Nicotine

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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. 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 arnd-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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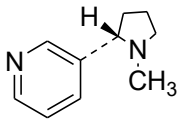
Nicotine



$C_{10}H_{14}N_2$ Mol. Wt. 162.2

Nicotine is a 3-[(2*S*)-1-methylpyrrolidin-2-yl]pyridine.

Nicotine contains not less than 99.0 per cent and 101.0 per cent of $C_{10}H_{14}N_2$, calculated on the anhydrous basis.

Category. Agonist at nicotinic acetylcholine receptors (nAChRs).

Description. A colourless or brownish viscous liquid, volatile, hygroscopic.

Identification

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

B. Specific optical rotation (see Tests).

Tests

Appearance of solution. Dissolve 1.0 g in *water* and dilute to 10.0 ml with *water*. The solution is clear (2.4.1) and not more intensely coloured than reference solution YS5, BYS5 or RS5 (2.4.1).

Specific optical rotation (2.4.22). -152° to -140°, determined at 20° in a 2.0 per cent w/v solution in *ethanol*.

Related Substances. Determine by liquid chromatography (2.4.14).

NOTE – Prepare solutions immediately before use.

Test Solution. Dissolve 20.0 mg of the substance under examination in *water* and dilute to 25.0 ml with *water*.

Reference *solution (a)*. A 0.008 per cent w/v solution of *nicotine IPRS* in *water*. Dilute 1.0 ml of the solution to 100.0 ml with *water*.

Reference *solution (b)*. Dissolve the contents of a vial of *nicotine for system suitability IPRS* (containing nicotine impurities A, B, C, D, E, F and G) in 1.0 ml of *water*.

Chromatographic system
– a stainless steel column 15 cm x 4.6 mm, packed with end capped polar embedded octadecylsilyl bonded to hybrid silica (5 µm) (such as Waters XTerra RP 18),
– mobile phase: A. a mixture of 900 ml of *water*, 25.0 ml of 6 per cent w/v solution of *glacial acetic acid* and 6.0 ml of *concentrated ammonia*, adjusted to pH 10.0 with *dilute ammonia solution* or *dilute glacial acetic acid* and dilute to 1000 ml with *water*,
B. *acetonitrile*,
– a gradient programme using the conditions given below,
– flow rate: 1 ml per minute,
– spectrophotometer set at 254 nm,
– injection volume: 20 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile Phase B (per cent v/v)
0	100	0
3	100	0
3.01	95	5

28	74	26
32	60	40
33	100	0
43	100	0

Name	Relative Retention Time
Nicotine impurity E[1]	0.30
Nicotine impurity C[2]	0.55
Nicotine impurity F[3]	0.70
Nicotine impurity A[4]	0.80
Nicotine impurity D[5]	0.86
Nicotine impurity G[6]	0.90
Nicotine (Retention time: about 17.8 minutes)	1.00
Nicotine impurity B[7]	1.60

[1](1*RS*,2S)-1-methyl-2-(pyridin-3-yl)pyrrolidine 1-oxide (nicotine N'-oxide),
[2](5*S*)-1-methyl-5-(pyridin-3-yl)pyrrolidin-2-one (cotinine),
[3]3-[(2*S*)-pyrrolidin-2-yl]pyridine (nornicotine),
[4](2*S*)-1,2,3,6-tetrahydro-2,3'-bipyridyl (anatabine),
[5]3-(4,5-dihydro-3*H*-pyrrol-2-yl)pyridine (myosmine),
[6]3-[(2*S*)-piperidin-2-yl]pyridine (anabasine),
[7]3-(1-methyl-1*H*-pyrrol-2-yl)pyridine (β-nicotyrine).

Inject reference solution (b) to identify the peaks due to nicotine impurity A, B, C, D, E, F and G.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to nicotine impurity G and nicotine is not less than 2.5.

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to nicotine impurity A, B, C, D, E, F and G, each of, is not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent) and the sum of the areas of all the secondary peaks is not more than 8 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.8 per cent). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Water (2.3.43). Not more than 0.5 per cent, determined on 1.0 g.

Assay. Dissolve 60.0 mg of substance under examination in 30.0 ml of *anhydrous acetic acid*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (2.4.25). Carry out a blank titration.

1 ml of *0.1 M perchloric acid* is equivalent to 0.00811 g of $C_{10}H_{14}N_2$.

Storage. Store protected from light and under nitrogen in an air tight container.

Solubility. Soluble in *water*, miscible with *ethanol*.