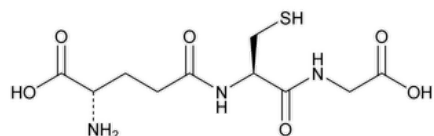


Status: Currently Official on 15-Feb-2025
 Official Date: Official as of 01-Jun-2023
 Document Type: Dietary Supplement Monographs
 DocId: GUID-AC406E18-3767-48C7-850B-C29FF498A6DB_5_en-US
 DOI: https://doi.org/10.31003/USPNF_M3372_05_01
 DOI Ref: nad3p

© 2025 USPC
 Do not distribute

Glutathione



$C_{10}H_{17}N_3O_6S$

307.32

Pentanoic acid, 2-amino-5-[(R)-1-(carboxymethylamino)-3-mercapto-1-oxopropan-2-ylamino]-5-oxo, (S);
 N-(N-L-γ-Glutamyl-L-cysteinyl)glycine CAS RN[®]: 70-18-8.

DEFINITION

Glutathione contains NLT 98.0% and NMT 101.0% of glutathione ($C_{10}H_{17}N_3O_6S$), calculated on the dried basis.

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy: 197K**
- **B. OPTICAL ROTATION, Specific Rotation(781S).**

Sample solution: 40 mg/mL in water

Acceptance criteria: -15.5° to -17.5° , at 20°

ASSAY

PROCEDURE

Sample: 500 mg of Glutathione previously dried

Blank: 50 mL of metaphosphoric acid (1 in 50)

Titrimetric system

(See [Titrimetry \(541\)](#).)

Mode: Direct titration

Titrant: 0.1 N iodine VS

Endpoint detection: Visual

Analysis: Dissolve the *Sample* in 50 mL of metaphosphoric acid (1 in 50) and titrate with the *Titrant*.

Calculate the percentage of glutathione ($C_{10}H_{17}N_3O_6S$) in the portion of Glutathione taken:

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

V_U = titrant volume of the *Sample* (mL)

V_B = titrant volume of the *Blank* (mL)

N = titrant normality (mEq/mL)

F = equivalency factor, 307.32 mg/mEq

W = weight of the *Sample* (mg)

Acceptance criteria: 98.0%–101.0% on the dried basis

IMPURITIES

AMMONIUM

Standard solution: 10 µg of ammonium from a diluted ammonium chloride solution

Sample solution: 50 mg of Glutathione

Silver manganese paper: Immerse strips of slow filter paper (Whatman® filter paper, grade 5 or equivalent) into a solution containing 8.5 mg/mL of manganese sulfate and 8.5 mg/mL of silver nitrate. Maintain for a few min and allow to dry over phosphorus pentoxide protected from acid and alkaline vapors.

Analysis: Transfer the *Sample solution* and the *Standard solution* to separate 25-mL jars fitted with caps, and dissolve in 1 mL of water. Add 0.30 g of magnesium oxide. Close immediately after placing a 5-mm square piece of *Silver manganese paper*, wetted with a few drops of water, under the caps. Swirl, avoiding projections of liquid, and allow to stand at 40° for 30 min.

Acceptance criteria: If the *Silver manganese paper* shows a gray color, it is not more intense than that of the Standard (NMT 200 ppm).

- **ARSENIC (211):** NMT 2 ppm
- **CHLORIDE AND SULFATE, Chloride(221):** Dissolve 0.7 g in water to make 15 mL. The solution shows no more chloride than corresponds to 0.20 mL of 0.020 N hydrochloric acid (NMT 200 ppm).
- **CHLORIDE AND SULFATE, Sulfate(221):** Dissolve 0.8 g in water to make 15 mL. The solution shows no more sulfate than corresponds to 0.25 mL of 0.020 N sulfuric acid (NMT 300 ppm).

Change to read:

- **IRON (241), Procedures, Procedure 1** ▲ (CN 1-JUN-2023) : NMT 10 ppm
- **RESIDUE ON IGNITION (281):** NMT 0.1%

• **RELATED COMPOUNDS**

Mobile phase: 6.8 g/L of potassium dihydrogen phosphate with 2.02 g/L of sodium 1-heptane sulfonate. Adjust with phosphoric acid to a pH of 3.0. Mix 970 mL of this solution with 30 mL of methanol.

System suitability solution: 0.1 mg/mL of [USP L-Phenylalanine RS](#), 0.5 mg/mL of [USP Glutathione RS](#), and 0.5 mg/mL of [USP Ascorbic Acid RS](#) in *Mobile phase*

Standard solution: 0.01 mg/mL of [USP Glutathione RS](#) in *Mobile phase*. [NOTE—This solution has a concentration equivalent to 2.0% of that of the *Sample solution*.]

Sample solution: 50 mg of Glutathione in 100 mL of *Mobile phase*. [NOTE—Allow the solution to stand for 5 min before use.]

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 5-μm packing L1

Column temperature: 30°

Flow rate: Adjust so that the retention time of glutathione is about 5 min.

Injection volume: 10 μL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 5.0 between the ascorbic acid and glutathione peaks; and NLT 5.0 between the glutathione and L-phenylalanine peaks

Relative standard deviation: NMT 1.5% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any impurity in the portion of Glutathione taken:

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

r_U = peak response of any peak from the *Sample solution* other than glutathione

r_S = peak response of the glutathione peak from the *Standard solution*

C_S = concentration of [USP Glutathione RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Glutathione in the *Sample solution* (mg/mL)

Acceptance criteria

Individual impurity: NMT 1.5% for the impurity with the relative retention time of about 4

Total impurities: NMT 2.0%

SPECIFIC TESTS

• **CLARITY AND COLOR OF SOLUTION**

Sample solution: 0.1 g/mL in water