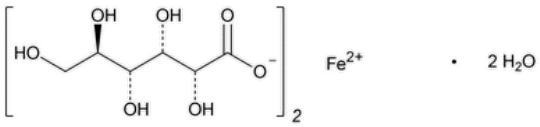
Printed on: Thu Nov 24 2022, 08:29:01 am
Printed by: XU SAI NAN
Status: Not Yet Official on 24-Nov-2022
Official Date: 01-Jun-2023
Document Type: USP & DS
DocId: GUID-9A0C69F8-DF6A-4449-AE66-DBBFC873DB23_3_en-US
DOI: https://doi.org/10.31003/USPNF_M32940_03_01
DOI Ref: 6w0fs

Ferrous Gluconate



$C_{12}H_{22}FeO_{14} \cdot 2H_2O$ 482.17

D-Gluconic acid, iron(2+) salt (2:1), dihydrate;
Iron(2+) gluconate (1:2) dihydrate CAS RN®: 12389-15-0.
Anhydrous 446.15 CAS RN®: 299-29-6.

DEFINITION

Ferrous Gluconate contains NLT 97.0% and NMT 102.0% of ferrous gluconate ($C_{12}H_{22}FeO_{14}$), calculated on the dried basis.

IDENTIFICATION

• **A. Thin-Layer Chromatography**

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

Sample solution: 10 mg/mL of Ferrous 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 *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*.

• **B. Ferrous Ion**

Sample solution: 5 mg/mL in water

Analysis: Add potassium ferricyanide TS to the *Sample solution*.

Acceptance criteria: The solution yields a dark blue precipitate.

ASSAY

• **Procedure**

Sample: 1.5 g of Ferrous Gluconate

Blank: Proceed as directed in the *Analysis* without the *Sample*.

Titrimetric system

(See *Titrimetry 〈541〉*.)

Mode: Direct titration

Titrant: 0.1 N ceric sulfate VS

Endpoint detection: Visual

Analysis: Dissolve the *Sample* in a mixture of 75 mL of water and 15 mL of 2 N sulfuric acid in a 300-mL conical flask. Add 250 mg of zinc dust, close the flask with a stopper containing a Bunsen valve, and allow to stand at room temperature for 20 min or until the solution becomes

colorless. Pass the solution through a filtering crucible containing a thin layer of zinc dust, and wash the crucible and contents with 10 mL of 2 N sulfuric acid, followed by 10 mL of water. [Note—Prepare and use the filtering crucible in a well-ventilated hood.]

Add orthophenanthroline TS, and immediately titrate the filtrate in the suction flask with *Titrant*. Perform a blank determination.

Calculate the percentage of ferrous gluconate ($C_{12}H_{22}FeO_{14}$) 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 = *Titrant* normality (mEq/mL)

F = equivalency factor, 446.2 mg/mEq

W = *Sample* weight (mg)

Acceptance criteria: 97.0%–102.0% on the dried basis

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: 1.0 g

Acceptance criteria: NMT 0.1%

- **Mercury** ⟨261⟩**:** NMT 3 ppm

Change to read:

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

Test preparation: Transfer 1.0 g of Ferrous Gluconate to a 100-mL round-bottom flask fitted with a 24/40 standard-taper joint. Add 40 mL of 9 N sulfuric acid and 2 mL of potassium bromide solution (3 in 10). Immediately connect to a suitable distillation apparatus that has a reservoir with a water jacket, cooled with circulating ice water, and heat to dissolve the Ferrous Gluconate. Distill, collect 25 mL of distillate, and transfer the distillate to the arsine generator flask. Wash the condenser and reservoir several times with small portions of water, add the washings to the distillate in the generator flask, add bromine TS until the solution is slightly yellow, and dilute with water to 35 mL. Proceed as directed in the chapter.

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 before use. 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.]

Ascorbic acid–sodium iodide solution: 100 mg/mL of ascorbic acid and 192.5 mg/mL of sodium iodide

Trioctylphosphine oxide solution: 50 mg/mL of trioctylphosphine oxide in 4-methyl-2-pentanone. [**Caution—**This solution causes irritation. Avoid contact with eyes, skin, and clothing. Take special precautions in disposing of unused portions of solutions to which this reagent is added.]

Standard solution: Transfer 5.0 mL of lead nitrate stock solution TS to a 100-mL volumetric flask, and dilute with water to volume. Transfer 2.0 mL of the resulting solution to a 50-mL volumetric flask, add 10 mL of 9 N hydrochloric acid and 10 mL of water. Add 20 mL of *Ascorbic acid–sodium iodide solution* and 5.0 mL of *Trioctylphosphine oxide solution*, shake for 30 s, and allow to separate. Add water to bring the organic solvent layer into the neck of the flask, shake again, and allow to separate. The organic layer is the *Standard solution*, and it contains 2 µg/mL of lead.

Sample solution: To a 50-mL volumetric flask add 1.0 g of Ferrous Gluconate, 10 mL of 9 N hydrochloric acid, 10 mL of water, 20 mL of *Ascorbic acid–sodium iodide solution*, and 5.0 mL of *Trioctylphosphine oxide solution*. Shake for 30 s, and allow to separate. Add water to bring the organic solvent layer into the neck of the flask, shake again, and allow to separate. The organic layer is the *Sample solution*.

Blank: To a 50-mL volumetric flask add 10 mL of 9 N hydrochloric acid, 10 mL of water, 20 mL of *Ascorbic acid–sodium iodide solution*, and 5.0 mL of *Trioctylphosphine oxide solution*. Shake for 30 s, and allow to separate. Add water to bring the organic solvent layer into the neck of the flask, shake again, and allow to separate. The organic layer is the *Blank*, and it contains 0 µg/mL of lead.

Instrumental conditions

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

Mode: Atomic absorption spectrophotometry

Analytical wavelength: 283.3 nm

Lamp: Lead hollow-cathode

Flame: Air–acetylene

System suitability

Samples: *Standard solution* and *Blank*

Suitability requirements: The absorbance of the *Standard solution* and the absorbance of the *Blank* are significantly different.

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*

Concomitantly determine the absorbances of the *Blank*, *Standard solution*, and *Sample solution*. Use the *Blank* to set the instrument to zero.

Acceptance criteria: The absorbance of the *Sample solution* does not exceed that of the *Standard solution* (NMT 10 ppm).

- **Limit of Ferric Iron**

Sample: 5 g of Ferrous Gluconate

Blank: Proceed as directed in the *Analysis* without the *Sample*.

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Direct titration

Titrant: 0.1 N sodium thiosulfate VS

Endpoint detection: Visual

Analysis: Dissolve the *Sample* in a mixture of 100 mL of water and 10 mL of hydrochloric acid, and add 3 g of potassium iodide. Shake, and allow to stand in the dark for 5 min. Titrate any liberated iodine with the *Titrant*, adding 3 mL of starch TS as the endpoint is approached. Perform a blank determination.

Calculate the percentage of ferric iron in the portion of Ferrous Gluconate 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 = *Titrant* normality (mEq/mL)

F = equivalency factor, 55.85 mg/mEq

W = *Sample* weight (mg)

Acceptance criteria: NMT 2.0%

- **Oxalic Acid**

Sample: 1.0 g

Analysis: Dissolve the *Sample* in 10 mL of water, add 2 mL of hydrochloric acid, and transfer to a separator. Extract successively with 50 mL and 20 mL of ether. Combine the ether extracts, add 10 mL of water, and evaporate the ether on a steam bath. Add 1 drop of 6 N acetic acid and 1 mL of a 50 mg/mL solution of calcium acetate.

Acceptance criteria: No turbidity is produced within 5 min.

- **Reducing Sugars**

Sample: 500 mg

Analysis: Dissolve the *Sample* in 10 mL of water, warm, and render alkaline with 1 mL of 6 N ammonium hydroxide. Pass hydrogen sulfide gas into the solution to precipitate the iron, and allow the solution to stand for 30 min to coagulate the precipitate. Filter, and wash the precipitate with two successive 5-mL portions of water. Acidify the combined filtrate and washings with hydrochloric acid, and add 2 mL of 3 N hydrochloric acid in excess. Boil the solution until the vapors no longer darken lead acetate paper, and continue to boil, if necessary, until it has been concentrated to 10 mL. Cool, add 5 mL of sodium carbonate TS and 20 mL of water, filter, and adjust the volume of the filtrate to 100 mL. To 5 mL of the filtrate add 2 mL of alkaline cupric tartrate TS, and boil for 1 min.

Acceptance criteria: No red precipitate is formed within 1 min.

SPECIFIC TESTS

- **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 16 h.

Acceptance criteria: 6.5%—10.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight 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
FERROUS GLUCONATE	Sandeep Putty Senior Scientist I	NBDS2020 Non-botanical Dietary Supplements

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 40(5)

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Current DocID: GUID-9A0C69F8-DF6A-4449-AE66-DBBFC873DB23_3_en-US
DOI: https://doi.org/10.31003/USPNF_M32940_03_01
DOI ref: 6w0fs