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Perindopril Erbumine Tablets

General Notices

Action and use

Angiotensin converting enzyme inhibitor.

DEFINITION

Perindopril Erbumine Tablets contain Perindopril Erbumine.

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

Content of perindopril erbumine, $C_{19}H_{32}N_2O_5,C_4H_{11}N$

92.5 to 105.0% of the stated amount.

IDENTIFICATION

A. Dissolve a quantity of the powdered tablets containing 50 mg of Perindopril Erbumine in 10 mL of *dichloromethane* and centrifuge for 5 minutes. Filter the supernatant liquid (Whatman GF/C is suitable), extract the filtrate with 10 mL of *water* and wash the upper aqueous layer with two 10-mL quantities of *hexane*. Evaporate the aqueous layer to dryness on a water bath and dry the residue at 60° at a pressure not exceeding 0.7 kPa, taking care to avoid excessive heating. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *infrared absorption spectrum* of *perindopril erbumine BPCRS*.
B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

TESTS

Dissolution

Comply with the requirements in 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 500 mL of 0.05M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 45 minutes withdraw a sample of the medium and filter. Dilute with 0.05M *hydrochloric acid*, if necessary, to produce a solution expected to contain 0.0004% w/v of Perindopril Erbumine.
(2) 0.0004% w/v of *perindopril erbumine BPCRS* in 0.05M *hydrochloric acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (7.5 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (3 µm) (Nucleosil 3 C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 215 nm.
(f) Inject 40 µL of each solution.

MOBILE PHASE

34 volumes of *acetonitrile* and 66 volumes of *water*, adjusted to pH 2.0 with a mixture of equal volumes of *perchloric acid* and *water*.

DETERMINATION OF CONTENT

Calculate the total content of perindopril erbumine, $C_{19}H_{32}N_2O_5,C_4H_{11}N$, in the medium from the chromatograms obtained and using the declared content of $C_{19}H_{32}N_2O_5,C_4H_{11}N$, in *perindopril erbumine BPCRS*.

LIMITS

The amount of perindopril erbumine 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 in mobile phase A.

(1) To a quantity of the powdered tablets containing 16 mg of Perindopril Erbumine, add 7 mL and mix with the aid of ultrasound. Dilute to 10 mL and filter.
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.16% w/v of *perindopril for peak identification EPCRS*.
(4) 0.01% w/v of *perindopril impurity standard BPCRS*.
(5) Dilute 2 volumes of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.0 mm) packed with spherical *octylsilyl silica gel for chromatography* (5 µm) (Inertsil C8 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use a column temperature of 60°.
(e) Use a detection wavelength of 215 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A *water* adjusted to pH 2.5 with a mixture of equal volumes of *perchloric acid* and *water*.

Mobile phase B 0.03% v/v solution of *perchloric acid* in *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-(5 - t)	95	5	isocratic
(5 - t)-(60 - t)	95→40	5→60	linear gradient
(60 – t)-(65 - t)	40→95	60→5	linear gradient

Use the chromatogram supplied with *perindopril for peak identification EPCRS* and the chromatogram obtained with solution (3) to identify the peaks due to impurities B, E, F, H and K. When the chromatograms are recorded under the

prescribed conditions, the relative retentions with reference to perindopril (retention time = about 25 minutes) are: impurity B = about 0.68; impurity K = about 0.72; impurity E = about 1.2; impurity F = about 1.6; impurity H = about 1.8 (impurity H may be eluted as 1 or 2 peaks).

Use the chromatogram supplied with *perindopril impurity standard BPCRS* and the chromatogram obtained with solution (4) to identify the peaks due to impurities C and D. When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to perindopril (retention time = about 25 minutes) are: impurity C = about 1.25; impurity D = about 1.3.

The isocratic step is described for a chromatographic system with a dwell volume (*D*) of 2 mL. If *D* is different from 2 mL, correct the gradient times with the value t, calculated using the following expression:

$$\frac{D-2}{flowrate}$$

SYSTEM SUITABILITY

The test is not valid unless:

the chromatogram obtained with solution (3) closely resembles the chromatogram supplied with *perindopril for peak identification EPCRS* and the *peak-to-valley* ratio is at least 3, where H_p is the height above the baseline of the peak due to impurity B and H_v is the height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity K.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B or F is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%);

the area of any peak corresponding to impurity C or D is not greater than 1.2 times the area of the principal peak in the chromatogram obtained with solution (2) (0.6%);

the area of any peak corresponding to impurity E is not greater than 0.8 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);

the area of any other *secondary peak* is not greater than half the area of the principal peak in the chromatogram obtained with solution (2) (0.25%);

the sum of the areas of all the *secondary peaks* excluding any peaks corresponding to impurities B, C, D, E and F is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.1%).

ASSAY

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

(1) To a quantity of the powdered tablets add sufficient of the mobile phase to produce a solution containing 0.004% w/v of Perindopril Erbumine, mix with the aid of ultrasound and filter.
(2) 0.004% w/v of *perindopril erbumine BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used but with an injection volume of 20 µL.

DETERMINATION OF CONTENT

Calculate the content of $C_{19}H_{32}N_2O_5,C_4H_{11}N$ in the tablets using the declared content of $C_{19}H_{32}N_2O_5,C_4H_{11}N$ in *perindopril erbumine BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Perindopril Erbumine.