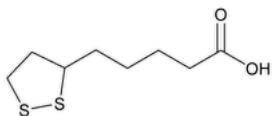


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Alpha Lipoic Acid



$C_8H_{14}O_2S_2$ 206.33

Thioctic acid;

1,2-Dithiolane-3-pentanoic acid;

1,2-Dithiolane-3-valeric acid CAS RN®: 1077-28-7.

DEFINITION

Alpha Lipoic Acid contains NLT 99.0% and NMT 101.0% of $C_8H_{14}O_2S_2$, calculated on the dried basis.

IDENTIFICATION

• **A.** The retention time of the peak for alpha lipoic acid of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

Change to read:

• **B.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197K ▲](#) (CN 1-MAY-2020)

ASSAY

• PROCEDURE

Buffer solution: 0.68 g/L of monobasic potassium phosphate

Mobile phase: Methanol, *Buffer solution*, and acetonitrile (58:46:9). Adjust with phosphoric acid solution (8.3 in 100) to a pH of 3.0–3.1.

Standard solution: 1.0 mg/mL of [USP Alpha Lipoic Acid RS](#) in *Mobile phase*

Sample solution: 1.0 mg/mL of Alpha Lipoic Acid in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 250-mm; packing L1

Column temperature: 35°

Flow rate: 1.2 mL/min

Injection size: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 10,000 theoretical plates

Tailing factor: NMT 2.0 for the alpha lipoic acid peak

Relative standard deviation: NMT 2.0% for alpha lipoic acid

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of alpha lipoic acid ($C_8H_{14}O_2S_2$) in the portion of Alpha Lipoic Acid taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

C_U = concentration of Alpha Lipoic Acid in the *Sample solution* (mg/mL)

Acceptance criteria: 99.0%–101.0% on the dried basis

IMPURITIES

- **RESIDUE ON IGNITION (281):** Less than 0.1%
- **CHROMATOGRAPHIC PURITY, PROCEDURE 1**

Buffer solution, Mobile phase, Standard solution, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

Diluted standard solution: Dilute the *Standard solution* (1 in 1000) with *Mobile phase*.

System suitability

Sample: *Diluted standard solution*

Suitability requirements

Signal-to-noise ratio: NLT 10

Relative standard deviation: NMT 10.0%

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Alpha Lipoic Acid taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

r_T = sum of the responses of all the peaks from the *Sample solution*

Acceptance criteria

Individual impurities: NMT 0.1%

Total impurities: NMT 2.0%

- **CHROMATOGRAPHIC PURITY, PROCEDURE 2**

[NOTE—Use low-actinic glassware.]

Standard solution A: 40.0 mg/mL of [USP Alpha Lipoic Acid RS](#) in dimethylformamide

Standard solution B: 20.0 mg/mL of [USP Alpha Lipoic Acid RS](#) in dimethylformamide, prepared from the dilution of *Standard solution A*

Standard solution C: 10.0 mg/mL of [USP Alpha Lipoic Acid RS](#) in dimethylformamide, prepared from the dilution of *Standard solution B*

Sample solution: 40.0 mg/mL of Alpha Lipoic Acid in dimethylformamide

Chromatographic system

(See [Chromatography \(621\)](#), [Thin-Layer Chromatography](#).)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 5 µL

Developing solvent system: *n*-Propyl alcohol, ethyl acetate, water, and 25% ammonia water (40:40:10:5). Allow the chamber to become saturated for at least 1 h.

Iodine vapor-saturated chamber: Transfer 4 g of iodine crystals to a small watch glass, and place in a chromatographic chamber. Allow the chamber to become saturated for at least 2 h.

Analysis

Samples: *Standard solution A, Standard solution B, Standard solution C, and Sample solution*

Proceed as directed in the chapter, except to develop until the solvent front has moved 10 cm. Remove the plate, and allow to air-dry until the ammonia disappears completely. Heat at 50° for 20 min, cool the plate, and place in the *Iodine vapor-saturated chamber* until the spots are visible. The R_F value for the alpha lipoic acid spot is 0.25–0.30 and for the polymeric lipoic acid spot is 0.

Acceptance criteria: No spot other than the alpha lipoic acid spot from the *Sample solution* is more intense than the spot at $R_F = 0$ from *Standard solution A*.

SPECIFIC TESTS

- **MELTING RANGE OR TEMPERATURE (741):** 60.0°–62.0°
- **OPTICAL ROTATION, Specific Rotation (781S)**

Sample solution: 50 mg/mL of Alpha Lipoic Acid, in dehydrated alcohol

Acceptance criteria: –1.0° to +1.0°

- **LOSS ON DRYING (731):** Dry a sample in vacuum at 40° for 3 h: it loses NMT 0.2% of its weight.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers.
- **USP REFERENCE STANDARDS (11).**
[USP Alpha Lipoic Acid RS](#)