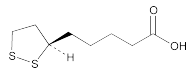
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Sodium Fluoride RS

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 [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

Change to read:

- **▲A.**▲*USP35* 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*.

Add the following:

▲• B. INFRARED ABSORPTION ⟨**197K**⟩▲*USP35*

ASSAY

Change to read:

- **PROCEDURE**
  ▲Buffer solution:▲*USP35* 0.68 g/L of monobasic potassium phosphate
  ▲▲*USP35*
  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.
  ▲▲*USP35*
  Standard solution: 1.0 mg/mL of USP Alpha Lipoic Acid RS in ▲*Mobile phase*▲*USP35*
  Sample solution: 1.0 mg/mL of Alpha Lipoic Acid in ▲*Mobile phase*▲*USP35*
  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▲*USP35* 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%
- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 10 ppm

Change to read:

- **CHROMATOGRAPHIC PURITY, PROCEDURE 1**
  Buffer solution, Mobile phase, Standard solution, ▲▲*USP35* **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%▲*USP35*
  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

Alpha Lipoic Acid Capsules

DEFINITION

Alpha Lipoic Acid Capsules contain NLT 90.0% and NMT 115.0% of the labeled amount of $C_8H_{14}O_2S_2$.

IDENTIFICATION

- The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Content of Alpha Lipoic Acid*.

STRENGTH

- **CONTENT OF ALPHA LIPOIC ACID**
  Mobile phase: 0.025 M phosphoric acid and acetonitrile (62:38)
  Standard solution: 0.05 mg/mL of USP Alpha Lipoic Acid RS in acetonitrile and water (1:1)
  Sample solution A (for hard gelatin Capsules)**:** Empty and mix thoroughly the contents of NLT 20 Capsules. Transfer a portion of the powder, equivalent to 100 mg of alpha lipoic acid, to a suitable container. Add 70 mL of a mixture of acetonitrile and water (1:1), and shake for 45 min by mechanical means. Transfer to a 100-mL volumetric flask, dilute with the mixture of acetonitrile and water (1:1) to volume, and filter a portion of this preparation, discarding the first 5 mL of the filtrate. Transfer 5.0 mL of the remaining filtrate to a 100-mL volumetric flask, and dilute with acetonitrile and water (1:1) to volume.
  Sample solution B (for soft gelatin Capsules)**:** Using a suitable cutting instrument, open a number of Capsules equivalent to 500 mg of alpha lipoic acid from a counted number of opened Capsules. Transfer the contents and the shells to a suitable container with stopper, add 500.0 mL of a mixture of acetonitrile and water (1:1), and shake for 45 min by mechanical means. Filter a portion of this preparation, discarding the first 5 mL of the filtrate. Transfer 5.0 mL of the remaining filtrate to a 100-mL volumetric flask, and dilute with acetonitrile and water (1:1) to volume.
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: LC
  Detector: UV 220 nm
  Column: 3.9-mm × 30-cm; packing L1
  Flow rate: 1.5 mL/min
  Injection size: 20 µL
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Column efficiency: NLT 1300 theoretical plates
  Tailing factor: NMT 1.2 for alpha lipoic acid
  Relative standard deviation: NMT 1.0%
  Analysis
  Samples: *Standard solution* and appropriate *Sample solution*
  Calculate the percentage of alpha lipoic acid in the portion of Capsules taken:

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

  r_U = peak response from *Sample solution A* or *Sample solution B*
  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 = nominal concentration of alpha lipoic acid in *Sample solution A* or *Sample solution B* (mg/mL)
  Acceptance criteria: 90.0%–115.0%

PERFORMANCE TESTS

- **DISINTEGRATION AND DISSOLUTION OF DIETARY SUPPLEMENTS ⟨2040⟩:** Meet the requirements for *Dissolution*
  Medium: Water; 900 mL
  Apparatus 1 (for hard gelatin Capsules)**:** 100 rpm
  Apparatus 2 (for soft gelatin Capsules)**:** 75 rpm
  Time: 60 min
  Standard solution: 1 mg/mL of USP Alpha Lipoic Acid RS in a mixture of acetonitrile and water (1:1). Dilute with water to obtain a concentration of 0.02 mg/mL.
  Sample solution: Withdraw a portion of the solution under test, and filter, discarding the first portion of the filtrate. Transfer an aliquot to a volumetric flask, and dilute with water to volume to obtain a solution having an expected concentration of 0.02 mg/mL of alpha lipoic acid.
  Mobile phase and **Chromatographic system:** Proceed as directed in the test for *Content of Alpha Lipoic Acid*.
  Injection size: 50 µL
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of alpha lipoic acid ($C_8H_{14}O_2S_2$) dissolved:

$$\text{Result} = (r_U/r_S) \times (V \times C \times D/L) \times 100$$

  r_U = peak area from the *Sample solution*
  r_S = peak area from the *Standard solution*
  V = volume of dissolution *Medium*, 900 mL
  C = concentration of USP Alpha Lipoic Acid RS in the *Standard solution* (mg/mL)
  D = dilution factor of the sample
  L = label claim of alpha lipoic acid (mg/Capsule)
  Tolerances: NLT 70% of the labeled amount of $C_8H_{14}O_2S_2$ is dissolved.
- **WEIGHT VARIATION OF DIETARY SUPPLEMENTS ⟨2091⟩:** Meet the requirements

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers.