Edition: BP 2025 (Ph. Eur. 11.6 update)

Haloperidol Tablets

General Notices

Action and use

Dopamine receptor antagonist; neuroleptic.

DEFINITION

Haloperidol Tablets contain Haloperidol.

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

Content of haloperidol, $C_{21}H_{23}ClFNO_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

To a quantity of the powdered tablets containing 10 mg of Haloperidol add 10 mL of *water* and 1 mL of 1M *sodium hydroxide* and extract with 10 mL of *ether*. Filter the ether extract through absorbent cotton, evaporate the filtrate to dryness and dry the residue at 60° at a pressure not exceeding 0.7 kPa. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of haloperidol *(RS 173)*.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.
(b) Use 900 mL of a solution containing of 0.2% w/v of *sodium chloride* and 8% v/v of 1M *hydrochloric acid* in *water*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium, filter and dilute with the dissolution medium if necessary, to produce a solution expected to contain 0.00017% w/v of Haloperidol.
(2) 0.00017% w/v of *haloperidol BPCRS* in dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 5 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil ODS is suitable).

(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 247 nm.
(f) Inject 50 µL of each solution.

MOBILE PHASE

45 volumes of *acetonitrile* and 55 volumes of a 1% w/v solution of *ammonium acetate*.

DETERMINATION OF CONTENT

Calculate the total content of haloperidol, $C_{21}H_{23}ClFNO_2$, in the medium from the chromatograms obtained and using the declared content of $C_{21}H_{23}ClFNO_2$, in *haloperidol BPCRS*.

LIMITS

The amount of haloperidol released is not less than 70% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 1 volume of mobile phase A and 9 volumes of mobile phase B (solution A). Prepare the solutions immediately before use and protect from light.

(1) Shake a quantity of powdered tablets containing 10 mg of Haloperidol with 15 mL of solution A and mix with the aid of ultrasound. Dilute to 20 mL and filter.
(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.05% w/v of *haloperidol for system suitability EPCRS*.
(4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Hypersil BDS is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 230 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

Mobile phase A 1.7% w/v of *tetrabutylammonium hydrogen sulfate*.

Mobile phase B *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-2	90	10	isocratic
2-17	90→50	10→50	linear gradient
17-22	50	50	isocratic
22-23	50→90	50→10	linear gradient
23-28	90	10	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to haloperidol (retention time about 8 minutes) are: impurity B, about 0.9 and impurity D, about 1.6.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity B and haloperidol is at least 3.0.

LIMITS

Identify any peak corresponding to impurity B in the chromatogram obtained with solution (1), using the chromatogram obtained with solution (3), and multiply the area of this peak by a correction factor of 0.7.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity D is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any peak corresponding to impurity B is not greater than 0.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the area of any other *secondary peak* is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of all *secondary peaks* 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 (4) (0.1%).

Uniformity of content

Tablets containing less than 2 mg and/or less than 2% w/w of Haloperidol comply with the requirements stated under Tablets using the following method of analysis. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Place one tablet in 10 mL of the mobile phase, disperse with the aid of ultrasound for 2 minutes and centrifuge. If necessary, dilute the supernatant liquid with the mobile phase to produce a solution containing 0.005% w/v of Haloperidol.
(2) 0.005% w/v of *haloperidol BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

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

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{23}ClFNO_2$ in each tablet using the declared content of $C_{21}H_{23}ClFNO_2$ in *haloperidol BPCRS*.

ASSAY

For tablets containing less than 2 mg and/or less than 2% w/w of Haloperidol

Use the average of the individual results determined in the test for Uniformity of content.

For tablets containing 2 mg or more and 2% w/w or more of Haloperidol

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

(1) Add 60 mL of the mobile phase to a quantity of the powdered tablets containing 20 mg of Haloperidol, disperse with the aid of ultrasound for 2 minutes, add sufficient mobile phase to produce 100 mL, mix and filter.
(2) 0.020% w/v of *haloperidol BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

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

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{23}ClFNO_2$ in the tablets using the declared content of $C_{21}H_{23}ClFNO_2$ in *haloperidol BPCRS*.

IMPURITIES

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