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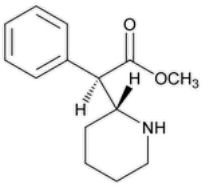
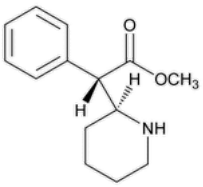
Methylphenidate Hydrochloride



• HCl



• HCl

$C_{14}H_{19}NO_2 \cdot HCl$ 269.77

2-Piperidineacetic acid, α-phenyl-, methyl ester, hydrochloride, (*R**,*R**)-(±)-;
Methyl α-phenyl-2-piperidineacetate hydrochloride;
(*RS*)-Methyl-2-phenyl-2-[(*RS*)-piperidin-2-yl] acetate, hydrochloride CAS RN®: 23655-65-4; UNII: 4B3SC438HI.

DEFINITION

Methylphenidate Hydrochloride contains NLT 98.0% and NMT 102.0% of methylphenidate hydrochloride ($C_{14}H_{19}NO_2 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M
• **B. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements
• **C.** 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**

Buffer: 2.7 g/L of monobasic potassium phosphate

Mobile phase: Methanol and *Buffer* (1:2). Adjust with phosphoric acid to a pH of 4.6 ± 0.1.

System suitability solution: 0.005 mg/mL of USP Methylphenidate Related Compound A RS and 0.5 mg/mL of USP Methylphenidate Hydrochloride RS in *Mobile phase*

Standard solution: 0.5 mg/mL of USP Methylphenidate Hydrochloride RS in *Mobile phase*

Sample solution: 0.5 mg/mL of Methylphenidate Hydrochloride in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 209 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of methylphenidate

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 2.5 between methylphenidate related compound A and methylphenidate

Tailing factor: NMT 3.0 for methylphenidate

Relative standard deviation: NMT 2.0% for methylphenidate

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of methylphenidate hydrochloride ($C_{14}H_{19}NO_2 \cdot HCl$) in the portion of Methylphenidate Hydrochloride taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

C_U = concentration of Methylphenidate Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities, Procedure 1**

Buffer, Mobile phase, System suitability solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Identify each impurity using the relative retention times in *Table 1*.

Calculate the percentage of each impurity in the portion of Methylphenidate Hydrochloride taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_T = sum of the responses of all impurity peaks including the methylphenidate peak from the *Sample solution*

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Erythro isomer[a]	0.58	0.15
Methylphenidate related compound A	0.85	0.5
Methylphenidate	1.0	—
Any individual unspecified impurity	—	0.10
Total impurities	—	1.0

[a] (*RS*)-Methyl-2-phenyl-2-[(*SR*)-piperidin-2-yl] acetate.

• **Organic Impurities, Procedure 2**

[Note—Perform this test only if ethylphenidate or *all-rac*-dimethyl 2,2'-(piperidine-1,2-diyl)bis(2-phenylacetate) is a known process impurity.]

Buffer A: 5.7 g of monobasic ammonium phosphate and 1.6 g of octanesulfonic acid sodium salt in 1 L of water

Buffer B: Add 4 mL of triethylamine to 1 L of *Buffer A*. Adjust with phosphoric acid to a pH of 2.9.

Solution A: Acetonitrile and *Buffer B* (14:86)

Solution B: Acetonitrile and *Buffer A* (80:20)

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	90	10
7	65	35
10	50	50

Time (min)	Solution A (%)	Solution B (%)
12	50	50
13	90	10
16	90	10

[NOTE—Equilibration of the chromatographic system at the initial conditions for a minimum of 30 min is recommended before the first injection.]

System suitability solution: 0.5 mg/mL of USP Methylphenidate Hydrochloride RS and 3 µg/mL each of USP Methylphenidate Related Compound A RS, phenylacetic acid, and USP Methylphenidate Hydrochloride Erythro Isomer Solution RS in *Solution A*

Standard solution: 0.5 µg/mL of USP Methylphenidate Hydrochloride RS in *Solution A*

Sample solution: 0.5 mg/mL of Methylphenidate Hydrochloride in *Solution A*. [NOTE—Allow the solution to stand for at least 2 h.]

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 3.9-mm × 15-cm; 5-µm packing L7

Column temperature: 40°

Flow rate: 2.8 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

[NOTE—See *Table 3* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.7 between methylphenidate related compound A and phenylacetic acid; NLT 3.6 between phenylacetic acid and erythro isomer

Tailing factor: NMT 2.0 for methylphenidate

Relative standard deviation: NMT 2.0% for methylphenidate; NMT 5.0% for methylphenidate related compound A, phenylacetic acid, and methylphenidate hydrochloride erythro isomer

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual impurity in the portion of Methylphenidate Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

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

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

C_U = concentration of Methylphenidate Hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. The reporting threshold is 0.05%.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Methylphenidate related compound A	0.55	1.1	0.2
Phenylacetic acid	0.67	1.0	0.1
Erythro isomer[a]	0.80	1.0	0.2
Methylphenidate	1.0	—	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Ethylphenidate[b]	1.22	0.9	0.1
Bis-methylphenidate[c]	1.80	2.6	0.1
Any individual unspecified impurity	—	1.0	0.1
Total impurities	—	—	0.5

[a] (*RS*)-Methyl-2-phenyl-2-[(*SR*)-piperidin-2-yl] acetate.

[b] Ethyl(*RS*)-2-phenyl-2-[(*RS*-piperidin-2-yl)]acetate.

[c] *all-rac*-Dimethyl 2,2'-(piperidine-1,2-diyl)bis(2-phenylacetate).

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry under vacuum at 60° for 4 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **Labeling:** If a test for *Organic Impurities* other than *Procedure 1* is used, then the labeling states the procedure with which the article complies.

Change to read:

• **USP Reference Standards ⟨11⟩**

USP Methylphenidate Hydrochloride RS

USP Methylphenidate Hydrochloride Erythro Isomer Solution RS

This solution contains 0.5 mg/mL of methylphenidate hydrochloride erythro isomer in methanol.

USP Methylphenidate Related Compound A RS

▲(*RS*)-2-Phenyl-2-[(*RS*)-piperidin-2-yl]acetic acid hydrochloride.▲ (ERR 1-Jun-2023)

$C_{13}H_{17}NO_2 \cdot HCl$ 255.74

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

Topic/Question	Contact	Expert Committee
METHYLPHENIDATE HYDROCHLORIDE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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