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Amlodipine and Atorvastatin Tablets

DEFINITION

Amlodipine and Atorvastatin Tablets contain an amount of amlodipine besylate equivalent to NLT 90.0% and NMT 110.0% of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) and an amount of atorvastatin calcium equivalent to NLT 94.5% and NMT 105.0% of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$). It may contain suitable antioxidants.

IDENTIFICATION

- A.** The UV spectrum of the major peaks of the *Sample solution* exhibits maxima and minima at the same wavelengths as that of the *Standard solution*, as obtained in the Assay.
- B.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

• **PROCEDURE**

Solution A: Dissolve 1.54 g of [ammonium acetate](#) in 1000 mL of [water](#) and add 2 mL of [triethylamine](#). Adjust with [acetic acid](#) to a pH of 5.0.

Mobile phase: [Acetonitrile](#), [methanol](#), and *Solution A* (38:15:47)

Buffer: Transfer 7 mL of [triethylamine](#) to a 1000-mL volumetric flask containing 900 mL of [water](#) and mix. Adjust with dilute [phosphoric acid](#) (1 in 100) to a pH of 3.0 and dilute with [water](#) to volume.

Diluent: [Acetonitrile](#), [methanol](#), and *Buffer* (3:7:10)

Standard stock solution 1: 0.35 mg/mL of [USP Amlodipine Besylate RS](#) in [methanol](#)

Standard stock solution 2: 0.44 mg/mL of [USP Atorvastatin Calcium RS](#) in [methanol](#)

Standard solution: Prepare solutions of [USP Amlodipine Besylate RS](#) and [USP Atorvastatin Calcium RS](#) in *Mobile phase* at concentrations given in [Table 1](#) from *Standard stock solution 1* and *Standard stock solution 2*.

Table 1

Strength of Tablet, Amlodipine/Atorvastatin (mg/mg)	Concentration of Amlodipine Besylate (mg/mL)	Concentration of Atorvastatin Calcium (mg/mL)
2.5/10, 5/20, 10/40	0.028	0.088
2.5/20, 5/40, 10/80	0.014	0.088
5/10, 10/20	0.028	0.044
2.5/40, 5/80	0.014	0.176
10/10	0.028	0.022

Sample solution: Transfer NLT 10 Tablets to a suitable volumetric flask. Add about 20% of the final volume of the volumetric flask size in *Diluent* and sonicate to disperse the Tablets. Add about 40% of the final volume of the volumetric flask size in *Diluent*, sonicate for 20 min, and dilute with *Diluent* to volume. Centrifuge and transfer a suitable quantity of the supernatant to an appropriate suitable volumetric flask. Dilute with *Mobile phase* to volume to obtain the nominal concentrations of amlodipine and atorvastatin similar to that of the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 237 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

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

Column temperature: 35°

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 3.5 times the retention time of amlodipine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for both peaks

Relative standard deviation: NMT 2.0% for both peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

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

M_{r1} = molecular weight of amlodipine, 408.88

M_{r2} = molecular weight of amlodipine besylate, 567.05

Calculate the percentage of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times [M \times (M_{r1}/M_{r2})] \times 100$$

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

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

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

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

M = number of moles of atorvastatin per mole of atorvastatin calcium, 2

M_{r1} = molecular weight of atorvastatin, ▲558.65▲ (CN 1-May-2024)

M_{r2} = molecular weight of atorvastatin calcium, ▲1155.36▲ (CN 1-May-2024)

Acceptance criteria

Amlodipine: 90.0%–110.0%

Atorvastatin: 94.5%–105.0%

PERFORMANCE TESTS

Change to read:

• [DISSOLUTION <711>](#)

Test 1

Solution A, Mobile phase, Standard stock solution 1, Standard stock solution 2, Chromatographic system, and System suitability: Proceed as directed in the Assay.

Medium: 0.1% [polysorbate 80](#) in [pH 6.8 phosphate buffer](#); 900 mL

Apparatus 2: 75 rpm

Time: 20 min

Standard solution: ($L_1/900$) mg/mL of amlodipine and ($L_2/900$) mg/mL of atorvastatin in *Medium* from *Standard stock solution 1* and *Standard stock solution 2*, where L_1 is the label claim of amlodipine in mg/Tablet and L_2 is the label claim of atorvastatin in mg/Tablet

Sample solution: Centrifuge the solution under test and use the supernatant.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times (M_{r1}/M_{r2}) \times (1/L) \times 100$$

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

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

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

V = volume of *Medium*, 900 mL

M_{r1} = molecular weight of amlodipine, 408.88

M_{r2} = molecular weight of amlodipine besylate, 567.05

L = label claim of amlodipine (mg/Tablet)

Calculate the percentage of the labeled amount of atorvastatin ($C_{33}H_{35}FN_2O_5$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times V \times [M \times (M_{r1}/M_{r2})] \times (1/L) \times 100$$

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

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

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

V = volume of *Medium*, 900 mL

M = number of moles of atorvastatin per mole of atorvastatin calcium, 2

M_{r1} = molecular weight of atorvastatin, ▲558.65▲ (CN 1-May-2024)

M_{r2} = molecular weight of atorvastatin calcium, ▲1155.36▲ (CN 1-May-2024)

L = label claim of atorvastatin (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of amlodipine ($C_{20}H_{25}ClN_2O_5$) and atorvastatin ($C_{33}H_{35}FN_2O_5$) are dissolved.

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

Medium: 0.05 M phosphate buffer prepared as follows. Dissolve 40.8 g of [potassium phosphate, monobasic](#) and 5 g of [sodium hydroxide](#) in 6 L of [water](#). Adjust with [1 N sodium hydroxide](#) or [phosphoric acid](#) to a pH of 6.8; 900 mL.

Apparatus 2: 75 rpm

Time: 30 min

Buffer: Dissolve 4.0 g of [sodium phosphate, monobasic](#) in 1200 mL of [water](#) and add 6 mL of [triethylamine](#). Adjust with [phosphoric acid](#) to a pH of 2.5.

Mobile phase: [Acetonitrile](#) and *Buffer* (40:60)

Diluent: [Acetonitrile](#) and [water](#) (50:50)

Standard stock solution 1: 155 µg/mL of [USP Amlodipine Besylate RS](#) in *Diluent*

Standard stock solution 2: 460 µg/mL of [USP Atorvastatin Calcium RS](#) in *Diluent*

Standard solution: Prepare solutions of [USP Amlodipine Besylate RS](#) and [USP Atorvastatin Calcium RS](#) at concentrations given in [Table 2](#) from *Standard stock solution 1* and *Standard stock solution 2*.

Table 2

Strength of Tablet, Amlodipine/Atorvastatin (mg/mg)	Volume of Standard Stock Solution 1 to Be Added (mL)	Volume of Standard Stock Solution 2 to Be Added (mL)	Volume of Diluent to Be Added (mL)	Final Volume with Medium (mL)	Final Concentration of USP Amlodipine Besylate RS/ USP Atorvastatin Calcium RS (µg/mL)
5/10	10	5	45	200	7.75/11.5
5/20	10	10	40	200	7.75/23
5/40	10	20	30	200	7.75/46
5/80	10	40	10	200	7.75/92
10/10	20	5	35	200	15.5/11.5
10/20	20	10	30	200	15.5/23

