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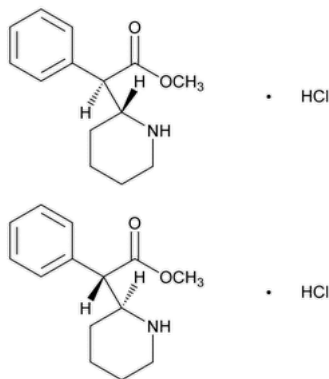
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Methylphenidate Hydrochloride


 $C_{14}H_{19}NO_2 \cdot HCl$ 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 $\times$ 25-cm; 5- μ m packing [L1](#)

Flow rate: 1.0 mL/min

Injection volume: 10 μ L

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