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

Phenoxybenzamine Capsules

General Notices

Action and use

Alpha-adrenoceptor antagonist; treatment of hypertension in phaeochromocytoma.

DEFINITION

Phenoxybenzamine Capsules contain Phenoxybenzamine Hydrochloride.

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

Content of phenoxybenzamine hydrochloride, $C_{18}H_{22}ClNO,HCl$

92.5 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions prepared in *methanol*.
(1) Shake a quantity of the powdered capsule contents containing 10 mg of Phenoxybenzamine Hydrochloride with 5 mL with *methanol*. Dilute to 10 mL and filter (a Whatman GF/C filter is suitable).
(2) 0.1% w/v of *phenoxybenzamine hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F* (Merck silica gel 60 plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 20 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and spray with *dilute potassium iodobismuthate solution*.

MOBILE PHASE

20 volumes of *dichloromethane* and 80 volumes of *acetone*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2).
B. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

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Comply with the requirements in 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 500 mL of 0.01M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 45 minutes withdraw a sample of the medium and filter. Use the filtered medium, diluted with 0.01M *hydrochloric acid* if necessary, to produce a solution expected to contain 0.002% w/v of Phenoxybenzamine Hydrochloride.
(2) 0.002% w/v of *phenoxybenzamine hydrochloride BPCRS* in 0.01M *hydrochloric acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5 µm) (Kromasil C8 is 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 268 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

45 volumes of a 0.22% w/v solution of *anhydrous sodium dihydrogen orthophosphate*, previously adjusted to pH 3.0 with *orthophosphoric acid*, and 55 volumes of *acetonitrile*.

When the chromatograms are recorded under the prescribed conditions, the retention time of phenoxybenzamine is about 11 minutes.

DETERMINATION OF CONTENT

Calculate the total content of phenoxybenzamine hydrochloride, $C_{18}H_{22}ClNO,HCl$, in the medium from the chromatograms obtained and using the declared content of $C_{18}H_{22}ClNO,HCl$ in *phenoxybenzamine hydrochloride BPCRS*.

LIMITS

The amount of phenoxybenzamine hydrochloride released is not less than 75% (Q) of the stated amount.

Related substances

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

(1) Shake a quantity of the capsule contents containing 80 mg of Phenoxybenzamine Hydrochloride with 50 mL and dilute to 100 mL.
(2) Dilute 1 volume of solution (1) to 100 volumes.
(3) Dilute 1 volume of solution (2) to 10 volumes.
(4) Add 0.5 mL of 0.1M *sodium hydroxide* to 10 mL of 0.08% w/v of *phenoxybenzamine hydrochloride BPCRS* in *acetonitrile* (generation of impurity B and impurity 1).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used with a flow rate of 0.6 mL per minute. For solution (1), allow the chromatography to proceed for 1.5 times the retention time of phenoxybenzamine.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to phenoxybenzamine (retention time about 35 minutes) are: impurity B, about 0.1 and impurity 1, about 0.15.

SYSTEM SUITABILITY

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The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity B and impurity 1 is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%);

the area of any peak corresponding to impurity 1 is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the area of any other *secondary peak* is not greater than 4 times the area of the principal peak in the chromatogram obtained with solution (3) (0.4%);

the sum of the areas of any other *secondary peaks* is not greater than 1.5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (3) (0.1%).

ASSAY

Weigh the contents of 20 capsules. Mix and powder if necessary. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in *acetonitrile*.

(1) Mix, with the aid of ultrasound and occasional swirling, a quantity of the capsule contents containing 50 mg of Phenoxybenzamine Hydrochloride with 30 mL of *acetonitrile*. Dilute to produce 50 mL and filter. Dilute 1 volume of the filtrate to 5 volumes.
(2) 0.02% w/v of *phenoxybenzamine hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

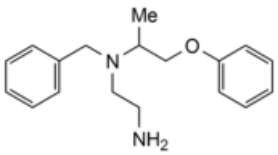
The chromatographic conditions described under Dissolution may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_{18}H_{22}ClNO,HCl$ in the capsules using the declared content of $C_{18}H_{22}ClNO,HCl$ in *phenoxybenzamine hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Phenoxybenzamine Hydrochloride and:



1. 2-(benzyl-[1-phenoxypropan-2-yl]amino)amine.

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