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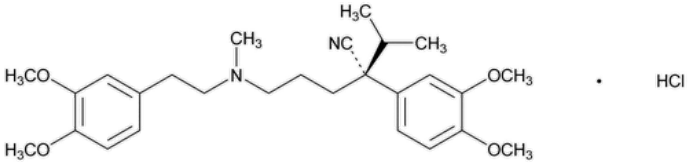
Verapamil Hydrochloride



$C_{27}H_{38}N_2O_4 \cdot HCl$ 491.06

Benzeneacetonitrile, α-[3-[[2-(3,4-dimethoxyphenyl)ethyl]methylamino]propyl]-3,4-dimethoxy-α-(1-methylethyl)-, monohydrochloride, (±)-; (±)-5-[(3,4-Dimethoxyphenethyl)methylamino]-2-(3,4-dimethoxyphenyl)-2-isopropylvaleronitrile monohydrochloride CAS RN®: 152-11-4; UNII: V3888OEY5R.

DEFINITION

Verapamil Hydrochloride contains NLT 98.0% and NMT 102.0% of Verapamil Hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

• **A.** **Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**

• **B.** The retention time of the major peak for verapamil in the *Sample solution* corresponds to that of *Standard solution B*, as obtained in the test for *Organic Impurities*.

• **C.** **Identification Tests—General, *Chloride* ⟨191⟩:** Meets the requirements

ASSAY

• **Procedure**

Buffer: 1.23 g/L of sodium acetate containing about 33 mL/L of glacial acetic acid

Mobile phase: Acetonitrile, 2-aminoheptane, and *Buffer* (300:5:700)

Standard solution: 1 mg/mL of USP Verapamil Hydrochloride RS in *Mobile phase*

Sample solution: 1 mg/mL of Verapamil Hydrochloride in *Mobile phase*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 278 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 0.9 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of verapamil

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$) in the portion of Verapamil Hydrochloride 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 = concentration of Verapamil Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Change to read:

• **Organic Impurities**

Buffer ▲and **Mobile phase:** Prepare▲ (ERR 1-Nov-2020) as directed in the *Assay*.

System suitability solution: 1.9 mg/mL of USP Verapamil Hydrochloride RS and 1.5 mg/mL of USP Verapamil Related Compound B RS in *Mobile phase*

Standard solution A: 5.6 µg/mL of USP Verapamil Hydrochloride RS in *Mobile phase*

Standard solution B: 9.4 µg/mL of USP Verapamil Hydrochloride RS in *Mobile phase*

Sample solution: 1.9 mg/mL of Verapamil Hydrochloride in *Mobile phase*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 278 nm

Column: 4.6-mm × 12.5- to 15-cm; packing L1

Flow rate: 0.9 mL/min

Injection volume: 10 µL

Run time: NLT 4 times the retention time of verapamil

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for verapamil related compound B and verapamil are 0.88 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the verapamil related compound B and verapamil peaks

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Sample solution*, *Standard solution A*, and *Standard solution B*

Acceptance criteria

Individual impurities: Any single peak response is not greater than that of the verapamil peak response from *Standard solution A* (0.3%).

Total impurities: The sum of the peak responses, other than that of verapamil, from the *Sample solution* is not greater than the verapamil peak response from *Standard solution B* (0.5%).

SPECIFIC TESTS

• **pH ⟨791⟩**

Sample solution: 50 mg/mL. Prepare with gentle heating.

Acceptance criteria: 4.5–6.5

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

• **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

Topic/Question	Contact	Expert Committee
VERAPAMIL HYDROCHLORIDE	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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