

1 Fenofibrate Tablets

2 フェノフィブラート錠

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

7 **Method of preparation** Prepare as directed under Tab-
8 lets, with Fenofibrate.

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

17 **Purity** Related substances—Conduct this procedure us-
18 ing light-resistant vessels. To 4 mL of the supernatant liquid
19 obtained in the Assay add a mixture of acetonitrile and wa-
20 ter (7:3) to make 10 mL, and use this solution as the sample
21 solution. Pipet 1 mL of this solution, and add a mixture of
22 acetonitrile and water (7:3) to make exactly 20 mL. Pipet 5
23 mL of this solution, add a mixture of acetonitrile and water
24 (7:3) to make exactly 50 mL, and use this solution as the
25 standard solution. Perform the test with exactly 10 μ L each
26 of the sample solution and standard solution as directed un-
27 der Liquid Chromatography <2.01> according to the follow-
28 ing conditions, and determine each peak area by the auto-
29 matic integration method: the area of the peak other than
30 fenofibrate and the related substance A having the relative
31 retention time of about 1.4 to fenofibrate obtained from the
32 sample solution, is not larger than 2/5 times the peak area
33 of fenofibrate from the standard solution, and the total area
34 of the peaks other than fenofibrate from the sample solution
35 is not larger than the peak area of fenofibrate from the stand-
36 ard solution.

37 *Operating conditions*—

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

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

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

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

50 *System suitability*—

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

57 System performance: When the procedure is run with 10
58 μ L of the standard solution under the above operating
59 conditions, the number of theoretical plates and the
60 symmetry factor of the peak of fenofibrate are not less than
61 10,000 and 0.8 to 1.5, respectively.

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

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

69 Conduct this procedure using light-resistant vessels. To 1
70 tablet of Fenofibrate Tablets add exactly 20 mL of a mixture
71 of acetonitrile and water (7:3), and shake until the tablet is
72 disintegrated. Centrifuge this solution, pipet V mL of the
73 supernatant liquid, equivalent to about 20 mg of fenofibrate
74 ($C_{20}H_{21}ClO_4$), and add a mixture of acetonitrile and water
75 (7:3) to make exactly 20 mL. Pipet 2 mL of this solution,
76 add exactly 2 mL of the internal standard solution, add a
77 mixture of acetonitrile and water (7:3) to make 50 mL, and
78 use this solution as the sample solution. Then, proceed as
79 directed in the Assay.

$$80 \quad \text{Amount (mg) of fenofibrate (C}_{20}\text{H}_{21}\text{ClO}_4\text{)}$$

$$81 \quad = M_s \times Q_T / Q_s \times 8 / V$$

82 M_s : Amount (mg) of Fenofibrate RS taken

83 **Dissolution** <6.10> When the test is performed at 50 rev-
84 olutions per minute according to the Paddle method, using
85 900 mL of a solution prepared by dissolving 1 g of poly-
86 sorbate 80 in water to make 100 mL as the dissolution me-
87 dium, the dissolution rate in 30 minutes of Fenofibrate Tab-
88 lets is not less than 75%.

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

100 for 4 hours, and dissolve in a mixture of acetonitrile and
 101 water (7:3) to make exactly 20 mL. Pipet 2 mL of this solu-
 102 tion add the dissolution medium to make exactly 20 mL,
 103 and use this solution as the standard solution. Perform the
 104 test with exactly 10 μL each of the sample solution and
 105 standard solution as directed under Liquid Chromatography
 106 <2.01> according to the following conditions, and determine
 107 the peak areas, A_T and A_S , of fenofibrate in each solution.

108 Dissolution rate (%) with respect to the labeled amount of
 109 fenofibrate ($\text{C}_{20}\text{H}_{21}\text{ClO}_4$)

$$110 = M_S \times A_T / A_S \times V' / V \times 1 / C \times 450$$

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

112 C : Labeled amount (mg) of fenofibrate ($\text{C}_{20}\text{H}_{21}\text{ClO}_4$) in 1
 113 tablet

114 *Operating conditions*—

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

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

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

122 *System suitability*—

123 System performance: When the procedure is run with 10
 124 μL of the standard solution under the above operating
 125 conditions, the number of theoretical plates and the
 126 symmetry factor of the peak of fenofibrate are not less than
 127 4000 and not more than 2.0, respectively.

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

132 **Assay** Conduct this procedure using light-resistant ves-
 133 sels. Weigh accurately the mass of not less than 20 tablets
 134 of Fenofibrate Tablets, and powder. Weigh accurately a
 135 portion of the powder, equivalent to about 50 mg of feno-
 136 fibrate ($\text{C}_{20}\text{H}_{21}\text{ClO}_4$), add 30 mL of a mixture of acetonitrile
 137 and water (7:3), shake thoroughly, and add a mixture of ac-
 138 etonitrile and water (7:3) to make exactly 50 mL. Centrifuge
 139 this solution, pipet 2 mL of the supernatant liquid, add ex-
 140 actly 2 mL of the internal standard solution, add a mixture
 141 of acetonitrile and water (7:3) to make 50 mL, and use this
 142 solution as the sample solution. Separately, weigh accu-
 143 rately about 50 mg of Fenofibrate RS, previously dried in
 144 vacuum over phosphorus (V) oxide at 60°C for 4 hours, and
 145 dissolve in a mixture of acetonitrile and water (7:3) to make
 146 exactly 50 mL. Pipet 2 mL of this solution, add exactly 2
 147 mL of the internal standard solution, add a mixture of ace-
 148 tonitrile and water (7:3) to make 50 mL, and use this solu-
 149 tion as the standard solution. Perform the test with 20 μL

150 each of the sample solution and standard solution as di-
 151 rected under Liquid Chromatography <2.01> according to
 152 the following conditions, and calculate the ratios, Q_T and Q_S ,
 153 of the peak area of fenofibrate to that of the internal stand-
 154 ard.

$$155 \text{ Amount (mg) of fenofibrate (C}_{20}\text{H}_{21}\text{ClO}_4) \\ 156 = M_S \times Q_T / Q_S$$

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

158 *Internal standard solution*—A solution of 4-chlorobenzophenon in a mixture of acetonitrile and water (7:3) (11 in
 159 10,000).
 160

161 *Operating conditions*—

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

164 *System suitability*—

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

167 **Containers and storage** Containers—Tight containers.

168 Storage—Light-resistant.

169 **Others**

170 Related substance A: Refer to it described in Fenofibrate.

171 **Add the following to 9.01 Reference**
 172 **Standards (1):**

173 **Fenofibrate RS**

174 **Add the following to 9.41 Reagents,**
 175 **Test Solutions:**

176 **4-Chlorobenzophenon** $\text{C}_6\text{H}_5\text{COC}_6\text{H}_4\text{Cl}$ A white,
 177 crystalline powder or powder.

178 *Identification*—Determine the absorption spectrum of a
 179 solution of 4-chlorobenzophenon in ethanol (99.5) (3 in
 180 50,000) as directed under Ultraviolet-visible Spectropho-
 181 tometry <2.24>: it exhibits a maximum between 256 nm and
 182 260 nm.

183 *Melting point*: 73 – 78°C

184 *Content*: not less than 98.0%. Assay—Dissolve 1 g of
 185 4-chlorobenzophenon in acetone to make 10 mL, and use
 186 this solution as the sample solution. Perform the test with 1
 187 μL of the sample solution as directed under Gas Chroma-
 188 tography <2.02> according to the following conditions. De-
 189 termine each peak area by the automatic integration method,
 190 and calculate the amount of 4-chlorobenzophenon by the
 191 area percentage method.

192 *Operating conditions*

193 Detector: A hydrogen flame-ionization detector.

194 Column: A fused silica column 0.25 mm in inside diam-
 195 eter and 30 m in length, coated with dimethylpolysiloxane
 196 for gas chromatography in thickness of 0.25 μm .

197 Column temperature: A constant temperature of about
198 220°C.

199 Injection port temperature: 270°C.

200 Detector temperature: 250°C.

201 Carrier gas: Helium.

202 Flow rate: 1.33 mL per minute.

203 Split ratio: 1:100.

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

206 System suitability

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

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