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Verapamil Hydrochloride Tablets

» Verapamil Hydrochloride Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$).

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—

USP Verapamil Hydrochloride RS

USP Verapamil Related Compound A RS

3,4-Dimethoxy-α-[3-(methylamino)propyl]-α-(1-methylethyl)-benzeneacetonitrile monohydrochloride.

$C_{17}H_{26}N_2O_2 \cdot HCl$ 326.87

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

USP Verapamil Related Compound E RS

3,4-Dimethoxybenzaldehyde.

USP Verapamil Related Compound F RS

(3,4-Dimethoxyphenyl)methanol.

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests* ⟨197⟩*, Infrared Spectroscopy: 197K*▲ (CN 1-May-2020) —

Test specimen—Transfer a portion of finely powdered Tablets, equivalent to about 25 mg of verapamil hydrochloride, to a separator. Add 25 mL of water, and shake by mechanical means for 30 minutes. Add 1 mL of 1 N sodium hydroxide, and extract with 25 mL of chloroform, shaking by mechanical means for 10 minutes. Pass the chloroform extract through a filter containing anhydrous sodium sulfate. Triturate the chloroform extract with 400 mg of potassium bromide and evaporate to dryness. Dry at 105° for 2 hours.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Dissolution ⟨711⟩—

Medium: 0.01 N hydrochloric acid; 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_{27}H_{38}N_2O_4 \cdot HCl$ dissolved from the difference between UV absorbances at the wavelengths of maximum absorbance at about 278 nm and 300 nm using filtered portions of the solution under test, suitably diluted with *Medium* if necessary, in comparison with a Standard solution having a known concentration of USP Verapamil Hydrochloride RS in the same *Medium*.

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{27}H_{38}N_2O_4 \cdot HCl$ is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩**:** meet the requirements.

Procedure for content uniformity—Transfer 1 Tablet to a 100-mL volumetric flask, add 50 mL of 0.01 N hydrochloric acid, and heat on a steam bath for 50 minutes. Sonicate the heated solution for about 10 minutes, cool, dilute with 0.01 N hydrochloric acid to volume, mix, and filter. Dilute an accurately measured portion of the filtrate quantitatively with 0.01 N hydrochloric acid to obtain a *Test preparation* containing about 48 µg of verapamil hydrochloride per mL. Dissolve an accurately weighed quantity of USP Verapamil Hydrochloride RS in 0.01 N hydrochloric acid to obtain a *Standard preparation* having a known concentration of about 48 µg per mL. Concomitantly determine the absorbances of the *Test preparation* and the *Standard preparation* in 1-cm cells at the wavelength of maximum absorbance at about 278 nm and the absorbance of the *Test preparation* at 300 nm, with a suitable spectrophotometer using 0.01 N hydrochloric acid as the blank. Calculate the quantity, in mg, of $C_{27}H_{38}N_2O_4 \cdot HCl$ in the Tablet taken by the formula:

$$(TC/D)(A_U/A_S)$$

in which T is the labeled quantity, in mg, of verapamil hydrochloride in the Tablet; C is the concentration, in µg per mL, of USP Verapamil Hydrochloride RS in the *Standard preparation; D* is the concentration, in µg per mL, of verapamil hydrochloride in the *Test preparation*, on the basis of the labeled quantity per Tablet and the extent of dilution; A_U is the difference between absorbances at 278 nm and 300 nm of the *Test preparation;* and A_S is the absorbance of the *Standard preparation* at 278 nm.

Related compounds—

Aqueous solvent mixture, Mobile phase, System suitability solution, and *Chromatographic system*—Proceed as directed in the *Assay.*

Standard solution—Dissolve accurately weighed quantities of USP Verapamil Hydrochloride RS, USP Verapamil Related Compound A RS, USP Verapamil Related Compound E RS, and USP Verapamil Related Compound F RS in *Mobile phase* to obtain a solution having known concentrations of about 1.6 mg of USP Verapamil Hydrochloride RS per mL and 0.0048 mg each of USP Verapamil Related Compound A RS, USP Verapamil Related Compound E RS, and USP Verapamil Related Compound F RS per mL.

Test solution—Use the *Assay preparation*.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, and allow the *Test solution* to elute for not less than four times the retention time for verapamil. Record the chromatograms, and measure all of the peak responses. [NOTE—The retention times are about 0.4 for verapamil related compound F, 0.5 for verapamil related compound A, 0.7 for verapamil related compound E, and 1.0 for verapamil.] Calculate the quantity, in mg, of each individual impurity in the portion of Tablets taken by the formula:

$$25C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of verapamil related compound A, verapamil related compound E, or verapamil related compound F in the *Standard solution* [NOTE—For calculating any other unspecified impurity, C is the concentration, in mg per mL, of USP Verapamil Hydrochloride RS in the *Standard solution*.]; and r_U and r_S are the peak responses of the appropriate impurity obtained from the *Test solution* and the *Standard solution*, respectively: not more than 0.3% of any specified impurity is found; and the sum of all impurities is not more than 1.0%.

Assay—

Aqueous solvent mixture—Prepare a 0.015 N sodium acetate solution containing about 33 mL of glacial acetic acid per L.

Mobile phase—Prepare a filtered and degassed mixture of *Aqueous solvent mixture,* acetonitrile, and 2-aminoheptane (70:30:0.5). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Verapamil Hydrochloride RS in *Mobile phase* to obtain a solution having a known concentration of about 1.6 mg per mL.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 40 mg of verapamil hydrochloride, to a stoppered centrifuge tube, and add 25 mL of *Mobile phase*. Shake by mechanical means for 15 minutes, centrifuge, and if necessary filter the supernatant.

System suitability solution—Dissolve suitable quantities of USP Verapamil Hydrochloride RS and USP Verapamil Related Compound B RS in *Mobile phase* to obtain a solution having known concentrations of about 1.9 mg per mL and 1.5 mg per mL, respectively.

Chromatographic system (see *CHROMATOGRAPHY* ⟨621⟩)—The liquid chromatograph is equipped with a 278-nm detector and a 4.6-mm × 12.5- to 15-cm column that contains packing L1. The flow rate is about 0.9 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.88 for verapamil related compound B and 1.0 for verapamil; the resolution, *R,* between the verapamil related compound B and verapamil peaks is not less than 1.5; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, and allow the *Assay preparation* to elute for not less than four times the retention time for verapamil. Record the chromatograms, and measure the responses for all of the major peaks. Calculate the quantity, in mg, of verapamil hydrochloride ($C_{27}H_{38}N_2O_4 \cdot HCl$) in the portion of Tablets taken by the formula:

$$25C(r_U/r_S)$$

in which C is the concentration, in mg per mL, of USP Verapamil Hydrochloride RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
VERAPAMIL HYDROCHLORIDE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Topic/Question	Contact	Expert Committee
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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