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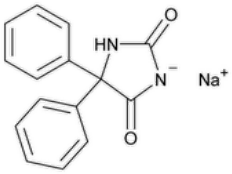
Phenytoin Sodium



$C_{15}H_{11}N_2NaO_2$ 274.25

2,4-Imidazolidinedione, 5,5-diphenyl-, monosodium salt;

5,5-Diphenylhydantoin sodium salt CAS RN®: 630-93-3; UNII: 4182431BJH.

DEFINITION

Phenytoin Sodium contains NLT 98.0% and NMT 102.0% of phenytoin sodium ($C_{15}H_{11}N_2NaO_2$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)
- **B.** Identification Tests—General, *Sodium* ⟨191⟩

Solution A: Dissolve 2.7 g of methoxyphenylacetic acid in 6 mL of tetramethylammonium hydroxide TS, and add 20 mL of dehydrated alcohol.

Solution B: 158 mg/mL of ammonium carbonate in water

Sample solution: Ignite 1 g, and cool. Add 2 mL of water to the residue, and neutralize the solution with hydrochloric acid. Filter, and dilute the filtrate with water to 4 mL.

Analysis: To 0.1 mL of the *Sample solution* add 1.5 mL of *Solution A*, and cool in ice water for 30 min. A voluminous, white, crystalline precipitate is formed. Place in water at 20°, and stir for 5 min.

Acceptance criteria: The precipitate does not disappear. Add 1 mL of ammonia TS. The precipitate dissolves completely. Add 1 mL of *Solution B*. No precipitate is formed.

- **C.** 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: 0.05 M monobasic ammonium phosphate buffer, adjusted with phosphoric acid to a pH of 2.5

Mobile phase: Acetonitrile, methanol, and *Buffer* (35:20:45)

System suitability solution: 0.1 mg/mL of USP Phenytoin RS and 0.15 mg/mL of benzoin in *Mobile phase*

Standard solution: 0.05 mg/mL of USP Phenytoin RS in *Mobile phase*

Sample solution: 0.05 mg/mL of Phenytoin Sodium in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

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

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

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

[Note—The relative retention times for phenytoin and benzoin are 1.0 and 1.3, respectively.]

Suitability requirements

Resolution: NLT 1.5 between phenytoin and benzoin, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phenytoin sodium ($C_{15}H_{11}N_2NaO_2$) in the portion of Phenytoin Sodium taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

M_{r1} = molecular weight of phenytoin sodium, 274.25

M_{r2} = molecular weight of phenytoin, 252.27

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

IMPURITIES

• **Organic Impurities**

Mobile phase, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.5 µg/mL of benzophenone, 1 µg/mL of USP Phenytoin RS, 9 µg/mL of USP Phenytoin Related Compound A RS, and 9 µg/mL of USP Phenytoin Related Compound B RS in *Mobile phase*

Sample solution: 1 mg/mL of Phenytoin Sodium in *Mobile phase*

System suitability

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

[Note—The relative retention times for phenytoin and benzoin are 1.0 and 1.3, respectively.]

Suitability requirements

Resolution: NLT 1.5 between phenytoin and benzoin, *System suitability solution*

Relative standard deviation: NMT 5.0% for each compound, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phenytoin related compound A, phenytoin related compound B, and benzophenone in the portion of Phenytoin Sodium taken:

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

r_U = peak response of phenytoin related compound A, phenytoin related compound B, or benzophenone from the *Sample solution*

r_S = peak response of phenytoin related compound A, phenytoin related compound B, or benzophenone from the *Standard solution*

C_S = concentration of the corresponding analyte in the *Standard solution* (µg/mL)

C_U = concentration of Phenytoin Sodium in the *Sample solution* (µg/mL)

Calculate the percentage of any unspecified impurity in the portion of Phenytoin Sodium taken:

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

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

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

C_S = concentration of USP Phenytoin RS in the *Standard solution* (µg/mL)

C_U = concentration of Phenytoin Sodium in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of phenytoin sodium, 274.25

M_{r2} = molecular weight of phenytoin, 252.27

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%, w/w)
Phenytoin related compound A	0.5	0.5
Phenytoin related compound B	0.6	0.9
Phenytoin	1.0	—
Benzophenone	2.9	0.1
Any individual unspecified impurity	—	0.10
Total impurities[a]	—	0.9

[a] Excluding benzophenone.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry at 105° for 4 h.

Acceptance criteria: NMT 2.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **USP Reference Standards ⟨11⟩**

USP Phenytoin RS

USP Phenytoin Related Compound A RS

Diphenylglycine.

$C_{14}H_{13}NO_2$ 227.26

USP Phenytoin Related Compound B RS

Diphenylhydantoic acid.

$C_{15}H_{14}N_2O_3$ 270.29

USP Phenytoin Sodium RS

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

Topic/Question	Contact	Expert Committee
PHENYTOIN SODIUM	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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