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Verapamil Hydrochloride Extended-Release Capsules

DEFINITION

Verapamil Hydrochloride Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Solution A: 0.01 N [sodium acetate](#) in water containing 33 mL/L of [glacial acetic acid](#)

Mobile phase: [Acetonitrile](#), [2-aminoheptane](#), and *Solution A* (30:0.5:70)

System suitability solution: 0.12 mg/mL of [USP Verapamil Hydrochloride RS](#) and 0.1 mg/mL of [USP Verapamil Related Compound B RS](#) in *Mobile phase*

Standard solution: 0.12 mg/mL of [USP Verapamil Hydrochloride RS](#) in *Mobile phase*

Sample stock solution: Nominally 1.2 mg/mL of verapamil hydrochloride prepared as follows. Transfer an equivalent to 240 mg of verapamil hydrochloride, from the pool of Capsule contents (NLT 20), to a 200-mL volumetric flask. Add about 150 mL of *Mobile phase* (prewarm the *Mobile phase* to 45°). While sonicating, stir for 1 h, cool to room temperature, dilute with *Mobile phase* to volume, and mix. Centrifuge a portion for 20 min, and use the supernatant.

Sample solution: Nominally 0.12 mg/mL of verapamil hydrochloride in *Mobile phase* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 278 nm. For *Identification B*, use a diode array detector in the range of 220–400 nm.

Column: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Flow rate: 1.2 mL/min

Injection volume: 20 μL

Run time: NLT 2 times the retention time of verapamil

System suitability

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

[NOTE—The relative retention times for verapamil related compound B and verapamil are 0.84 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between verapamil and verapamil related compound B, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$) in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1

Medium: 0.1 N [hydrochloric acid](#); 900 mL

Apparatus 2: 100 rpm. Use a wire helix sinker as necessary.

Times: 2, 4, 8, and 24 h

Solution A, Mobile phase, and Chromatographic system: Proceed as directed in the Assay, except for the *Injection volume*.

Injection volume: 30 μ L

System suitability solution: 0.25 mg/mL of [USP Verapamil Hydrochloride RS](#) and 0.2 mg/mL of [USP Verapamil Related Compound B RS](#) in *Medium*

Standard solution: 0.267 mg/mL of [USP Verapamil Hydrochloride RS](#) in *Medium*

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

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between verapamil and verapamil related compound B, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$) dissolved at each time point (*i*):

$$Q_2 = (r_U/r_S) \times (C_S/L) \times V \times 100$$

$$Q_4 = (Q_2 \times V_{S1}/V) + [(r_U/r_S) \times (C_S/L) \times (V - V_{S1}) \times 100]$$

$$Q_8 = (Q_2 \times V_{S1}/V) + \{Q_4 \times V_{S2}/[V - (V_{S1} + V_{S2})]\} + \{(r_U/r_S) \times (C_S/L) \times [V - (V_{S1} + V_{S2})] \times 100\}$$

$$Q_{24} = (Q_2 \times V_{S1}/V) + \{Q_4 \times V_{S2}/[V - (V_{S1} + V_{S2})]\} + \{Q_8 \times V_{S3}/[V - (V_{S1} + V_{S2} + V_{S3})]\} + \{(r_U/r_S) \times (C_S/L) \times [V - (V_{S1} + V_{S2} + V_{S3})] \times 100\}$$

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

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

C_S = concentration of [USP Verapamil Hydrochloride RS](#) in the *Standard solution*

L = label claim (mg/Capsule)

V = initial volume of *Medium*, 900 mL

V_{Si} = volume of *Medium* taken at each time point (mL)

Tolerances: See [Table 1](#).

Table 1

Time (h)	Amount Dissolved (%)
2	10–25
4	15–40
8	40–65
24	NLT 80



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