Fenofibrate Tablets

フェノフィブラート錠

Fenofibrate Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$: 360.83).

Method of preparation Prepare as directed under Tablets, with Fenofibrate.

Identification To a quantity of powdered Fenofibrate Tablets, equivalent to 10 mg of Fenofibrate, add 10 mL of a mixture of acetonitrile and water (7:3), shake, and centrifuge. To 1 mL of the supernatant liquid add a mixture of acetonitrile and water (7:3) to make 100 mL. Determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits a maximum between 285 nm and 289 nm.

Purity Related substances—Conduct this procedure using light-resistant vessels. To 4 mL of the supernatant liquid obtained in the Assay add a mixture of acetonitrile and water (7:3) to make 10 mL, and use this solution as the sample solution. Pipet 1 mL of this solution, and add a mixture of acetonitrile and water (7:3) to make exactly 20 mL. Pipet 5 mL of this solution, add a mixture of acetonitrile and water (7:3) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* according to the following conditions, and determine each peak area by the automatic integration method: the area of the peak other than fenofibrate and the related substance A having the relative retention time of about 1.4 to fenofibrate obtained from the sample solution, is not larger than 2/5 times the peak area of fenofibrate from the standard solution, and the total area of the peaks other than fenofibrate from the sample solution is not larger than the peak area of fenofibrate from the standard solution.

Operating conditions—

Detector, column temperature, and mobile phase: Proceed as directed in the operating conditions in the Assay under Fenofibrate.

Column: A stainless steel column 4.6 mm in inside diameter and 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Flow rate: Adjust so that the retention time of fenofibrate is about 21 minutes.

Time span of measurement: About 2 times as long as the retention time of fenofibrate, beginning after the solvent peak.

System suitability—

Test for required detectability: Pipet 1 mL of the standard solution, and add a mixture of acetonitrile and water (7:3) to make exactly 10 mL. Confirm that the peak area of fenofibrate obtained with 10 μL of this solution is equivalent to 7 to 13% of that with 10 μL of the standard solution.

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of fenofibrate are not less than 10,000 and 0.8 to 1.5, respectively.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of fenofibrate is not more than 3.0%.

Uniformity of dosage units *<6.02>* Perform the Mass variation test, or the Content uniformity test according to the following method: it meets the requirement.

Conduct this procedure using light-resistant vessels. To 1 tablet of Fenofibrate Tablets add exactly 20 mL of a mixture of acetonitrile and water (7:3), and shake until the tablet is disintegrated. Centrifuge this solution, pipet V mL of the supernatant liquid, equivalent to about 20 mg of fenofibrate ($C_{20}H_{21}ClO_4$), and add a mixture of acetonitrile and water (7:3) to make exactly 20 mL. Pipet 2 mL of this solution, add exactly 2 mL of the internal standard solution, add a mixture of acetonitrile and water (7:3) to make 50 mL, and use this solution as the sample solution. Then, proceed as directed in the Assay.

$$\text{Amount (mg) of fenofibrate } (C_{20}H_{21}ClO_4) = M_S \times Q_T / Q_S \times 8 / V$$

M_S: Amount (mg) of Fenofibrate RS taken

Dissolution *<6.10>* When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of a solution prepared by dissolving 1 g of polysorbate 80 in water to make 100 mL as the dissolution medium, the dissolution rate in 30 minutes of Fenofibrate Tablets is not less than 75%.

Conduct this procedure using light-resistant vessels. Start the test with 1 tablet of Fenofibrate Tablets, withdraw not less than 10 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 5 mL or more of the filtrate, pipet V mL of the subsequent filtrate, add the dissolution medium to make exactly V' mL so that each mL contains about 59 μg of fenofibrate ($C_{20}H_{21}ClO_4$), and use this solution as the sample solution. Separately, weigh accurately about 12 mg of Fenofibrate RS, previously dried in vacuum over phosphorus (V) oxide at 60℃

for 4 hours, and dissolve in a mixture of acetonitrile and water (7:3) to make exactly 20 mL. Pipet 2 mL of this solution add the dissolution medium to make exactly 20 mL, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine the peak areas, A_T and A_S, of fenofibrate in each solution.

Dissolution rate (%) with respect to the labeled amount of fenofibrate ($C_{20}H_{21}ClO_4$)

$$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 450$$

M_S: Amount (mg) of Fenofibrate RS for assay taken

C: Labeled amount (mg) of fenofibrate ($C_{20}H_{21}ClO_4$) in 1 tablet

Operating conditions—

Detector, column, and column temperature: Proceed as directed in the operating conditions in the Assay under Fenofibrate.

Mobile phase: A mixture of acetonitrile and 0.02 mol/L phosphate buffer solution (pH 3.0) (8:2).

Flow rate: Adjust so that the retention time of fenofibrate is about 4 minutes.

System suitability—

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of fenofibrate are not less than 4000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of fenofibrate is not more than 2.0%.

Assay Conduct this procedure using light-resistant vessels. Weigh accurately the mass of not less than 20 tablets of Fenofibrate Tablets, and powder. Weigh accurately a portion of the powder, equivalent to about 50 mg of fenofibrate ($C_{20}H_{21}ClO_4$), add 30 mL of a mixture of acetonitrile and water (7:3), shake thoroughly, and add a mixture of acetonitrile and water (7:3) to make exactly 50 mL. Centrifuge this solution, pipet 2 mL of the supernatant liquid, add exactly 2 mL of the internal standard solution, add a mixture of acetonitrile and water (7:3) to make 50 mL, and use this solution as the sample solution. Separately, weigh accurately about 50 mg of Fenofibrate RS, previously dried in vacuum over phosphorus (V) oxide at 60℃ for 4 hours, and dissolve in a mixture of acetonitrile and water (7:3) to make exactly 50 mL. Pipet 2 mL of this solution, add exactly 2 mL of the internal standard solution, add a mixture of acetonitrile and water (7:3) to make 50 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of fenofibrate to that of the internal standard.

Amount (mg) of fenofibrate ($C_{20}H_{21}ClO_4$)

$$= M_S \times Q_T / Q_S$$

M_S: Amount (mg) of Fenofibrate RS for assay taken

Internal standard solution—A solution of 4-chlorobenzophenon in a mixture of acetonitrile and water (7:3) (11 in 10,000).

Operating conditions—

Proceed as directed in the operating conditions in the Assay under Fenofibrate.

System suitability—

Proceed as directed in the system suitability in the Assay under Fenofibrate.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Others

Related substance A: Refer to it described in Fenofibrate.

Add the following to 9.01 Reference Standards (1):

Fenofibrate RS

Add the following to 9.41 Reagents, Test Solutions:

4-Chlorobenzophenon $C_6H_5COC_6H_4Cl$ A white, crystalline powder or powder.

Identification—Determine the absorption spectrum of a solution of 4-chlorobenzophenon in ethanol (99.5) (3 in 50,000) as directed under Ultraviolet-visible Spectrophotometry <*2.24*>: it exhibits a maximum between 256 nm and 260 nm.

Melting point: 73 – 78℃

Content: not less than 98.0%. Assay—Dissolve 1 g of 4-chlorobenzophenon in acetone to make 10 mL, and use this solution as the sample solution. Perform the test with 1 μL of the sample solution as directed under Gas Chromatography <*2.02*> according to the following conditions. Determine each peak area by the automatic integration method, and calculate the amount of 4-chlorobenzophenon by the area percentage method.

Operating conditions

Detector: A hydrogen flame-ionization detector.

Column: A fused silica column 0.25 mm in inside diameter and 30 m in length, coated with dimethylpolysiloxane for gas chromatography in thickness of 0.25μm.

Column temperature: A constant temperature of about 220℃.

Injection port temperature: 270℃.

Detector temperature: 250℃.

Carrier gas: Helium.

Flow rate: 1.33 mL per minute.

Split ratio: 1:100.

Time span of measurement: About 3 times as long as the retention time of 4-chlorobenzophenon.

System suitability

System performance: To 1 mL of the sample solution add acetone to make 10 mL. When the procedure is run with 1 μL of this solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of 4-chlorobenzophenon are not less than 50,000 and not more than 1.2, respectively.

System repeatability: To 1 mL of the sample solution add acetone to make 10 mL. When the test is repeated 6 times with 1 μL of this solution under the above operating conditions, the relative standard deviation of the peak area of 4-chlorobenzophenon is not more than 2.0%.