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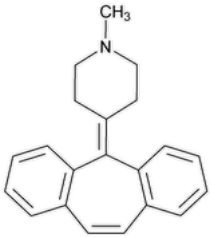
Cyproheptadine Hydrochloride



• HCl • $1½\ H_2O$

$C_{21}H_{21}N \cdot HCl \cdot 1½H_2O$ 350.88
$C_{21}H_{21}N \cdot HCl$ 323.87

Piperidine, 4-(5*H*-dibenzo[*a*,*d*]cycloheptен-5-ylidene)-1-methyl-, hydrochloride, sesquihydrate;
4-(5*H*-Dibenzo[*a*,*d*]cycloheptен-5-ylidene)-1-methylpiperidine hydrochloride sesquihydrate CAS RN®: 41354-29-4; UNII: NJ82J0F8QC.
Anhydrous CAS RN®: 969-33-5; UNII: 0S9323MCT0.

DEFINITION

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

IDENTIFICATION

Change to read:

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

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

ASSAY

• **Procedure**

Solution A: 1 mL/L of trifluoroacetic acid in water

Solution B: Acetonitrile and *Solution A* (38:62)

Solution C: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution B (%)	Solution C (%)
0.0	100	0
6.0	100	0
6.1	15	85
9.0	15	85
9.1	100	0
12	100	0

Diluent: Acetonitrile and water (38:62)

Standard solution: 40 µg/mL of USP Cyproheptadine Hydrochloride RS in *Diluent*. Sonication may be used to aid dissolution.

Sample solution: 40 µg/mL of Cyproheptadine Hydrochloride in *Diluent*. Sonication may be used to aid dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 266 nm

Column: 4.6-mm × 15-cm; 2.7-µm packing L60

Flow rate: 1 mL/min

Injection volume: 15 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cyproheptadine hydrochloride ($C_{21}H_{21}N \cdot HCl$) in the portion of Cyproheptadine Hydrochloride 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 Cyproheptadine Hydrochloride RS in the *Standard solution* (µg/mL)

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Solution A, Solution B, Solution C, Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard stock solution: 50 µg/mL each of USP Cyproheptadine Hydrochloride RS, USP Cyproheptadine Related Compound A RS, USP Amitriptyline Related Compound A RS, and USP Cyproheptadine Related Compound C RS, prepared as follows. Transfer a suitable quantity of each Reference Standard to an appropriate volumetric flask. Add 38% of the total flask volume of acetonitrile to dissolve, and then dilute with water to volume.

Standard solution: 0.75 µg/mL each of USP Cyproheptadine Hydrochloride RS, USP Cyproheptadine Related Compound A RS, USP Amitriptyline Related Compound A RS, and USP Cyproheptadine Related Compound C RS from the *Standard stock solution* in *Diluent*

Sensitivity solution: 0.25 µg/mL each of USP Cyproheptadine Hydrochloride RS, USP Cyproheptadine Related Compound A RS, USP Amitriptyline Related Compound A RS, and USP Cyproheptadine Related Compound C RS from the *Standard stock solution* in *Diluent*

Sample solution: 500 µg/mL of Cyproheptadine Hydrochloride in *Diluent*. Sonication may be used to aid dissolution.

System suitability

Samples: *Standard solution* and *Sensitivity solution*

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 3.0 between amitriptyline related compound A and cyproheptadine related compound A, *Standard solution*

Relative standard deviation: NMT 5.0% for cyproheptadine, cyproheptadine related compound A, amitriptyline related compound A, and cyproheptadine related compound C, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cyproheptadine related compound A, amitriptyline related compound A, and cyproheptadine related compound C in the portion of Cyproheptadine Hydrochloride taken:

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

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

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

C_S = concentration of the appropriate USP Reference Standard in the *Standard solution* (µg/mL)

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

Calculate the percentage of any individual unknown impurity in the portion of Cyproheptadine Hydrochloride taken:

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

r_U = peak response of any individual unknown impurity from the *Sample solution*

r_S = peak response of cyproheptadine hydrochloride from the *Standard solution*

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

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

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

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Cyproheptadine related compound C	0.7	0.15
Cyproheptadine	1.0	—
Amitriptyline related compound A	2.5	0.15
Cyproheptadine related compound A	2.6	0.15
Any individual unknown impurity	—	0.10
Total impurities	—	0.5

SPECIFIC TESTS

• **Water Determination ⟨921⟩, *Method I*:** 7.0%–9.0%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Amitriptyline Related Compound A RS
Dibenzosuberone.
$C_{15}H_{12}O$ 208.26

USP Cyproheptadine Hydrochloride RS

USP Cyproheptadine Related Compound A RS
5*H*-Dibenzo[*a*,*d*]cycloheptene.
$C_{15}H_{12}$ 192.26

USP Cyproheptadine Related Compound C RS
5-(1-Methyl-piperidin-4-yl)-5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol.
$C_{21}H_{23}NO$ 305.41

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

Topic/Question	Contact	Expert Committee
CYPROHEPTADINE HYDROCHLORIDE	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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