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Methadone Hydrochloride Tablets

DEFINITION
Methadone Hydrochloride Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of methadone hydrochloride ($C_{21}H_{27}NO \cdot HCl$).

IDENTIFICATION

Change to read:

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

Sample: Equivalent to 5 mg of methadone hydrochloride from a quantity of finely powered Tablets

▲▲ (USP 1-Aug-2024)

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

Analysis: Shake the *Sample* 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: Meet the requirements

Add the following:

▲• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Aug-2024)

ASSAY

Change to read:

• **Procedure**

Mobile phase: Acetonitrile and 0.03 M monobasic potassium phosphate (40:60). Adjust with phosphoric acid to a pH of 3.2.

Standard solution: 0.4 mg/mL of USP Methadone Hydrochloride RS in *Mobile phase*

Sample solution: ▲Nominally 0.4 mg/mL of methadone hydrochloride in *Mobile phase* prepared as follows. Transfer an amount of finely powdered Tablets (NLT 20) equivalent to 10 mg of methadone hydrochloride to a 25-mL volumetric flask. Add 10 mL of *Mobile phase*, and sonicate briefly. Shake by mechanical means for about 15 min, dilute with *Mobile phase* to volume. Pass through a suitable filter of 0.45-µm pore size.▲ (USP 1-Aug-2024)

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; ▲10-µm▲ (USP 1-Aug-2024) packing L11

Flow rate: 1.5 mL/min

Injection volume: 10 µL

▲**Run time:** NLT 1.5 times the retention time of methadone▲ (USP 1-Aug-2024)

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT ▲1.0%▲ (USP 1-Aug-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of methadone hydrochloride ($C_{21}H_{27}NO \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response of methadone from the *Sample solution*

r_S = peak response of methadone 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: 93.0%–107.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: Water; 500 mL

Apparatus 1: 100 rpm

Time: 45 min

▲Determine the percentage of the labeled amounts of methadone hydrochloride ($C_{21}H_{27}NO \cdot HCl$) dissolved by using one of the following procedures.

Spectroscopic procedure▲ (USP 1-Aug-2024)

Standard solution: USP Methadone Hydrochloride RS in *Medium*

Sample solution: ▲Pass a portion of the solution under test through a suitable filter. Transfer a volume of the filtrate equivalent to about 400 µg of methadone hydrochloride into a suitable separator. Add 1 mL of glacial acetic acid and 20 mL of a solution of bromocresol purple prepared by dissolving 200 mg of bromocresol purple in 1000 mL of dilute glacial acetic acid (1 in 50). Mix, and extract with 20.0 mL of chloroform.▲ (USP 1-Aug-2024)

Instrumental conditions

Mode: Vis

Analytical wavelength: 405 nm

Analysis

▲**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of methadone hydrochloride ($C_{21}H_{27}NO \cdot HCl$) dissolved in comparison with the chloroform extract similarly prepared from the *Standard solution*:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of 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)

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Chromatographic procedure

Buffer: Dissolve 9.8 g of phosphoric acid in 1000 mL of water. Adjust with triethylamine to a pH of 3.6.

Mobile phase: Acetonitrile and *Buffer* (30:70)

Standard stock solution: 0.25 mg/mL of USP Methadone Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Methadone Hydrochloride RS to a volumetric flask and add acetonitrile to 20% of the flask volume. Add water to 60% of the flask volume and sonicate for about 5 min to dissolve. Dilute with water to volume.

Standard solution: 20 µg/mL of USP Methadone Hydrochloride RS in *Medium* from the *Standard stock solution*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 292 nm

Column: 4.6-mm × 10-cm; 3.5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 1.3 times the retention time of methadone

System suitability

Sample: *Standard solution*

Suitability requirements

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 methadone hydrochloride ($C_{21}H_{27}NO \cdot HCl$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response of methadone from the *Sample solution*

r_S = peak response of methadone from the *Standard solution*

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

L = label claim (mg/Tablet)

V = volume of *Medium*, 500 mL▲ (USP 1-Aug-2024)

Tolerances: NLT 75% (*Q*) of the labeled amount of methadone hydrochloride ($C_{21}H_{27}NO \cdot HCl$) is dissolved

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

Add the following:

▲IMPURITIES

• **Organic Impurities**

Buffer: Dissolve 9.8 g of phosphoric acid in 1000 mL of water. Adjust with triethylamine to a pH of 3.6.

Mobile phase: Acetonitrile and *Buffer* (30:70)

Diluent: Acetonitrile and *Buffer* (40:60)

Standard stock solution A: 0.25 mg/mL of USP Methadone Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Methadone Hydrochloride RS to a volumetric flask and add acetonitrile to 20% of the flask volume. Add water to 60% of the flask volume and sonicate for about 5 min to dissolve. Dilute with water to volume.

Standard stock solution B: 0.1 mg/mL of USP Methadone Hydrochloride RS in *Mobile phase* from *Standard stock solution A*

Standard solution: 0.5 µg/mL of USP Methadone Hydrochloride RS in *Diluent* from *Standard stock solution B*

Sensitivity solution: 0.25 µg/mL of USP Methadone Hydrochloride RS in *Diluent* from the *Standard solution*

Sample solution: Nominally 0.5 mg/mL of methadone hydrochloride prepared as follows. Transfer Tablets (NLT 5) equivalent to 50 mg of methadone hydrochloride to a 100-mL volumetric flask. Add 80 mL of *Diluent* and shake for about 60 min. Dilute with *Diluent* to volume. Pass through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 3.5-µm packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 3.5 times the retention time of methadone

System suitability

Samples: *Standard solution* and *Sensitivity solution*

Suitability requirements

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual degradation product in the portion of Tablets taken:

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

r_U = peak response of any individual degradation product from the *Sample solution*

r_S = peak response of methadone from the *Standard solution*

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

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

Acceptance criteria: The reporting threshold is 0.05%.

Any individual degradation product: NMT 0.2%

Total degradation products: NMT 1.2%▲ (USP 1-Aug-2024)

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in well-closed containers. ▲Store at controlled room temperature and protect from light.▲ (USP 1-Aug-2024)

• **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 TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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