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Morphine Sulfate Extended-Release Capsules

DEFINITION

Morphine Sulfate Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of morphine sulfate pentahydrate $[(C_{17}H_{19}NO_3)_{3/2} \cdot H_2SO_4 \cdot 5H_2O]$.

IDENTIFICATION

- A.**
Standard solution and Sample solution: Prepare as directed in the Assay.
Analysis: Inject 10 µL each of the *Standard solution* and the *Sample solution* using the *Chromatographic system* except for the *Injection volume* in the Assay.
Acceptance criteria: The UV absorption spectrum of the morphine peak of the *Sample solution* and of the *Standard solution* exhibits maxima and minima at the same wavelengths, as obtained in the Assay.
- 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**
Diluent: Water. Adjust with [phosphoric acid](#) to a pH of 3.6.
Buffer solution: 13.8 mg/mL of [monobasic sodium phosphate](#)
Solution A: Acetonitrile, [triethylamine](#), *Buffer solution*, and water (25: 0.5: 100: 874.5). Adjust with [phosphoric acid](#) to a pH of 3.6.
Solution B: Acetonitrile
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
33	100	0
44	85	15
54	85	15
55	100	0
65	100	0

- System suitability solution:** 400 µg/mL of [USP Morphine Sulfate RS](#) and 10 µg/mL each of [USP Morphine Related Compound A RS](#) and [USP Morphine Related Compound B RS](#) (pseudomorphine) in *Diluent*
- Standard solution:** 1.0 mg/mL of [USP Morphine Sulfate RS](#) in *Diluent*
- Sample stock solution:** Transfer a weighed portion of the contents from NLT 20 Capsules, nominally equivalent to 250 mg of morphine sulfate pentahydrate, to a 100-mL volumetric flask. Add 5 mL of methanol and mix well for NLT 30 min with gentle swirling about every 5 min. Add *Diluent* up to half of the flask volume and sonicate for NLT 5 min to dissolve. Dilute with *Diluent* to volume.
- Sample solution:** Nominally 1.0 mg/mL of morphine sulfate pentahydrate from the *Sample stock solution* in *Diluent*. Pass through a suitable filter and use the clear filtrate.
- Chromatographic system**
(See [Chromatography \(621\), System Suitability](#).)
- Mode:** LC
- Detector:** UV 245 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.
- Columns**
Guard: Packing [L1](#)

Analytical: 3.9-mm × 30-cm; 10-μm packing [L1](#)

Flow rate: 2 mL/min

Injection volume: 40 μL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between the morphine related compound A and morphine sulfate peaks, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of morphine sulfate pentahydrate $[(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O]$ 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 from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of [USP Morphine Sulfate RS](#) in the *Standard solution* (mg/mL), calculated on the anhydrous basis

C_U = nominal concentration of morphine sulfate pentahydrate in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of morphine sulfate pentahydrate, 758.83

M_{r2} = molecular weight of anhydrous morphine sulfate, 668.77

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1

pH 7.5 phosphate buffer: 6.8 mg/mL of [monobasic potassium phosphate](#) and 1.6 mg/mL of [sodium hydroxide](#). Adjust with [phosphoric acid](#) or [2 N sodium hydroxide](#) to a pH of 7.5.

Medium: Prepare as directed in [Dissolution \(711\)](#), [Procedure, Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms, Method B Procedure](#), observing the following exceptions. Perform *Acid Stage* testing, using 500 mL of [0.1 N hydrochloric acid](#) for 1 h; and perform *Buffer Stage* testing, using 500 mL of *pH 7.5 phosphate buffer* for NLT 8 h.

Apparatus 1: 100 rpm

Times: 1, 4, 6, and 9 h

Mobile phase: Methanol, [glacial acetic acid](#), and water (280:10:720), containing 0.73 g of [sodium 1-heptanesulfonate](#) for each 1.01 L of the solvent mixture

System suitability solution: 0.1 mg/mL each of [phenol](#) and [USP Morphine Sulfate RS](#) in *Mobile phase*

Standard solution: [USP Morphine Sulfate RS](#) in *pH 7.5 phosphate buffer* to obtain a solution with a known concentration corresponding to that of the *Sample solution*

Sample solution: Sample per [Dissolution \(711\)](#).

Chromatographic system

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

Mode: LC

Detector: UV 284 nm

Column: 3.9-mm × 30-cm; 10-μm packing [L1](#)

Flow rate: 2 mL/min

Injection volume: 25 μL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for phenol and morphine sulfate are about 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the phenol and morphine sulfate peaks

Tailing factor: NMT 2.0 for the morphine sulfate peak

Relative standard deviation: NMT 2.0% for the morphine sulfate peak

Analysis

Samples: *Standard solution* and *Sample solution*

Tolerances: See [Table 2](#).

Table 2