Edition: BP 2025 (Ph. Eur. 11.6 update)

Verapamil Tablets

General Notices

Action and use

Calcium channel blocker.

DEFINITION

Verapamil Tablets contain Verapamil Hydrochloride. They are coated.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of verapamil hydrochloride, $C_{27}H_{38}N_2O_4$,HCl

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing 0.1 g of Verapamil Hydrochloride with 25 mL of 0.1M *hydrochloric acid*, filter, extract the filtrate with 25 mL of *ether*, discard the extract and make the aqueous solution just alkaline with 2M *potassium carbonate sesquihydrate*. Extract with 25 mL of *ether*, filter the ether layer through *anhydrous sodium sulfate* and evaporate to dryness. The *infrared absorption spectrum* of a thin film of the oily residue, Appendix II A, is concordant with the *reference spectrum* of verapamil (*RS 359*).

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of 0.01M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 30 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium, if necessary, to produce a solution expected to contain 0.004% w/v of verapamil hydrochloride, at the maximum at 278 nm, Appendix II B, using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a 0.004% w/v solution of *verapamil hydrochloride BPCRS* in the dissolution medium using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of verapamil hydrochloride, $C_{27}H_{38}N_2O_4$, HCl in the medium from the absorbances obtained and using the declared content of $C_{27}H_{38}N_2O_4$, HCl in *verapamil hydrochloride BPCRS*.

LIMITS

The amount of verapamil hydrochloride released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in the mobile phase.

(1) Shake a quantity of the powdered tablets containing 0.24 g of Verapamil Hydrochloride with 90 mL of solvent, add sufficient solvent to produce 100 mL, centrifuge and use the supernatant liquid.
(2) Dilute 1 volume of solution (1) to 50 volumes. Further dilute 1 volume to 10 volumes.
(3) 0.005% w/v of *verapamil hydrochloride BPCRS* and 0.005% w/v of *verapamil impurity I EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Hypersil ODS is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.85 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 278 nm.
(f) Inject 10 µL of each solution.
(g) Allow the chromatography to proceed for 4 times the retention time of verapamil.

MOBILE PHASE

1 volume of *2-heptylamine*, 4.7 volumes of *glacial acetic acid*, 58 volumes of *acetonitrile* and 137 volumes of 0.01M *sodium acetate*.

When the chromatograms are recorded under the prescribed conditions, the retention times relative to verapamil (retention time about 6 minutes) are: impurity I, about 0.9 and impurity M, about 2.4.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity I and verapamil is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any such peaks is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%).

Disregard any peak with an area less than half of the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in the mobile phase.

(1) Shake a quantity of the powdered tablets containing 0.24 g of Verapamil Hydrochloride with 90 mL of solvent, add to produce 100 mL and filter. Dilute 1 volume of the filtrate to 20 volumes.
(2) 0.012% w/v of *verapamil hydrochloride BPCRS*.
(3) 0.005% w/v of *verapamil hydrochloride BPCRS* and 0.005% w/v of *verapamil impurity I EPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity I and verapamil is at least 2.0.

DETERMINATION OF CONTENT

Calculate the content of verapamil hydrochloride, $C_{27}H_{38}N_2O_4$,HCl, in the tablets from the chromatograms obtained and using the declared content of $C_{27}H_{38}N_2O_4$,HCl in *verapamil hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities D, E, F, G, I, J, K and M listed under Verapamil Hydrochloride.