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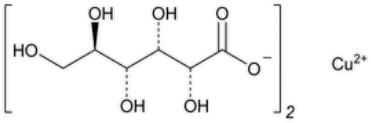
Copper Gluconate



$C_{12}H_{22}CuO_{14}$ 453.84

Copper, bis(D-gluconato-O^1,O^2)-;

Copper D-gluconate (1:2) CAS RN®: 527-09-3; UNII: RV823G6G67.

DEFINITION

Copper Gluconate contains NLT 98.0% and NMT 102.0% of copper gluconate ($C_{12}H_{22}CuO_{14}$).

IDENTIFICATION

- **A. Identification Tests—General, *Copper*⟨191⟩:** A 50-mg/mL solution meets the requirements.
- **B. Thin-Layer Chromatographic Identification Test**

Standard solution: 10 mg/mL of USP Potassium Gluconate RS

Sample solution: 10 mg/mL of Copper Gluconate, heating in a water bath at 60°, if necessary, to dissolve

Chromatographic system

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

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel

Application volume: 5 µL

Developing solvent system: Alcohol, ethyl acetate, ammonium hydroxide, and water (50:10:10:30)

Spray reagent: Dissolve 2.5 g of ammonium molybdate in 50 mL of 2 N sulfuric acid in a 100-mL volumetric flask, add 1.0 g of ceric sulfate, swirl to dissolve, and dilute with 2 N sulfuric acid to volume.

Analysis

Samples: *Standard solution* and *Sample solution*

Develop the chromatogram until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, and dry at 110° for 20 min. Allow to cool, and spray with the *Spray reagent*. Heat the plate at 110° for about 10 min.

Acceptance criteria: The principal spot of the *Sample solution* corresponds in color, size, and R_F value to that of the *Standard solution*.

ASSAY

- **Procedure**

Sample: 1.5 g of Copper Gluconate

Blank: 100 mL of water

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Indirect titration

Titrant: 0.1 N sodium thiosulfate VS

Endpoint detection: Visual

Analysis: Dissolve the *Sample* in 100 mL of water. Add 2 mL of glacial acetic acid and 5 g potassium iodide, mix, and titrate with *Titrant* to a light yellow color. Add 2 g of ammonium thiocyanate, and mix. Add 3 mL of starch TS, and continue titrating to a milk-white endpoint. Perform the blank determination.

Calculate the percentage of copper gluconate ($C_{12}H_{22}CuO_{14}$) in the *Sample* taken:

$$\text{Result} = \{[(V_S - V_B) \times N \times F]/W\} \times 100$$

V_S = *Titrant* volume consumed by the *Sample* (mL)

V_B = *Titrant* volume consumed by the *Blank* (mL)

N = actual normality of the *Titrant* (mEq/mL)

F = equivalency factor, 453.8 mg/mEq

W = *Sample* weight (mg)

Acceptance criteria: 98.0%–102.0%

IMPURITIES

• **Chloride and Sulfate,** *Chloride*⟨221⟩

Standard solution: 1.0 mL of 0.020 N hydrochloric acid

Sample: 1.0 g

Acceptance criteria: NMT 0.07%

• **Chloride and Sulfate,** *Sulfate*⟨221⟩

Standard solution: 1.0 mL of 0.020 N sulfuric acid

Sample: 2.0 g

Acceptance criteria: NMT 0.05%

Change to read:

• ▲**Arsenic** ⟨211⟩*, Procedures, Procedure 1*▲ (CN 1-Jun-2023)

Test preparation: 1.0 g in 35 mL of water

Acceptance criteria: NMT 3 ppm

• **Limit of Lead**

[Note—For the preparation of all aqueous solutions and for the rinsing of glassware before use, use water that has been passed through a strong-acid, strong-base, mixed-bed ion-exchange resin. Select all reagents to have as low a content of lead as practicable, and store all reagent solutions in containers of borosilicate glass. Cleanse glassware before use by soaking in warm 8 N nitric acid for 30 min and by rinsing with deionized water.]

Standard stock solution: Transfer 10.0 mL of lead nitrate stock solution TS to a 100-mL volumetric flask. Add 40 mL of water and 5 mL of nitric acid, and dilute with water to volume.

Standard solution: Transfer 0.40 mL of *Standard stock solution* to a 100-mL volumetric flask. Add 50 mL of water and 1 mL of nitric acid, and dilute with water to volume. This solution contains 0.04 µg/mL of lead.

Sample stock solution: Transfer 4 g of Copper Gluconate to a 100-mL volumetric flask. Add 50 mL of water and 5 mL of nitric acid, and sonicate to dissolve the specimen. Dilute with water to volume. Transfer 4.0 mL of this solution to a second 100-mL volumetric flask. Add 50 mL of water and 1 mL of nitric acid, dilute with water to volume, and mix.

Blank: Transfer 1.2 mL of nitric acid to a 100-mL volumetric flask and dilute with water to volume.

Sample solution A: Mix 10.0 mL of the *Sample stock solution* with 10.0 mL of *Blank*. This solution contains 0.00 µg/mL of added lead from the *Standard solution*.

Sample solution B: Mix 10.0 mL of the *Sample stock solution* with 4.0 mL of the *Standard solution* and 6.0 mL of *Blank*. This solution contains 0.008 µg/mL of added lead from the *Standard solution*.

Sample solution C: Mix 10.0 mL of the *Sample stock solution* with 7.0 mL of the *Standard solution* and 3.0 mL of *Blank*. This solution contains 0.014 µg/mL of added lead from the *Standard solution*.

Sample solution D: Mix 10.0 mL of the *Sample stock solution* with 10.0 mL of the *Standard solution*. This solution contains 0.020 µg/mL of added lead from the *Standard solution*.

Instrumental conditions

(See *Atomic Absorption Spectroscopy* ⟨852⟩.)

Mode: Graphite furnace atomic absorption spectrophotometry

Analytical wavelength: 283.3 nm

Lamp: Lead hollow-cathode

Argon flow rate: 3 L/min, or as noted

Graphite tube temperature: See *Table 1*.

Table 1

Temperature (°)	Time (s)
70	10
90	60
120	15
250 (no gas flow)	5
250	10
250 (no gas flow)	2
2000	3.2

Injection volume: 20 µL

Analysis

Samples: *Blank* and *Sample solutions A,B, C,* and *D*

The graphite tube is temperature-programmed to reach 2000° in about 2 min, as shown in *Table 1*. When the temperature reaches 2000°, determine the absorbance at 283.3 nm, corrected for background absorption. Inject the *Sample solutions* and *Blank*, and determine the absorbances. Correct the absorbance values from the *Sample solutions* by subtracting from each the absorbance value from the *Blank*. Plot the corrected absorbances of the *Sample solutions* versus their added lead concentrations, in µg/mL. Draw the straight line best fitting the four points, and extrapolate the line until it intercepts the concentration axis. From the intercept, determine the concentration, *C*, in µg/mL, of lead in *Sample solution A*.

Calculate the content of lead in the portion of Copper Gluconate taken:

$$\text{Result} = (C \times V)/W$$

C = concentration of lead in the *Sample solution A* (µg/mL), determined from the intercept of the linear regression line

V = volume of solvent taken to prepare the *Sample solution A* (mL)

W = weight of Calcium Gluconate taken to prepare the *Sample solution A* (g)

Acceptance criteria: NMT 25 µg/g

- **Reducing Substances**

Sample: 1.0 g of Copper Gluconate

Blank: 10 mL of water

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Residual titration

Titrant: 0.1 N iodine VS

Back-titrant: 0.1 N sodium thiosulfate VS

Endpoint detection: Visual

Analysis: Transfer the *Sample* to a 250-mL conical flask, add 10 mL of water to dissolve the *Sample*, then add 25 mL of alkaline cupric citrate TS. Cover the flask, boil gently for 5 min, accurately timed, and cool rapidly to room temperature. Add 25 mL of 0.6 N acetic acid, 10.0 mL of *Titrant*, and 10 mL of 3 N hydrochloric acid, and titrate with *Back-titrant*, adding 3 mL of starch TS as the endpoint is approached. Perform the blank determination.

Calculate the percentage of reducing substances (as dextrose) in the *Sample* taken:

$$\text{Result} = \{[(V_B - V_S) \times N \times F]/W\} \times 100$$

V_B = *Back-titrant* volume consumed by the *Blank* (mL)

V_S = *Back-titrant* volume consumed by the *Sample* (mL)

N = actual normality of the *Back-titrant* (mEq/mL)

F = equivalency factor, 27 mg/mEq

W = *Sample* weight (mg)

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨11⟩
  USP Potassium Gluconate RS

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

Topic/Question	Contact	Expert Committee
COPPER GLUCONATE	Nagaphani Batchu Senior Scientist I, Documentary Standards	NBDS2020 Non-botanical Dietary Supplements

Chromatographic Database Information: Chromatographic Database

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