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

Hydroxyzine Tablets

General Notices

Action and use

Histamine H_1 receptor antagonist.

DEFINITION

Hydroxyzine Tablets contain Hydroxyzine Hydrochloride.

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

Content of hydroxyzine hydrochloride, $C_{21}H_{27}ClN_2O_2,2HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. In the Assay, the retention time of the principal peak in the chromatogram obtained with solution (1) is the same as that of the peak due to hydroxyzine hydrochloride in the chromatogram obtained with solution (2).
B. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions, prepared in a solution containing 1 volume of *methanol* and 1 volume of *dichloromethane* (solution A).
(1) Shake a quantity of the powdered tablets containing 100 mg of Hydroxyzine Hydrochloride with 5 mL of solution A, add sufficient solution A to produce 10 mL, centrifuge and use the supernatant liquid.
(2) 1% w/v of *hydroxyzine hydrochloride BPCRS*.
(3) 0.5% w/v each of *hydroxyzine hydrochloride BPCRS* and *meclozine hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a *silica gel G plate*.
(b) Use the mobile phase described below.
(c) Apply 2 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air, spray with *potassium iodobismuthate solution R2*, heat at 110° for 5 minutes and allow to cool.

MOBILE PHASE

1 volume of 13.5M *ammonia*, 24 volumes of *ethanol* and 75 volumes of *toluene*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows two clearly separated spots.

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).

TESTS

Dissolution

Carry out the procedure protected from light. Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 75 revolutions per minute.
(b) Use 900 mL of *water*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium if necessary to produce a solution expected to contain 0.0011% w/v of Hydroxyzine Hydrochloride, at the maximum at 230 nm, Appendix II B using *water* in the reference cell.
(2) Measure the *absorbance* of a 0.0011% w/v solution of *hydroxyzine hydrochloride BPCRS* using *water* in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of hydroxyzine hydrochloride, $C_{21}H_{27}ClN_2O_2,2HCl$, in the medium from the absorbances obtained and using the declared content of $C_{21}H_{27}ClN_2O_2,2HCl$ in *hydroxyzine hydrochloride BPCRS*.

LIMITS

The amount of hydroxyzine 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 in the mobile phase.

(1) Shake a quantity of the powdered tablets containing 50 mg of Hydroxyzine Hydrochloride with 10 mL of the mobile phase, add sufficient mobile phase to produce 50 mL and filter.
(2) Dilute 2 volumes of solution (1) to 100 volumes. Further dilute 1 volume of this solution to 10 volumes.
(3) 0.1% w/v of *hydroxyzine hydrochloride BPCRS*.
(4) Dilute 1 volume of solution (1) to 100 volumes. Further dilute 1 volume of the resulting solution to 20 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Luna C18 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 230 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for 3 times the retention time of hydroxyzine.

MOBILE PHASE

14 volumes of *triethylamine*, 300 volumes of *acetonitrile* and 686 volumes of a 0.075% w/v solution of *sodium methanesulfonate*, adjust the mobile phase to pH 2.7 with *sulfuric acid*.

When the chromatograms are recorded under the prescribed conditions the retention time of hydroxyzine is about 9 min.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 10, where H_p is the height above the baseline of the peak immediately before the peak due to hydroxyzine and H_v is the height above the baseline of the lowest point of the curve separating this peak from the peak due to hydroxyzine.

LIMITS

In the chromatogram obtained with solution (1):

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

the sum of the areas of any *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.05%).

ASSAY

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

(1) Shake a quantity of the powdered tablets containing 50 mg of Hydroxyzine Hydrochloride with 10 mL of *water* for 20 minutes, add 125 mL of *methanol* and shake for a further 30 minutes. Add a sufficient quantity of a 30% v/v solution of *acetonitrile* to produce 250 mL, filter and dilute 5 volumes of the filtrate to 10 volumes with a 30% v/v solution of *acetonitrile*.
(2) 0.01% w/v of *hydroxyzine hydrochloride BPCRS* in a 30% v/v solution of *acetonitrile*.
(3) 0.01% w/v of *hydroxyzine hydrochloride BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3);

the *peak-to-valley ratio* is at least 10, where H_p is the height above the baseline of the peak immediately before the peak due to hydroxyzine and H_v is the height above the baseline of the lowest point of the curve separating this peak from the peak due to hydroxyzine.

DETERMINATION OF CONTENT

Calculate the content of $C_{21}H_{27}ClN_2O_2,2HCl$ in the tablets using the declared content of $C_{21}H_{27}ClN_2O_2,2HCl$ in *hydroxyzine hydrochloride BPCRS*.