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Extended Phenytoin Sodium Capsules

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DEFINITION

Extended Phenytoin Sodium Capsules contain NLT 95.0% and NMT 105.0% of the labeled amount of phenytoin sodium ($C_{15}H_{11}N_2NaO_2$).

IDENTIFICATION

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

Sample: 300 mg of phenytoin sodium from the contents of Capsules in 50 mL of [water](#) in a separator. Add 10 mL of [3 N hydrochloric acid](#), and extract with three successive portions, measuring 100, 60, and 30 mL, respectively, of [ether](#) and [chloroform](#) (1:2). Evaporate the combined extracts, and dry the residue of phenytoin at 105° for 4 h.

Acceptance criteria: The spectrum of the *Sample* corresponds to that of a similarly prepared [USP Phenytoin RS](#).

• **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

Change to read:

• **PROCEDURE**

Buffer: 0.05 M [monobasic potassium phosphate](#). Adjust with [phosphoric acid](#) to a pH of 3.5.

Mobile phase: [Methanol](#) and *Buffer* (55:45)

Standard solution: 0.6 mg/mL of [USP Phenytoin RS](#) in *Mobile phase*. [NOTE—Dissolve the required quantity of phenytoin in a small amount of [methanol](#) before diluting with *Mobile phase*.]

Sample stock solution: Transfer the contents of 10 Capsules to a 250-mL volumetric flask. Add 150 mL of [methanol](#), and sonicate for 20 min. Cool to room temperature, and dilute with [methanol](#) to volume.

Sample solution: Nominally 0.6 mg/mL of phenytoin $\blacktriangle$ sodium $\blacktriangle$ (ERR 1-Jan-2022) from the *Sample stock solution* in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 229 nm

Column: 4.6-mm × 25-cm; packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 10 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 3000 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

r_U = peak response of phenytoin 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* (mg/mL)

C_u = nominal concentration of phenytoin ▲sodium▲ (ERR 1-Jan-2022) 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: 95.0%–105.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1

Medium: [Water](#); 900 mL

Apparatus 1: 50 rpm

Times: 30, 60, and 120 min

Mobile phase: [Methanol](#) and [water](#) (70:30)

Standard solution: Dissolve [USP Phenytoin RS](#) in [methanol](#), and dilute with [water](#) to obtain a concentration similar to that of the *Sample solution*.

Sample solution: Pass a portion of the solution under test through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 229 nm

Column: 4.6-mm × 25-cm; packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 3200 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of phenytoin sodium ($C_{15}H_{11}N_2NaO_2$) dissolved:

$$\text{Result} = (r_u/r_s) \times C_s \times (M_{r1}/M_{r2}) \times V \times (100/L)$$

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)

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

M_{r2} = molecular weight of phenytoin, 252.27

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

Tolerances (for products labeled as 30-mg Capsules): The percentage of the labeled amount of phenytoin sodium ($C_{15}H_{11}N_2NaO_2$) dissolved is NMT 40% (Q) in 30 min, 56% (Q) in 60 min, and NLT 65% (Q) in 120 min. The requirements are met if the quantities dissolved from the Capsules tested conform to [Table 1](#).

Table 1

Stage	Number Tested	Acceptance Criteria
S_1	6	Each unit is within the range between $Q - 15\%$ and $Q - 5\%$, is within the range $Q' \pm 10\%$, and is NLT $Q'' + 5\%$ at the stated <i>Times</i> .
S_2	6	Average of 12 units ($S_1 + S_2$) is within the range between $Q - 10\%$ and Q , is within the range $Q' \pm 8\%$, and is NLT Q'' ; no unit is outside the range between $Q - 20\%$ and $Q + 10\%$, no unit is outside the range $Q' \pm 18\%$, and no unit is less than $Q'' - 10\%$ at the stated <i>Times</i> .
S_3	12	Average of 24 units ($S_1 + S_2 + S_3$) is within the range between $Q - 10\%$ and Q , is within the range $Q' \pm 8\%$, and is NLT Q'' ; NMT 2 units are outside the range between $Q - 20\%$ and $Q + 10\%$, and no unit is outside the range $Q - 30\%$ and $Q + 20\%$; NMT 2 units are outside the range $Q' \pm 18\%$, and no unit is outside the range $Q' \pm 25\%$; NMT 2 units are less than $Q'' - 10\%$, and no unit is less than $Q'' - 20\%$ at the stated <i>Times</i> .

Tolerances (for products labeled as 100-mg Capsules): The percentage of the labeled amount of phenytoin sodium ($C_{15}H_{11}N_2NaO_2$) dissolved is NMT 45% (Q) in 30 min, 60% (Q') in 60 min, and NLT 70% (Q'') in 120 min. The requirements are met if the quantities dissolved from the Capsules tested conform to [Table 2](#).

Table 2

Stage	Number Tested	Acceptance Criteria
S_1	6	Each unit is within the range between $Q - 25\%$ and $Q - 5\%$, is equal to $Q' \pm 20\%$, and is NLT $Q'' + 5\%$ at the stated <i>Times</i> .
S_2	6	Average of 12 units ($S_1 + S_2$) is within the range between $Q - 20\%$ and Q , is within the range $Q' \pm 15\%$, and is NLT Q'' ; no unit is outside the range between $Q - 30\%$ and $Q + 10\%$, no unit is outside the range $Q' \pm 25\%$, and no unit is less than $Q'' - 10\%$ at the stated <i>Times</i> .
S_3	12	Average of 24 units ($S_1 + S_2 + S_3$) is within the range between $Q - 20\%$ and Q , is within the range $Q' \pm 15\%$, and is NLT Q'' ; NMT 2 units are outside the range between $Q - 30\%$ and $Q + 10\%$, and no unit is outside the range between $Q - 40\%$ and $Q + 20\%$; NMT 2 units are outside the range $Q' \pm 25\%$ and no unit is outside the