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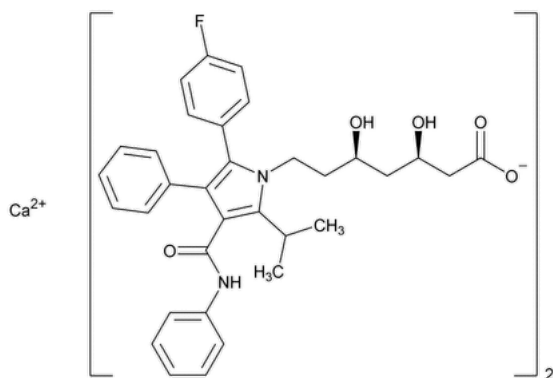
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Atorvastatin Calcium


 $C_{66}H_{68}CaF_2N_4O_{10}$ 1155.36

1*H*-Pyrrole-1-heptanoic acid, 2-(4-fluorophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-, calcium salt (2:1), [*R*-(*R**,*R**)]-;

Calcium (β*R*,δ*R*)-2-(*p*-fluorophenyl)-β,δ-dihydroxy-5-isopropyl-3-phenyl-4-(phenylcarbamoyl)pyrrole-1-heptanoate (1:2);

[(3*R*,5*R*)-7-[3-(Phenylcarbamoyl)-5-(4-fluorophenyl)-2-isopropyl-4-phenyl-1*H*-pyrrol-1-yl]-3,5-dihydroxyheptanoic acid, calcium salt]

Anhydrous CAS RN®: 134523-03-8; UNII: C0GEJ5QCSO.

 $C_{66}H_{68}CaF_2N_4O_{10} \cdot 3H_2O$ 1209.41

Trihydrate CAS RN®: 344423-98-9; UNII: 48A5M73Z4Q.

 $C_{66}H_{68}CaF_2N_4O_{10} \cdot C_3H_8O_2$

Propylene glycol solvate 1231.46

DEFINITION

Atorvastatin Calcium contains NLT 98.0% and NMT 102.0% of atorvastatin calcium ($C_{66}H_{68}CaF_2N_4O_{10}$), calculated on the anhydrous and solvent-free basis. If labeled as a propylene glycol solvate, it contains NLT 98.0% and NMT 102.0% of atorvastatin calcium ($C_{66}H_{68}CaF_2N_4O_{10}$), calculated on the anhydrous, propylene glycol-free, and solvent-free basis. It may contain a suitable antioxidant.

IDENTIFICATION

• A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197K

[NOTE—If a difference appears in the IR spectra of the analyte and the standard, separately dissolve equal portions of the sample specimen and the USP Reference Standard in equal volumes of methanol, evaporate the solution to dryness in similar containers under identical conditions, and repeat the test on the residues.]

• B. CALCIUM

Diluent: Methanol, water, and hydrochloric acid (75:25:2)

Sample solution: 0.05 mg/mL of Atorvastatin Calcium in *Diluent*

Blank: *Diluent*

Analysis

Samples: *Sample solution* and *Blank*

Instrumental conditions

(See [Atomic Absorption Spectroscopy \(852\)](#).)

Mode: Atomic absorption spectrophotometry

Analytical wavelength: Calcium emission line at 422.7 nm

Flame: Air–acetylene

Acceptance criteria: The *Sample solution* exhibits a significant absorption at the calcium emission line at 422.7 nm.

ASSAY

• PROCEDURE

Buffer: 3.9 g/L of ammonium acetate in water. Adjust with glacial acetic acid to a pH of 5.0 ± 0.1.

Solution A: Acetonitrile, stabilizer-free tetrahydrofuran, and *Buffer* (21:12:67)

Solution B: Acetonitrile, stabilizer-free tetrahydrofuran, and *Buffer* (61:12:27)

Mobile phase: See [Table 1](#). [NOTE—If necessary, adjust the *Mobile phase* by increasing or decreasing the percentage of acetonitrile or the pH of the ammonium acetate solution to achieve a retention time of 26–34 min for the atorvastatin peak.]

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
40	100	0
70	20	80
85	0	100
100	0	100
105	100	0
115	100	0

Diluent: *N,N*-dimethylformamide

System suitability solution: 0.05 mg/mL of [USP Atorvastatin Calcium RS](#) and 0.06 mg/mL of [USP Atorvastatin Related Compound B RS](#) in *Diluent*

Standard solution: 0.4 mg/mL of [USP Atorvastatin Calcium RS](#) in *Diluent*. [NOTE—Use sonication if necessary.]

Sample solution: 0.4 mg/mL of Atorvastatin Calcium in *Diluent*. [NOTE—Use sonication if necessary.]

Chromatographic system

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

[NOTE—If significant fronting of the peaks for atorvastatin related compound B and atorvastatin is observed, use the following diluent to prepare the *Sample solution*, the *Standard solution*, and the *System suitability solution*: acetonitrile, stabilizer-free tetrahydrofuran, and water (1:1:2).]

Mode: LC

Detector: UV 244 nm

Column: 4.6-mm × 25-cm; 5-μm packing L7

Column temperature: 35°

Flow rate: 1.5 mL/min

Injection volume: 20 μL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between the peaks for atorvastatin related compound B and atorvastatin, *System suitability solution*

Tailing factor: NMT 1.6, *Standard solution*

Relative standard deviation: NMT 0.6%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of atorvastatin calcium ($C_{66}H_{68}CaF_2N_4O_{10}$) in the portion of Atorvastatin Calcium 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 Atorvastatin Calcium RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the anhydrous and solvent-free basis. If labeled as a propylene glycol solvate, 98.0%–102.0% on the anhydrous, propylene glycol-free, and solvent-free basis.

OTHER COMPONENTS

• **CONTENT OF PROPYLENE GLYCOL** (if labeled as a propylene glycol solvate)

Diluent: Dimethylsulfoxide

Standard solution: 0.125 mg/mL of propylene glycol in *Diluent*

Sample solution: 2.5 mg/mL of Atorvastatin Calcium (as propylene glycol solvate) in *Diluent*. Use sonication as needed to achieve a complete dissolution.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 75-m; 3-μm coating of G43

Temperatures

Injection port: 230°

Detector: 250°

Column: See [Table 2](#).

Table 2

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
100	0	100	1
100	10	140	5
140	30	225	3

Carrier gas: Helium

Flow rate: 6.0 mL/min

Injection volume: 1 μL

Injection type: Splitless, using a suitable inlet liner

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of propylene glycol in the portion of Atorvastatin Calcium as propylene glycol solvate taken:

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

r_U = peak response of propylene glycol from the *Sample solution*

r_S = peak response of propylene glycol from the *Standard solution*

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

C_U = concentration of Atorvastatin Calcium (as propylene glycol solvate) in the *Sample solution* (mg/mL)

Acceptance criteria: 5.4%–7.3%

IMPURITIES

• **ORGANIC IMPURITIES, PROCEDURE 1:** [NOTE—On the basis of the synthetic route or of the solid state nature of the drug substance, perform either *Procedure 1* or *Procedure 2*. *Procedure 2* may be suitable when atorvastatin lactone, atorvastatin epoxy tetrahydrofuran analog, and atorvastatin acetoneide are possible related compounds, and it may be suitable for an amorphous form of the drug substance.]

Buffer, Solution A, Solution B, Mobile phase, Diluent, System suitability solution, and Chromatographic system: Proceed as directed in the Assay.

Standard solution: 1.5 μg/mL each of [USP Atorvastatin Related Compound A RS](#), [USP Atorvastatin Related Compound B RS](#), [USP Atorvastatin Related Compound C RS](#), and [USP Atorvastatin Related Compound D RS](#) in *Diluent*

Sample solution: 1 mg/mL of Atorvastatin Calcium in *Diluent*. [NOTE—Use sonication if necessary.]

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.5 between the peaks for atorvastatin related compound B and atorvastatin

Analysis

Samples: *Standard solution* and *Sample solution*