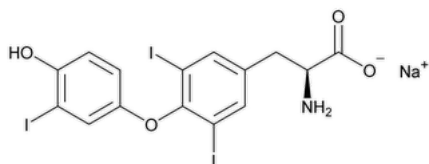


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Liothyronine Sodium



$C_{15}H_{11}I_3NNaO_4$ 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 CAS RN®: 55-06-1; UNII: GCA9VV7D2N.

DEFINITION

Change to read:

Liothyronine Sodium is the sodium salt of L-3,3',5-triiodothyronine. It contains NLT 95.0% and NMT Δ 102.0% $\blacktriangle$ (USP 1-May-2021) of liothyronine sodium ($C_{15}H_{11}I_3NNaO_4$), calculated on the dried basis.

IDENTIFICATION

Delete the following:

$\blacktriangle$ 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%. $\blacktriangle$ (USP 1-May-2021)

Add the following:

$\blacktriangle$ A. [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197K or 197A $\blacktriangle$ (USP 1-May-2021)

Change to read:

• B. $\blacktriangle$ The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay. $\blacktriangle$ (USP 1-May-2021)

• C. [IDENTIFICATION TESTS—GENERAL \(191\)](#), [Chemical Identification Tests, Sodium](#): The residue from the ignition of Liothyronine Sodium meets the requirements.

Delete the following:

$\blacktriangle$ D. The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay. $\blacktriangle$ (USP 1-May-2021)

ASSAY

Change to read:

• PROCEDURE

Mobile phase: Mixture of [acetonitrile](#) and [water](#) (40:60) 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 dilution (1:100) of this solution using *Mobile phase*.

Liothyronine stock solution: 0.4 mg/mL of [USP Liothyronine RS](#) in *Solution A*

Standard solution: 10 μ g/mL of liothyronine from *Liothyronine stock solution* and 0.5 μ g/mL of levothyroxine from *Levothyroxine stock solution*, in *Mobile phase*

Sample solution: 10 μ g/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 ▲0.73%▲ (USP 1-May-2021) 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%–▲102.0%▲ (USP 1-May-2021) on the dried basis**IMPURITIES****Change to read:**• **CHLORIDE CONTENT**▲**Sample solution:** Dissolve 500 mg of Liothyronine Sodium in 100 mL of a 2-g/L solution of [sodium hydroxide](#).**Analysis:** Add 25 mL of diluted [nitric acid](#) to the *Sample solution*, and titrate with [0.05 N silver nitrate VS](#), determining the endpoint potentiometrically. Perform a blank determination and make any necessary corrections. Each milliliter of [0.05 N silver nitrate](#) is equivalent to 1.77 mg of chloride.**Acceptance criteria:** NMT 1.2% on the dried basis (equivalent to NMT 2.0% of sodium chloride)▲ (USP 1-May-2021)**Delete the following:**▲• **LIMIT OF LEVOTHYROXINE SODIUM****Mobile phase, Levothyroxine stock solution, Standard solution, 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***Analysis****Samples:** *Levothyroxine 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 Standard solution* C_S = concentration of [USP Levothyroxine RS](#) in the *Levothyroxine 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▲ (USP 1-May-2021)**Add the following:**▲• **ORGANIC IMPURITIES****Solution A:** 4.9 g/L of [sulfamic acid](#) and 0.75 g/L of [sodium hydroxide](#) in [water](#). Adjust with [2 N sodium hydroxide](#) to a pH of 2.0.