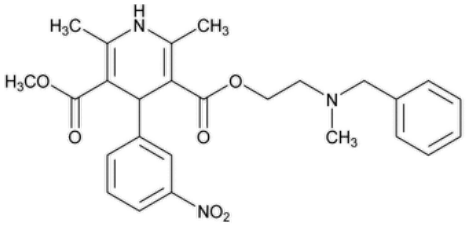
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-Aug-2024
Document Type: USP Monographs
DocId: GUID-FA3EE285-C60A-440B-B5B4-15518E76B450_6_en-US
DOI: https://doi.org/10.31003/USPNF_M56600_06_01
DOI Ref: bnr78

Nicardipine Hydrochloride



• HCl

$C_{26}H_{29}N_3O_6 \cdot HCl$ 515.99

3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl 2-[methyl(phenylmethyl)amino]ethyl ester, monohydrochloride; 2-(Benzylmethylamino)ethyl methyl 1,4-dihydro-2,6-dimethyl-4-(*m*-nitrophenyl)-3,5-pyridinedicarboxylate monohydrochloride CAS RN®: 54527-84-3; UNII: K5BC5011K3.

Nicardipine free base

$C_{26}H_{29}N_3O_6$ 479.53 CAS RN®: 55985-32-5; UNII: CZ5312222S.

DEFINITION

Nicardipine Hydrochloride contains NLT 98.0% and NMT 102.0% of nicardipine hydrochloride ($C_{26}H_{29}N_3O_6 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

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

• **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: 2.5 mg/mL in methanol

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Protect all solutions from light.

Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust the solution with potassium hydroxide to a pH of 4.8.

Solution A: Acetonitrile and methanol (90:10)

Mobile phase: *Solution A* and *Buffer* (38:62)

System suitability solution: 0.02 mg/mL each of USP Nicardipine Hydrochloride RS, USP Nicardipine Related Compound B RS, USP Nicardipine Related Compound C RS, and USP Nicardipine Related Compound D RS in *Mobile phase*

Standard solution: 0.1 mg/mL of USP Nicardipine Hydrochloride RS in *Mobile phase*

Sample solution: 0.1 mg/mL of Nicardipine Hydrochloride in *Mobile phase*. [Note—Sonication may be necessary for complete dissolution.]

Chromatographic system

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

Mode: LC

Detector: UV 237 nm

Column: 4.6-mm × 25-cm; 4-µm packing L7

Column temperature: 35°

Flow rate: 1.2 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of the nicardipine peak

System suitability

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

[NOTE—The relative retention times for nicardipine, nicardipine related compound D, nicardipine related compound C, and nicardipine related compound B are 1.00, 1.10, 1.43, and 1.93 respectively.]

Suitability requirements

Resolution: NLT 1.5 between nicardipine and nicardipine related compound D, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nicardipine hydrochloride ($C_{26}H_{29}N_3O_6 \cdot HCl$) in the portion of Nicardipine Hydrochloride taken:

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

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

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

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

C_U = concentration of Nicardipine 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%

• **ORGANIC IMPURITIES**

Protect all solutions from light.

Buffer, Solution A, Mobile phase, and **System suitability solution:** Prepare as directed in the *Assay*.

Standard solution 1: 3 µg/mL of USP Nicardipine Hydrochloride RS in *Mobile phase*

Standard solution 2: 0.6 µg/mL of USP Nicardipine Related Compound B RS in *Mobile phase*

Sensitivity solution: 0.3 µg/mL of USP Nicardipine Hydrochloride RS from *Standard solution 1* in *Mobile phase*

Sample solution: 0.6 mg/mL of Nicardipine Hydrochloride in *Mobile phase*. [NOTE—Sonication may be necessary for complete dissolution.]

Chromatographic system: Proceed as directed in the *Assay*, except for the *Run time*.

Run time: NLT 4 times the retention time of nicardipine

System suitability

Samples: *System suitability solution*, *Standard solution 1*, *Standard solution 2*, and *Sensitivity solution*

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

Suitability requirements

Resolution: NLT 1.5 between nicardipine and nicardipine related compound D; NLT 1.5 between nicardipine related compound D and nicardipine related compound C, *System suitability solution*

Relative standard deviation: NMT 2%, *Standard solution 1* and *Standard solution 2*

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

Analysis

Samples: *Standard solution 1*, *Standard solution 2*, and *Sample solution*

Calculate the percentage of nicardipine related compound B in the portion of Nicardipine Hydrochloride taken:

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

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

r_S = peak response of nicardipine related compound B from *Standard solution 2*

C_S = concentration of USP Nicardipine Related Compound B RS in *Standard solution 2* (µg/mL)

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

Calculate the percentage of nicardipine related compound C and nicardipine related compound D or any unspecified impurity in the portion of Nicardipine Hydrochloride taken:

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

r_U = peak response of each specified and unspecified impurity from the *Sample solution*

r_S = peak response of nicardipine from *Standard solution 1*

C_S = concentration of USP Nicardipine Hydrochloride RS in *Standard solution 1* (µg/mL)

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

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Nicardipine	1.0	—
Nicardipine related compound D (nicardipine bis analog)	1.1	0.5
Nicardipine related compound C (nicardipine dimethyl ester)	1.4	0.5
Nicardipine related compound B (nicardipine pyridine analog)	2.0	0.1
Any unspecified impurity	—	0.10
Total impurities	—	1.0

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105°, protected from light, to constant weight.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tightly closed containers, protected from light. Store at room temperature.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Nicardipine Hydrochloride RS

USP Nicardipine Related Compound B RS

▲3-{2-[Benzyl(methyl)amino]ethyl} 5-methyl 2,6-dimethyl-4-(3-nitrophenyl)pyridine-3,5-dicarboxylate oxalate.▲ (ERR 1-Aug-2024)

$C_{26}H_{27}N_3O_6 \cdot C_2H_2O_4$ 567.55

USP Nicardipine Related Compound C RS

Dimethyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate.

$C_{17}H_{18}N_2O_6$ 346.34

USP Nicardipine Related Compound D RS

▲Bis{2-[benzyl(methyl)amino]ethyl} 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate dihydrochloride.▲ (ERR 1-Aug-2024)

$C_{35}H_{40}N_4O_6 \cdot 2HCl$ 685.64

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

Topic/Question	Contact	Expert Committee
NICARDIPINE HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 46(6)

Current DocID: GUID-FA3EE285-C60A-440B-B5B4-15518E76B450_6_en-US

DOI: https://doi.org/10.31003/USPNF_M56600_06_01

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