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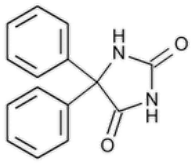
Phenytoin



$C_{15}H_{12}N_2O_2$ 252.27
2,4-Imidazolidinedione, 5,5-diphenyl-;
5,5-Diphenylhydantoin CAS RN®: 57-41-0; UNII: 6158TKW0C5.

DEFINITION

Phenytoin contains NLT 98.0% and NMT 102.0% of phenytoin ($C_{15}H_{12}N_2O_2$), 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 major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: Prepare a 0.05 M monobasic potassium phosphate solution and adjust with phosphoric acid to a pH of 2.5.

Solution B: Methanol and acetonitrile (60:40)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
23	60	40
38	42	58
45	30	70
50	30	70
51	60	40
55	60	40

Diluent: *Solution B* and water (1:1)

Standard solution: 0.2 mg/mL of USP Phenytoin RS in *Diluent*. Dissolve with the aid of sonication if necessary.

Sample solution: 0.2 mg/mL of Phenytoin in *Diluent*. Dissolve with the aid of sonication if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of phenytoin ($C_{15}H_{12}N_2O_2$) in the portion of Phenytoin taken:

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

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 the *Sample solution* (mg/mL)

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

IMPURITIES

• **Organic Impurities**

Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 1 µg/mL of USP Phenytoin RS, 5 µg/mL of USP Phenytoin Related Compound A RS, 9 µg/mL of USP Phenytoin Related Compound B RS, and 1 µg/mL of USP Benzophenone RS in *Diluent*

Sample solution: 1 mg/mL of Phenytoin in *Diluent*

System suitability

Sample: *Standard solution*

[Note—The relative retention times are given in *Table 2*.]

Suitability requirements

Signal-to-noise ratio: NLT 10

Relative standard deviation: NMT 5.0% for the phenytoin peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified impurity in the portion of Phenytoin taken:

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

r_U = peak area of specified impurity from the *Sample solution*

r_S = peak area of corresponding impurity from the *Standard solution*

C_S = concentration of corresponding impurity in the *Standard solution* (mg/mL)

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

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

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

r_U = peak area for each unspecified impurity

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

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

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

Acceptance criteria: See *Table 2*. Disregard any impurity less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Phenytoin related compound A	0.14	0.5
Phenytoin related compound B	0.53	0.9
Phenytoin	1.0	—
Benzophenone	2.11	0.1
Benzil	2.23	—
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 1.0%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Benzophenone RS

Diphenylmethanone.

$C_{13}H_{10}O$ 182.22

USP Phenytoin RS

USP Phenytoin Related Compound A RS

2,2-Diphenylglycine.

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

USP Phenytoin Related Compound B RS

2,2-Diphenyl-2-ureidoacetic acid.

$C_{15}H_{14}N_2O_3$ 270.28

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

Topic/Question	Contact	Expert Committee
PHENYTOIN	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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