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Verapamil Prolonged-release Capsules

General Notices

Prolonged-release Verapamil Capsules

Verapamil Prolonged-release Capsules from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Action and use

Calcium channel blocker.

DEFINITION

Verapamil Prolonged-release Capsules contain Verapamil Hydrochloride. They are formulated so that the medicament is released over a period of several hours.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Verapamil Hydrochloride. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

The capsules comply with the requirements stated under Capsules 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 contents of the capsules containing 0.1 g of Verapamil Hydrochloride with 25 mL of 0.1M *hydrochloric acid* for 10 minutes, filter, extract the filtrate with 25 mL of *ether*, discard the extract and make the aqueous solution 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

Related substances

Prepare a solution containing equal volumes of 0.01M *hydrochloric acid* and *methanol* (solvent A).

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in solvent A.

(1) To a quantity of the contents of the capsules containing 0.24 g of Verapamil Hydrochloride add 95 mL of solvent A, mix with the aid of ultrasound for 5 minutes, shaking occasionally, add sufficient solvent A to produce 100 mL and mix.

Centrifuge 50 mL of the resulting solution; dilute the supernatant liquid with sufficient of solvent A to produce a solution containing 0.072% w/v of Verapamil Hydrochloride and filter through a 0.45-µm filter.
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (3 µm) (Spherisorb ODS 2 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.8 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 278 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for six times the retention time of verapamil (retention time = about 5.6 minutes).

MOBILE PHASE

3 volumes of *2-heptylamine*, 300 volumes of *acetonitrile* and 700 volumes of a solution containing 0.082% w/v of *anhydrous sodium acetate* and 3.3% v/v of *anhydrous acetic acid*.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of all the *secondary peaks* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (3) (0.1%).

ASSAY

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

(1) Dissolve a quantity of the mixed contents of 20 capsules containing 0.12 g of Verapamil Hydrochloride in *methanol* and mix with the aid of ultrasound for 30 minutes, followed by shaking for 10 minutes. Add sufficient *methanol* to produce a solution containing 0.048% w/v of Verapamil Hydrochloride, mix and filter.
(2) 0.048% w/v of *verapamil hydrochloride BPCRS* in *methanol*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (30 cm × 3.9 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (µ-Bondapak C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 280 nm.
(f) Inject 25 µL of each solution.

MOBILE PHASE

3 volumes of a 0.164% w/v solution of *anhydrous sodium acetate* previously adjusted to pH 7.0 with a 5% v/v solution of *glacial acetic acid* and 7 volumes of *acetonitrile*.

DETERMINATION OF CONTENT

Calculate the content of $C_{27}H_{38}N_2O_4$,HCl in the capsules 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 and K listed under Verapamil Hydrochloride.