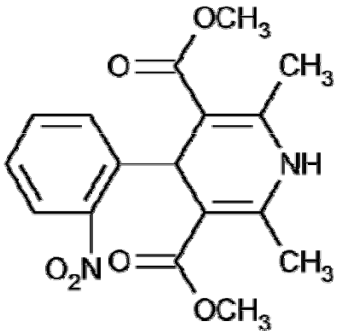
Nifedipine

USP Method Nifedipine RS
USP Method Nifedipine Assay



Original Manufacturer: Bayer (patent expired)

Brand Name: Adalat, Nifediac, Cordipin, Nifedical, and Procardia

Nifedipine is a dihydropyridine calcium channel blocker. Its main uses are as an antianginal (especially in Prinzmetal's angina) and antihypertensive, although a large number of other indications have recently been found for this agent, such as Raynaud's phenomenon, premature labor, and painful spasms of the esophagus in cancer and tetanus patients. It is also commonly used for the small subset of pulmonary hypertension patients whose symptoms respond to calcium channel blockers.

The approved uses for Nifedipine are the long-term treatment of hypertension (high blood pressure) and angina pectoris.

Merck Millipore is a division of Merck KGaA, Darmstadt, Germany

www.merck-chemicals.com/chromatography
chromatography@merckgroup.com

Nifedipine

USP34 – NF29 S1

USP Columns:

C-18-IP Ultrasphere. Assay and Related Compounds 5-µm, Beckman Instruments.
Alternative column Luna C18(2), Phenomenex

Equivalent Column:

Purospher®STAR RP-18 endcapped (5 µm) 250x4.6 mm (1.50252.0001)

Recommended Solvents and Reagents:

Acetonitrile	isocratic grade for liquid chromatography LiChrosolv®	(1.14291)
Methanol	for liquid chromatography LiChrosolv®	(1.06018)
Water	Water for chromatography LiChrosolv® or freshly purified water from Milli-Q water purification system	(1.15333)

USP Standards

Nifedipine (125 mg)	USP Product Number:	1463508
Nifedipine Nitrophenylpyridine Analog (25 mg)	USP Product Number:	1463600
Nifedipine Nitrosophenylpyridine Analog (25 mg)	USP Product Number:	1463701

Merck Millipore is a division of Merck KGaA, Darmstadt, Germany
www.merck-chemicals.com/chromatography
chromatography@merckgroup.com

USP Method for Nifedipine Assay

Assay

[note—Protect the Standard preparation and the Assay preparation from actinic light. Conduct the Assay promptly after preparation of the Standard preparation and the Assay preparation.]

Mobile phase

Prepare a suitable mixture of water, acetonitrile, and methanol (50:25:25), and degas.
Make adjustments if necessary (*see System Suitability under Chromatography 621*).

Standard preparation

Dissolve an accurately weighed quantity of USP Nifedipine RS in methanol (about 1 mg per mL), and quantitatively dilute with Mobile phase to obtain a solution having a known concentration of about 0.1 mg per mL.

Assay preparation

Transfer about 25 mg of Nifedipine, accurately weighed, to a 250-mL volumetric flask. Dissolve in 25 mL of methanol, dilute with Mobile phase to volume, and mix to obtain a solution having a concentration of about 0.1 mg per mL.

Chromatographic system (*see Chromatography 621*)

The liquid chromatograph is equipped with a 235-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure:

Column efficiency is not less than 4000 theoretical plates;
Tailing factor is not more than 1.5;
Relative standard deviation for replicate injections is not more than 1.0%.

Procedure

Separately inject equal volumes (about 25 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for the major peaks.
Calculate the quantity, in mg, of $C_{17}H_{18}N_2O_6$ in the portion of Nifedipine taken by the formula:

$$250C(r_U/r_S)$$

C = concentration in mg/mL, of Nifedipine RS in the Standard preparation, and where r_U and r_S are the peak responses obtained from the Assay preparation and the Standard preparation, respectively.

USP Method for Nifedipine RS

Related compounds

[note—Protect the Standard Nifedipine solution and the Test preparation from actinic light. Conduct this test promptly after preparation of the Standard Nifedipine solution and the Test solution.]

Mobile phase: *(Prepare as directed in the Assay)*

Standard Nifedipine solution

Dissolve an accurately weighed quantity of USP Nifedipine RS in methanol (about 1 mg per mL), and dilute quantitatively with Mobile phase to obtain a solution having a known concentration of about 0.3 mg per mL.

Reference solution 1:

Dissolve an accurately weighed quantity of USP Nifedipine Nitrophenylpyridine Analog RS in methanol (about 1 mg per mL), and dilute quantitatively with Mobile phase to obtain a solution having a known concentration of about 0.6 µg per mL.

Reference solution 2

Dissolve an accurately weighed quantity of USP Nifedipine Nitrosophenylpyridine Analog RS in methanol (about 1 mg per mL), and dilute quantitatively with Mobile phase to obtain a solution having a known concentration of about 0.6 µg per mL.

Standard solution

Transfer 5.0 mL of each of the two Reference solutions to a container, add 5.0 mL Mobile phase, and mix.

Test solution

Prepare as directed for the Assay preparation in the Assay.

System suitability solution

Mix equal volumes of the Standard Nifedipine solution and of each of the two Reference solutions.

Chromatographic system

Prepare as directed in the Assay. Chromatograph the System suitability preparation, and record the peak responses as directed for Procedure: Resolution, R, between the nitrophenylpyridine analog and nitrosophenylpyridine analog peaks is not less than (NLT) 1.5; the resolution, R, between the nitrosophenylpyridine analog and Nifedipine peaks is NLT 1.0; and the relative standard deviation of the response for each analog in replicate injections is not more than 10%. The relative retention times are about 0.8 for the nitrophenylpyridine analog, about 0.9 for the nitrosophenylpyridine analog, and 1.0 for Nifedipine.

Procedure

Separately inject equal volumes (about 25 µL) of the Standard and the Test solution into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of each related compound in the portion of Nifedipine taken by the formula:

$250C(r_U/r_S)$ C= conc. in mg/mL, of the appropriate USP Nifedipine Analog RS, in the Standard solution; r_U and r_S = peak responses for the corresponding related compound obtained from the Test solution and the Standard solution, respectively.

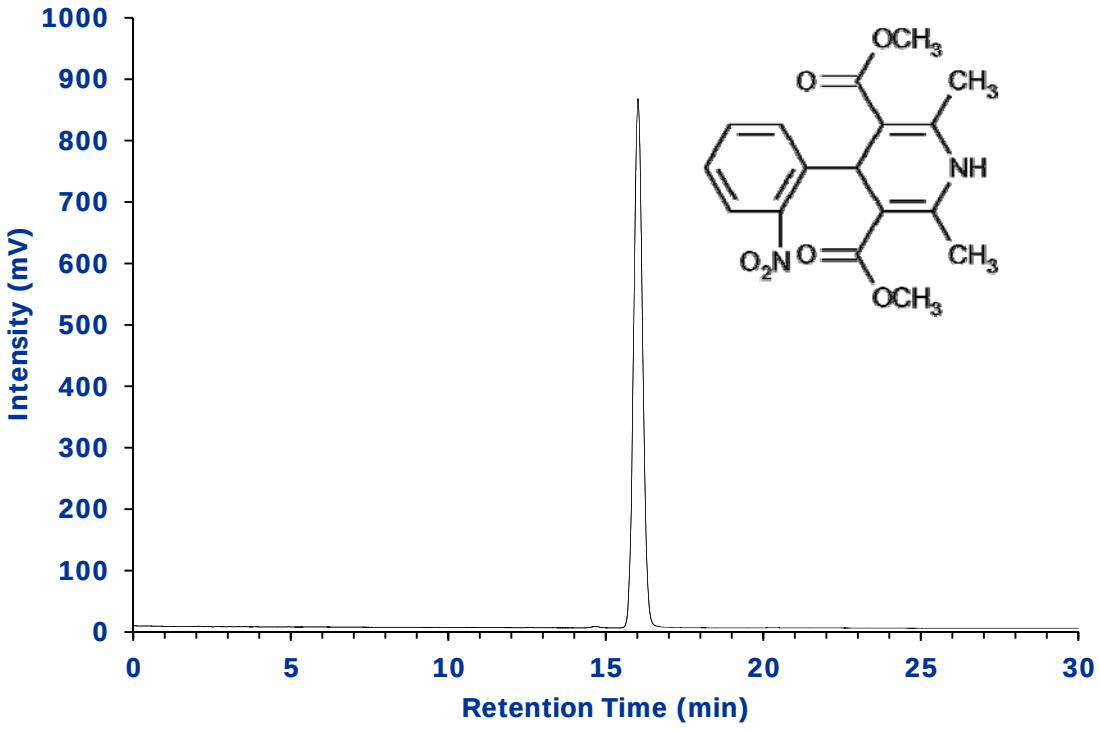
NMT 0.2% of each of dimethyl 4-(2-nitrophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate and dimethyl- 4-(2-nitrosophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate, corresponding to Nifedipine Nitrophenylpyridine Analog and Nifedipine Nitrosophenylpyridine Analog, respectively, is found.

USP Method for Nifedipine

Purospher®STAR RP-18endcapped

Chromatographic Conditions

Column:	Purospher®STAR RP-18endcapped (5 µm) 250x4.0 mm	1.50252.0001
Injection:	25 µL	
Detection:	Shimadzu Prominence, UV 254 nm	
Cell:	10 µL	
Flow Rate:	1.0 mL/min	
Mobile Phase (v/v):	Acetonitrile, Methanol and Water in a mixture (25:25:50)	
Temperature:	Ambient	
Diluent	Mobile phase	
Sample:	100 ppm (0.1 mg/mL) of Nifedipine	
Pressure Drop:	208 Bar (3016 psi)	



Chromatographic Data

No	Compound	Time (min)	Relative Retention Time (RRT)	Asymmetry (T_{USP})	Plates (N)
1	Nifedipine	16.0	1.00	1.1	15035

Merck Millipore is a division of Merck KGaA, Darmstadt, Germany
www.merck-chemicals.com/chromatography
chromatography@merckgroup.com