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# Pilocarpine Hydrochloride

$C_{11}H_{16}N_2O_2 \cdot HCl$ 244.72

2(3*H*)-Furanone, 3-ethyldihydro-4-[(1-methyl-1*H*-imidazol-5-yl)methyl]-, monohydrochloride, (3*S*-*cis*)-;

Pilocarpine monohydrochloride CAS RN®: 54-71-7; UNII: 0WW6D218XJ.

## DEFINITION

Pilocarpine Hydrochloride contains NLT 98.0% and NMT 102.0% of $C_{11}H_{16}N_2O_2 \cdot HCl$, calculated on the dried basis.

## IDENTIFICATION

***Change to read:***

- **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197M**▲ (CN 1-May-2020)
- **B.** **Identification Tests—General, *Chloride*⟨191⟩:** Meets the requirements

  **Sample solution:** 50 mg/mL

## ASSAY

- **Procedure**

  **Buffer:** 4.4 g/L of dibasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 6.5 ± 0.1.

  **Mobile phase:** Acetonitrile, methanol, and *Buffer* (2:35:63)

  **Standard solution:** 0.5 mg/mL of USP Pilocarpine Hydrochloride RS in water. [Note—Sonicate if necessary.]

  **System suitability solution:** Transfer a known quantity of USP Pilocarpine Hydrochloride RS in a suitable volumetric flask, and add water, equivalent to 10% of the volume of the flask, to dissolve. [Note—Sonicate as needed.] Add 0.1 N sodium hydroxide, equivalent to 10% of the volume of the flask, quench immediately with the same volume of 0.1 N hydrochloric acid, and mix. Dilute with water to volume. [Note—The initial concentration of USP Pilocarpine Hydrochloride RS is 0.5 mg/mL. Isopilocarpine is formed in the *System suitability solution* preparation.]

  **Sample solution:** 0.5 mg/mL of Pilocarpine Hydrochloride in water. [Note—Sonicate if necessary.]

  **Chromatographic system**

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

  **Mode:** LC

  **Detector:** UV 215 nm

  **Column:** 4.6-mm × 15-cm; 3-µm packing L11

  **Column temperature:** 35°

  **Flow rate:** 1.0 mL/min

  **Injection size:** 10 µL

  **System suitability**

  **Samples:** *Standard solution* and *System suitability solution*

  **Suitability requirements**

  **Resolution:** NLT 1.5 between isopilocarpine and pilocarpine, *System suitability solution*

  **Tailing factor:** NMT 2.0, *Standard solution*

  **Relative standard deviation:** NMT 2.0%, *Standard solution*

  **Analysis**

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

  Calculate the percentage of $C_{11}H_{16}N_2O_2 \cdot HCl$ in the portion of Pilocarpine Hydrochloride taken:

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

  $r_U$ = peak area from the *Sample solution*

$r_S$ = peak area from the *Standard solution*

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

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

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

## IMPURITIES

### Organic Impurities

- **Procedure 1: Related Compounds**

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

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

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 215 nm

**Column:** 4.6-mm × 15-cm; 3-µm packing L11

**Column temperature:** 35°

**Flow rate:** 1.0 mL/min

**Run time:** NLT 5 times the retention time of the pilocarpine peak

**Injection size:** 10 µL

**System suitability**

**Samples:** *Standard solution*, *System suitability solution*, and *Sensitivity solution*

**Suitability requirements**

**Resolution:** NLT 1.5 between isopilocarpine and pilocarpine, *System suitability solution*

**Signal-to-noise ratio:** NLT 10 for the pilocarpine peak, *Sensitivity solution*

**Relative standard deviation:** NMT 2.0% for the pilocarpine peak, *Standard solution*

**Analysis**

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

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

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

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

$r_S$ = peak area of pilocarpine from the *Standard solution*

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

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

**Acceptance criteria**

**Individual impurities:** See *Impurity Table 1*. [Note—Disregard any unspecified impurity peaks less than 0.05%.]

**Total impurities:** NMT 1.0%

**Impurity Table 1**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Isopilocarpine[a] | 0.94 | 1.0 |
| Pilocarpine | 1.00 | — |
| Pilocarpic acid[b] | 1.15 | 0.5 |
| Isopilocarpic acid[c] | 1.19 | 0.1 |

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Any unspecified impurity | — | 0.1 |

[a] (3*R*,4*R*)-3-Ethyl-4-[(1-methyl-1*H*-imidazol-5-yl)methyl]dihydrofuran-2(3*H*)-one.

[b] (2*S*,3*R*)-2-Ethyl-4-hydroxy-3-[(1-methyl-1*H*-imidazol-5-yl)methyl]butanoic acid.

[c] (2*R*,3*R*)-2-Ethyl-4-hydroxy-3-[(1-methyl-1*H*-imidazol-5-yl)methyl]butanoic acid.

- **Procedure 2: Other Alkaloids**

**Sample solution:** 10 mg/mL in water

**Analysis:** Divide the *Sample solution* into two portions. To one portion add a few drops of 6 N ammonium hydroxide, and to the other, add a few drops of potassium dichromate TS.

**Acceptance criteria:** No turbidity is produced in either solution.

## SPECIFIC TESTS

- **Optical Rotation, *Specific Rotation*⟨781S⟩:** +88.5° to +91.5°

**Sample solution:** 20 mg/mL, in water

- **Loss on Drying ⟨731⟩:** Dry a sample at 105° for 2 h: it loses NMT 3.0% of its weight.
- **Readily Carbonizable Substances Test ⟨271⟩**

**Sample solution:** 50 mg/mL in sulfuric acid

**Acceptance criteria:** The solution has no more color than *Matching Fluid B*.

## ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at room temperature.
- **USP Reference Standards ⟨11⟩**

USP Pilocarpine Hydrochloride RS

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| PILOCARPINE HYDROCHLORIDE | Documentary Standards Support | SM32020 Small Molecules 3 |
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | SM32020 Small Molecules 3 |

**Chromatographic Database Information:** Chromatographic Database

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