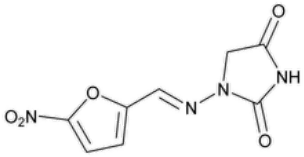
Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-3674B11A-F643-487A-83FC-76CC26EF4AB8_3_en-US
DOI: https://doi.org/10.31003/USPNF_M56770_03_01
DOI Ref: aeb73

Nitrofurantoin



$C_8H_6N_4O_5$ (anhydrous) 238.16
$C_8H_6N_4O_5 \cdot H_2O$ 256.18
2,4-Imidazolidinedione, 1-[[(5-nitro-2-furanyl)methylene] amino]-;
1-[(5-nitrofurfurylidene)amino]hydantoin CAS RN®: 67-20-9; UNII: 927AH8112L.
Monohydrate CAS RN®: 17140-81-7; UNII: E1QI2CQQ1I.

DEFINITION

Nitrofurantoin is anhydrous or contains one molecule of water of hydration. It contains NLT 98.0% and NMT 102.0% of $C_8H_6N_4O_5$, calculated on the anhydrous basis.

[Note—Nitrofurantoin and solutions of it are discolored by alkali and by exposure to light and are decomposed upon contact with metals other than stainless steel and aluminum.]

IDENTIFICATION

Change to read:

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

  Sample: Previously dried at 140° for 30 min

  Acceptance criteria: Meets the requirements

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

ASSAY

- **Procedure**

  Buffer: Dissolve 6.8 g of monobasic potassium phosphate in 500 mL of water. Add about 30 mL of 1.0 N sodium hydroxide sufficient to adjust to a pH of 7.0, and dilute with water to 1 L.

  Mobile phase: Acetonitrile and *Buffer* (12:88)

  Internal standard solution: 1 mg/mL of acetanilide in water

  Standard solution: 0.56 mg/mL of USP Nitrofurantoin RS prepared as follows. Dissolve 50 mg of USP Nitrofurantoin RS in 40.0 mL of dimethylformamide, and add 50.0 mL of *Internal standard solution.*

  Sample solution: 0.56 mg/mL of Nitrofurantoin prepared as directed for *Standard solution*

  Chromatographic system

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

  [Note—Adjust the operating parameters so that the retention time of the nitrofurantoin peak is about 8 min and the peak heights are about half full-scale.]

  Mode: LC

  Detector: UV 254 nm

  Column: 3.9-mm × 30-cm; packing L1

  Injection size: 5–10 µL

  System suitability

  Sample: *Standard solution*

  Suitability requirements

  Resolution: NLT 3.0 between the acetanilide and nitrofurantoin peaks

Relative standard deviation: NMT 2.0% determined from the ratio of the peak responses

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of nitrofurantoin ($C_8H_6N_4O_5$) in the portion of Nitrofurantoin taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = internal standard ratio (peak response of nitrofurantoin/peak response of acetanilide) from the *Sample solution*

R_S = internal standard ratio (peak response of nitrofurantoin/peak response of acetanilide) from the *Standard solution*

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

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

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

IMPURITIES

• **Limit of Nitrofurfural Diacetate**

Standard solution: 100 µg/mL of USP Nitrofurfural Diacetate RS in dimethylformamide and acetone (1:10)

Sample solution: Dissolve 100 mg of Nitrofurantoin in 1 mL of dimethylformamide, and dilute with acetone to 10.0 mL.

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Chloroform and methanol (9:1)

Spray reagent: Dissolve 0.75 g of phenylhydrazine hydrochloride in 50 mL of water, and decolorize with activated charcoal. Add 25 mL of hydrochloric acid, and mix with water to produce 200 mL.

Analysis

Samples: *Standard solution* and *Sample solution*

Proceed as directed in the chapter. Develop in the *Developing solvent system* until the solvent front has moved three-fourths the length of the plate, allow to air-dry for 5 min, and heat the plate at 105° for 5 min. While it is still warm, locate the spots by spraying the plate with *Spray reagent*.

Acceptance criteria: Any spot produced by the *Sample solution*, at an R_F value of 0.7, is not greater in size or intensity than that produced by the *Standard solution* at the same R_F value: NMT 1.0% of nitrofurfural diacetate is found.

• **Limit of Nitrofurazone**

Buffer: Prepare as directed in the *Assay*.

Mobile phase: Tetrahydrofuran and *Buffer* (10:90)

System suitability stock solution: 5.0 µg/mL each of USP Nitrofurazone RS and USP Nitrofurantoin RS in dimethylformamide

System suitability solution: 0.5 µg/mL each of USP Nitrofurazone RS and USP Nitrofurantoin RS in *Mobile phase* from *System suitability stock solution*

Standard stock solution: 5.0 µg/mL of USP Nitrofurazone RS in dimethylformamide

Standard solution: 0.5 µg/mL of USP Nitrofurazone RS in water from *Standard stock solution*

Sample solution: Dissolve 100 mg of Nitrofurantoin in 2.0 mL of dimethylformamide, and add 20.0 mL of water. Mix, and allow to stand for 15 min to allow a precipitate to form. Pass a portion of the solution through a suitable nylon filter of 0.45-µm pore size.

Chromatographic system

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

[Note—Adjust the operating parameters so that the retention time of the nitrofurazone peak is about 10.5 min and its height is about 0.1 half full-scale.]

Mode: LC

Detector: UV 375 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 1.6 mL/min

Injection size: 60–100 µL

System suitability

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

Suitability requirements

Resolution: NLT 4.0 between the nitrofurazone and nitrofurantoin peaks, *System suitability solution*

Relative standard deviation: NMT 2.0% determined from the peak height, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: The height of any peak appearing in the *Sample solution* at a retention time corresponding to that of the main peak from the *Standard solution* is NMT the height of the main peak from the *Standard solution* (NMT 0.01%).

SPECIFIC TESTS

• **Water Determination,** *Method III* ⟨921⟩

Analysis: Dry a sample at 140° for 30 min.

Acceptance criteria: For the anhydrous form, it loses NMT 1.0% of its weight; for the hydrous form, it loses 6.5%–7.5% of its weight.

• **Specific Surface Area** ⟨846⟩ (where it is labeled as being in the form of macrocrystals)

Sample: Outgas a portion of the powder to be placed under test at 150° for 10 min at ambient pressure with nitrogen.

Acceptance criteria: 0.045–0.20 m^2/g

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **Labeling:** Label it to indicate whether it is anhydrous or hydrous. Nitrofurantoin in the form of macrocrystals is so labeled. The labeling states the specific surface area and which method, specified under *Specific Surface Area* ⟨846⟩, is used.

• **USP Reference Standards** ⟨11⟩

USP Nitrofurantoin RS		
USP Nitrofurazone RS		
USP Nitrofurfural Diacetate RS	$C_9H_9NO_7$	243.17

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

Topic/Question	Contact	Expert Committee
NITROFURANTOIN	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 35(1)

Current DocID: GUID-3674B11A-F643-487A-83FC-76CC26EF4AB8_3_en-US

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