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Mexiletine Capsules

General Notices

Action and use

Class I antiarrhythmic; treatment of myotonia.

DEFINITION

Mexiletine Capsules contain Mexiletine Hydrochloride.

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

Content of mexiletine hydrochloride, $C_{11}H_{17}NO,HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the contents of the capsules containing the 50 mg of Mexiletine Hydrochloride with 10 mL of *methanol* for 15 minutes, filter (Whatman GF/C filter paper is suitable), evaporate to dryness on a rotary evaporator and dry the residue at 105° for 2 hours. The *infrared absorption spectrum* of the dried residue, Appendix II A, is concordant with the *reference spectrum* of mexiletine hydrochloride *(RS 233)*.

TESTS

Dissolution

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

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

After 30 minutes withdraw a sample of the medium and filter. Dilute the filtrate with 0.01M *hydrochloric acid*, if necessary, to give a solution expected to contain 0.02% w/v of Mexiletine Hydrochloride. Measure the *absorbance* of this solution, Appendix II B, at the maximum at 260 nm, using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of mexiletine hydrochloride, $C_{11}H_{17}NO,HCl$, in the medium taking 11.6 as the value of A(1%, 1 cm) at the maximum at 260 nm.

LIMITS

The amount of mexiletine hydrochloride released is not less than 80% (Q) of the stated amount.

Related substances

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

(1) Mix, with the aid of ultrasound, a quantity of the contents of the capsules containing 0.2 g of Mexiletine Hydrochloride with 10 mL of the mobile phase, filter through a 0.4-µm glass microfibre filter (Whatman GF/C is suitable) and use the filtrate.
(2) Dilute 1 volume of solution (1) to 10 volumes with the mobile phase.
(3) 0.01% w/v of *mexiletine impurity C EPCRS* and 0.08% w/v of *2,6-dimethylphenol* (impurity A) in the mobile phase. Mix 1 volume of this solution with 2 volumes of solution (2) and add sufficient mobile phase to produce 100 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Kromasil 100-5 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 262 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for 5.5 times the retention time of mexiletine.

MOBILE PHASE

35 volumes of solution A and 65 volumes of *methanol R2*.

Solution A Dissolve 11.5 g of *anhydrous sodium acetate* in 500 mL of *water*, add 3.2 mL of *glacial acetic acid*, mix and allow to cool. Adjust the pH to 4.8 with *glacial acetic acid* and add sufficient *water* to produce 1000 mL.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to mexiletine (retention time about 4 minutes) are: impurity C, about 0.7 and impurity A, about 1.8.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity C and mexiletine is at least 5.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than 2.5 times the area of the peak due to impurity A in the chromatogram obtained with solution (3) (0.1%);

the area of any peak corresponding to impurity C is not greater than 20 times the area of the peak due to impurity C in the chromatogram obtained with solution (3) (0.1%);

the area of any other *secondary peak* is not greater than half the area of the peak due to mexiletine in the chromatogram obtained with solution (3) (0.1%).

The total impurity content is not greater than 0.5%.

Disregard any peak with an area less than 0.25 times the area of the peak due to mexiletine in the chromatogram obtained with solution (3) (0.05%).

ASSAY

Weigh the contents of 20 capsules. Mix and powder if necessary. Shake a quantity of capsule contents containing 50 mg of Mexiletine Hydrochloride with 50 mL of 0.01M *hydrochloric acid* for 30 minutes. Dilute to 100 mL with 0.01M *hydrochloric*

acid and centrifuge. Measure the *absorbance* of the supernatant liquid at the maximum at 260 nm, Appendix II B. Calculate the content of $C_{11}H_{17}NO,HCl$ taking 11.6 as the value of A(1%, 1 cm) at the maximum at 260 nm.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B and C listed under Mexiletine Hydrochloride.