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Gemfibrozil Capsules

General Notices

Action and use

Fibrate lipid-regulating drug.

DEFINITION

Gemfibrozil Capsules contain Gemfibrozil.

The capsules comply with the requirements stated under Capsules and with the following requirements.

Content of gemfibrozil, $C_{15}H_{22}O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the contents of the capsules containing about 0.5 g of Gemfibrozil with 10 mL of *n-hexane* for 10 minutes, filter through a filter paper previously washed with 20 mL of *n-hexane*, evaporate the filtrate to dryness on a water bath and then dry over *silica gel* at a pressure of 2 kPa for 2 hours or until a waxy solid is obtained. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of gemfibrozil *(RS 167)*.

TESTS

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia 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 900 mL of 0.2M *phosphate buffer pH 7.5*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a 10 mL sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium if necessary, at the maximum at 276 nm, Appendix II B using 0.2M *phosphate buffer pH 7.5* in the reference cell.
(2) Measure the *absorbance* of a suitable solution of *gemfibrozil BPCRS,* adding the minimum volume of 0.1M *sodium hydroxide*, if necessary, to complete dissolution, and using 0.2M *phosphate buffer pH 7.5* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of gemfibrozil, $C_{15}H_{22}O_3$, in the medium from the absorbances obtained and using the declared content of $C_{15}H_{22}O_3$, in *gemfibrozil BPCRS*.

Related substances

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

(1) Shake a quantity of the contents of the capsules containing 0.4 g of Gemfibrozil with 100 mL of *methanol* and filter
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase and further dilute 1 volume of this solution to 5 volumes with the mobile phase.
(3) 0.0004% w/v of *gemfibrozil impurity E BPCRS* in the mobile phase.
(4) 0.001% w/v of *gemfibrozil methyl ester BPCRS* and 0.0004% w/v of *gemfibrozil impurity E BPCRS* in solution (2).

CHROMATOGRAPHIC CONDITIONS

The chromatographic procedure described under Assay may be used. For solution (1) allow the chromatography to proceed for twice the retention time of the principal peak.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to gemfibrozil and gemfibrozil methyl ester is at least 4.0 and the *resolution* between the peaks due to gemfibrozil methyl ester and gemfibrozil impurity E is at least 1.2.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to gemfibrozil impurity E is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.1%);

the area of any other *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 *secondary peaks* other than any peak corresponding to gemfibrozil impurity E is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

ASSAY

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

(1) Add 50 mL of *methanol* to a quantity of the mixed contents of 20 capsules containing 0.15 g of Gemfibrozil, shake on a mechanical shaker for 10 minutes, add 20 mL of *water*, 1 mL of *glacial acetic acid* and sufficient *methanol* to produce 100 mL, mix and filter (Whatman GF/C paper is suitable), discarding the first 20 mL of filtrate. Dilute 1 volume of the filtrate to 5 volumes with the mobile phase.
(2) Dissolve 30 mg of *gemfibrozil BPCRS* in 80 mL of *methanol*, add 1 mL of *glacial acetic acid* and dilute to 100 mL with *water*.
(3) 0.01% w/v of *gemfibrozil methyl ester BPCRS* in a solution prepared by diluting 1 volume of solution (1) to 3 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Spherisorb ODS 2 or Regis C18 are suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 276 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

1 volume of *glacial acetic acid*, 19 volumes of *water* and 80 volumes of *methanol*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to gemfibrozil and gemfibrozil methyl ester is at least 4.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{15}H_{22}O_3$ in the capsules from the chromatograms obtained using the declared content of $C_{15}H_{22}O_3$ in *gemfibrozil BPCRS*.