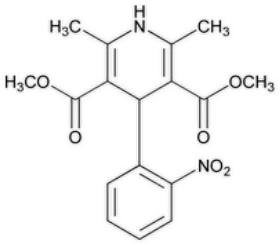
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-2B9498D9-116D-4396-AA44-1546CFF57E5D_4_en-US
DOI: https://doi.org/10.31003/USPNF_M56640_04_01
DOI Ref: blk5c

Nifedipine



$C_{17}H_{18}N_2O_6$ 346.33

3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-, dimethyl ester;

Dimethyl 1,4-dihydro-2,6-dimethyl-4-(*o*-nitrophenyl)-3,5-pyridinedicarboxylate CAS RN®: 21829-25-4; UNII: I9ZF7L6G2L.

DEFINITION

Nifedipine contains NLT 98.0% and NMT 102.0% of nifedipine ($C_{17}H_{18}N_2O_6$), calculated on the dried basis.

[NOTE—Nifedipine, when exposed to daylight and certain wavelengths of artificial light, readily converts to a nitrosophenylpyridine derivative. Exposure to UV light leads to the formation of a nitrophenylpyridine derivative. Perform the *Assay* and other tests in the dark or under golden fluorescent or other low-actinic light. Use low-actinic glassware.]

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-MAY-2020) **:** Do not dry samples.

• **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**

Protect the *Standard solution* and the *Sample solution* from actinic light. Conduct the *Assay* promptly after preparation of the *Standard solution* and the *Sample solution*.

Mobile phase: Acetonitrile, methanol, and water (25:25:50)

Standard stock solution: 1 mg/mL of USP Nifedipine RS in methanol

Standard solution: 0.1 mg/mL in *Mobile phase* from *Standard stock solution*

Sample solution: 0.1 mg/mL of Nifedipine prepared as follows. Transfer about 25 mg of Nifedipine to a 250-mL flask, dissolve in 25 mL of methanol, and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 25 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 4000 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nifedipine ($C_{17}H_{18}N_2O_6$) in the portion of Nifedipine 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 Nifedipine RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%, an ignition temperature of 600° being used

• **Organic Impurities**

Protect *Standard stock solution B* and the *Sample solution* from actinic light. Conduct this test promptly after preparation of *Standard stock solution B* and the *Sample solution*.

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

Standard stock solution A: 1 mg/mL of USP Nifedipine RS in methanol

Standard solution A: 0.3 mg/mL of USP Nifedipine RS in *Mobile phase* from *Standard stock solution A*

Standard stock solution B: 1 mg/mL of USP Nifedipine Nitrophenylpyridine Analog RS in methanol

Standard solution B: 0.6 µg/mL of USP Nifedipine Nitrophenylpyridine Analog RS in *Mobile phase* from *Standard stock solution B*

Standard stock solution C: 1 mg/mL of USP Nifedipine Nitrosophenylpyridine Analog RS in methanol

Standard solution C: 0.6 µg/mL of USP Nifedipine Nitrosophenylpyridine Analog RS from *Standard stock solution C*, diluted with *Mobile phase*

Standard solution D: *Mobile phase*, *Standard solution B*, and *Standard solution C* (1:1:1)

System suitability solution: *Standard solution A*, *Standard solution B*, and *Standard solution C* (1:1:1)

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.5 between nifedipine nitrophenylpyridine analog and nifedipine nitrosophenylpyridine analog; NLT 1.0 between the nifedipine nitrosophenylpyridine analog and nifedipine

Relative standard deviation: NMT 10% for both nifedipine nitrophenylpyridine analog and nifedipine nitrosophenylpyridine analog

Analysis

Samples: *Sample solution* and *Standard solution D*

Calculate the percentage of nifedipine nitrophenylpyridine analog and nifedipine nitrosophenylpyridine analog in the portion of Nifedipine taken:

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

r_U = peak response of nifedipine nitrophenylpyridine analog or nifedipine nitrosophenylpyridine analog from the *Sample solution*

r_S = peak response of nifedipine nitrophenylpyridine analog or nifedipine nitrosophenylpyridine analog from *Standard solution D*

C_S = concentration of USP Nifedipine Nitrophenylpyridine Analog RS or USP Nifedipine Nitrosophenylpyridine Analog RS in *Standard solution D* (mg/mL)

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Nifedipine nitrophenylpyridine analog[a]	0.8	0.2
Nifedipine nitrosophenylpyridine analog[b]	0.9	0.2
Nifedipine	1.0	—

[a] Dimethyl 4-(2-nitrophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate.

[b] Dimethyl 4-(2-nitrosophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate.

• **Limit of Chloride and Sulfate**

Standard solution A: Add 5.0 mL of water to 10 mL of 8.2 µg/mL of sodium chloride (corresponding to 5 µg/mL of chloride).

Standard solution B: Equivalent to 10 µg/mL of sulfate from potassium sulfate in water

Sample solution: To 5.0 g of Nifedipine add 4.0 mL of 6 N acetic acid and 46 mL of water. Bring carefully to a boil on a hot plate. Cool, pass through filter paper that is free of chloride and sulfate, and use the filtrate.

Chloride: Pipet 2.5 mL of the *Sample solution* into a 50-mL color-comparison tube, and add 12.5 mL of water. Into a matched color-comparison tube, pipet 10 mL of *Standard solution A*. To each tube add 0.15 mL of 0.3 M nitric acid and 0.3 mL of silver nitrate TS, and mix.

Acceptance criteria: NMT 0.02%; the opalescence exhibited by the *Sample solution* does not exceed that of *Standard solution A*.

Sulfate: Pipet into each of two 50-mL matched color-comparison tubes 1.5 mL of *Standard solution B*. To each tube add, successively and with continuous shaking, 0.75 mL of alcohol, 0.5 mL of a 6.1% aqueous solution of barium chloride, and 0.25 mL of 6 N acetic acid. Shake for an additional 30 s. Pipet into one tube, designated the standard tube, 15 mL of *Standard solution B*. Pipet into the other tube, designated the sample tube, 3 mL of *Sample solution* and 12 mL of water.

Acceptance criteria: NMT 0.05%; the turbidity exhibited by the *Sample solution* in the sample tube does not exceed that of *Standard solution B* in the standard tube.

• **Perchloric Acid Titration**

Sample solution: Dissolve 4 g of Nifedipine in 160 mL of glacial acetic acid in a 250-mL conical flask with the aid of an ultrasonic bath.

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N perchloric acid VS

Endpoint: Visual

Analysis: Add 3 drops of *p*-naphtholbenzein TS to the *Sample solution*, and titrate with *Titrant* to a green endpoint.

Acceptance criteria: NMT 0.12 mL of 0.1 N perchloric acid is consumed for each g of Nifedipine.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry a sample at 105° to constant weight.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **USP Reference Standards** ⟨11⟩

USP Nifedipine RS

USP Nifedipine Nitrophenylpyridine Analog RS

Dimethyl 4-(2-nitrophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate.

$C_{17}H_{16}N_2O_6$ 344.33

USP Nifedipine Nitrosophenylpyridine Analog RS

Dimethyl 4-(2-nitrosophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate.

$C_{17}H_{16}N_2O_5$ 328.33

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

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

Topic/Question	Contact	Expert Committee
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. PF 38(4)

Current DocID: GUID-2B9498D9-116D-4396-AA44-1546CFF57E5D_4_en-US
DOI: https://doi.org/10.31003/USPNF_M56640_04_01
DOI ref: blk5c