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Nifedipine Extended-Release Tablets

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DEFINITION

Nifedipine Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$). [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 assays and tests in the dark or under golden fluorescent or other low-actinic light. Use low-actinic glassware.]

IDENTIFICATION

- **A.** The retention time of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **B.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Ultraviolet-Visible Spectroscopy](#): 197U

Standard stock solution and Sample stock solution: Prepare as directed in the Assay.

Standard solution: 0.02 mg/mL of [USP Nifedipine RS](#) in *Mobile phase* from the *Standard stock solution*

Sample solution: Nominally 0.02 mg/mL of nifedipine in *Mobile phase* from the *Sample stock solution*

ASSAY

• PROCEDURE

[NOTE—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 of [USP Nifedipine RS](#) from the *Standard stock solution* in *Mobile phase*

Sample stock solution: Dissolve an amount equivalent to 420 mg of nifedipine from powdered Tablets in 130 mL of [water](#) in a 250-mL volumetric flask; or transfer the intact Tablets to a 400-mL, high-speed blender cup containing 130 mL of [water](#). Homogenize until a uniform suspension is achieved (about 2 min), and transfer the suspension with the aid of a mixture of [acetonitrile](#) and [methanol](#) (1:1) to a 250-mL volumetric flask. Dilute with a mixture of [acetonitrile](#) and [methanol](#) (1:1) to volume, and stir for 30 min. Centrifuge the resulting suspension to obtain a clear supernatant.

Sample solution: Nominally 0.1 mg/mL of nifedipine prepared as follows. Transfer 3.0 mL of the *Sample stock solution* to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and filter. [NOTE—Reserve a portion of this solution for use as the *Sample solution* in the test for *Organic Impurities*.]

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 265 nm

Columns

Guard: 2.1-mm × 3-cm; packing [L1](#)

Analytical: 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 the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) in the portion of Tablets 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 = nominal concentration of nifedipine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION \(711\)](#)

Test 1: If the product complies with this test, the labeling indicates that it meets *USP Dissolution Test 1*.

Medium: [Water](#); 50 mL

Apparatus 7: (See [Drug Release \(724\)](#).) 15–30 cycles/min. Do not use the reciprocating disk; use a 25-cm Plexiglas rod, the perimeter of the Tablets being affixed to the rod with a water-insoluble glue. The solution containers are 25-mm test tubes, 150–200 mm in length, and the water bath is maintained at $37 \pm 0.5^\circ$. At the end of each specified test interval, the systems are transferred to the next row of new test tubes containing 50 mL of fresh *Medium*.

Times: 4, 8, 12, 16, 20, and 24 h

Diluent: [Methanol](#) and [water](#) (1:1)

Standard solution: Transfer 50 mg of [USP Nifedipine RS](#) to a 100-mL volumetric flask. Dissolve in 50 mL of [methanol](#), and dilute with [water](#) to volume. Quantitatively dilute this solution with *Diluent* to obtain solutions having suitable known concentrations.

Sample solution: Use portions of the solution under test, passed through a suitable filter of 0.4- μ m pore size, suitably diluted with [methanol](#), and stepwise if necessary, with *Diluent* to obtain a final mixture consisting of equal parts of [methanol](#) and [water](#).

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 338 nm

Cell: 0.5 cm

Analysis: Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) released in the *Sample solution* at each 4-h interval from UV absorbances. [NOTE –For the 4-h time period, determine the absorbance at 456 nm, and use this determination to correct for excipient interference.]

Tolerances: See [Table 1](#).

Table 1

Time (h)	Amount Dissolved ^a (%)
4	5–17
8	—
12	43–80
16	—
20	—
24	NLT 80

^a The amount dissolved is expressed in terms of the labeled Tablet strength rather than in terms of the labeled total contents.

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$), released at the times specified, conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Solution A: Dissolve 330.9 g of [dibasic sodium phosphate](#) and 38 g of [citric acid](#) in [water](#) in a 1-L volumetric flask. Add 10 mL of [phosphoric acid](#), and dilute with [water](#) to volume.

Medium: Mix 125.0 mL of *Solution A* and 1 L of 10% [sodium dodecyl sulfate](#) solution, and dilute to 10 L. Adjust, if necessary, to a pH of 6.8; 900 mL.

Apparatus 2: 50 rpm, with sinkers (see [Dissolution \(711\)](#), [Figure 2a](#))

Times: 3, 6, and 12 h

Mobile phase: [Acetonitrile](#) and [water](#) (7:3)

Standard stock solution: 1.11 mg/mL of [USP Nifedipine RS](#) in [methanol](#)

Standard solution: 0.1 mg/mL of [USP Nifedipine RS](#) from the *Standard stock solution* in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 350 nm

Column: 4.0-mm × 125-mm; 3-μm packing [L1](#)

Temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 theoretical plates

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved.

Tolerances: See [Table 2](#).

Table 2

Time (h)	Amount Dissolved (%)
3	10–30
6	40–65
12	NLT 80

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$), dissolved at the times specified, conform to [Dissolution \(711\)](#).

[Acceptance Table 2](#).

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

For Tablets labeled to contain 30 mg of nifedipine: Phase 1

Medium: 0.05 M phosphate buffer, pH 7.5; 900 mL

Apparatus 2: 100 rpm

Time: 1 h

Standard solution: 0.034 mg/mL of [USP Nifedipine RS](#) in *Medium*. [NOTE—If necessary, a volume of [methanol](#), not exceeding 10% of the final volume, can be used to help solubilize nifedipine.]

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 238 nm**Cell:** 0.5 cm

Analysis: [NOTE—After the run, take the Tablet out of the dissolution vessel, adapt a sinker to it, and transfer the Tablet with the sinker to the dissolution vessel containing the *Medium for Phase 2*.] Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) released in *Phase 1*, using filtered portions of the *Sample solution*, in comparison with the *Standard solution*, using the *Medium* as the blank.

For Tablets labeled to contain 30 mg of nifedipine: Phase 2**Medium:** 0.5% [sodium dodecyl sulfate](#) in [simulated gastric fluid](#) without enzyme, pH 1.2; 900 mL**Apparatus 2:** 100 rpm**Times:** 1, 4, 8, and 12 h

Standard solution: 0.034 mg/mL of [USP Nifedipine RS](#) in *Medium*. [NOTE—If necessary, a volume of [methanol](#), not exceeding 10% of the final volume, can be used to help solubilize nifedipine.]

Sample solution: Pass a portion of the solution under test through a suitable filter.**Instrumental conditions**(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)**Mode:** UV**Analytical wavelength:** 238 nm

Analysis: Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) released in *Phase 2*, using filtered portions of the *Sample solution*, in comparison with the *Standard solution*, using *Medium* as the blank.

Tolerances: See [Table 3](#).**Table 3**

Time (h)	Amount Dissolved ^a (%)
1	NMT 30
4	30–55
8	NLT 60
12	NLT 80

^a For each dosage unit, add the amount dissolved in phosphate buffer, pH 7.5 from *Phase 1* to the amount dissolved at each time point in *Phase 2*.

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$), dissolved at the times specified, conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

For Tablets labeled to contain 60 mg of nifedipine: Phase 1**Medium:** 0.05 M phosphate buffer, pH 7.5; 900 mL**Apparatus 2:** 100 rpm**Time:** 25 min

Standard solution: 0.067 mg/mL of [USP Nifedipine RS](#) in *Medium*. [NOTE—If necessary, a volume of [methanol](#), not exceeding 10% of the final volume, can be used to help solubilize nifedipine.]

Sample solution: Pass a portion of the solution under test through a suitable filter.**Instrumental conditions**(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)**Mode:** UV**Analytical wavelength:** 238 nm

Analysis: [NOTE—After the run, take the Tablet out of the dissolution vessel, adapt a sinker to it, and transfer the Tablet with the sinker to the dissolution vessel containing the *Medium for Phase 2*.] Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) released in *Phase 1*, using filtered portions of the *Sample solution*, in comparison with the *Standard solution*, using the *Medium* as the blank.

For Tablets labeled to contain 60 mg of nifedipine: Phase 2**Medium:** 0.5% [sodium dodecyl sulfate](#) in [simulated gastric fluid](#) without enzyme, pH 1.2; 900 mL**Apparatus 2:** 100 rpm**Times:** 1, 4, 8, and 12 h

Standard solution: 0.067 mg/mL of [USP Nifedipine RS](#) in *Medium*. [NOTE—If necessary, a volume of [methanol](#), not exceeding 10% of the final volume, can be used to help solubilize nifedipine.]

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 238 nm

Analysis: Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) released in *Phase 2*, using filtered portions of the *Sample solution*, in comparison with the *Standard solution*, using the *Medium* as the blank.

Tolerances: See [Table 4](#).

Table 4

Time (h)	Amount Dissolved ^a (%)
1	NMT 30
4	40–70
8	NLT 70
12	NLT 80

^a For each dosage unit, add the amount dissolved in phosphate buffer, pH 7.5 from *Phase 1* to the amount dissolved at each time point in *Phase 2*.

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$), released in vivo and dissolved at the times specified, conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 4: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 4*.

Medium: 0.5% [sodium dodecyl sulfate](#) in [simulated gastric fluid](#) without enzyme, pH 1.2; 900 mL

Apparatus 2: 100 rpm

Times: 1, 4, and 12 h

Standard solution: 0.067 mg/mL of [USP Nifedipine RS](#) for Tablets labeled to contain 60 mg, and 0.034 mg/mL of [USP Nifedipine RS](#) for Tablets labeled to contain 30 mg, in *Medium*. [NOTE—If necessary, a volume of [methanol](#), not exceeding 10% of the final volume, can be used to help solubilize nifedipine.]

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: UV 238 nm

Cell: 1 cm

Analysis: Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) released, using filtered portions of the *Sample solution*, in comparison with the *Standard solution*, using the *Medium* as the blank.

Tolerances: See [Table 5](#) and [Table 6](#).

Table 5. For Tablets Labeled to Contain 30 mg of Nifedipine

Time (h)	Amount Dissolved (%)
1	12–35
4	44–67
12	NLT 80

Table 6. For Tablets Labeled to Contain 60 mg of Nifedipine

Time (h)	Amount Dissolved (%)
1	10–30
4	40–63
12	NLT 80

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$), released at the times specified, conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 5: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 5*.

Medium: [Water](#); 50 mL

Apparatus 7: (See [Drug Release \(724\)](#).) Use a 25-cm Plexiglas rod, the perimeter of the Tablets being affixed to the rod with a water-insoluble glue; 30 dips/min. The solution containers are 25-mm test tubes, 150–200 mm in length, and the water bath is maintained at $37 \pm 0.5^\circ$.

Times: 4, 12, and 24 h

Diluent A: [Methanol](#) and [acetonitrile](#) (1:1)

Diluent B: *Diluent A* and [water](#) (1:1)

Standard stock solution: 0.50 mg/mL of [USP Nifedipine RS](#) prepared as follows. Transfer a suitable amount of [USP Nifedipine RS](#) to an appropriate volumetric flask. Dissolve in 50% of the flask volume of *Diluent A*. Dilute with [water](#) to volume.

Standard solutions: 0.01, 0.05, and 0.20 mg/mL solutions, from the *Standard stock solution* in *Diluent B*, that are used at 4-, 12-, and 24-h samplings

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 338 nm

Cell: 0.5 cm

Analysis: [NOTE—For the 4-h time period, filter the solution under test, and determine the absorbance at 456 nm. Use this absorbance value to correct for excipient interference at the other time points.] Determine the amount of nifedipine released at each interval on portions of the *Sample solution* passed through a suitable filter of 0.45- μ m pore size, suitably diluted, if necessary, with *Diluent A* and [water](#) to obtain a final mixture of [water](#), [methanol](#), and [acetonitrile](#) (2:1:1), in comparison with the appropriate *Standard solution*, using *Diluent B* as the blank.

Tolerances: See [Table 7](#).

Table 7

Time (h)	Amount Dissolved (%)
4	NMT 14
12	39–75
24	NLT 75

The cumulative percentages of the labeled amount of nifedipine, dissolved at the times specified, conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 6: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.

Medium: [Simulated gastric fluid](#) without enzyme containing 0.5% of [sodium dodecyl sulfate](#), pH 1.2; 900 mL, deaerated

Apparatus 1: 100 rpm

Times: 1, 4, and 12 h

Standard stock solution: 0.33 mg/mL of [USP Nifedipine RS](#) in [methanol](#)

Standard solution: Quantitatively dilute the *Standard stock solution* with *Medium* to obtain a solution having a concentration of about 0.033 mg/mL.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 329 nm

Cell: 0.5 cm

Blank: *Medium*

Tolerances: See [Table 8](#).

Table 8

Time (h)	Amount Dissolved (%)
1	NMT 15
4	20–40
12	NLT 80

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 7: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 7*.

Medium: [Simulated gastric fluid](#) without enzyme containing 0.5% [sodium dodecyl sulfate](#), pH 1.2; 900 mL

Apparatus 2: 100 rpm, with three-prong sinker

Times: 1, 4, and 12 h

Standard solution: ($L/900$) mg/mL of [USP Nifedipine RS](#) in *Medium*, where L is the label claim, in mg/Tablet, of nifedipine. A small amount of [methanol](#), not exceeding 6%–7% of the final volume of the first dilution, can be used to solubilize nifedipine.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 238 nm

Cell: 1 mm, flow cell

Blank: *Medium*

Tolerances: See [Table 9](#).

Table 9

Time (h)	Amount Dissolved (%)
1	NMT 15
4	25–50
12	NLT 80

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 8: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 8*.

Acid stage medium: [Simulated gastric fluid](#) without enzyme containing 3% [polysorbate 80](#), pH 1.2; 250 mL

Apparatus 3: 20 dpm, 20-mesh polypropylene screen on the bottom; 1 min drip time. The Tablet is automatically transferred by the apparatus to the next set of vessels for each time point.

Time: 1 h

Buffer stage medium: 0.01 M sodium phosphate buffer, pH 6.8, containing 3% [polysorbate 80](#) (dissolve 8.3 g of [monobasic sodium phosphate](#) and 1 g of [sodium hydroxide](#) in 6 L of [water](#), adjust with either diluted [sodium hydroxide](#) or [phosphoric acid](#) to a pH of 6.8 ± 0.05, and add 180 g of [polysorbate 80](#)); 250 mL

Times: 2, 8, 12, and 24 h

Mobile phase: [Acetonitrile](#), [methanol](#), and [water](#) (35:35:30)

Standard stock solution: 1 mg/mL of [USP Nifedipine RS](#) in *Buffer stage medium*. An amount of [methanol](#), about 40% of the final volume, can be used to dissolve nifedipine.

Standard solution: (L/1000) mg/mL in *Buffer stage medium*, from the *Standard stock solution*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 338 nm

Column: 4.6-mm × 25-cm; packing [L1](#)

Temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 4000 theoretical plates

Tailing factor: NMT 1.7

Relative standard deviation: NMT 2.0%

Analysis: Calculate the percentage of the labeled amount of nifedipine dissolved at each time point.

At 1 h:

$$D_1 = (r_U/r_S) \times (C_S/L) \times V \times 100$$

At 2 h:

$$D = (r_U/r_S) \times (C_S/L) \times V \times 100$$

$$D_2 = D_1 + D$$

At 8 h:

$$D = (r_U/r_S) \times (C_S/L) \times V \times 100$$

$$D_8 = D_2 + D$$

At 12 h:

$$D = (r_U/r_S) \times (C_S/L) \times V \times 100$$

$$D_{12} = D_8 + D$$

At 24 h:

$$D = (r_U/r_S) \times (C_S/L) \times V \times 100$$

$$D_{24} = D_{12} + D$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

L = label claim (mg/Tablet)

V = volume of *Medium*, 250 mL

Tolerances

Acid stage: NMT 5% of the labeled amount of nifedipine is dissolved in 1 h.

Buffer stage: See [Table 10](#).

Table 10

Time (h)	Amount Dissolved (%)
1	NMT 5
2	0–10
8	25–60
12	45–85
24	NLT 80

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at the times specified conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 9: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 9*.

Medium: 0.03 M phosphate/citrate buffer, pH 6.8 with 1% [sodium dodecyl sulfate](#) (to a solution of 4.1 g/L of [dibasic sodium phosphate](#) and 0.475 g/L of [citric acid](#) monohydrate in [water](#), add 10 g/L of [sodium dodecyl sulfate](#). Adjust if necessary, with [phosphoric acid](#) to a pH of 6.8); 900 mL

Apparatus 2: 50 rpm, with a suitable sinker

Times: 3, 6, and 12 h

Standard stock solution: 0.33 mg/mL of [USP Nifedipine RS](#) in [methanol](#)

Standard solution: Prepare the corresponding [USP Nifedipine RS](#) solutions in *Medium* as directed in [Table 11](#).

Table 11

Tablet Strength (mg)	Concentration (mg/mL)
30	0.033
60	0.066
90	0.099

Sample solution: Pass a portion of the solution under test at each time point through a suitable filter.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 346 nm

Cell: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solutions and Sample solution*

Calculate the concentration (C_i) of nifedipine ($C_{17}H_{18}N_2O_6$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (A_U/A_S) \times C_S$$

A_U = absorbance of the *Sample solution* at each time point

A_S = absorbance of the *Standard solution*

C_S = concentration of [USP Nifedipine RS](#) in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_i \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_s)] + (C_1 \times V_s)\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{[C_3 \times [V - (2 \times V_s)]] + [(C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

C_i = concentration of nifedipine in the *Sample solution* at the specified time point (*i*) (mg/mL)

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

V_s = volume of the *Sample solution* withdrawn at each time point (*i*) (mL)

Tolerances: See [Table 12](#).

Table 12

Time Point (<i>i</i>)	Time (h)	Amount Dissolved (%)	
		Tablets Labeled to Contain 30 mg and 60 mg of Nifedipine	Tablets Labeled to Contain 90 mg of Nifedipine
1	3	15–40	10–35
2	6	43–73	40–65
3	12	NLT 80	NLT 80

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at the times specified conform to [Dissolution \(711\)](#).

[Acceptance Table 2](#).

Test 10: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 10*.

Medium: pH 6.8 phosphate buffer with 0.5% [sodium dodecyl sulfate](#) (transfer 442.1 g of [dibasic sodium phosphate](#) and 38 g of [citric acid](#) in a 1-L volumetric flask. Add [water](#) to dissolve, add 10 mL of [phosphoric acid](#), and dilute with [water](#) to volume. Transfer 60 g of [sodium dodecyl sulfate](#) to a suitable container. Add 150 mL of the phosphate solution above and 11,850 mL of [water](#). Mix well and adjust with [phosphoric acid](#) or [sodium hydroxide](#) to a pH of 6.8); 900 mL

Apparatus 2: 50 rpm, with sinkers (see [Dissolution \(711\)](#), [Figure 2a](#))

Times: 2, 8, and 16 h

Mobile phase: [Methanol](#) and [water](#) (60:40)

Standard solution: 0.06 mg/mL of [USP Nifedipine RS](#) prepared as follows. Transfer 12 mg of [USP Nifedipine RS](#) into a 200-mL volumetric flask. Add 20 mL of [methanol](#), and dilute with *Medium* to volume. [NOTE—Sonication may be needed to aid dissolution.]

Sample solution: Withdraw a 10-mL aliquot at each time point. Pass a portion of the solution under test through a suitable filter.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 380 nm

Column: 4.6-mm × 7.5-mm; 3.5-μm packing [L60](#)

Temperature: 45°

Flow rate: 1 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 3000 theoretical plates

Tailing factor: NMT 1.5
Relative standard deviation: NMT 3.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of nifedipine ($C_{17}H_{18}N_2O_6$) in the sample withdrawn from the vessel at each time point (i):

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

r_U = peak response of nifedipine in the *Sample solution* at each time point

r_S = peak response of nifedipine in the *Standard solution*

C_S = concentration of [USP Nifedipine RS](#) in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{[C_3 \times [V - (2 \times V_S)]] + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of nifedipine in the *Sample solution* at the specified time point (i) (mg/mL)

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point (i) (mL)

Tolerances: See [Table 13](#).

Table 13

Time Point (i)	Time (h)	Amount Dissolved (%)	
		Tablets Labeled to Contain 30 and 60 mg of Nifedipine	Tablets Labeled to Contain 90 mg of Nifedipine
1	2	NMT 30	NMT 15
2	8	53–83	35–58
3	16	NLT 80	NLT 75

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at the times specified conform to [Dissolution \(711\)](#).

[Acceptance Table 2](#).

Test 11: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 11*.

Medium: 1.25% [sodium dodecyl sulfate](#) in [water](#) (transfer 12.5 g of [sodium dodecyl sulfate](#) to 1 L of [water](#)); 900 mL

Apparatus 2: 100 rpm

Times: 1, 2, 4, and 10 h

Standard solution: 0.033 mg/mL of [USP Nifedipine RS](#) for Tablets labeled to contain 30 mg prepared as follows. Transfer an appropriate amount of [USP Nifedipine RS](#) into a suitable volumetric flask. Add [methanol](#) to 1% volume of the flask, and dilute with *Medium* to volume.

[NOTE—Sonication may be needed to aid the dissolution.]

Sample solution: A portion of the solution under test at the time points specified

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelengths: 230–246 nm, from the difference between first derivative values at the wavelengths of maximum and minimum in the wavelength range from 230 to 246 nm

Cell: 1 mm

Blank: *Medium*

Analysis: Use an automatic dissolution system with an appropriate dissolution software. Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved, using portions of the *Sample solution*, in comparison with the *Standard solution*.

Tolerances: See [Table 14](#).

Table 14. For Tablets Labeled to Contain 30 mg of Nifedipine

Time (h)	Amount Dissolved (%)
1	NMT 25
2	15–40
4	35–70
10	NLT 85

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$), dissolved at the times specified, conform to [Dissolution \(711\)](#), [Acceptance Table 2](#).

Test 12: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 12*.

Medium: pH 6.8 phosphate buffer with 1.25% [sodium dodecyl sulfate](#) (transfer 6 g of [monobasic sodium phosphate](#) and 112 mL of 0.2 N [sodium hydroxide](#) in a 1-L volumetric flask containing 800 mL of [water](#). Mix to dissolve, and dilute with [water](#) to volume. Adjust with [phosphoric acid](#) or [sodium hydroxide](#) to a pH of 6.8. Transfer 12.5 g of [sodium dodecyl sulfate](#) in 1 L of the phosphate solution); 900 mL

Apparatus 2: 50 rpm

Times: 2, 6, 8, and 16 h

Standard solution: 0.067 mg/mL of [USP Nifedipine RS](#) for Tablets labeled to contain 60 mg prepared as follows. Transfer an appropriate amount of [USP Nifedipine RS](#) into a suitable volumetric flask. Add [methanol](#) to 1% volume of the flask, and dilute with *Medium* to volume. [NOTE—Sonication may be needed to aid the dissolution.]

Sample solution: A portion of the solution under test at the time points specified

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelengths: 230–246 nm, from the difference between first derivative values at the wavelengths of maximum and minimum in the wavelength range from 230 to 246 nm

Cell: 1 mm

Blank: *Medium*

Analysis: Use an automatic dissolution system with an appropriate dissolution software. Determine the amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved, using portions of the *Sample solution*, in comparison with the *Standard solution*.

Tolerances: See [Table 15](#).

Table 15. For Tablets Labeled to Contain 60 mg of Nifedipine

Time (h)	Amount Dissolved (%)
2	NMT 20
6	28–53
8	43–68
16	NLT 80

The cumulative percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$), dissolved at the times specified, conform to [Dissolution \(711\), Acceptance Table 2](#).

Test 13: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 13*.

Medium: 0.5% [sodium dodecyl sulfate](#) in [simulated gastric fluid](#) without enzyme, pH 1.2; 900 mL

Apparatus 2: 100 rpm, with suitable sinkers

Times

For Tablets labeled to contain 30 and 60 mg of nifedipine: 1, 4, 6, and 10 h

For Tablets labeled to contain 90 mg of nifedipine: 1, 4, 6, and 12 h

Mobile phase: [Acetonitrile](#), [methanol](#), [water](#), and [phosphoric acid](#) (25:30:45:0.1)

Standard stock solution: 1.68 mg/mL of [USP Nifedipine RS](#) in [methanol](#)

Standard solution: A known concentration of [USP Nifedipine RS](#) in *Medium* from *Standard stock solution*, prepared as directed in [Table 16](#)

Table 16

Tablet Strength (mg)	Concentration (mg/mL)
30	0.0336
60	0.0672
90	0.1008

Sample solution: At each specified time point, withdraw a 10-mL aliquot and replace with the same volume of *Medium*. Pass a portion of the solution under test through a suitable filter and discard the first few milliliters of the filtrate.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 338 nm

Column: 4.6-mm × 15-cm; 5-μm packing [L1](#)

Flow rate: 2.0 mL/min

Injection volume: 20 μL

Run time: NLT 1.6 times the retention time of nifedipine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of nifedipine ($C_{17}H_{18}N_2O_6$) in the sample withdrawn from the vessel at each time point (i):

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

r_U = peak response of nifedipine in the *Sample solution* at each time point

r_S = peak response of nifedipine in the *Standard solution*

C_S = concentration of [USP Nifedipine RS](#) in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at each time point (i):

$$\text{Result}_1 = C_i \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_i \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_i) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_i) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of nifedipine in the *Sample solution* at the specified time point (*i*) (mg/mL)

V = volume of the *Medium*, 900 mL

L = label claim (mg/Tablet)

V_s = volume of the *Sample solution* withdrawn at each time point (*i*) (mL)

Tolerances: See [Table 17](#) and [Table 18](#).

Table 17. For Tablets Labeled to Contain 30 and 60 mg of Nifedipine

Time (h)	Amount Dissolved (%)
1	3–13
4	29–54
6	52–77
10	NLT 80

Table 18. For Tablets Labeled to Contain 90 mg of Nifedipine

Time (h)	Amount Dissolved (%)
1	3–13
4	27–52
6	45–70
12	NLT 80

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at the times specified conform to [Dissolution \(711\)](#).

[Acceptance Table 2](#).

Test 15: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 15*.

Medium: pH 6.8 phosphate buffer with 0.5% [sodium dodecyl sulfate](#) (transfer 7.8 g of [sodium phosphate monobasic dihydrate](#) and 0.9 g of [sodium hydroxide](#) in 1 L of water. Adjust with 1 N [sodium hydroxide](#) or [phosphoric acid](#) to a pH of 6.8. Transfer 5 g of [sodium dodecyl sulfate](#) in 1 L of the phosphate solution); 900 mL

Apparatus 2: 50 rpm, with suitable sinkers

Times: 2, 8, 12, and 24 h

Mobile phase: [Methanol](#) and [water](#) (60:40)

Standard solution: 0.06 mg/mL of [USP Nifedipine RS](#) for Tablets labeled to contain 60 or 90 mg, and 0.03 mg/mL of [USP Nifedipine RS](#) for Tablets labeled to contain 30 mg, in *Medium*.

[NOTE—If necessary, a volume of [methanol](#), not exceeding 10% of the final volume, can be used to help solubilize nifedipine.]

Sample solution: At each specified time point, withdraw a 10-mL aliquot. Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size, discarding the first 2–3 mL of the filtrate.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 380 nm

Column: 4.6-mm $\times$ 7.5-cm, 3.5 μ m packing [L60](#)

Temperature: 45°

Flow rate: 1 mL/min

Injection volume: 20 μ L

Run time: NLT 2 times the retention time of nifedipine

System suitability

Sample: Standard solution

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 3.0%

Analysis

Samples: Standard solution and Sample solution

Calculate the concentration (C_i) of nifedipine ($C_{17}H_{18}N_2O_6$) in the sample withdrawn from the vessel at each time point (i):

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

r_U = peak response of nifedipine in the Sample solution at each time point

r_S = peak response of nifedipine in the Standard solution

C_S = concentration of [USP Nifedipine RS](#) in the Standard solution (mg/mL)

Calculate the percentage of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at each time point (i):

$$\text{Result}_1 = C_i \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{[C_3 \times [V - (2 \times V_S)]] + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{[C_4 \times [V - (3 \times V_S)]] + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of nifedipine in the Sample solution at the specified time point (i) (mg/mL)

V = volume of Medium, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the Sample solution withdrawn at each time point (i) (mL)

Tolerances: See [Table 19](#).

Table 19

Time (h)	Amount Dissolved (%)
2	NMT 20
8	29–49
12	51–71
24	NLT 80

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at the times specified conform to [Dissolution <711>](#).

[Acceptance Table 2](#).

Test 16: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 16*.

Medium: pH 6.8 phosphate buffer with 1.0% [sodium dodecyl sulfate](#) (add 10 g/L of [sodium dodecyl sulfate](#) to a solution of 4.1 g/L of [anhydrous dibasic sodium phosphate](#), 0.13 mL/L of [phosphoric acid](#) and 0.475 g/L of [anhydrous citric acid](#) in [water](#); adjust, if necessary, with [phosphoric acid](#) or [sodium hydroxide](#) to a pH of 6.8); 900 mL, deaerated

Apparatus 2: 50 rpm, with a suitable sinker

Times: 2, 8, 12 and 20 h

Mobile phase: [Acetonitrile](#) and [water](#) (50:50)

Standard stock solution: 1 mg/mL of [USP Nifedipine RS](#) in [methanol](#)

Standard solution: (L/900) mg/mL of [USP Nifedipine RS](#) in *Medium*, from the *Standard stock solution*, where L is the label claim in mg/Tablet

Sample solution: Pass a portion of the solution under test through a suitable filter at each time point.

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 350 nm

Column: 4.6-mm × 15-cm; 5-µm packing [L1](#)

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 25 µL

Run time: NLT 1.6 times the retention time of nifedipine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of nifedipine ($C_{17}H_{18}N_2O_6$) in the sample withdrawn from the vessel at each time point (i):

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

r_U = peak response of nifedipine in the *Sample solution*

r_S = peak response of nifedipine in the *Standard solution*

C_S = concentration of [USP Nifedipine RS](#) in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = \{[C_2 \times (V - V_S)] + (C_1 \times V_S)\} \times (1/L) \times 100$$

$$\text{Result}_3 = \{[C_3 \times [V - (2 \times V_S)]] + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

$$\text{Result}_4 = \{[C_4 \times [V - (3 \times V_S)]] + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of nifedipine in the portion of sample withdrawn at each time point (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_S = volume of the *Sample solution* withdrawn at each time point (mL)

Tolerances: See [Table 20](#).

Table 20

Time (h)	Amount Dissolved (%)
2	NMT 10
8	21–41
12	42–62

Time (h)	Amount Dissolved (%)
20	NLT 80

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at the times specified conform to [Dissolution <711>](#), [Acceptance Table 2](#).

▲**Test 17:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 17*.

Medium

For Tablets labeled to contain 30 mg or 60 mg of nifedipine: [Simulated gastric fluid TS](#) without enzyme. Adjust with [hydrochloric acid](#) or [sodium hydroxide](#) to a pH of 1.2. To this add 5 mL of [sodium dodecyl sulfate](#); 900 mL.

For Tablets labeled to contain 90 mg of nifedipine: [Simulated gastric fluid TS](#) without enzyme. Adjust with [hydrochloric acid](#) or [sodium hydroxide](#) to a pH of 1.2. To this add 1 mL of [sodium dodecyl sulfate](#); 900 mL.

Apparatus 2: 100 rpm, with 3-prong sinkers

Times: 1, 6, and 14 h

Solution A: Add 1 mL of [phosphoric acid](#) to 1000 mL of [water](#).

Mobile phase: [Acetonitrile](#), [methanol](#), and *Solution A* (25:25:50)

Standard stock solution: 0.33 mg/mL of [USP Nifedipine RS](#) prepared as follows. Transfer a suitable quantity of [USP Nifedipine RS](#) into an appropriate volumetric flask. Add 20% of the flask volume of [methanol](#). Sonicate to dissolve, if necessary, and dilute with *Medium* to volume. Prepare the *Standard solution* immediately after preparation of the *Standard stock solution*.

Standard solution: ($L/900$) mg/mL of [USP Nifedipine RS](#) in *Medium* from the *Standard stock solution*, where L is the label claim in mg/Tablet

Sample solution: At each specified time point, withdraw a known volume of the solution and replace with the same volume of *Medium*.

Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Chromatographic system

(See [Chromatography <621>](#), *System Suitability*.)

Mode: LC

Detector: UV 238 nm

Column: 4.6-mm $\times$ 15-cm, 5- μ m packing [L1](#)

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 10 μ L

Run time: NLT 2.0 times the retention time of nifedipine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.8–2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of nifedipine ($C_{17}H_{18}N_2O_6$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (r_i/r_s) \times C_s$$

r_i = peak response of nifedipine from the *Sample solution* at each time point

r_s = peak response of nifedipine from the *Standard solution*

C_s = concentration of [USP Nifedipine RS](#) in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_s)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

C_i = concentration of nifedipine in the portion of the *Sample solution* withdrawn at the time point (*i*) (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_s = volume of the *Sample solution* withdrawn at each time point *i* and replaced with *Medium* (mL)

Tolerances: See [Table 21](#).

Table 21

Time Point (<i>i</i>)	Time (h)	Amount Dissolved (for Tablets labeled to contain 30 or 60 mg of nifedipine) (%)	Amount Dissolved (for Tablets labeled to contain 90 mg of nifedipine) (%)
1	1	NMT 12	NMT 10
2	6	40–60	43–63
3	14	NLT 80	NLT 80

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at the times specified conform to [Dissolution \(711\)](#).

[Acceptance Table 2](#).

Test 18: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 18*.

Ensure that the laser hole of the Tablets are on the upper side during the drop of the Tablets into the dissolution apparatus.

Medium: [Simulated gastric fluid TS](#) without enzyme. Adjust with [hydrochloric acid](#) or [sodium hydroxide](#) to a pH of 1.2. To this add 5 mL of [sodium dodecyl sulfate](#); 900 mL, deaerated, if necessary.

Apparatus 1: 100 rpm

Times: 4, 12, and 24 h

Mobile phase: [Acetonitrile](#), [methanol](#), and [water](#) (35:35:30)

Standard stock solution: 2.2 mg/mL of [USP Nifedipine RS](#) in [methanol](#). Sonicate to dissolve.

Standard solution: ($L/900$) mg/mL of [USP Nifedipine RS](#) in *Medium* from the *Standard stock solution*, where L is the label claim in mg/Tablet

Sample solution: At the times specified, withdraw a portion of the solution under test and replace with the same volume of *Medium*. Pass a portion of the solution under test through a suitable filter of 0.45- μ m pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 338 nm

Column: 4.6-mm $\times$ 25-cm, 5- μ m packing [L1](#)

Column temperature: 30°

Flow rate: 1.5 mL/min

Injection volume: 10 μ L

Run time: NLT 2.0 times the retention time of nifedipine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of nifedipine ($C_{17}H_{18}N_2O_6$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result}_i = (r_i/r_s) \times C_s$$

r_i = peak response of nifedipine from the *Sample solution* at each time point

r_s = peak response of nifedipine from the *Standard solution*

C_s = concentration of [USP Nifedipine RS](#) in the *Standard solution* (mg/mL)

Calculate the percentage of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at each time point (*i*):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_s)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_s]\} \times (1/L) \times 100$$

C_i = concentration of nifedipine in the portion of the *Sample solution* at the time point (*i*) (mg/mL)

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

V_s = volume of the *Sample solution* withdrawn at each time point *i* and replaced with *Medium* (mL)

Tolerances: See [Table 22](#).

Table 22

Time Point (i)	Time (h)	Amount Dissolved (%)
1	4	NMT 20
2	12	40–60
3	24	NLT 80

The percentages of the labeled amount of nifedipine ($C_{17}H_{18}N_2O_6$) dissolved at the times specified conform to [Dissolution <711>](#).

[Acceptance Table 2](#).▲ (RB 1-Sep-2024)

- [UNIFORMITY OF DOSAGE UNITS <905>](#): Meet the requirements

IMPURITIES

- **ORGANIC IMPURITIES**

[NOTE—Conduct this test promptly after preparation of the *Standard nifedipine solution* and the *Sample solution*.]

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

Quantitative limit stock solution A: 1 mg/mL of [USP Nifedipine Nitrophenylpyridine Analog RS](#) in [methanol](#)

Quantitative limit solution A: 6 µg/mL of [USP Nifedipine Nitrophenylpyridine Analog RS](#) from *Quantitative limit stock solution A* in *Mobile phase*

Quantitative limit stock solution B: 1 mg/mL of [USP Nifedipine Nitrosophenylpyridine Analog RS](#) in [methanol](#)

Quantitative limit solution B: 1.5 µg/mL of [USP Nifedipine Nitrosophenylpyridine Analog RS](#) from *Quantitative limit stock solution B* in *Mobile phase*

Standard nifedipine stock solution: 1 mg/mL of [USP Nifedipine RS](#) in [methanol](#)

Standard nifedipine solution: 0.3 mg/mL of [USP Nifedipine RS](#) from *Standard nifedipine stock solution* in *Mobile phase*

System suitability solution: *Quantitative limit solution A*, *Quantitative limit solution B*, and *Standard nifedipine solution* (1:1:1)

Standard solution: *Mobile phase*, *Quantitative limit solution A*, and *Quantitative limit solution B* (1:1:1)

[NOTE—Each mL of this solution contains about 2 µg of [USP Nifedipine Nitrophenylpyridine Analog RS](#) and 0.5 µg of [USP Nifedipine Nitrosophenylpyridine Analog RS](#).]

Sample solution: Use a portion of the *Sample solution* prepared as directed in the Assay.

Chromatographic system

(See [Chromatography <621>](#), [System Suitability](#).)

Mode: LC

Detector: UV 265 nm**Columns****Guard:** 2.1-mm × 3-cm; packing [L1](#)**Analytical:** 4.6-mm × 25-cm; packing [L1](#)**Flow rate:** 1 mL/min**Injection volume:** 25 µL**System suitability****Sample:** *System suitability solution***Suitability requirements****Resolution:** NLT 1.5 between the nitrophenylpyridine analog and nitrosophenylpyridine analog peaks; NLT 1.0 between the nitrosophenylpyridine analog and nifedipine peaks**Relative standard deviation:** NMT 10% for each analog**Analysis****Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of each analog in the portion of Tablets taken:

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

 r_U = peak response of each analog from the *Sample solution* r_S = peak response of each analog from the *Standard solution* C_S = concentration of the appropriate analog USP Reference Standard in the *Standard solution* (µg/mL) C_U = nominal concentration of nifedipine in the *Sample solution* (µg/mL)**Acceptance criteria:** NMT 2.0% of nifedipine nitrophenylpyridine analog and NMT 0.5% of nifedipine nitrosophenylpyridine analog, both relative to the nifedipine content**ADDITIONAL REQUIREMENTS**

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
- **LABELING:** The labeling indicates the *Dissolution* test with which the product complies.
- **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 EXTENDED-RELEASE TABLETS	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:**

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