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

Imipramine Tablets

General Notices

Action and use

Monoamine reuptake inhibitor; tricyclic antidepressant.

DEFINITION

Imipramine Tablets contain Imipramine Hydrochloride.

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

Content of imipramine hydrochloride, $C_{19}H_{24}N_2,HCl$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Dissolve a quantity of powdered tablets containing 100 mg of Imipramine Hydrochloride in 10 mL of *acetone* and filter. Evaporate the filtrate to approximately 3 mL under a stream of *nitrogen* and add *diethyl ether* until a precipitate is formed and filter. Wash the precipitate with *diethyl ether* and dry under vacuum at 105 °C for 30 minutes. Dissolve the precipitate in 10 mL of *acetone*, add *diethyl ether* until a precipitate is formed and filter. Dry the precipitate under vacuum at 105 °C for 30 minutes. The *infrared absorption* spectrum of the dried residue, Appendix II A, is concordant with the reference spectrum of imipramine hydrochloride (*RS 509*).

TESTS

Dissolution

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

(a) Use Apparatus 1, rotating the basket at 100 revolutions per minute.

(b) Use 900 mL of 0.1M *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 0.1M *hydrochloric acid* if necessary, expected to contain 0.0011% w/v of Imipramine Hydrochloride.
(2) 0.0011% w/v of imipramine hydrochloride BPCRS in 0.1M *hydrochloric acid*.
(3) 0.1% w/v *imipramine for system suitability EPCRS* (containing impurity B) in 0.1M *hydrochloric acid*

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm x 4.6 mm) packed with *end-capped polar-embedded octadecylsilyl amorphous organosilica polymer* (5µm) (X-Terra RP18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 220 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

40 volumes of *acetonitrile* and 60 volumes of a 0.52% w/v solution of *dipotassium hydrogen orthophosphate*, previously adjusted to pH 7.0 with *orthophosphoric acid*.

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 imipramine is at least 4.5.

the *symmetry factor* is between 0.8 to 2.0.

DETERMINATION OF CONTENT

Calculate the total content of imipramine hydrochloride, $C_{19}H_{24}N_2$,HCl in the medium from the chromatograms obtained using the declared content of $C_{19}H_{24}N_2$,HCl in *imipramine hydrochloride BPCRS*.

LIMITS

The amount of imipramine 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 following solutions.

(1) To 80 mL of the mobile phase add 10 whole tablets and mix with the aid of ultrasound for 30 minutes. Shake for a further 30 minutes and add sufficient of the mobile phase to produce a solution containing 0.1% w/v of Imipramine Hydrochloride and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase and dilute 1 volume of this solution to 5 volumes with the same solvent.
(3) 0.0003% w/v of *iminodibenzyl* in the mobile phase.
(4) 0.1% w/v *imipramine for system suitability EPCRS* (containing impurity B) in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used allowing the chromatography to proceed for 2.5 times the retention time of imipramine for solution (1).

When the chromatograms are recorded under the prescribed conditions, the *relative retention* of impurity B with respect to Imipramine (retention time, about 7 minutes) is about 0.7.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity B and imipramine is at least 4.5.

in the chromatogram obtained with solution (2), the *symmetry factor* of the principal peak is between 0.8 to 2.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to iminodibenzyl is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (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 impurities is not greater than 1.0%.

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

ASSAY

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

(1) To 80 mL of the mobile phase add 10 whole tablets and mix with the aid of ultrasound for 30 minutes. Shake for a further 30 minutes and add sufficient of the mobile phase to produce a solution containing 0.1% w/v of Imipramine Hydrochloride and filter. Dilute 1 volume of the filtrate to 10 volumes with the mobile phase.
(2) 0.01% w/v of *imipramine hydrochloride BPCRS* in the mobile phase.
(3) 0.1% w/v *imipramine for system suitability EPCRS* (containing impurity B) in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity B and imipramine is at least 4.5.

in the chromatogram obtained with solution (2), the *symmetry factor* of the principal peak is between 0.8 to 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{19}H_{24}N_2$,HCl in the tablets from the chromatograms obtained and using the declared content of $C_{19}H_{24}N_2$,HCl in *imipramine hydrochloride BPCRS*.