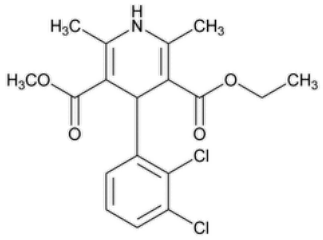
https://trungtamthuoc.com/

Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Dec-2022
Document Type: USP Monographs
DocId: GUID-F74659C6-B9CB-4E34-BA9C-AA0195814E3C_6_en-US
DOI: https://doi.org/10.31003/USPNF_M32655_06_01
DOI Ref: 4d4j5

© 2025 USPC
Do not distribute

Felodipine



$C_{18}H_{19}Cl_2NO_4$ 384.25

3,5-Pyridinedicarboxylic acid 4-(2,3-dichlorophenyl)-1,4-dihydro-2,6-dimethyl-, ethyl methyl ester, (±)-;

Ethyl methyl 4-(2,3-dichlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate CAS RN®: 72509-76-3.

DEFINITION

Felodipine contains NLT 98.0% and NMT 101.0% of felodipine ($C_{18}H_{19}Cl_2NO_4$), 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*.

ASSAY

- **Procedure**

Buffer: Dissolve 6.9 g of sodium phosphate monobasic dihydrate in 400 mL of water, add 8.0 mL of 1 M phosphoric acid, and dilute with water to 1 L. [Note—The pH of this solution is around 3.0.]

Mobile phase: Acetonitrile, methanol, and *Buffer* (40:20:40)

System suitability stock solution: 0.05 mg/mL of USP Felodipine RS and 0.1 mg/mL of USP Felodipine Related Compound A RS in *Mobile phase*

System suitability solution: 0.5 µg/mL of USP Felodipine RS and 1 µg/mL of USP Felodipine Related Compound A RS in *Mobile phase* from the *System suitability stock solution*. [Note—Pass the solution through a suitable filter of 0.2-µm pore size.]

Standard solution: 0.3 mg/mL of USP Felodipine RS in *Mobile phase*. [Note—Prepare fresh before analysis. Pass the solution through a suitable filter of 0.2-µm pore size.]

Sample solution: 0.3 mg/mL of Felodipine in *Mobile phase*. [Note—Prepare fresh before analysis. Pass the solution through a suitable filter of 0.2-µm pore size.]

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

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

Flow rate: 1 mL/min

Injection volume: 20 µL for the *System suitability solution* and 40 µL for the *Standard solution* and the *Sample solution*

Run time: NLT 2 times the retention time of felodipine

System suitability

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

[Note—The relative retention times for felodipine related compound A and felodipine are 0.83 and 1.00, respectively.]

Suitability requirements

Resolution: NLT 2.5 between felodipine related compound A and felodipine, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 0.37%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of felodipine ($C_{18}H_{19}Cl_2NO_4$) in the portion of Felodipine taken:

OFFICIAL

www.webofpharma.com

https://trungtamthuoc.com/

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

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

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

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

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

Acceptance criteria: 98.0%–101.0% on the dried basis

IMPURITIES

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

• **Limit of Ethyl 3-Aminocrotonate**

Buffer: 2.84 g/L of sodium phosphate, dibasic, anhydrous in water prepared as follows. Dissolve 2.84 g of sodium phosphate, dibasic, anhydrous in 1000 mL of water. Adjust with phosphoric acid to a pH of 7.0.

Mobile phase: Acetonitrile and *Buffer* (57:43)

Standard solution: 30 µg/mL of USP Ethyl 3-Aminocrotonate RS in *Mobile phase*. Prepare fresh before analysis.

Sample solution: 20 mg/mL of Felodipine in *Mobile phase*. Sonicate the solution for 10 min. Prepare fresh before analysis. [Note—Pass the solution through a suitable filter of 0.2-µm pore size.]

Chromatographic system

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

Mode: LC

Detector: Refractive index

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

Temperatures

Column: 35°

Detector: 35°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 4 times the retention time of ethyl 3-aminocrotonate for the *Standard solution*; NLT 8 times the retention time of ethyl 3-aminocrotonate for the *Sample solution*

System suitability

Sample: *Standard solution*

Requirements

Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ethyl 3-aminocrotonate in the portion of Felodipine taken:

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

r_U = peak response of ethyl 3-aminocrotonate from the *Sample solution*

r_S = peak response of ethyl 3-aminocrotonate from the *Standard solution*

C_S = concentration of USP Ethyl 3-Aminocrotonate RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 0.15%

Change to read:

• **Organic Impurities**

Buffer, Mobile phase, System suitability solution, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*▲, and use 40 µL injection volume for the *Sensitivity solution*.▲ (ERR 1-Dec-2022)

Sensitivity solution: 0.15 µg/mL of USP Felodipine RS in *Mobile phase* from the *Standard solution*. [Note—Prepare fresh before analysis.]

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

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

Suitability requirements

Resolution: NLT 2.5 between the felodipine related compound A and felodipine, *System suitability solution*

Relative standard deviation: NMT 10.0%, *Sensitivity solution*

Analysis

OFFICIAL

www.webofpharma.com

https://trungtamthuoc.com/

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Felodipine taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak response for each impurity

r_T = sum of all the peak responses

F = relative response factor (see *Table 1*)

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

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Methyl benzylidene acetoacetate[a]	0.55	1.17	0.15
Dimethyl felodipine[b]	0.70	1.0	—
Felodipine related compound A	0.83	0.44	0.15
Felodipine	1.00	1.0	—
Diethyl felodipine[c]	1.44	1.0	—
Sum of dimethyl felodipine and diethyl felodipine	—	—	1.0
Any unspecified impurity	—	1.0	0.10
Total impurities[d]	—	—	1.5

[a] Methyl 2-(2,3-dichlorobenzylidene)-3-oxobutanoate.

[b] Dimethyl 4-(2,3-dichlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate.

[c] Diethyl 4-(2,3-dichlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate.

[d] Total impurities include the sum of the results from the tests for *Organic Impurities* and *Limit of Ethyl 3-Aminocrotonate*.

SPECIFIC TESTS

- **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.5%

- **Color of Solution**

Sample solution: 20 mg/mL of Felodipine in methanol

Instrumental conditions

Mode: Vis

Analytical wavelength: 440 nm

Cell: 5 cm

Blank: Methanol

Acceptance criteria: NMT 0.2 absorbance

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**

USP Ethyl 3-Aminocrotonate RS

Ethyl (*Z*)-3-aminobut-2-enoate.

$C_6H_{11}NO_2$ 129.16

USP Felodipine RS

USP Felodipine Related Compound A RS

3-Ethyl 5-methyl 4-(2,3-dichlorophenyl)-2,6-dimethylpyridine-3,5-dicarboxylate.

$C_{18}H_{17}Cl_2NO_4$ 382.24

OFFICIAL

www.webofpharma.com

https://trungtamthuoc.com/

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 44(5)

Current DocID: GUID-F74659C6-B9CB-4E34-BA9C-AA0195814E3C_6_en-US

DOI: https://doi.org/10.31003/USPNF_M32655_06_01

DOI ref: 4d4j5

OFFICIAL

www.webofpharma.com