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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](#)

Most Recently Appeared In:

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