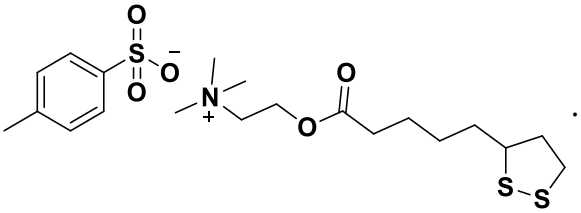
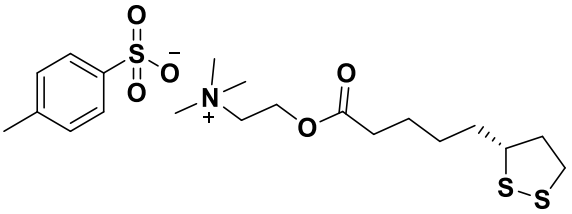
What is claimed is:

1. Lipoic acid choline ester tosylate having structure:

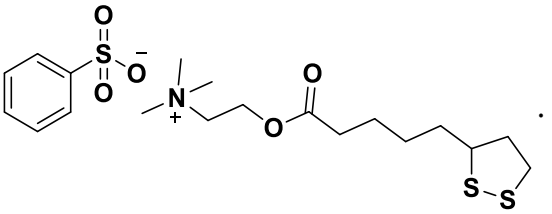


2. (R) Lipoic acid choline ester tosylate having structure:

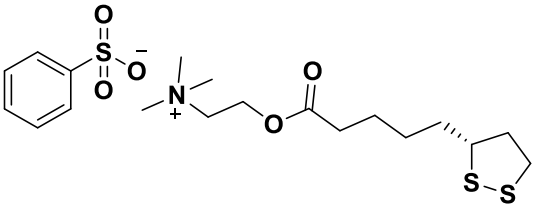


having at least 90% enantiomeric excess of the R isomer.

3. Lipoic acid choline ester besylate having structure:



4. (R) Lipoic acid choline ester besylate having structure:



having at least 90% enantiomeric excess of the R isomer.

5. A crystal form A of lipoic acid choline ester tosylate characterized by an X ray diffraction pattern having three or more peaks at 2θ values selected from 21.9, 24.9, 25.9, 26.7, 27.1, 30.4, and 32.1 ± 0.2 °2θ.

6. The crystal form A of lipoic acid choline ester tosylate according to claim 5, characterized by an X ray diffraction pattern having four, five, six, or seven peaks at 2θ

values selected from 11.4, 15.2, 18.4, 19.0, 19.4, 19.8, 21.9, 22.9, 24.9, 25.9, 26.7, 27.1, 29.6, 30.4, 32.1± 0.2 °2θ.

7. A crystal form B of lipoic acid choline ester tosylate characterized by an X ray diffraction pattern having three or more peaks at 2θ values selected from 7.7, 20.7, 21.4, 24.3, and 25.37 ± 0.2 °2θ.

8. The crystal form B of lipoic acid choline ester tosylate according to claim7, characterized by an X ray diffraction pattern having four or five peaks at 2θ values selected from 7.7, 20.7, 21.4, 24.3, and 25.37 ± 0.2 °2θ.

9. A lipoic acid choline ester tosylate composition, comprising at least 90 weight % of the crystalline form B according to claim 7 or 8, based on the weight of the composition.

10. A crystal form of lipoic acid choline ester besylate characterized by an X ray diffraction pattern having three or more peaks at 2θ values selected from 4.3, 12.7, 18.4, 19.0, 19.9, 20.6, 20.8, 21.3, 23.3, 24.2, 25.5, 27.6, 31.4, 33.2, 35.0, 35.4 ± 0.2 °2θ.

11. A method of preparing lipoic acid choline ester tosylate, comprising:
reacting lipoic acid with an activating agent, optionally in a solvent, and optionally in the presence of a base, to yield an activated lipoic acid intermediate, and
reacting the activated lipoic acid intermediate with choline tosylate, optionally in a solvent, and optionally in the presence of a base, to yield lipoic acid choline ester tosylate.

12. The method according to claim 11, with one or more of the following:
the activating agent is carbonyldiimidazole;
the reaction of lipoic acid with the activating agent is carried out in a solvent and the presence of a base;
the reaction of lipoic acid with an activating agent is carried out at temperatures below 25 °C;
the reaction of activated lipoic acid intermediate with the choline tosylate is carried out in a solvent and in the presence of a base; and
the reaction of activated lipoic acid intermediate with choline tosylate is carried out at temperatures below 25 °C, or below 30 °C.

13. A pharmaceutical composition, comprising an effective amount of lipoic acid choline ester tosylate or lipoic acid choline ester besylate, according to any of claims 0-10, and a pharmaceutically acceptable excipient.

14. A pharmaceutical composition, comprising:

a lipoic acid choline ester tosylate or lipoic acid choline ester besylate, according to any of claims 1-10,
hydroxypropyl-β-cyclodextrin,
optionally, a tonicity agent,
optionally, a viscosity modifying agent,
optionally, a buffer, and
optionally, a preservative.

15. The pharmaceutical composition according to claim 14, comprising

about 0.5% w/v to about 5% w/v (based on the lipoic acid choline ester) of the lipoic acid choline ester salt,
about 1.5% w/v to about 25% w/v of hydroxypropyl-β-cyclodextrin,
up to 300 mM of a tonicity agent,
0% w/v to about 20% w/v of a viscosity modifying agent,
0% w/v to about 1% w/v of a buffer, and
0% w/v to about 0.5% w/v of a preservative.

16. The pharmaceutical composition according to any of claims 13-15, comprising about 0.01% w/v to about 20% w/v of a viscosity modifying agent.

17. The pharmaceutical composition according to claim 16, wherein the viscosity modifying agent is selected from the group consisting of cellulosic agents and is present in an amount of about 0.01% w/v to about 1% w/v.

18. The pharmaceutical composition according to claim 17, wherein the viscosity modifying agent comprises or is substantially all hydroxypropylmethyl cellulose.

19. The pharmaceutical composition according to claim 18, comprising about 1 mM to about 150 mM of a tonicity agent selected from the group consisting of sodium chloride, potassium chloride, and mixtures thereof, or about 1 mM to about 300 mM of a tonicity agent selected from the group consisting of mannitol, dextrose, and mixtures thereof.

20. The pharmaceutical composition according to claim 19, wherein the tonicity agent comprises or is substantially all sodium chloride.

21. The pharmaceutical composition according to any of claims 13-20, comprising about 0.01% w/v to about 1% w/v of a buffer.

22. The pharmaceutical composition according to claim 21, wherein the buffer is selected from the group consisting of phosphate buffers (e.g., sodium phosphate monobasic monohydrate, sodium phosphate dibasic anhydrous), acetate buffer, citrate buffer, borate buffers, and HBSS (Hank's Balanced Salt Solution).

23. The pharmaceutical composition according to claim 21 wherein the buffer comprises or is substantially all acetate buffer.

24. The pharmaceutical composition according to any of claims 13-23, comprising 0% w/v to about 0.5% w/v of a preservative selected from the group consisting of benzalkonium chloride, sorbic acid, boric acid, and mixtures thereof.

25. The pharmaceutical composition according to any of claims 13-24, having a pH of about 4.3 to about 4.7.

26. The pharmaceutical composition according to any of claims 13-25, wherein the pharmaceutical composition does not include a biochemical energy source.

27. The pharmaceutical composition according to any of claims 13-26, wherein the pharmaceutical composition does not include benzalkonium chloride.

28. The pharmaceutical composition according to any of claims 13-27, wherein the pharmaceutical composition does not include a preservative and wherein the pharmaceutical composition meets US Pharmacopoeia preservation standards for sterile parenteral multi-dose compositions.

29. The pharmaceutical composition according to any of claims 13-28, comprising hydroxypropyl-β-cyclodextrin in an amount about equimolar to the lipoic acid choline ester salt or about 1.5% w/v, about 2.5% w/v, about 3.2% w/v, about 3.3% w/v, about 6.3% w/v, about 6.7% w/v, about 11.2% w/v, about 11.5% w/v, about 15.0% w/v, or about 19.6% w/v of hydroxypropyl-β-cyclodextrin.

30. The pharmaceutical composition according to any of claims 13-29, having an osmolality of about 250 mOsm to about 425 mOsm.

31. A lipoic acid choline ester for use in treating or preventing a disease or disorder associated with oxidative damage, wherein a lipoic acid choline ester salt at a total daily dose of about 0.1 mg to about 5 mg of lipoic acid choline ester, about 0.2 mg to about 3 mg of lipoic acid choline ester, about 0.4 mg to about 2.5 mg of lipoic acid choline ester, or of about 0.2 mg, about 0.4 mg, about 0.5 mg, about 0.8 mg, about 0.9 mg, about 1 mg, about 1.1 mg, about 1.2 mg, about 1.4 mg, about 1.5 mg, about 1.6 mg, about 2.1 mg, about 2.4 mg, about 2.8 mg, or about 3.2 mg, of lipoic acid choline ester is to be ocularly administered to a patient, and
wherein the lipoic acid choline ester is in a salt form selected from the group consisting of lipoic acid choline ester tosylate, lipoic acid choline ester besylate, lipoic acid choline ester chloride or lipoic acid choline ester iodide.

32. The lipoic acid choline ester for use according to claim 31, wherein the lipoic acid choline ester is to be administered to the patient in the form of a pharmaceutical composition according to any of claims 13-30.

33. The lipoic acid choline ester for use according to claim 32, wherein a total daily dose of lipoic acid choline ester tosylate of about 0.2 mg to about 7 mg, or about 0.5 mg to about 5 mg, or about 0.7 mg to about 3.5 mg, or about 0.3 mg, about 0.6 mg, about 0.8 mg, about 1.0 mg, about 1.5 mg, about 1.7 mg, about 2.0 mg, about 2.2 mg, about 2.3 mg, about 2.5 mg, about 2.6 mg, about 3.0 mg, about 3.4, about 3.9, about 4.5, about 5.0, about 6.0, or about 6.7 mg is to be ocularly administered to a patient.

34. A lipoic acid choline ester for use in improving distance corrected near vision acuity (DCNVA) in a subject in need thereof, wherein an effective amount of a pharmaceutical

composition according to any of claims 13-30 is to be ocularly administered to a patient to the subject.

35. The lipoic acid choline ester for use of any of claims 31-34, wherein the subject suffers from a disease or disorder associated with oxidative damage.

36. The lipoic acid choline ester for use of any of claims 31-35, wherein the disease or disorder associated with oxidative damage is presbyopia or cataract.