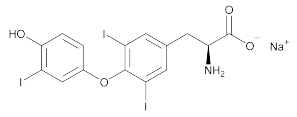
Liothyronine Sodium



$C_{15}H_{11}I_3NNaO_4$ 672.96

L-Tyrosine, *O*-(4-hydroxy-3-iodophenyl)-3,5-diiodo-, monosodium salt;
Monosodium L-3-[4-(4-hydroxy-3-iodophenoxy)-3,5-diiodophenyl]alanine [55-06-1].

DEFINITION

Liothyronine Sodium is the sodium salt of L-3,3′,5-triiodothyronine. It contains NLT 95.0% and NMT 101.0% of liothyronine sodium ($C_{15}H_{11}I_3NNaO_4$), calculated on the dried basis.

IDENTIFICATION

- **A.**
  Diluent: Solution of hydrochloric acid in 80% alcohol (1 in 50)
  Sample solution: 0.1-mg/mL solution in *Diluent*
  Acceptance criteria: The UV absorption spectrum of the *Sample solution* exhibits maxima at the same wavelengths as those of a similar solution of USP Liothyronine RS, concomitantly measured; and the respective absorptivities, both calculated on the dried basis in terms of the acid at the wavelength of maximum absorbance at about 297 nm, do not differ by more than 5.0%.
- **B.**
  Analysis: Heat 50 mg with a few drops of sulfuric acid in a porcelain crucible.
  Acceptance criteria: Violet vapors of iodine are evolved.
- **C. IDENTIFICATION TESTS—GENERAL ⟨191⟩, *Sodium*:** The residue from the ignition of Liothyronine Sodium meets the requirements.
- **D.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **PROCEDURE**
  Mobile phase: Mixture of acetonitrile and water (4:6) that contains 0.5 mL of phosphoric acid in each liter of the mixture
  Solution A: Dissolve 400 mg of sodium hydroxide in 500 mL of water. Cool, and add 500 mL of methanol.
  Levothyroxine stock solution: 0.4 mg/mL of USP Levothyroxine RS in *Solution A*. Make a 1:100 dilution of this solution using *Mobile phase*.
  Liothyronine stock solution: 0.4 mg/mL of USP Liothyronine RS in *Solution A*
  Standard solution: 10 µg/mL of liothyronine from *Liothyronine stock solution* and 0.5 µg/mL of levothyroxine from *Levothyroxine stock solution*, in *Mobile phase*
  Sample solution: 10 µg/mL of Liothyronine Sodium in *Mobile phase*
  [NOTE—A small amount of 0.01 M methanolic sodium hydroxide can be used to facilitate the dissolution of the sample.]
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 225 nm
  Column: 4.6-mm × 25-cm; packing L10
  Flow rate: 1.5 mL/min
  Injection volume: 100 µL
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Resolution: NLT 5.0 between levothyroxine and liothyronine
  Relative standard deviation: NMT 2.0% for liothyronine
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of liothyronine sodium ($C_{15}H_{11}I_3NNaO_4$) in the portion of Liothyronine Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of liothyronine from the *Sample solution*
r_S = peak response of liothyronine from the *Standard solution*
C_S = concentration of USP Liothyronine RS in the *Standard solution* (µg/mL)
C_U = concentration of Liothyronine Sodium in the *Sample solution* (µg/mL)
M_{r1} = molecular weight of liothyronine sodium, 672.96
M_{r2} = molecular weight of liothyronine, 650.97

Acceptance criteria: 95.0%–101.0% on the dried basis

IMPURITIES

- **CHLORIDE CONTENT**
  Sample solution: Transfer 100 mg of Liothyronine Sodium, previously dried, into a platinum dish. Ignite over a low flame, protecting the dish from air currents during the ignition. When carbonization is complete, cool the dish, add 2 drops of water, and break up the charred mass thoroughly with a stirring rod. Add 10 mL of water and 5 mL of ammonium hydroxide, and mix. Transfer the slurry to a glass-stoppered, 50-mL flask, and wash the platinum dish and the stirring rod with water, adding the washings to the flask, until the volume of the solution is about 25 mL. Add 10 mL of silver nitrate solution (1 in 20), shake thoroughly, and filter through a retentive paper into a 50-mL color-comparison tube. Wash the flask and the filter paper with 10 mL of water, and add the washings to the tube. Acidify the combined filtrate and washings to litmus with nitric acid, and dilute with water to 50 mL.
  Control solution: Mix 5 mL of ammonium hydroxide, 20 mL of water, and 10 mL of silver nitrate solution (1 in 20). Filter the mixture through a retentive paper into a 50-mL color-comparison tube, and then wash the filter paper with 10 mL of water into the tube. Acidify the contents of the tube to litmus with nitric acid, and dilute with water to 50 mL.
  Sodium chloride solution: 1-mg/mL solution of sodium chloride in water
  Analysis: Add the *Sodium chloride solution* in 0.1-mL increments to the *Control solution* until the turbidity of the *Control solution* matches that of the *Sample solution*.
  Acceptance criteria: NMT 2.0 mL of *Sodium chloride solution* is required (1.2%).

Change to read:

- **LIMIT OF LEVOTHYROXINE SODIUM**

Mobile phase, •**Levothyroxine stock solution, Standard solution,**• (IRA 1-Sep-2016) **Sample solution, Chromatographic system,** and **System suitability:** Proceed as directed in the *Assay*.

•**Levothyroxine standard solution:** 0.5 µg/mL of levothyroxine from *Levothyroxine stock solution*, in *Mobile phase*• (IRA 1-Sep-2016)

Analysis

Samples: •*Levothyroxine*• (IRA 1-Sep-2016) *standard solution* and *Sample solution*

Calculate the percentage of levothyroxine sodium ($C_{15}H_{10}I_4NNaO_4$) in the portion of Liothyronine Sodium taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of levothyroxine from the *Sample solution*

r_S = peak response of levothyroxine from the •*Levothyroxine*• (IRA 1-Sep-2016) *standard solution*

C_S = concentration of USP Levothyroxine RS in the •*Levothyroxine*• (IRA 1-Sep-2016) *standard solution* (µg/mL)

C_U = concentration of Liothyronine Sodium in the *Sample solution* (µg/mL)

M_{r1} = molecular weight of levothyroxine sodium, 798.85

M_{r2} = molecular weight of levothyroxine, 776.87

Acceptance criteria: NMT 5.0% of levothyroxine sodium

SPECIFIC TESTS

- **SODIUM CONTENT**

Analysis: Transfer 100 mg, previously dried, into a platinum dish. Add 8–10 drops of sulfuric acid, and ignite to constant weight, taking care to avoid spattering. Each mg of residue is equivalent to 0.324 mg of sodium (Na).

Correct the result for the quantity of sodium equivalent to the sodium chloride (NaCl) found in the test for *Chloride Content*.

Acceptance criteria: 2.9%–4.0%

- **OPTICAL ROTATION** ⟨**781S**⟩**,** *Procedures***,** *Specific Rotation*

Diluent: A mixture of alcohol and 1.2 N hydrochloric acid (4:1)

Sample solution: 20 mg/mL in *Diluent*

Acceptance criteria: +18° to +22°

- **LOSS ON DRYING** ⟨**731**⟩

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 4.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- **USP REFERENCE STANDARDS** ⟨**11**⟩

USP Levothyroxine RS

USP Liothyronine RS