Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
CYCLOBENZAPRINE HYDROCHLORIDE EXTENDED-RELEASE CAPSULES	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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