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Morphine Sulfate Compounded Suppositories

DEFINITION

Morphine Sulfate Compounded Suppositories contain NLT 90.0% and NMT 110.0% of the labeled amount of morphine sulfate pentahydrate $[(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O]$.

Prepare Morphine Sulfate Compounded Suppositories in Fatty Acid Base or Polyethylene Glycol Base as follows (see *Pharmaceutical Compounding—Nonsterile Preparations ⟨795⟩*).

Morphine Sulfate	50 mg
Silica Gel	25 mg
Fatty Acid Base or Polyethylene Glycol Base, a sufficient quantity to make	1 suppository

Calibrate the actual molds with the *Base* that is used for preparing the Suppositories, and adjust the formula accordingly. Thoroughly mix the *Morphine Sulfate* and *Silica Gel* to obtain a uniform powder. Heat the *Base* slowly and evenly until melted. Slowly add the powder to the melted *Base* with stirring. Mix thoroughly, and pour into molds. Cool, trim, and wrap.

ASSAY

• **Suppositories in Fatty Acid Base**

Mobile phase: Dissolve 5.5 g of sodium 1-heptanesulfonate in 700 mL of water, and add 300 mL of methanol and 10 mL of glacial acetic acid. Filter and degas.

System suitability solution: 0.24 mg/mL of USP Morphine Sulfate RS and 0.15 mg/mL of phenol in *Mobile phase*

Standard solution: 0.5 mg/mL of USP Morphine Sulfate RS in *Mobile phase*. Prepare a fresh solution daily.

Sample solution: Transfer 1 Suppository to a 60-mL separator containing 20 mL of chloroform and 20 mL of 0.01 N hydrochloric acid, and shake to dissolve the Suppository. Transfer the chloroform layer to a 250-mL separator. Extract the aqueous layer with a second 20-mL portion of chloroform, and combine the chloroform extracts in the 250-mL separator. Wash the chloroform extracts with two additional 20-mL portions of 0.01 N hydrochloric acid, combine the aqueous layers in a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Pass through a filter of 0.45-µm or finer pore size, discarding the first 4 mL of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 284 nm

Column: 4.6-mm × 25-cm; packing L1

Column temperature: 30°

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 phenol and morphine sulfate are about 0.7 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between phenol and morphine sulfate, *System suitability solution*

Tailing factor: NMT 2.0 for the morphine sulfate peak

Relative standard deviation: NMT 2.0% for replicate injections, *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 Suppository:

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

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) (corrected for moisture content by titrimetric determination)

C_U = nominal concentration of morphine sulfate 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%

• **Suppositories in Polyethylene Glycol Base**

Mobile phase, System suitability solution, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay* for *Suppositories in Fatty Acid Base*.

Sample solution: Transfer 1 Suppository to a 100-mL volumetric flask, and add 70 mL of *Mobile phase*. Sonicate for 15 min to dissolve the Suppository, cool, dilute with *Mobile phase* to volume, and mix. Pass a 10-mL portion of the solution through a filter of 0.45-µm or finer pore size, discarding the first 4 mL of filtrate.

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 Suppository:

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

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) (corrected for moisture content by titrimetric determination)

C_U = nominal concentration of morphine sulfate 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

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements for *Weight Variation*

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Package in tight containers, and store in a refrigerator. Do not dispense or store Polyethylene Glycol Base Suppositories in polystyrene containers.

• **Beyond-Use Date:** NMT 90 days after the date on which they were compounded when stored in a refrigerator

• **Labeling:** Label Morphine Sulfate Compounded Suppositories to state whether they are in a Fatty Acid Base or in a Polyethylene Glycol Base. Label to indicate that they are for rectal use only. Label to state that they are to be stored in a refrigerator. Label it to state the *Beyond-Use Date*.

• **USP Reference Standards ⟨11⟩**

USP Morphine Sulfate RS

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

Topic/Question	Contact	Expert Committee
MORPHINE SULFATE COMPOUNDED SUPPOSITORIES	Brian Serumaga Science Program Manager	CMP2020 Compounding 2020
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CMP2020 Compounding 2020

Chromatographic Database Information: Chromatographic Database

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