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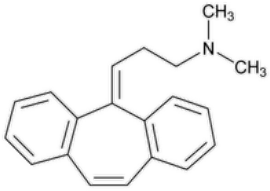
Cyclobenzaprine Hydrochloride



• HCl

$C_{20}H_{21}N \cdot HCl$ 311.85

1-Propanamine, 3-(5*H*-dibenzo[*a*,*d*]cyclohepten-5-ylidene)-*N*,*N*-dimethyl-, hydrochloride;

N,*N*-Dimethyl-5*H*-dibenzo[*a*,*d*]cycloheptene-$\Delta^{5,\gamma}$-propylamine hydrochloride CAS RN®: 6202-23-9; UNII: 0VE05JYS2P.

DEFINITION

Cyclobenzaprine Hydrochloride contains NLT 98.0% and NMT 102.0% of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

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

• **C.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride***

Sample solution: 20 mg/mL of Cyclobenzaprine Hydrochloride in water

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Mobile phase: Dissolve 2.0 g of ammonium acetate in 350 mL of water. Add 650 mL of methanol, and adjust with 25% ammonium hydroxide to a pH of 8.9.

Standard solution: 0.2 mg/mL of USP Cyclobenzaprine Hydrochloride RS in *Mobile phase*

Sample solution: 0.2 mg/mL of Cyclobenzaprine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

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

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of cyclobenzaprine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cyclobenzaprine hydrochloride ($C_{20}H_{21}N \cdot HCl$) in the portion of Cyclobenzaprine Hydrochloride taken:

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

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 = concentration of Cyclobenzaprine Hydrochloride in the *Sample solution* (mg/mL)

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Change to read:

• **Organic Impurities**

Buffer: 5.7 g/L of ammonium acetate in water. Adjust with 25% ammonium hydroxide to a pH of 7.2.

Mobile phase: Methanol and *Buffer* (65:35)

System suitability solution: 0.5 mg/mL of USP Cyclobenzaprine Hydrochloride RS and 0.75 µg/mL each of USP Cyclobenzaprine Related Compound A RS and USP Cyclobenzaprine Related Compound B RS in *Mobile phase*

Standard solution: 0.5 µg/mL of USP Cyclobenzaprine Hydrochloride RS in *Mobile phase*

Sample solution: 500 µg/mL of Cyclobenzaprine Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 3.5 times the retention time of cyclobenzaprine

System suitability

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

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

Suitability requirements

Resolution: NLT 1.5 between cyclobenzaprine related compound A and cyclobenzaprine related compound B, *System suitability solution*

Tailing factor: NMT 2.0 for the cyclobenzaprine peak, *System suitability solution*

Relative standard deviation: NMT 5.0% for cyclobenzaprine, *Standard solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of each specified impurity and any individual unspecified impurity in the portion of Cyclobenzaprine Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity 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* (µg/mL)

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

F = relative response factor for each impurity (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

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Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%, w/w)
Cyclobenzaprine related compound A	0.51	0.35	0.15
Cyclobenzaprine related compound B	0.57	1.0	0.15
Cyclobenzaprine *N*-oxide[a]	0.74	▲1.0▲ (RB 1-May-2020)	0.15
Dibenzocycloheptenol[b]	0.87	0.45	0.1
Cyclobenzaprine	1.0	—	—
Amitriptyline[c]	1.3	0.48	0.15
Dibenzocycloheptenone[d]	1.6	▲1.4▲ (RB 1-May-2020)	0.15
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] 3-(5*H*-Dibenzo[*a*,*d*]cyclohepten-5-ylidene)-*N*,*N*-dimethyl-1-propanamine *N*-oxide.

[b] 5*H*-Dibenzo[*a*,*d*]cycloheptene-5-ol.

[c] 10,11-Dihydro-*N*,*N*-dimethyl-5*H*-dibenzo[*a*,*d*]cycloheptene-$\Delta^{5,\gamma}$-propylamine.

[d] Dibenzo[*a*,*d*]cyclohepten-5-one.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° to constant weight.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards** ⟨11⟩

USP Cyclobenzaprine Hydrochloride RS

USP Cyclobenzaprine Related Compound A RS

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

$C_{20}H_{23}NO$ 293.40

USP Cyclobenzaprine Related Compound B RS

3-(5*H*-Dibenzo[*a*,*d*]cyclohepten-5-ylidene)-*N*-methyl-1-propanamine hydrochloride.

$C_{19}H_{19}N \cdot HCl$ 297.82

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

Topic/Question	Contact	Expert Committee
CYCLOBENZAPRINE HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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