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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 µL

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

The percentages of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$) 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*.

Medium, Apparatus 2, Times, Solution A, Mobile phase, System suitability solution, Standard solution, Sample solution, Chromatographic system, System suitability, and **Analysis:** Proceed as directed in *Test 1*.

Tolerances: See *Table 2*.

Table 2

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

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Solution A, Mobile phase, and **Sample stock solution:** Prepare as directed in the *Assay*.

System suitability solution: 6 µg/mL of USP Verapamil Hydrochloride RS and 4.8 µg/mL of USP Verapamil Related Compound B RS in *Mobile phase*

Standard solution: 6 µg/mL of USP Verapamil Hydrochloride RS in *Mobile phase*

Sample solution: Use the *Sample stock solution*.

Chromatographic system: Proceed as directed in the *Assay*, except for the *Injection volume* and *Run time*.

Injection volume: 50 µL

Run time: NLT 5 times the retention time of verapamil

System suitability

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

[Note—See *Table 3* for relative retention times.]

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 each unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of each unspecified degradation product 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* (µg/mL)

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

Acceptance criteria: See *Table 3*.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Verapamil related compound B[a]	0.84	—
Verapamil	1.0	—
Any individual unspecified degradation product	—	0.2
Total degradation products	—	0.5

[a] For resolution measurement only. Do not include it in the total.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Verapamil Hydrochloride RS

USP Verapamil Related Compound B RS

Benzeneacetonitrile, α-[2-[[2-(3,4-dimethoxyphenyl)-ethyl]methylamino]ethyl]-3,4-dimethoxy-α-(1-methylethyl)-, monohydrochloride.

$C_{26}H_{36}N_2O_4 \cdot HCl$ 477.05

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

Topic/Question	Contact	Expert Committee
VERAPAMIL HYDROCHLORIDE EXTENDED-RELEASE CAPSULES	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

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