Pilocarpine Hydrochloride

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Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

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Document History and Schedule for the Adoption Process

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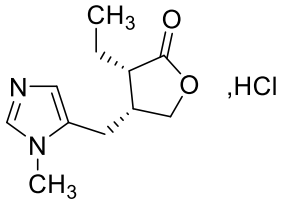
Pilocarpine Hydrochloride



$C_{11}H_{16}N_2O_2$,HCl Mol. Wt. 244.7

Pilocarpine Hydrochloride is 2(3*H*)-Furanone, 3-ethyldihydro-4-[(1-methyl-1*H*-imidazol-5-yl)methyl]-, monohydrochloride, (3*S*-*cis*).

Pilocarpine Hydrochloride contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{11}H_{16}N_2O_2$,HCl, calculated on the dried basis.

Category. Cholinoceptor agonist.

Description. A white or almost white, crystalline powder or colourless crystals, hygroscopic.

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *pilocarpine hydrochloride IPRS* or with the reference spectrum of pilocarpine hydrochloride.

B. It gives reaction (A) of chlorides (2.3.1).

Tests

Specific optical rotation (2.4.22). + 88.5 ° to + 91.5°, determined in a 2.0 per cent w/v solution in *water*.

Other alkaloids. Dissolve 1 g in 100 ml of *water* and divide into two portions. To one portion, add few drops of *6 M ammonium hydroxide* and to the another, add few drops of *dilute potassium dichromate*; No turbidity is produced in either solution.

Related substances. Determine by liquid chromatography (2.4.14).

Test solution Dissolve 50 mg of the substance under examination in *water,* with the aid of ultrasound and dilute to 100.0 ml with the *water.*

Reference solution (a). A 0.05 per cent w/v solution of *pilocarpine hydrochloride IPRS* in *water.*

Reference solution (b). Dilute 5.0 ml of reference solution (a) to100.0 ml with *water.*

Reference solution (c). Dissolve 25 mg of *pilocarpine hydrochloride IPRS* in 5 ml of *water* with the aid of ultrasound. Add 5 ml of *0.1 M sodium hydroxide*, quench immediately with 5 ml of *0.1 M hydrochloric acid*, mix and dilute with *water* to 50 ml with *water* (Isopilocarpine formed).

Reference solution (d). Dilute 1.0 ml of reference solution (b) to100.0 ml with *water.*

Chromatographic system

-stainless steel column 15 cm x 4.6 mm, packed with phenyl groups bonded to porous silica (5 µm) (Such as Luna Phenyl-Hexyl),

-column temperature: 35°,

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-mobile phase: a mixture of 63 volumes of a buffer solution prepared by dissolving 4.4 g of *dipotassium hydrogen phosphate* in 1000 ml of *water,* adjusted to pH 6.5 with *orthophosphoric acid,* 35 volumes of *methanol* and 2 volumes of *acetonitrile,*
- flow rate: 1 ml per minute,
- spectrophotometer set at 215 nm,
- injection volume: 10 µl.

Name	Relative retention time
Isopilocarpine[1]	0.94
Pilocarpine	1.0
Pilocarpic acid[2]	1.15
Isopilocarpic acid[3]	1.19

[1](3*R*,4*R*)-3-Ethyl-4-[(1-methyl-1*H*-imidazol-5-yl)methyl]dihydrofuran-2(3*H*)-one,
[2] (2*S*,3*R*)-2-Ethyl-4-hydroxy-3-[(1-methyl-1*H*-imidazol-5-yl)methyl]butanoic acid,
[3](2*R*,3*R*)-2-Ethyl-4-hydroxy-3-[(1-methyl-1*H*-imidazol-5-yl)methyl]butanoic acid.

Inject reference solution (a), (c) and (d). The test is not valid unless the resolution between the peaks due to isopilocarpine and pilocarpine is not less than 1.5 in the chromatogram obtained with reference solution (c), the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (a) and the signal-to-noise ratio is not less than 10 in the chromatogram obtained with reference solution (d).

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to isopilocarpine is not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent), the area of any peak corresponding to pilocarpic acid is not more than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent), the area of any peak corresponding to isopilocarpic acid is not more than 0.02 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent), the area of any other secondary peak is not more than 0.02 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent) and the sum of areas of all the secondary peaks is not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent). Ignore any peak with an area less than 0.01 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Sulphated ash (2.3.18). Not more than 0.1 per cent.

Loss on drying (2.4.19). Not more than 3.0 per cent, determined on 1.0 g by drying in an oven at 105° for 2 hours.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances.

Inject reference solution (a) and (c). The test is not valid unless the resolution between the peaks due to isopilocarpine and pilocarpine is not less than 1.5 in the chromatogram obtained with reference solution (c), the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution.

Calculate the content of $C_{11}H_{16}N_2O_2$,HCl.

Storage. Store protected from light and moisture, at a temperature not exceeding 30°.

Solubility.

Pilocarpine Hydrochloride. Very soluble in *water* and freely soluble in *ethanol (95 per cent).*

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