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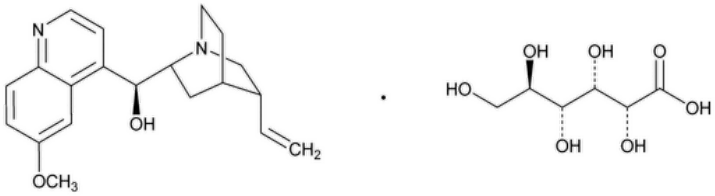
Quinidine Gluconate



$C_{20}H_{24}N_2O_2 \cdot C_6H_{12}O_7$ 520.57

Cinchonan-9-ol, 6'-methoxy-, (9*S*)-, mono-D-gluconate (salt);

Quinidine mono-D-gluconate (salt) CAS RN®: 7054-25-3; UNII: R6875N380F.

DEFINITION

Quinidine Gluconate is the gluconate of an alkaloid that may be obtained from various species of *Cinchona* and their hybrids, from *Remijia pedunculata* Flückiger (Fam. Rubiaceae), or prepared from quinine. Quinidine Gluconate contains NLT 99.0% and NMT 100.5% of total alkaloid salt, calculated as quinidine gluconate ($C_{20}H_{24}N_2O_2 \cdot C_6H_{12}O_7$) on the dried basis.

IDENTIFICATION

- **A.**

  Sample solution: 1-in-2000 solution of Quinidine Gluconate in dilute sulfuric acid (1 in 350)

  Acceptance criteria: The *Sample solution* exhibits a vivid blue fluorescence. On the addition of a few drops of hydrochloric acid, the fluorescence disappears.

- **B.** The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in *Organic Impurities*.

- **C.**

  Sample solution: 20 mg/mL of Quinidine Gluconate

  Acceptance criteria: The *Sample solution* is dextrorotatory.

- **D.**

  Sample: Dissolve 700 mg of Quinidine Gluconate in 5 mL of water with the aid of heat. Add 1 mL of glacial acetic acid and 200 mg of phenylhydrazine hydrochloride.

  Analysis: Heat in a water bath for 15 min, cool, and scratch the inner surface of the tube with a glass rod.

  Acceptance criteria: Orange crystals are formed.

ASSAY

- **Procedure**

  Sample solution: Dissolve 150 mg of Quinidine Gluconate in 10 mL of glacial acetic acid, heating gently if necessary, and cool the solution.

  Titrimetric system

  Mode: Titrimetry

  Titrant: 0.1 N perchloric acid VS

  Endpoint detection: Visual

  Analysis: To the *Sample solution* add 20 mL of acetic anhydride and 4 drops of *p*-naphtholbenzein TS, and titrate with *Titrant* from a 10-mL microburet to a green endpoint. Perform a blank determination, and make any necessary corrections (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 26.03 mg of total alkaloid salt, calculated as quinidine gluconate ($C_{20}H_{24}N_2O_2 \cdot C_6H_{12}O_7$).

  Acceptance criteria: 99.0%–100.5% on the dried basis

IMPURITIES

- **Residue on Ignition** ⟨281⟩**:** NMT 0.15%
- **Organic Impurities**

Standard solution A: 6 mg/mL of USP Quinidine Gluconate RS in diluted alcohol

Standard solution B: 0.06 mg/mL of USP Quinidine Gluconate RS in diluted alcohol from *Standard solution A*

Standard solution C: 0.04 mg/mL of USP Quininone RS (corresponding to 0.06 mg of the gluconate) and 0.08 mg/mL of cinchonine (corresponding to 0.12 mg of the gluconate) in diluted alcohol

Sample solution: 6 mg/mL of Quinidine Gluconate in diluted alcohol

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Chloroform, acetone, and diethylamine (50:40:10)

Analysis

Samples: *Standard solution A, Standard solution B, Standard solution C*, and *Sample solution*

Proceed as directed in the chapter. The solvent chamber is used without previous equilibration. When the solvent front has moved about 15 cm, remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate. Spray with glacial acetic acid. Locate the spots on the plate by examination under long-wavelength UV light. Then spray the plate with potassium iodoplatinate TS.

Acceptance criteria: Any spot produced by the *Sample solution* at the R_F value of a spot produced by *Standard solution C* is not greater in size or intensity than that corresponding spot. Apart from these spots and from the spots appearing at the R_F value of Quinidine Gluconate and dihydroquinidine gluconate (the two spots most evident from *Standard solution A*), any additional fluorescent spot is not greater in size or intensity than the principal spot of *Standard solution B*. After treatment with potassium iodoplatinate TS, any spot produced by the *Sample solution* is not greater in size or intensity than a corresponding spot from *Standard solution C*.

• **Limit of Dihydroquinidine Gluconate**

Solution A: Add 35.0 mL of methanesulfonic acid to 20.0 mL of glacial acetic acid, and dilute with water to 500 mL.

Solution B: Dissolve 10.0 mL of diethylamine in water to prepare a 100-mL solution.

Mobile phase: Acetonitrile, *Solution A*, *Solution B*, and water (100:20:20:860). Adjust with *Solution B* to a pH of 2.6.

System suitability solution: 0.2 mg/mL each of quinidine gluconate and dihydroquinidine hydrochloride prepared as follows. Dissolve a suitable quantity of each quinidine gluconate and dihydroquinidine hydrochloride in about 10% of total volume of methanol, and dilute with *Mobile phase* to volume.

Sample solution: 0.26 mg/mL of Quinidine Gluconate in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 235 nm

Column: 3.9-mm × 30-cm; packing L1

Injection volume: 50 µL

System suitability

Sample: *System suitability solution*

[Note—The relative retention times for quinidine and dihydroquinidine are 1 and 1.5, respectively.]

Suitability requirements

Resolution: NLT 2.5 between quinidine and dihydroquinidine

Relative standard deviation: NMT 2.0%

Analysis

Sample: *Sample solution*

Acceptance criteria: 20%; the response of the dihydroquinidine peak is NMT 0.25 that of the quinidine peak.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry a sample at 105° for 1 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers. Store at controlled room temperature.

• **USP Reference Standards ⟨11⟩**

USP Quinidine Gluconate RS		
USP Quininone RS	$C_{20}H_{22}N_2O_2$	322.40

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

Topic/Question	Contact	Expert Committee
QUINIDINE GLUCONATE	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

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