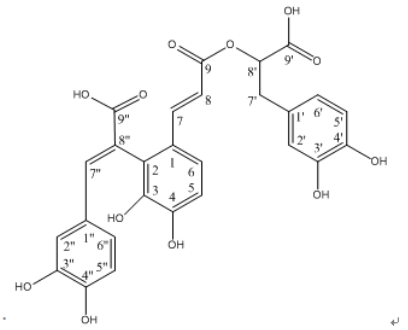
What's claimed is:

1. A salvianolic acid T represented by the structural formula (I), its pharmaceutically acceptable salts, chiral isomers, solvates ~~and hydrolysable esters.~~



2. A preparation method of the salvianolic acid T according to claim 1, wherein, the method includes the following steps:

(1a) extraction:extracting Radix Salviae Miltiorrhizae crude drug or a mixture of Radix Salviae Miltiorrhizae and other crude drugs with water, concentrating the filtrate to obtain a water extract, then adding alcohol to precipitate and obtain a supernatant, concentrating the supernatant to obtain an alcohol extract;

(1b) separation: diluting the alcohol extract of the step (1a) in water, applying on the macroporous absorbent resin , washing the resin with an acidic aqueous solution to remove impurities and then eluting the resin with ethanol to obtain an ethanol eluent, concentrating the ethanol eluent to obtain an extract;

Or, replacing the above steps (1a) and (1b) by the following step (1):

(1)Synthesis:dissolving salvianolic acid B in the water, heating ;

(2) purification: adjusting the pH of the reaction liquid obtained in the step (1) to be acidic or purifying the extract obtained in the step (1b) by the preparative high pressure liquid chromatograph, with C18 reversed phase silica gel column as the chromatographic packing, acetonitrile-water-formic acid as the eluent, carrying out isocratic elution or gradient elution, with

a detection wavelength of 280nm; monitoring the elution process by high performance liquid chromatography, collecting the eluent containing salvianolic acid T; concentrating to obtain the salvianolic acid T.

3. A preparation method of the chiral isomers of salvianolic acid T according to claim 1, wherein, the method includes the following steps:

(1a) extraction: extracting Radix Salviae Miltiorrhizae crude drug or a mixture of Radix Salviae Miltiorrhizae and other crude drugs with water, concentrating the filtrate to obtain a water extract, then adding alcohol to precipitate and obtain a supernatant, concentrating the supernatant to obtain an alcohol extract;

(1b) separation: diluting the alcohol extract obtained in the step (1a) with water, applying on the macroporous absorbent resin, washing the resin with an acidic aqueous solution to remove impurities and then eluting the resin with ethanol to obtain an ethanol eluent, concentrating the ethanol eluent to obtain an extract;

Or, replacing the above steps (1a) and (1b) by the following step (1) :

(1)Synthesis: dissolving salvianolic acid B in the water, heating;

(2) purification: adjusting the pH of the reaction liquid obtained in the step(1) to be acidic or purifying the extract obtained in the step (1b) by the preparative high pressure liquid chromatograph, with C18 reversed phase silica gel column as the chromatographic packing, acetonitrile-water-formic acid as the eluent, carrying out isocratic elution, with a detection wavelength of 280nm; monitoring the elution process by high performance liquid chromatography, combining the eluent containing salvianolic acid T ; concentrating to obtain the salvianolic acid T.

(3) preparation of the chiral isomers:separating the chiral isomers from the salvianolic acid T obtained in step (2) by preparative liquid chromatograph, with reversed phase chiral column as the chromatographic column, acetonitrile-water-formic acid as the eluent, carrying out isocratic elution or gradient elution, with a detection wavelength of 280nm; monitoring the elution process

by high performance liquid chromatography, collecting the eluent containing (*S*)-salvianolic acid T and (*R*)-salvianolic acid T separately, freeze-drying to obtain the pure products of (*S*)-salvianolic acid T and (*R*)-salvianolic acid T.

4. The preparation method according to claim 2 or 3, wherein, in the step (1a), the said Radix Salviae Miltiorrhizae crude drug or the mixture of Radix Salviae Miltiorrhizae and other crude drugs are decoction pieces, crushed particles or powders, the said other crude drugs are Radix Notoginseng or Radix Astragali or the combination of the two that which are compatible with the Radix Salviae Miltiorrhizae.

5. The preparation method according to claim 2 or 3, wherein, in the step (1a), the said water-extraction is as follows: decocting the crude drug with water of 4-8 times the volume of the crude drug for 1.5-4h; filtrating; concentrating the filtrate to obtain a water extract with a relative density of 1.10-1.30(80℃).

6. The preparation method according to claim 2 or 3, wherein, in the step (1a), the said water-extraction is as follows: decocting the crude drug with water of 6 times the volume of the crude drug for 3h; filtrating; concentrating the filtrate to obtain a water extract with a relative density of 1.22 (80℃).

7. The preparation method according to claim 2 or 3, wherein, in the step (1a), an alkali aqueous solution is used in the said water-extraction step, the said alkali is at least one selected from the group consisting of sodium bicarbonate solution, sodium carbonate aqueous solution, Potassium hydrogen carbonate solution,Potassium carbonate solution, sodium hydroxide aqueous solution, potassium hydroxide aqueous solution.

8. The preparation method according to claim 7， wherein, the said alkali aqueous solution is a sodium bicarbonate aqueous solution in a concentration of 0.3%-0.45% (w/v).

9. The preparation method according to claim 2 or 3, wherein, in the step (1a), the said alcohol-precipitation is as follows: adding 95% (v/v) ethanol into the water extract to precipitate

until the content of the ethanol being 50%-70% (v/v) (25℃), and standing still for 8-36h; obtaining the supernatant, recovering ethanol under reduced pressure condition, concentrating to obtain an Alcohol extract with a relative density of 1.25-1.5(60℃).

10. The preparation method according to claim 2 or 3, wherein, in the step (1a), the said alcohol-precipitation is as follows: adding 95% (v/v) ethanol into the water extract to precipitate until the content of the ethanol being 60% (v/v)(25℃), and standing still for 24h; obtaining the supernatant, recovering ethanol under reduced pressure condition, concentrating to obtain an Alcohol extract with a relative density of 1.32 (60℃).

11. The preparation method according to claim 2 or 3, wherein, in the step (1b), the said macroporous adsorptive resin can be non-polar or weak polar macroporous adsorptive resin.

12. The preparation method according to claim 11，wherein, the non-polar or weak polar macroporous adsorptive resin is AB-8 type, HPD450 type, D101 type, or X5 type macroporous adsorptive resin.

13. The preparation method according to claim 12，wherein, the non-polar or weak polar macroporous adsorptive resin is AB-8 type.

14. The preparation method according to claim 2 or 3, wherein, in the step (1b), the weight ratio of the crude drug used in the step(1a) to the macroporous absorbent resin is 5:1-1:1.

15. The preparation method according to claim 14，wherein, , the weight ratio of the crude drug used in the step(1a) to the macroporous absorbent resin is 3:1。

16. The preparation method according to claim 2 or 3, wherein, in the step (1b), the said acidic aqueous solution is at least one selected from the group consisting of hydrochloric acid aqueous solution, sulfuric acid aqueous solution, nitric acid aqueous solution and acetic acid aqueous solution or the combination of them; the pH of the solution is adjusted into 1.0-5.0, washing with the acidic aqueous solution until the eluent being nearly colorless.

17. The preparation method according to claim 16，wherein, the said acidic aqueous solution is hydrochloric acid aqueous solution; the pH of the solution is adjusted into 3.0.

18. The preparation method according to claim 2 or 3, wherein, in the step (1b), 4-10 times of 50%-95% (v/v) ethanol is used to wash the column, then the eluent is concentrated to obtain an extract without alcoholic smell.

19. The preparation method according to claim 18，wherein, 5 times of 95% (v/v) ethanol is used to wash the column.

20. The preparation method according to claim 2 or 3, wherein, in the step (1), the reaction raw material is salvianolic acid B or its salts.

21. The preparation method according to claim 2 or 3, wherein, in the step (1), the mass ratio of the said salvianolic acid B to the said aqueous solution is 1:0.1-1:100000，the reaction temperature is 10-150℃，the reaction time is 10 min to 24h.

22. The preparation method according to claim 2 or 3, wherein, in the step (1), the mass ratio of the said salvianolic acid B to the said aqueous solution is 1:200，the reaction temperature is 90℃，the reaction time is 1h.

23. The preparation method according to claim 2 or 3, wherein, in the step (1), the said aqueous solution is acidic aqueous solution, neutral aqueous solution or alkaline aqueous solution.

24. The preparation method according to claim 2 or 3, wherein, in the step (1), the said aqueous solution is alkaline aqueous solution, the said alkaline aqueous solution is at least selected from the following aqueous solutions:sodium bicarbonate solution, sodium carbonate aqueous solution, potassium hydrogen carbonate solution, potassium carbonate solution, sodium hydroxide aqueous solution and potassium hydroxide aqueous solution.

25. The preparation method according to claim 8，wherein, the said alkaline aqueous solution is sodium bicarbonate solution with a concentration of 0.05%-0.45% (w/v).

26. The preparation method according to claim 2 or 3, wherein, in the step (2), any one or combination of the hydrochloric acid aqueous solution, sulfuric acid aqueous solution, aqueous solution of nitric acid and acetic acid aqueous solution is used to adjust the pH of the reaction liquid into 1.0-6.0.

27. The preparation method according to claim 26，wherein, the hydrochloric acid aqueous solution is used to adjust the reaction liquid into 3.0.

28. The preparation method according to claim 2 or 3, wherein, in the step (2), the said high pressure liquid chromatograph is dynamic axial high pressure liquid chromatograph, the chromatographic packing is C18 reversed phase silica gel column, dissolving the reaction liquid the pH of which is adjusted in the step(1) or the extract obtained in the said step(1b) with mobile phase, the said mobile phase is acetonitrile:water:formic acid (volume ratio)=(10:90:1)-(90:10:1); the eluent uses the above ratio of the mobile phase, the elution is isocratic elution or gradient elution; the flow rate is 300mL/min; the detection wavelength is 280nm；high performance liquid chromatography is used to monitor the elution process, collecting the components the retention time of which is 21.2-24.0min, concentrating to dry, obtaining salvianolic acid T sample.

29. The preparation method according to claim 28, wherein, the said mobile phase is acetonitrile:water:formic acid(volume ratio)=(10:90:1)-(50:50:1).

30. The preparation method according to claim 28, wherein, the said mobile phase is acetonitrile:water:formic acid (volume ratio) =15:85:1.

31. The preparation method according to claim 28, wherein, the said elution uses mobile phase of acetonitrile:water:formic acid(volume ratio)=15:85:1 to carry out the isocratic elution.

32. The preparation method according to claim 3, wherein, in the step (3), preparative liquid chromatography is used to carry out the chiral isomer separation, the chromatographic column is reversed phase column, dissolving the salvianolic acid T sample obtained in the step (2) with mobile phase, the said mobile phase is acetonitrile:water:formic acid (volume ratio)=(90:10:1)-

(10:90:1); the eluent uses the above ratio of the mobile phase, the elution is isocratic elution or gradient elution; the flow rate is 25mL/min; the detection wavelength is 280nm; high performance liquid chromatography is used to Monitor the elution process, collecting the (S)-salvianolic acid T component with a retention time of 19.5-21.1min, (R)-salvianolic acid T component with a retention time of 23.9-25.3min separately, freeze-drying after low temperature centration, obtaining (S)-salvianolic acid T pure product and (R)-salvianolic acid T pure product.

33. The preparation method according to claim 32, wherein, the said mobile phase is acetonitrile:water:formic acid(volume ratio)=17:83:1.

34. The preparation method according to claim 32, wherein, the said elution uses the mobile phase of acetonitrile:water:formic acid (volume ratio)=17:83:1 to carry out isocratic elution.

35. The preparation method according to claim 32, wherein, the said low temperature is 10-40℃.

36. The preparation method according to claim 32, wherein, the said low temperature is 30℃。

37. A pharmaceutical composition comprising the said salvianolic acid T, its pharmaceutically acceptable salts, chiral isomers, solvates ~~and hydrolysable esters~~ according to claim 1.

38. An antioxidant comprising the said salvianolic acid T, its pharmaceutically acceptable salts, chiral isomers, solvates ~~and hydrolysable esters~~ according to claim 1.

39. A free radical scavenger comprising the said salvianolic acid T, its pharmaceutically acceptable salts, chiral isomers, solvates ~~and hydrolysable esters~~ according to claim 1.

40. A use of the salvianolic acid T, its pharmaceutically acceptable salts, chiral isomers, solvates ~~and hydrolysable esters~~ according to claim 1 in preparing drugs for treating acute myocardial infarction and acute myocardial ischemia.

41. A use of the salvianolic acid T, its pharmaceutically acceptable salts, chiral isomers, solvates ~~and hydrolysable esters~~ according to claim 1 in preparing drugs for treating pulmonary

fibrosis disease.

42. A use of the salvianolic acid T, its pharmaceutically acceptable salts, chiral isomers, solvates ~~and hydrolysable esters~~ according to claim 1 in preparing antioxygens.

~~43. Using the salvianolic acid T, its pharmaceutically acceptable salts, chiral isomers, solvates and hydrolysable esters according to claim 1 for treating acute myocardial infarction, acute myocardial ischemia or pulmonary fibrosis disease.~~

~~44. Using the salvianolic acid T, its pharmaceutically acceptable salts, chiral isomers, solvates and hydrolysable esters according to claim 1 for delaying senility.~~

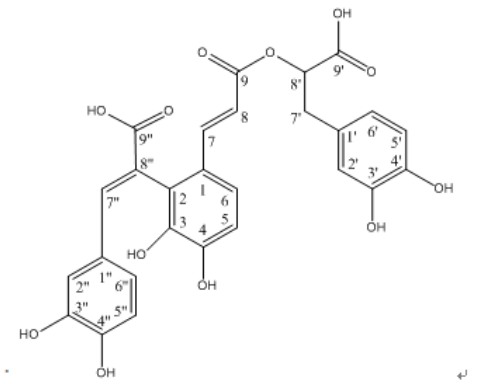
~~45. Using the salvianolic acid T, its pharmaceutically acceptable salts, chiral isomers, solvates and hydrolysable esters according to claim 1for antioxidation.~~

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NEW SALVIANOLIC ACID COMPOUND T, PREPARATION METHOD THEREFOR, AND USE THEREOF

Abstract

The present invention relates to the medical field, specifically a salvianolic acid T as described in structural formula (I), a chiral isomer thereof, a preparation method therefor, pharmaceutical compositions, antioxidants, and free radical scavengers thereof, and a use of the compound.



Structural formula（I）

Fig 1.