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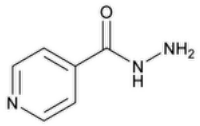
Isoniazid



$C_6H_7N_3O$ 137.14

4-Pyridinecarboxylic acid, hydrazide;

Isonicotinic acid hydrazide CAS RN®: 54-85-3; UNII: V83O1VOZ8L.

DEFINITION

Isoniazid contains NLT 98.0% and NMT 102.0% of isoniazid ($C_6H_7N_3O$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **B.** The retention time of the isoniazid peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 13.6 g/L of monobasic potassium phosphate adjusted with 10 N sodium hydroxide to a pH of 6.9. Add 30 mg/L of triethanolamine.

Mobile phase: Methanol and *Buffer* (5:95)

Standard solution: 0.32 mg/mL of USP Isoniazid RS in *Mobile phase*

Sample solution: 0.32 mg/mL of Isoniazid in *Mobile phase*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing: NMT 2.0 for the isoniazid peak

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of isoniazid ($C_6H_7N_3O$) in the portion of Isoniazid taken:

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

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

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

C_S = concentration of USP Isoniazid RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

• **Organic Impurities**

Buffer and **Mobile phase:** Proceed as directed in the *Assay*.

System suitability solution: 1.0 µg/mL each of USP Isoniazid RS, isoniacin, isonicotinamide, picolinohydrazide, and isonicotinonitrile in *Mobile phase*

Standard solution: 1.0 µg/mL of USP Isoniazid RS in *Mobile phase*

Sample solution: 1.0 mg/mL of Isoniazid in *Mobile phase*

Chromatographic system: Proceed as directed in the *Assay*, except for the following.

Detector: UV 266 nm

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between any adjacent peak pair, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Isoniazid taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

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

C_S = concentration of USP Isoniazid RS in the *Standard solution* (mg/mL)

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. Disregard any peak less than 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Isoniacin[a]	0.50	0.69	0.1
Isoniazid	1.0	1.0	—
Isonicotinamide	1.4	0.70	0.1
Picolinohydrazide[b]	2.1	1.2	0.1
Isonicotinonitrile[c]	3.9	0.74	0.1
Any unspecified impurity	—	1.0	0.10
Total impurities	—	—	2.0

[a] Isonicotinic acid.

[b] 2-Isoniazid.

[c] 4-Cyanopyridine.

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: In a solution (1 in 10)

Acceptance criteria: 6.0–7.5

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 4 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at 25°, excursions permitted between 15° and 30°.

- **USP Reference Standards** ⟨11⟩

  USP Isoniazid RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ISONIAZID	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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