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Zuclopenthixol Tablets

General Notices

Action and use

Dopamine receptor antagonist; neuroleptic.

DEFINITION

Zuclopenthixol Tablets contain Zuclopenthixol Hydrochloride.

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

Content of zuclopenthixol, $C_{22}H_{25}ClN_2OS$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. To a quantity of the powdered tablets containing the equivalent of 20 mg of zuclopenthixol add 40 mL of 0.1M hydrochloric acid, heat on a water bath for 30 minutes, shaking occasionally, cool, dilute to 200 mL with water and shake thoroughly. Centrifuge a portion of the resulting solution and dilute 20 mL of the supernatant liquid to 200 mL with water. Measure the absorbance, Appendix II B at 230 nm using 0.002M hydrochloric acid in the reference cell. The light absorption, Appendix II B, in the range 205 to 350 nm of a 0.0015% w/v solution in ethanol (96%) exhibits maxima at 230, 268 and 325 nm.
B. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Dissolution

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

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 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 30 minutes withdraw a sample of the medium, filter and dilute with the dissolution medium, if necessary, to produce a solution expected to contain the equivalent of 0.0002% w/v of zuclopenthixol.
(2) 0.00024% w/v of *zuclopenthixol hydrochloride BPCRS* in the dissolution medium.

(3) 0.002% w/v each of *zuclopenthixol hydrochloride BPCRS* and *trans-clopenthixol hydrochloride BPCRS* (impurity B) in solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 2.1 mm) packed with *octylsilyl silica gel for chromatography* (3.5 µm) (Symmetry Shield RP18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 0.6 mL per minute.
(d) Use a column temperature maintained at 40°.
(e) Use a detection wavelength of 270 nm.
(f) Inject 250 µL of each solution.
(g) allow the chromatography to proceed for 1.5 times the retention time of zuclopenthixol (retention time about 6 miuntes).

MOBILE PHASE

2 volumes of trifluoroacetic acid, 9 volumes of acetonitrile and 41 volumes of water.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks corresponding to zuclopenthixol and trans-clopenthixol hydrochloride is at least 2.0.

DETERMINATION OF CONTENT

Calculate the total content of zuclopenthixol, $C_{22}H_{25}ClN_2OS$, in the medium from the chromatograms obtained and the declared content of $C_{22}H_{25}ClN_2OS$, in zuclopenthixol hydrochloride BPCRS.

LIMITS

The amount of zuclopenthixol 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 protected from light.

Solution A 18 volumes of acetonitrile and 82 volumes of water.
(1) Shake a quantity of the powdered tablets containing the equivalent of 25 mg of zuclopenthixol with 5 mL of Solution A with the aid of ultrasound. Add 15 mL of Solution A, place in a water bath for 20 minutes, allow to cool and dilute to 25 mL with solution A.
(2) Dilute 1 volume of solution (1) to 100 volumes with solution A, further dilute 1 volume of this solution to 5 volumes with solution A.
(3) Dilute 3 volumes of solution (1) to 100 volumes with solution A.
(4) 0.002% w/v each of *zuclopenthixol hydrochloride BPCRS* and *trans-clopenthixol hydrochloride BPCRS* (impurity B) in solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (5 cm × 2.1 mm) packed with *octadecylsilyl silica gel for chromatography* (3.5 µm) (Symmetry Shield RP18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 0.6 ml per minute.
(d) Use a column temperature 40°.
(e) Use a detection wavelength of 270 nm.
(f) Inject 5 µL of each solution.

MOBILE PHASE

Mobile phase A 1 volume of *trifluoroacetic acid* and 25 volumes of water.

Mobile phase B 1 volume of trifluoroacetic acid and 25 volumes of acetonitrile.

Mobile phase C *methanol*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Mobile phase C (% v/v)	Comment
0-8	82	18	0	isocratic
8-17	82→5	18→10	0→85	linear gradient
17-19	5→82	10→18	85→0	linear gradient
19-30	82	18	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the retention times relative to zuclopenthixol (retention time about 6 minutes) are: impurity A, about 0.1; trans-clopenthixol hydrochloride, about 1.2.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks corresponding to zuclopenthixol and trans-clopenthixol hydrochloride is at least 2.0.

LIMITS

In the chromatogram obtained with solution (1):

The area of any peak due to trans-zuclopenthixol is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (3%).

The area of any peak due to zuclopenthixol impurity A is not greater than 1.5 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 the area of the principal peak in the chromatogram obtained with solution (2) (0.2%).

The sum of the areas of any secondary peak, excluding trans-clopenthixol hydrochloride, is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (1%).

Disregard any peak with an area of less than half the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

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

Solution A 18 volumes of acetonitrile and 82 volumes of water.
(1) To a quantity of the powdered tablets containing the equivalent of 25 mg of zuclopenthixol add 50 mL of solution A and mix with the aid of ultrasound. Add 150 mL of solution A and place in a water bath for 20 minutes, allow to cool and dilute to 250 mL with solution A.
(2) 0.012% w/v of zuclopenthixol hydrochloride BPCRS in solution A.
(3) 0.002% w/v each of *zuclopenthixol hydrochloride BPCRS* and *trans-clopenthixol hydrochloride BPCRS* (impurity B) in solution A.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under the Dissolution may be used, with an injection volume of 5µL.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks corresponding to zuclopenthixol and trans-clopenthixol hydrochloride is at least 2.0.

DETERMINATION OF CONTENT

Calculate the total content of zuclopenthixol, $C_{22}H_{25}ClN_2OS$, in the medium from the chromatograms obtained and the declared content of $C_{22}H_{25}ClN_2OS$, in zuclopenthixol hydrochloride BPCRS.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of zuclopenthixol.

IMPURITIES

The impurities limited by the requirements of this monograph include those shown under Zuclopenthixol Hydrochloride.