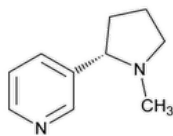


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Nicotine

Change to read:



$C_{10}H_{14}N_2$ ▲162.24▲ (USP 1-Aug-2022)
3-(1-Methyl-2-pyrrolidinyl)pyridine;
β-Pyridyl-α-N-methyl pyrrolidine CAS RN®: 54-11-5; UNII: 6M3C89ZY6R.

Change to read:

DEFINITION

Nicotine contains NLT ▲98.0%▲ (USP 1-Aug-2022) and NMT ▲102.0 %▲ (USP 1-Aug-2022) of nicotine ($C_{10}H_{14}N_2$), calculated on the anhydrous basis.

IDENTIFICATION

• A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy](#): 197F

Standard: Transfer an amount of [USP Nicotine Bitartrate Dihydrate RS](#) equivalent to 100 mg of nicotine to a 100-mL glass-stoppered tube. Add 20 mL of 1 M [ammonium hydroxide](#), 5 mL of 10 M [sodium hydroxide](#), and 20 mL of [n-hexane](#). Shake for 5 min, and allow the phases to separate. Transfer the upper hexane phase to an evaporating dish, and evaporate on a steam bath.

Sample: Nicotine
Acceptance criteria: Meets the requirements

Change to read:

• B. The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the ▲Assay.▲ (USP 1-Aug-2022)

ASSAY

Change to read:

• PROCEDURE

▲**Solution A:** Add 25 mL of 1 M [glacial acetic acid](#) to 900 mL of [water](#), and then add 6 mL of [ammonium hydroxide](#). Adjust with either 2 M [glacial acetic acid](#) or 2 M [ammonium hydroxide](#) to a pH of 10.0, and dilute with [water](#) to 1000 mL.

Solution B: [Acetonitrile](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
3	100	0
3.01	95	5
28	74	

Time (min)	Solution A (%)	Solution B (%)
32	60	40
34	100	0
40	100	0

System suitability solution: 1.5 mg/mL of [USP Nicotine Bitartrate Dihydrate RS](#) and 6 µg/mL each of [USP Nicotine Related Compound A RS](#), [USP Nicotine Related Compound B RS](#), [USP Nicotine Related Compound C RS](#), [USP Nicotine Related Compound D RS](#), [USP Nicotine Related Compound E RS](#), [USP Nicotine Related Compound F RS](#), and [USP Nicotine Related Compound G RS](#) in [water](#). [NOTE—The concentration of each related compound is in terms of the free base.]

Standard solution: 2.4 mg/mL of [USP Nicotine Bitartrate Dihydrate RS](#) in [water](#)

Sample solution: 0.8 mg/mL of Nicotine in [water](#)

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 15-cm; 5-µm packing [L1](#)

Flow rate: 1.0 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—See [Table 2](#) for the relative retention times.]

Suitability requirements

Resolution: NLT 2.5 between nicotine and nicotine related compound G, *System suitability solution*

Tailing factor: NMT 2.0 for nicotine, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nicotine (C₁₀H₁₄N₂) in the portion of Nicotine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of nicotine from the *Sample solution*

r_S = peak response of nicotine from the *Standard solution*

C_S = concentration of [USP Nicotine Bitartrate Dihydrate RS](#) on the anhydrous basis in the *Standard solution* (mg/mL)

C_U = concentration of Nicotine in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of nicotine, 162.24

M_{r2} = molecular weight of anhydrous nicotine bitartrate, 462.41

▲ (USP 1-Aug-2022)

Acceptance criteria: ▲98.0%–102.0%▲ (USP 1-Aug-2022) on the anhydrous basis

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

▲**Solution A, Solution B, Mobile phase, System suitability solution, Sample solution, and Chromatographic system:** Proceed as directed in the Assay.▲ (USP 1-Aug-2022)

Standard solution: 2.5 µg/mL of [USP Nicotine Bitartrate Dihydrate RS](#) in [water](#)

Sensitivity solution: 1.2 µg/mL of [USP Nicotine Bitartrate Dihydrate RS](#) in [water](#), from the *Standard solution*



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