Haloperidol decanoate

C_{31}H_{41}ClFNO_{3}  \quad M, 530.1

**DEFINITION**
Haloperidol decanoate contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of 4-[4-(4-chlorophenyl)-1-[4-(4-fluorophenyl)-1-[4-(4-hydroxypiperidin-1-yl)-phenyl]butan-1-one, calculated with reference to the dried substance.

**CHARACTERS**
A white or almost white powder, practically insoluble in water, very soluble in alcohol, in methanol and in methylene chloride.

It melts at about 42 °C.

**IDENTIFICATION**
A. Examine by infrared absorption spectrophotometry (2.2.24), comparing with the spectrum obtained with haloperidol decanoate CRS. Examine the substances prepared as mulls in liquid paraffin R.

B. To 0.1 g in a porcelain crucible add 0.5 g of sodium carbonate R. Heat over an open flame for 10 min. Allow to cool. Take up the residue with 5 ml of dilute nitric acid R and filter. To 1 ml of the filtrate add 1 ml of water R. The solution gives reaction (a) of chlorides (2.3.1).

**TESTS**

**Appearance of solution.** Dissolve 2.0 g in methylene chloride R and dilute to 20 ml with the same solvent. The solution is clear (2.2.1) and not more intensely coloured than reference solution B_{2} (2.2.2, Method II).

**Related substances.** Examine by liquid chromatography (2.2.29). Prepare the solutions immediately before use and protect from light.

**Test solution.** Dissolve 0.100 g of the substance to be examined in methanol R and dilute to 10.0 ml with the same solvent.

**Reference solution (a).** Dissolve 2.5 mg of bromperidol decanoate CRS and 2.5 mg of haloperidol decanoate CRS in methanol R and dilute to 50.0 ml with the same solvent.

**Reference solution (b).** Dilute 5.0 ml of the test solution to 100.0 ml with methanol R. Dilute 1.0 ml of this solution to 10.0 ml with methanol R.

The chromatographic procedure may be carried out using:
– a stainless steel column 0.1 m long and 4.0 mm in internal diameter packed with base-deactivated octadecylsilyl silica gel for chromatography R (3 µm),
– as mobile phase at a flow rate of 1.5 ml/min the following linear gradient programme:

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Mobile phase A (per cent V/V)</th>
<th>Mobile phase B (per cent V/V)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 30</td>
<td>80 → 40</td>
<td>20 → 60</td>
<td>linear gradient</td>
</tr>
<tr>
<td>30 - 35</td>
<td>40</td>
<td>60</td>
<td>isocratic elution</td>
</tr>
<tr>
<td>35 - 40</td>
<td>40 → 80</td>
<td>60 → 20</td>
<td>switch to initial eluent composition</td>
</tr>
<tr>
<td>40 - 60</td>
<td>80</td>
<td>20</td>
<td>restart gradient</td>
</tr>
</tbody>
</table>

– as detector a spectrophotometer set at 230 nm. Equilibrate the column for at least 30 min with acetonitrile R and then equilibrate at the initial eluent composition for at least 5 min.

Adjust the sensitivity of the system so that the height of the principal peak in the chromatogram obtained with 10 µl of reference solution (b) is at least 50 per cent of the full scale of the recorder.

Inject 10 µl of reference solution (a). When the chromatogram is recorded in the prescribed conditions the retention times are: haloperidol decanoate about 24 min and bromperidol decanoate about 24.5 min. The test is not valid unless the resolution between the peaks due to haloperidol decanoate and bromperidol decanoate is at least 1.5. If necessary, adjust the gradient or the time programme for the linear gradient elution.

Inject 10 µl of methanol R as a blank, 10 µl of the test solution and 10 µl of reference solution (b). In the chromatogram obtained with the test solution: the area of any peak apart from the principal peak, is not greater than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent); the sum of the areas of all the peaks apart from the principal peak, is not greater than three times the area of the principal peak in the chromatogram obtained with the reference solution (b) (1.5 per cent). Disregard any peak due to the blank and
any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b).

**Loss on drying** (2.2.32). Not more than 0.5 per cent, determined on 1.000 g by drying in vacuo at 30 °C.

**Sulphated ash** (2.4.14). Not more than 0.1 per cent, determined on 1.0 g in a platinum crucible.

**ASSAY**

Dissolve 0.425 g in 50 ml of a mixture of 1 volume of anhydrous acetic acid R and 7 volumes of methyl ethyl ketone R. Titrate with 0.1 M perchloric acid using 0.2 ml of naphtholbenzein solution R as indicator.

1 ml of 0.1 M perchloric acid is equivalent to 53.01 mg of C₃₁H₄₁ClFNO₃.

**STORAGE**

Store at room temperature below 25 °C, protected from light.

**IMPURITIES**

*Specified impurities: A, B, C, D, E, F, G, H, I, J, K.*

*Other detectable impurities: L.*

A. \( R₁ = F, R₂ = R₃ = R₄ = H \): 1-[4-(4-fluorophenyl)-4-oxobutyl]-4-phenylpiperidin-4-yl decanoate.

B. \( R₁ = R₂ = H, R₃ = F, R₄ = Cl \): 4-(4-chlorophenyl)-1-[4-(2-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate.

C. \( R₁ = F, R₂ = C₂H₅, R₃ = H, R₄ = Cl \): 4-(4-chlorophenyl)-1-[4-(3-ethyl-4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate.

D. 4-(4-chlorophenyl)-1-[4-[4-(4-chlorophenyl)-4-hydroxy]piperidin-1-yl][phenyl]-4-oxobutyl]piperidin-4-yl decanoate.

E. \( R = H, R' = Cl \): 4-(4'-chlorobiphenyl-4-yl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate.

F. \( R = Cl, R' = H \): 4-(3’-chlorobiphenyl-4-yl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate.

G. haloperidol,

H. \( n = 5 \): 4-(4-chlorophenyl)-1-[4(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl octanoate.

I. \( n = 6 \): 4-(4-chlorophenyl)-1-[4(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl nonanoate.

J. \( n = 8 \): 4-(4-chlorophenyl)-1-[4(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl undecanoate.

K. \( n = 9 \): 4-(4-chlorophenyl)-1-[4(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl dodecanoate.

L. 1-(4-fluorophenyl)ethanone.

**HALOTHANE**

Halothanum

\( C₂HBrClF₃ \)

**DEFINITION**

Halothane is \((RS)-2\)-bromo-2-chloro-1,1,1-trifluoroethane to which 0.01 per cent \( m/m \) of thymol has been added.

**CHARACTERS**

A clear, colourless, mobile, heavy, non-flammable liquid, slightly soluble in water, miscible with ethanol and with trichloroethylene.

**IDENTIFICATION**

*First identification: B.*

*Second identification: A, C.*

A. It complies with the test for distillation range (see Tests).