Dicyclomine Hydrochloride

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

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.

Document History and Schedule for the Adoption Process

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Draft revision published on IPC website for public comments	--
Further follow-up action as required.	

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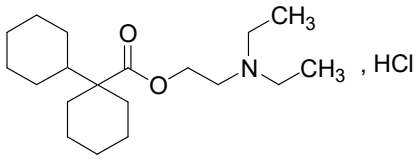
Change **to: Dicyclomine Hydrochloride**

Dicycloverine Hydrochloride



$C_{19}H_{35}NO_2$,HCl Mol.Wt. 346.0

Dicyclomine Hydrochloride is 2-diethylaminoethyl bicyclohexyl-1-carboxylate hydrochloride.

Dicyclomine Hydrochloride contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{19}H_{35}NO_2$,HCl calculated on the dried basis.

Category. Antispasmodic.

Description. A white or almost white, crystalline powder

Identification

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

B. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

C. It gives reaction of chlorides (2.3.1).

Tests

pH (2.4.24). 5.0 to 5.5, determined in 1.0 per cent w/v solution.

Limit of dicyclomine related compound A. Determine by liquid chromatography (2.4.14).

*Solvent mixture.*70 volumes of *acetonitrile* and 30 volumes of *water.*

Test solution. Dissolve 0.1 g of the substance under examination in the solvent mixture with the aid of ultrasound and dilute to 50.0 ml with the solvent mixture.

Reference solution (a). A 0.0003 per cent w/v solution of *dicyclomine hydrochloride related compound A ([1,1'-Bi(cyclohexane)]-1-carboxylic acid) IPRS* in the solvent mixture.

Reference solution (b). Dilute 5.0 ml of reference solution (a) to 10.0 ml with the solvent mixture

Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with octylsilane bonded to porous silica (3.5µm) (Such as X Bridge BEH C8),
- mobile phase: a mixture of 55 volumes of *acetonitrile* and 45 volumes of a buffer solution prepared by dissolving 2.72 g of *potassium dihydrogen orthophosphate* in 900 ml of *water*, adjusted to pH 3.5 with *orthophosphoric acid* and dilute to 1000 ml with *water*,
- flow rate: 1 ml per minute,

- spectrophotometer set at 215 nm,
- injection volume: 100 µl.

Inject reference solution (a) and (b) The test is not valid unless the relative standard deviation for replicate injections is not more than 5.0 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 (b).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to dicyclomine hydrochloride related compound A is not more than 1.33 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent).

Related substances. Determine by liquid chromatography (2.4.14).

NOTE--Use freshly prepared solutions.

*Solvent mixture.*70 volumes of *acetonitrile* and 30 volumes of *water.*

Test solution. Dissolve 40 mg of the substance under examination in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

Reference solution (a). A 0.04 per cent w/v solution of *dicyclomine hydrochloride IPRS* in the solvent mixture.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 100.0 ml with the solvent mixture. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (c). Dilute 5.0 ml of reference solution (b) to 10.0 ml with the solvent mixture.

Chromatographic system
- a stainless steel column 15 cm x 4.6 mm, packed with octylsilane bonded to porous silica (3.5 µm), (Such as X Bridge BEH C8),
- mobile phase: a mixture of 70 volumes of *acetonitrile* and 30 volumes of a buffer solution prepared by dissolving 2.72 g of *potassium dihydrogen orthophosphate* in 900 ml of *water*, adjusted to pH 7.5 with 10 per cent w/v of *sodium hydroxide solution* and dilute to 1000 ml with *water*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 215 nm,
- injection volume: 50 µl

Name	Relative retention time	Correction factor
Dicyclomine -1-ene [1]	0.8	0.34
Dicyclomine	1.0	--

[1]2-(Diethylamino) ethyl [1,1′-bi(cyclohexan)]-1′-ene-1-carboxylate,

Inject reference solution (a), (b) and (c). The test is not valid unless the resolution between the peaks due to dicylomine and dicylomine-1-ene is not less than 2.0 in the chromatogram obtained with reference solution (a), the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (b) and the signal-to-noise ratio is not less than 10 in the chromatogram obtained with reference solution (c).

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to dicyclomine-1-e is not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent) and the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent).

The sum of all the impurities found in the test of Limit of dicyclomine related compound A and Related substances is not more than (0.7 per cent).

Heavy metals (2.3.13). 1.0 g complies with the limit test for heavy metals, Method B (20 ppm).

Loss on drying (2.4.19). Not more than 1.0 per cent, determined on 1.0 g by drying in an oven at 105° for 4 hours.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances with the following modifications.

Inject reference solution (a). The tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 1.0 per cent.

Inject reference solution (a) and the test solution.

Calculate the content of $C_{19}H_{35}NO_2$,HCl.

Storage. Store protected from moisture.