

## 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].

Alpha Lipoic Acid contains not less than 99.0 percent and not more than 101.0 percent of  $C_8H_{14}O_2S_2$ , calculated on the dried basis.

**Packaging and storage**— Preserve in well-closed containers.

**Identification**— The retention time of the peak for alpha lipoic acid in the chromatogram of the Assay preparation corresponds to that in the chromatogram of the Standard preparation, as obtained in the Assay.

Melting range [741](#) : between 60.0 and 62.0 .

Specific rotation [781S](#) : between  $-1.0$  and  $+1.0$  .

**Test solution**— Transfer 2.5 g of Alpha Lipoic Acid, accurately weighed, to a 50-mL volumetric flask, dissolve in 30 mL of dehydrated alcohol, and dilute with dehydrated alcohol to volume.

Loss on drying [731](#) — Dry it in vacuum at 40 for 3 hours: it loses not more than 0.2% of its weight.

Residue on ignition [281](#) : less than 0.1%.

Heavy metals, Method II [231](#) : 0.001%.

Limit of 6,8-epitrithiooctanoic acid— Using the chromatograms of the Standard preparation and the Assay preparation, as obtained in the Assay, calculate the percentage of 6,8-epitrithiooctanoic acid in the portion of Alpha Lipoic Acid taken by the formula:

$$P_S (C_S / C_U)(r_U / r_S)$$

in which  $P_S$  is the labeled percentage of 6,8-epitrithiooctanoic acid in [USP Alpha Lipoic Acid RS](#);  $C_S$  and  $C_U$  are the concentrations, in mg per mL, of [USP Alpha Lipoic Acid RS](#) and Alpha Lipoic Acid in the Standard preparation and the Assay preparation, respectively; and  $r_U$  and  $r_S$  are the peak areas of 6,8-epitrithiooctanoic acid obtained from the Assay preparation and the Standard preparation, respectively: not more than 0.1% is found.

**Limit of polymer content—**

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture.

**Test solution—** Dissolve an accurately weighed quantity of Alpha Lipoic Acid in dimethylformamide to obtain a solution having a concentration of about 40.0 mg per mL.

Standard solution 1— Dissolve an accurately weighed quantity of [USP Alpha Lipoic Acid RS](#) in dimethylformamide to obtain a solution having a known concentration of about 40.0 mg per mL.

This solution contains 2.0% of polymer. Store in low-actinic glassware.

Standard solution 2— Dilute an aliquot of Standard solution 1 with a sufficient amount of dimethylformamide to obtain a solution having a known concentration of about 20.0 mg per mL.

This solution contains 1.0% of polymer.

Standard solution 3— Dilute an aliquot of Standard solution 2 with a sufficient amount of dimethylformamide to obtain a solution having a known concentration of about 10.0 mg per mL.

This solution contains 0.5% of polymer.

Application volume: 5  $\mu$ L of each solution.

Developing solvent system: a mixture of n-propyl alcohol, ethyl acetate, water, and 25 percent ammonia water (40:40:10:5). Allow the chamber to become saturated for at least 1 hour.

Iodine vapor saturated chamber— Transfer 4.0 g of iodine crystals, accurately weighed, to a small watch glass, and place into the chromatography chamber. Allow the chamber to become saturated for at least 2 hours.

**Procedure—** Proceed as directed for Thin-Layer Chromatography under [Chromatography](#)

[621](#) , except to develop the chromatogram 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 minutes, cool the plate, and place in the Iodine vapor saturated chamber until the spots are visible. The chromatograms exhibit a spot due to alpha lipoic acid polymer at an RF value of 0.0 and a spot due to alpha lipoic acid at an RF value between 0.25 and 0.30. The spot due to polymeric alpha lipoic acid in the chromatogram obtained from the Test solution is not more intense than the spot in the chromatogram obtained from Standard solution 1: not more than 2% is found.

**Assay—**

0.005 M Phosphate solution— Dissolve 1.36 g of monobasic potassium phosphate in 2000 mL of water.

Phosphoric acid solution— Transfer 8.3 mL of phosphoric acid to a 100-mL volumetric flask, and dilute with water to volume.

Mobile phase— Prepare a suitable filtered and degassed mixture of methanol, 0.005 M Phosphate solution, and acetonitrile (1160:920:180). Adjust with Phosphoric acid solution to a pH of 3.0 to 3.1.

Solvent buffer— Prepare a suitable filtered and degassed mixture of 0.005 M Phosphate solution and acetonitrile (1:1). Adjust with Phosphoric acid solution to a pH of 3.5 to 3.7.

Standard preparation— Dissolve an accurately weighed quantity of [USP Alpha Lipoic Acid RS](#) in Solvent buffer to obtain a solution having a known concentration of about 1.0 mg per mL.

Assay preparation— Dissolve an accurately weighed quantity of Alpha Lipoic Acid in Solvent buffer to obtain a solution having a concentration of about 1.0 mg per mL.

**Chromatographic system**— The liquid chromatograph is equipped with a 215-nm detector and a 4.6-mm × 250-mm column that contains packing L1. The flow rate is about 1.2 mL per minute.

The column temperature is maintained at 35 °. Chromatograph the Standard preparation, and record the peak responses as directed for Procedure: the retention times for alpha lipoic acid and 6,8-epitriethiooctanoic acid are about 6.5 minutes and 13 minutes, respectively; the column efficiency is not less than 15,000 theoretical plates; the tailing factor for the alpha lipoic acid peak is not more than 2; and the relative standard deviation for replicate injections is not more than 2.0%.

**Procedure**— Separately inject equal volumes (about 20 µL) of the Standard preparation and the Assay preparation into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the percentage of C<sub>8</sub>H<sub>14</sub>O<sub>2</sub>S<sub>2</sub> in the portion of Alpha Lipoic Acid taken by the formula:  $P_S (C_S / C_U)(r_U/r_S)$

in which P<sub>S</sub> is the percentage of alpha lipoic acid in [USP Alpha Lipoic Acid RS](#); C<sub>S</sub> is the concentration, in mg per mL, of [USP Alpha Lipoic Acid RS](#) in the Standard preparation; C<sub>U</sub> is the concentration of Alpha Lipoic Acid in the Assay preparation; and r<sub>U</sub> and r<sub>S</sub> are the peak areas for alpha lipoic acid obtained from the Assay preparation and the Standard preparation, respectively.