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Methadone Hydrochloride Oral Solution

DEFINITION

Methadone Hydrochloride Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of methadone hydrochloride ($C_{21}H_{27}NO \cdot HCl$).

IDENTIFICATION

- **A. Thin-Layer Chromatographic Identification Test ⟨201⟩**

  Sample solution: A volume of Oral Solution equivalent to 5 mg of methadone hydrochloride

  Developing solvent system: Alcohol, glacial acetic acid, and water (5:3:2)

  Analysis: Shake the *Sample solution* with 5 mL of sodium carbonate TS, and extract with 5 mL of chloroform. Proceed as directed using iodoplatinate TS to visualize the spots.

  Acceptance criteria: Meets the requirements

- **B. Identification Tests—General, *Chloride*⟨191⟩:** Meets the requirements

ASSAY

- **Procedure**

  Mobile phase: Acetonitrile and 0.033 M monobasic potassium phosphate (40:60). Adjust dropwise with phosphoric acid to a pH of 4.0.

  Internal standard solution: 250 µg/mL of pyrilamine maleate

  Standard solution: Transfer 20 mg of USP Methadone Hydrochloride RS to a 25-mL volumetric flask. Add 2.0 mL of *Internal standard solution*, and dilute with water to volume.

  Sample solution: Transfer a volume of Oral Solution equivalent to 20 mg of methadone hydrochloride to a 125-mL separator. Extract the specimen with two 50-mL portions of ether, collecting the ether extracts in a second separator. Wash the combined ether extracts with 2 mL of water, and discard the ether extract. Transfer the aqueous wash and the aqueous specimen to a 25-mL volumetric flask. Add 2.0 mL of *Internal standard solution*, and dilute with water to volume. Pass the solution through a filter of 5-µm pore size.

  Chromatographic system

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

  Mode: LC

  Detector: UV 254 nm

  Column: 3.9-mm × 30-cm; packing L11

  Flow rate: 1.3 mL/min

  Injection volume: 10 µL

  System suitability

  Sample: *Standard solution*

  The retention times for the internal standard and methadone hydrochloride are about 5.5 and 9 min, respectively.

  Suitability requirements

  Relative standard deviation: NMT 2.0%

  Analysis

  Samples: *Standard solution* and *Sample solution*

  Calculate the percentage of methadone hydrochloride ($C_{21}H_{27}NO \cdot HCl$) in the Oral Solution taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

  R_U = peak response ratio of methadone hydrochloride to the internal standard from the *Sample solution*

  R_S = peak response ratio of methadone hydrochloride to the internal standard from the *Standard solution*

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

C_U = nominal concentration of methadone hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

• **Alcohol Determination,** *Method II*⟨611⟩(if present)**:** 90.0%–115.0% of the labeled amount of C_2H_5OH, determined by the gas chromatographic procedure using acetone as the internal standard

PERFORMANCE TESTS

• **Uniformity of Dosage Units** ⟨905⟩**:** Meets the requirements for Oral Solution packaged in single-unit containers

• **Deliverable Volume** ⟨698⟩**:** Meets the requirements for Oral Solution packaged in multiple-unit containers

SPECIFIC TESTS

• **pH** ⟨791⟩**:** 1.0–4.0

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, protected from light, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩
USP Methadone Hydrochloride RS

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

Topic/Question	Contact	Expert Committee
METHADONE HYDROCHLORIDE ORAL SOLUTION	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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