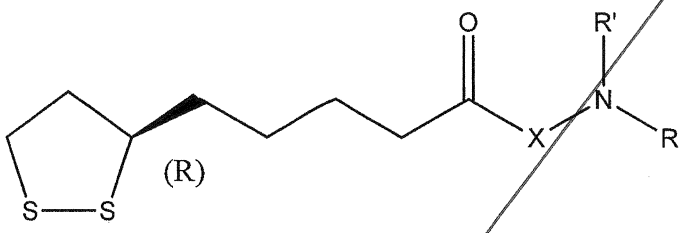
CLAIMS

What is claimed is:

1. A compound represented by Structural Formula (I):

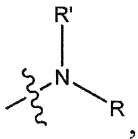


(I),

or a pharmaceutically acceptable salt or prodrug thereof, substantially separated from the (S)-lipoyl stereoisomer(s), or a pharmaceutically acceptable salt or prodrug thereof, wherein:

R is (C_1-C_{18})alkyl, (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{18})alkyl and is substituted with at least one acidic substituent selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH, wherein the aryl of the (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{18})alkyl is optionally further substituted with one or more substituents selected from the group consisting of hydroxy, halo, (C_1-C_3)alkyl, halo(C_1-C_3)alkyl, cyano, nitro, (C_1-C_3)alkoxy and thio(C_1-C_3)alkyl;

R' is hydrogen or (C_1-C_{18})alkyl, wherein (C_1-C_{18})alkyl is optionally substituted with one or more acidic substituents selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH; and

X is absent or is an amino acid, wherein the amino acid is oriented to form an amide linkage with 

, provided that the compound of Structural Formula (I) is not *N*-(R)-lipoyl-glutamylalanine, *N*-(R)-lipoyl-aminoethylphosphonic acid, or (R)-5-(5-(1,2-dithiolan-3-yl)pentanamido)-2-hydroxybenzoic acid.

2. The compound of Claim 1, wherein R is (C_1-C_3)alkyl.

3. The compound of Claim 1, wherein R is (C_6)aryl.

4. The compound of Claim 1, wherein R is (C_6)aryl$(C_1$-$C_3)$alkyl.

5. The compound of any one of Claims 1 to 4, wherein X is an amino acid and R' is hydrogen, or a pharmaceutically acceptable salt or prodrug thereof.

6. The compound of any one of Claims 1 to 5, wherein X is aspartic acid, tyrosine, glutamic acid or alanine, or a pharmaceutically acceptable salt or prodrug thereof.

7. The compound of any one of Claims 1 to 6, wherein R is $(C_1$-$C_3)$alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$, or a pharmaceutically acceptable salt or prodrug thereof.

8. The compound of Claim 1, wherein X is absent and R' is hydrogen, or a pharmaceutically acceptable salt or prodrug thereof.

9. The compound of Claim 8, wherein R is $(C_1$-$C_3)$alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$, or a pharmaceutically acceptable salt or prodrug thereof.

10. The compound of Claim 8, wherein R is (C_6)aryl$(C_1$-$C_3)$alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$, and wherein aryl is optionally substituted with halo and hydroxy, or a pharmaceutically acceptable salt or prodrug thereof.

11. The compound of Claim 8, wherein R is (C_2)alkyl substituted with one or two acidic substituents each independently selected from -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H and -OPO_3H_2, or a pharmaceutically acceptable salt or prodrug thereof.

12. The compound of Claim 8, wherein R is (C_6)aryl substituted with one acidic substituent selected from -CO_2H, -SO_3H, -PO_3H_2,-OSO_3H and -OPO_3H_2, or a pharmaceutically acceptable salt or prodrug thereof.

13. The compound of Claim 1, wherein R' is (C_1-C_3)alkyl.

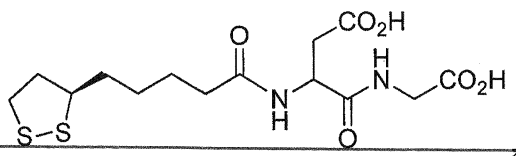
14. The compound of Claim 1, 2 or 13, wherein X is absent and R and R' are each (C_1-C_3)alkyl substituted with one acidic substituent selected from -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H and -OPO_3H_2.

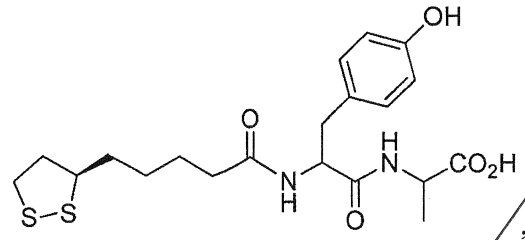
15. The compound of any one of Claims 1 to 14, wherein the pharmaceutically acceptable salt comprises a monovalent cation or a divalent cation.

16. The compound of any one of Claims 1 to 14, wherein the pharmaceutically acceptable salt comprises an amine.

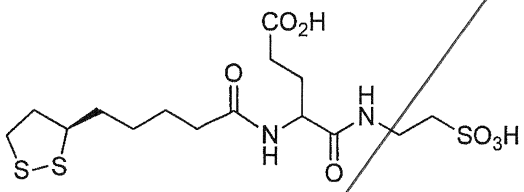
17. The compound of any one of Claims 1 to 14, wherein the pharmaceutically acceptable salt comprises lysine.

18. The compound of Claim 1, wherein the compound is represented by one of the following structural formulas:

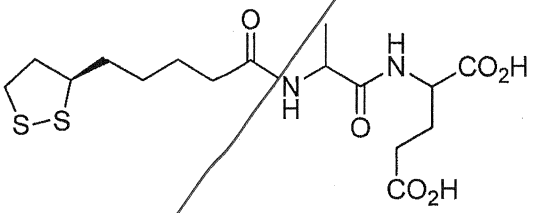



OH
O
H
N
N
CO2H
S–S
O
H
N
O

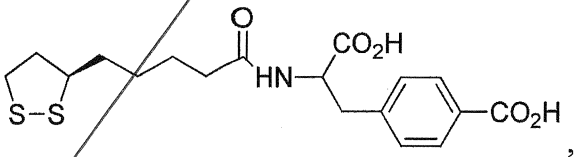
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CO2H
O
H
N
N
SO3H
S–S
O

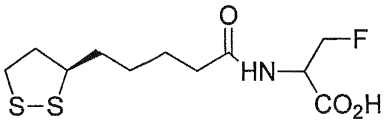
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O
H
N
N
CO2H
S–S
O
CO2H

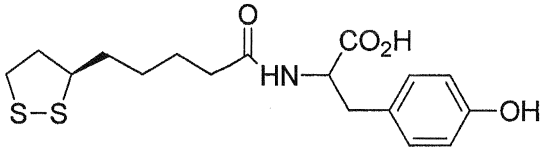
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O
CO2H
HN
S–S
CO2H

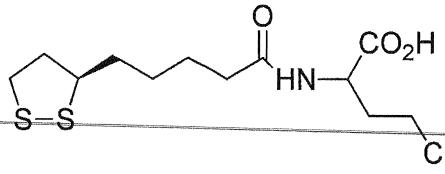
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O
F
HN
S–S
CO2H

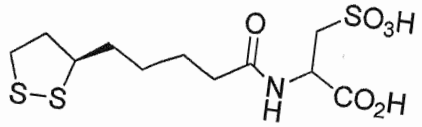
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O
CO2H
HN
S–S
OH

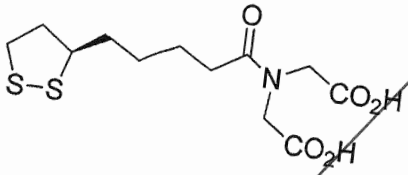
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O
CO2H
HN
S–S
CO2H

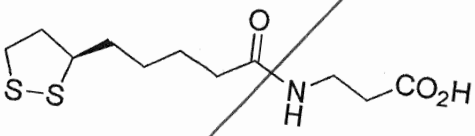
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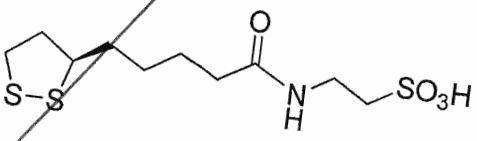
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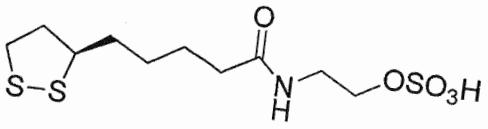
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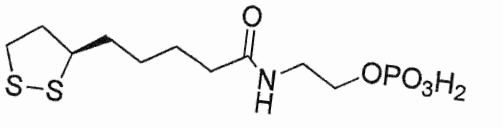
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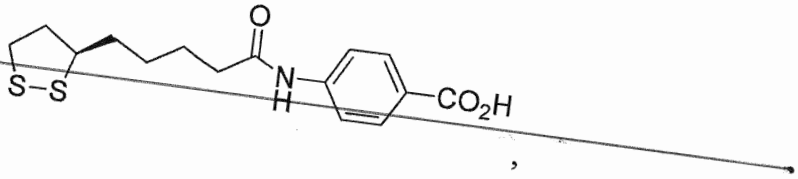
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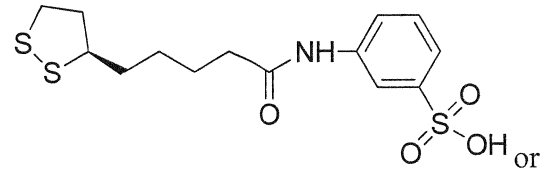
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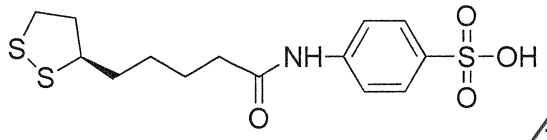
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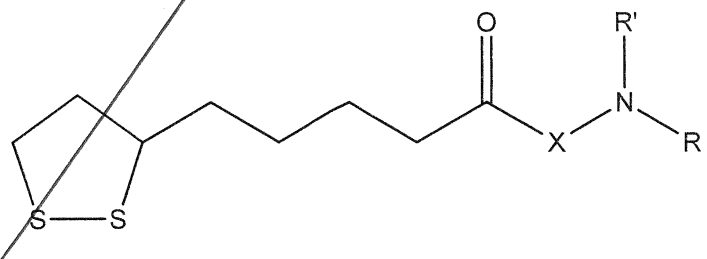
or



19. A composition, comprising a pharmaceutically acceptable carrier or diluent and one or more compounds of any one of Claims 1 to 18, or a pharmaceutically acceptable salt or prodrug thereof.

20. Use of an effective amount of the composition of Claim 19 in the manufacture of a medicament for treating an ischemic injury or an ischemia-reperfusion injury in a subject in need thereof.

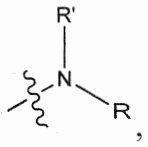
21. Use of an effective amount of a compound represented by Structural Formula (Ia):



(Ia),

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

R is $(C_1\text{-}C_{18})$alkyl, $(C_6\text{-}C_{18})$aryl or $(C_6\text{-}C_{18})$aryl$(C_1\text{-}C_{18})$alkyl and is substituted with at least one acidic substituent selected from the group consisting of $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$, $-OPO_3H_2$, $-B(OH)_2$ and -NHOH, wherein the aryl of the $(C_6\text{-}C_{18})$aryl or $(C_6\text{-}C_{18})$aryl$(C_1\text{-}C_{18})$alkyl is optionally further substituted with one or more substituents selected

from the group consisting of hydroxy, halo, (C_1-C_3)alkyl, halo(C_1-C_3)alkyl, cyano, nitro, (C_1-C_3)alkoxy and thio(C_1-C_3)alkyl;
R' is hydrogen or (C_1-C_{18})alkyl, wherein (C_1-C_{18})alkyl is optionally substituted with one or more acidic substituents selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH; and
X is absent or is an amino acid, wherein the amino acid is oriented to form an amide linkage with ,
provided that the compound of Structural Formula (Ia) is not *N*-lipoyl-glutamylalanine, *N*-lipoyl-aspartylglycine, *N*-lipoyl-glutamylglycine or 5-(5-(1,2-dithiolan-3-yl)pentanamido)-2-hydroxybenzoic acid
in the manufacture of a medicament for treating ischemic injury or ischemia-reperfusion injury in a subject in need thereof.

22. The use of Claim 21, wherein the compound is an (R)-lipoyl stereoisomer of a compound represented by Structural Formula (Ia), or a pharmaceutically acceptable salt or prodrug thereof, substantially separated from the (S)-lipoyl stereoisomer(s), or a pharmaceutically acceptable salt or prodrug thereof.

23. The use of Claim 21 or 22, wherein R is (C_1-C_3)alkyl.

24. The use of Claim 21 or 22, wherein R is (C_6)aryl.

25. The use of Claim 21 or 22, wherein R is (C_6)aryl(C_1-C_3)alkyl.

26. The use of any one of Claims 21 to 25, wherein X is an amino acid and R' is hydrogen, or a pharmaceutically acceptable salt or prodrug thereof.

27. The use of any one of Claims 21 to 26, wherein X is aspartic acid, tyrosine, glutamic acid or alanine, or a pharmaceutically acceptable salt or prodrug thereof.

28. The use of any one of Claims 21 to 27, wherein R is $(C_1\text{-}C_3)$alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$, or a pharmaceutically acceptable salt or prodrug thereof.

29. The use of Claim 21 or 22, wherein X is absent and R' is hydrogen, or a pharmaceutically acceptable salt or prodrug thereof.

30. The use of Claim 29, wherein R is $(C_1\text{-}C_3)$alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$, or a pharmaceutically acceptable salt or prodrug thereof.

31. The use of Claim 29, wherein R is (C_6)aryl$(C_1\text{-}C_3)$alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$, and wherein aryl is optionally substituted with halo or hydroxy, or a pharmaceutically acceptable salt or prodrug thereof.

32. The use of Claim 29, wherein R is (C_2)alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$, or a pharmaceutically acceptable salt or prodrug thereof.

33. The use of Claim 29, wherein R is (C_6)aryl substituted with one acidic substituent selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$, or a pharmaceutically acceptable salt or prodrug thereof.

34. The use of Claim 21 or 22, wherein R' is (C_1-C_3)alkyl.

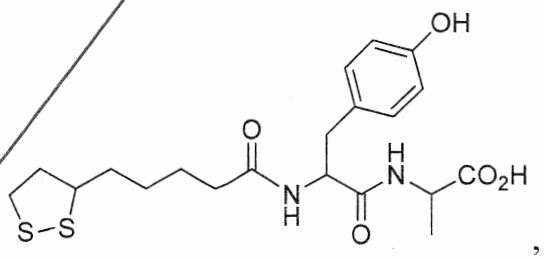
35. The use of Claim 21, 22, 23 or 34, wherein X is absent and R and R' are each (C_1-C_3)alkyl substituted with one acidic substituent selected from -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H and -OPO_3H_2.

36. The use of any one of Claims 21 to 35, wherein the pharmaceutically acceptable salt comprises a monovalent cation or a divalent cation.

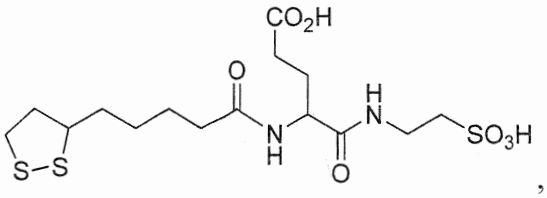
37. The use of any one of Claims 21 to 35, wherein the pharmaceutically acceptable salt comprises an amine.

38. The use of any one of Claims 21 to 35, wherein the pharmaceutically acceptable salt comprises lysine.

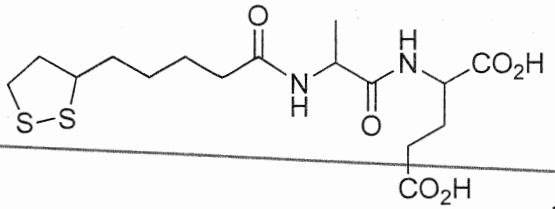
39. The use of Claim 21 or 22, wherein the compound is represented by one of the following structural formulas:



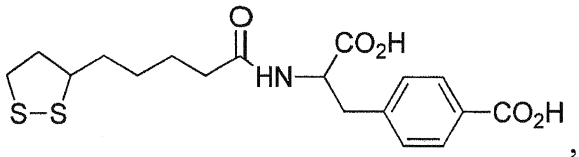
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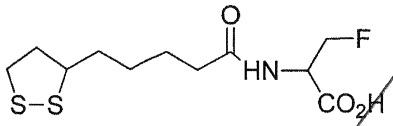
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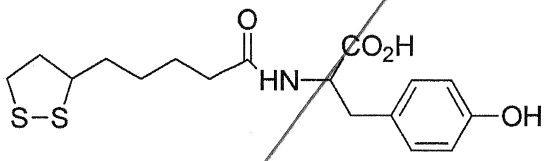
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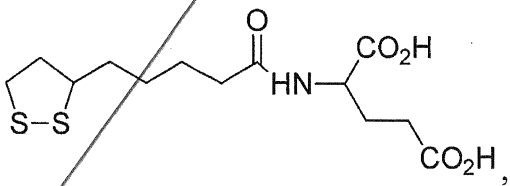
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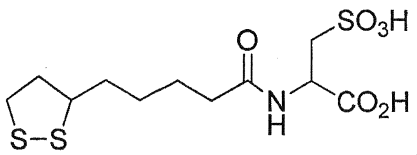
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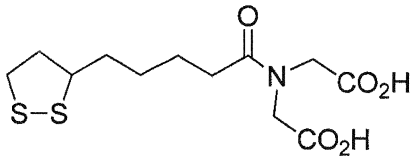
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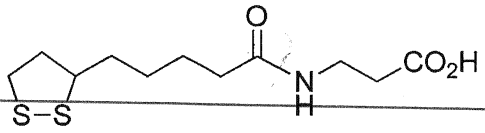
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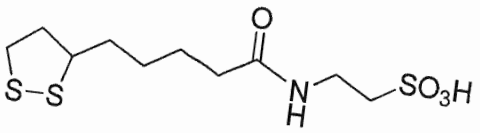
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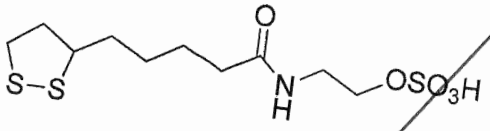
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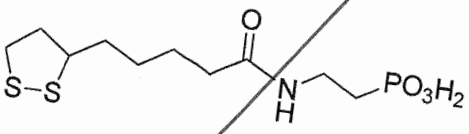
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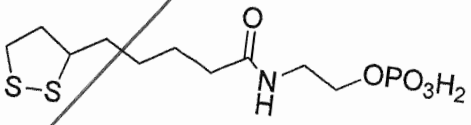
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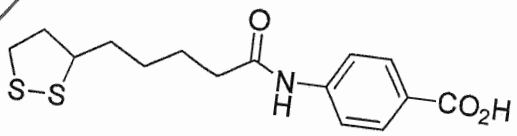
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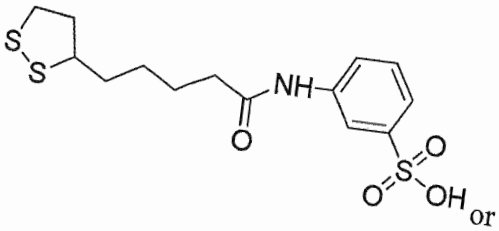
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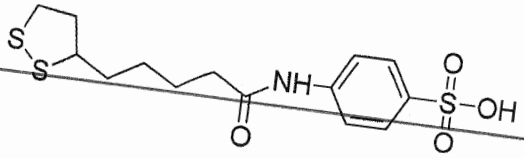
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or



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40. The use of any one of Claims 21 to 39, wherein the ischemia-reperfusion injury is selected from the group consisting of a cerebrovascular ischemia-reperfusion injury, a renal ischemia-reperfusion injury, a hepatic ischemia-reperfusion injury, an ischemia-reperfusion cardiomyopathy, a cutaneous ischemia-reperfusion injury, a bowel ischemia-reperfusion injury, an intestinal ischemia-reperfusion injury, a gastric ischemia-reperfusion injury, a pulmonary ischemia-reperfusion injury, a pancreatic ischemia-reperfusion injury, a skeletal muscle ischemia-reperfusion injury, an abdominal muscle ischemia-reperfusion injury, a limb ischemia-reperfusion injury, ischemia-reperfusion colitis, a mesenteric ischemia-reperfusion injury and a silent ischemia-reperfusion injury.

41. The use of any one of Claims 21 to 39, wherein the ischemic injury is a myocardial ischemic injury.

42. The use of any one of Claims 21 to 39, wherein the ischemic injury is consequent to an ischemia selected from the group consisting of a cardiovascular ischemia, a cerebrovascular ischemia, a renal ischemia, a hepatic ischemia, a ischemia-reperfusion cardiomyopathy, a cutaneous ischemia, a bowel ischemia, an intestinal ischemia, a gastric ischemia, a pulmonary ischemia, a pancreatic ischemia, a skeletal muscle ischemia, an abdominal muscle ischemia, a limb ischemia, an ischemia-reperfusion colitis, a mesenteric ischemia and a silent ischemia.

43. The use of any one of Claims 21 to 39, wherein the ischemia-reperfusion injury is a myocardial ischemia-reperfusion injury.

44. The use of Claim 43, wherein the myocardial ischemia-reperfusion injury is consequent to a myocardial infarction.

45. The use of Claim 44, wherein the myocardial infarction is an acute myocardial infarction.

46. The use of any one of Claims 21 to 39, wherein the ischemia-reperfusion injury is a cerebral ischemia-reperfusion injury.

47. The use of Claim 46, wherein the cerebral ischemia-reperfusion injury is consequent to a stroke.

48. The use of any one of Claims 21 to 39, wherein the ischemic injury or ischemia-reperfusion injury includes peri-operative cardiac damage.

49. The use of any one of Claims 21 to 39, wherein the ischemia-reperfusion injury is a renal ischemia-reperfusion injury.

50. The use of any one of Claims 21 to 39, wherein the ischemic injury or ischemia-reperfusion injury is consequent to a therapeutic intervention.

51. The use of any one of Claims 21 to 39, wherein the therapeutic intervention is selected from the group consisting of a coronary artery bypass graft surgery, a coronary angioplasty surgery, a transplant surgery and a cardiopulmonary bypass surgery.

52. The use of any one of Claims 21 to 39, wherein the subject is a human.

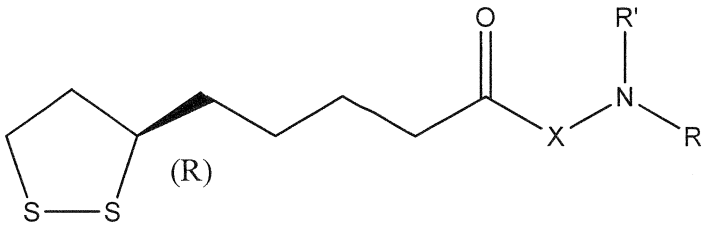
53. The use of any one of Claims 21 to 39, wherein the compound or pharmaceutically acceptable salt thereof is to be administered to the subject orally.

54. The use of any one of Claims 21 to 39, wherein the compound or pharmaceutically acceptable salt thereof is to be administered to the subject intravenously.

CLAIMS

What is claimed is:

1. A compound represented by Structural Formula (I):



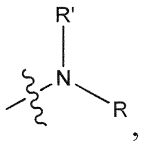
(I),

or a pharmaceutically acceptable salt thereof, wherein:

the enantiomeric excess or diastereomeric excess of the compound or pharmaceutically acceptable salt thereof is at least or about 90%;

R is (C_1-C_{18})alkyl, (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{18})alkyl and is substituted with at least one acidic substituent selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH, wherein the aryl of the (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{18})alkyl is optionally further substituted with one or more substituents selected from the group consisting of hydroxy, halo, (C_1-C_3)alkyl, halo(C_1-C_3)alkyl, cyano, nitro, (C_1-C_3)alkoxy and thio(C_1-C_3)alkyl;

R' is hydrogen or (C_1-C_{18})alkyl, wherein (C_1-C_{18})alkyl is optionally substituted with one or more acidic substituents selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH; and

X is absent or is an amino acid, wherein the amino acid is aspartic acid, tyrosine, glutamic acid or alanine and is oriented to form an amide linkage with 

, provided that the compound of Structural Formula (I) is not *N*-(R)-lipoyl-glutamylalanine, *N*-(R)-lipoyl-aminoethylphosphonic acid, or (R)-5-(5-(1,2-dithiolan-3-yl)pentanamido)-2-hydroxybenzoic acid.

2. The compound of Claim 1, wherein X is absent.

3. The compound of Claim 1, wherein X is an amino acid and R′ is hydrogen.

4. The compound of Claim 1, wherein R is: $(C_1\text{-}C_3)$alkyl substituted with at least one acidic substituent selected from the group consisting of $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$, $-OPO_3H_2$, $-B(OH)_2$ and -NHOH; or (C_6)aryl substituted with at least one acidic substituent selected from the group consisting of $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$, $-OPO_3H_2$, $-B(OH)_2$ and -NHOH, wherein the aryl of the (C_6)aryl is optionally further substituted with one or more substituents selected from the group consisting of hydroxy, halo, $(C_1\text{-}C_3)$alkyl, halo$(C_1\text{-}C_3)$alkyl, cyano, nitro, $(C_1\text{-}C_3)$alkoxy and thio$(C_1\text{-}C_3)$alkyl; or (C_6)aryl$(C_1\text{-}C_3)$alkyl substituted with at least one acidic substituent selected from the group consisting of $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$, $-OPO_3H_2$, $-B(OH)_2$ and -NHOH, wherein the aryl of the (C_6)aryl$(C_1\text{-}C_3)$alkyl is optionally further substituted with one or more substituents selected from the group consisting of hydroxy, halo, $(C_1\text{-}C_3)$alkyl, halo$(C_1\text{-}C_3)$alkyl, cyano, nitro, $(C_1\text{-}C_3)$alkoxy and thio$(C_1\text{-}C_3)$alkyl; or

$(C_1\text{-}C_3)$alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$.

5. The compound of Claim 1, wherein X is absent and R' is hydrogen.

6. The compound of Claim 5, wherein R is:

$(C_1\text{-}C_3)$alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$; or

(C_6)aryl$(C_1\text{-}C_3)$alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$, and wherein aryl is optionally substituted with halo and hydroxy; or

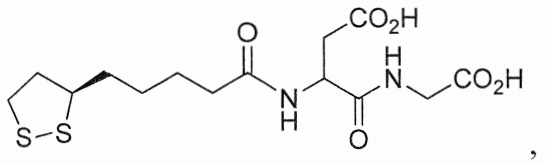
(C_2)alkyl substituted with one or two acidic substituents each independently selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ and $-OPO_3H_2$; or

(C_6)aryl substituted with one acidic substituent selected from $-CO_2H$, $-SO_3H$, $-PO_3H_2$,$-OSO_3H$ and $-OPO_3H_2$.

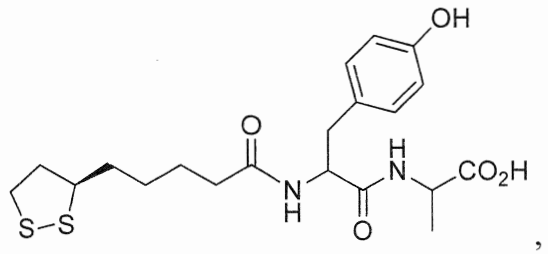
7. The compound of Claim 1, wherein R' is (C_1-C_3) alkyl substituted with at least one acidic substituent selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H and -OPO_3H_2.

8. The compound of Claim 1 or Claim 7, wherein X is absent and R and R' are each (C_1-C_3)alkyl substituted with one acidic substituent selected from -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H and -OPO_3H_2.

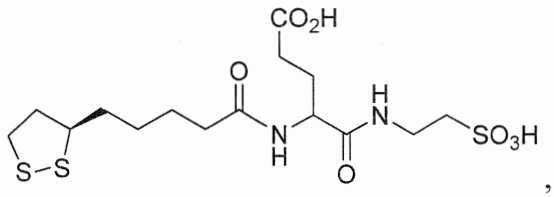
9. The compound of Claim 1, wherein the compound is represented by one of the following structural formulas:



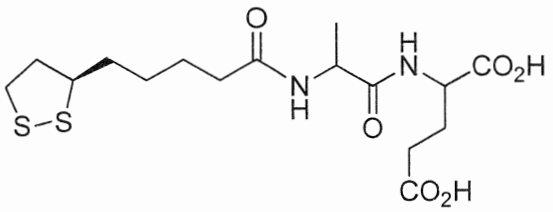
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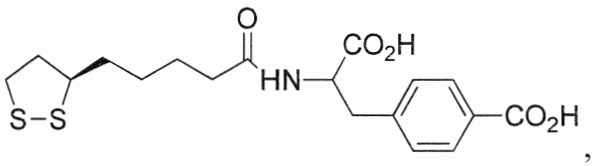
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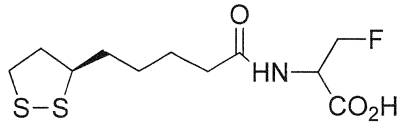
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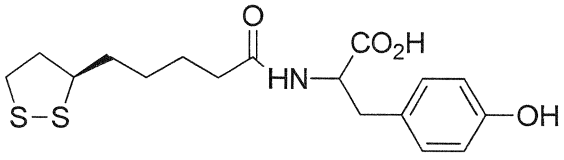
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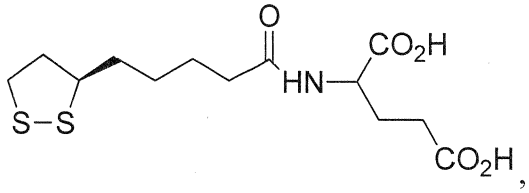
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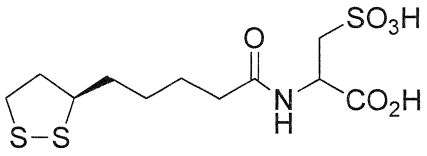
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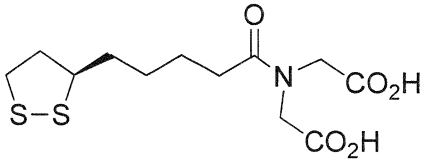
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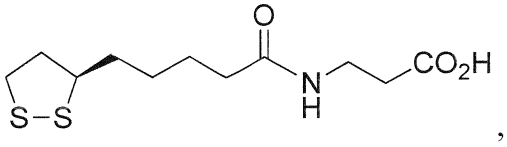
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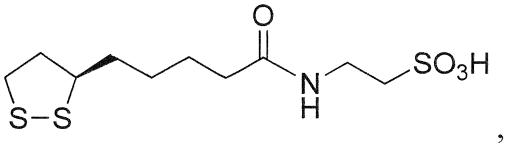
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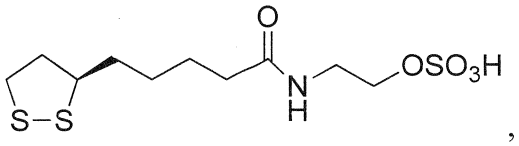
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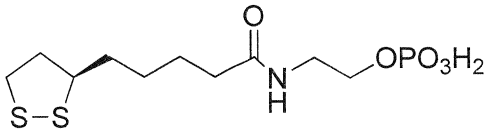
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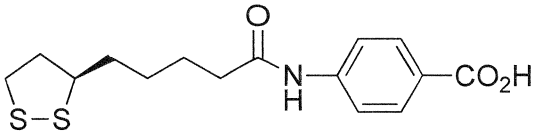
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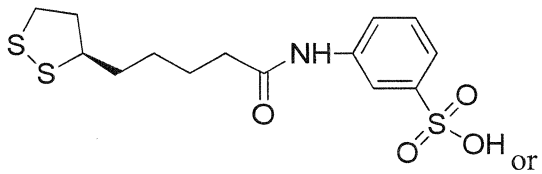
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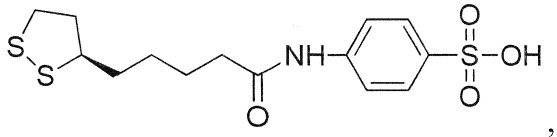
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or

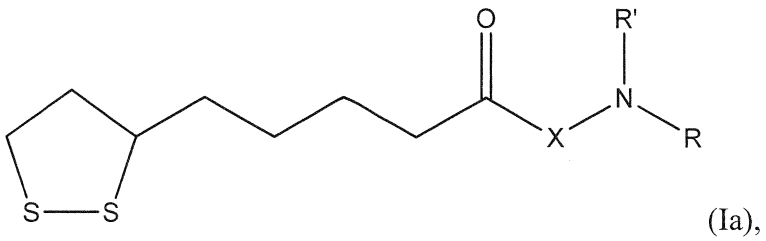


,

or a pharmaceutically acceptable salt thereof.

10. A composition, comprising a pharmaceutically acceptable carrier or diluent and one or more compounds of any one of Claims 1 to 9, or a pharmaceutically acceptable salt thereof.

11. Use of an effective amount of a compound represented by Structural Formula (Ia):

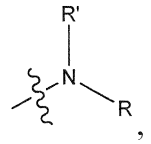


(Ia),

or a pharmaceutically acceptable salt thereof, wherein:

R is (C_1-C_{18})alkyl, (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{18})alkyl and is substituted with at least one acidic substituent selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH, wherein the aryl of the (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{18})alkyl is optionally further substituted with one or more substituents selected from the group consisting of hydroxy, halo, (C_1-C_3)alkyl, halo(C_1-C_3)alkyl, cyano, nitro, (C_1-C_3)alkoxy and thio(C_1-C_3)alkyl;

R' is hydrogen or (C_1-C_{18})alkyl, wherein (C_1-C_{18})alkyl is optionally substituted with one or more acidic substituents selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH; and

X is an amino acid, wherein the amino acid is oriented to form an amide linkage with 

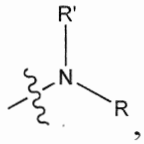
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provided that the compound of Structural Formula (Ia) is not *N*-lipoyl-glutamylalanine, *N*-lipoyl-aspartylglycine, or *N*-lipoyl-glutamylglycine; or

the compound is an (R)-lipoyl stereoisomer of a compound represented by Structural Formula (Ia), or a pharmaceutically acceptable salt thereof and the enantiomeric excess or diastereomeric excess of the compound or pharmaceutically acceptable salt thereof is at least or about 90%; and

R is (C_1-C_{18})alkyl, (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{18})alkyl and is substituted with at least one acidic substituent selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH, wherein the aryl of the (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{18})alkyl is optionally further substituted with one or more substituents selected from the group consisting of hydroxy, halo, (C_1-C_3)alkyl, halo(C_1-C_3)alkyl, cyano, nitro, (C_1-C_3)alkoxy and thio(C_1-C_3)alkyl;

R' is hydrogen or (C_1-C_{18})alkyl, wherein (C_1-C_{18})alkyl is optionally substituted with one or more acidic substituents selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH; and

X is absent or is an amino acid, wherein the amino acid is oriented to form an amide linkage with 

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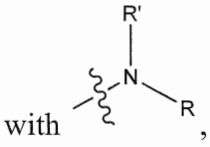
provided that the compound of Structural Formula (Ia) is not *N*-lipoyl-glutamylalanine, *N*-lipoyl-aspartylglycine, *N*-lipoyl-glutamylglycine or 5-(5-(1,2-dithiolan-3-yl)pentanamido)-2-hydroxybenzoic acid in the manufacture of a medicament for treating ischemic injury or ischemia reperfusion injury in a subject in need thereof.

12. The use of Claim 11, wherein:

R is (C_1-C_{18})alkyl, (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{18})alkyl and is substituted with at least one acidic substituent selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH, wherein the aryl of the (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{18})alkyl is optionally further substituted with one or more substituents selected from the group consisting of hydroxy, halo, (C_1-C_3)alkyl, halo(C_1-C_3)alkyl, cyano, nitro, (C_1-C_3)alkoxy and thio(C_1-C_3)alkyl;

R' is hydrogen or (C_1-C_{18})alkyl, wherein (C_1-C_{18})alkyl is optionally substituted with one or more acidic substituents selected from the group consisting of -CO_2H, -SO_3H, -PO_3H_2, -OSO_3H, -OPO_3H_2, -$B(OH)_2$ and -NHOH; and

X is an amino acid, wherein the amino acid is oriented to form an amide linkage

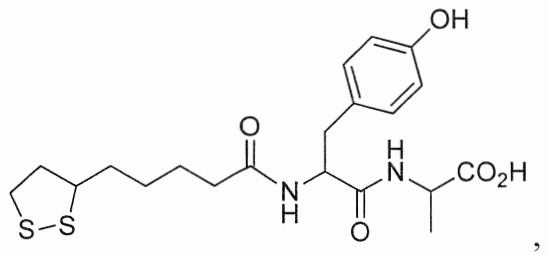


with ,

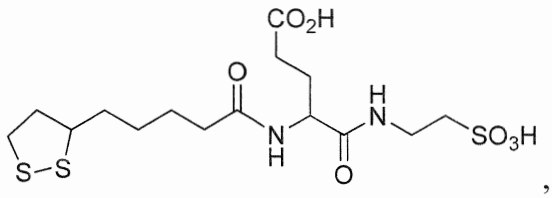
provided that the compound of Structural Formula (Ia) is not *N*-lipoyl-glutamylalanine, *N*-lipoyl-aspartylglycine, or *N*-lipoyl-glutamylglycine.

13 The use of Claim 12, wherein the compound is an (R)-lipoyl stereoisomer of a compound represented by Structural Formula (Ia), or a pharmaceutically acceptable salt thereof, and the enantiomeric excess or diastereomeric excess of the compound or pharmaceutically acceptable salt thereof is at least or about 90.

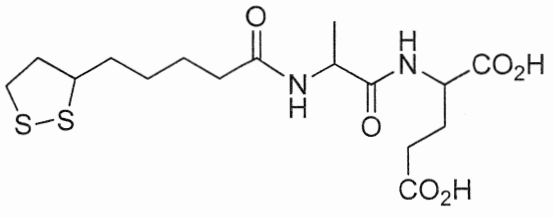
14. The use of any one of Claims 11 to 13, wherein the compound is represented by one of the following structural formulas:



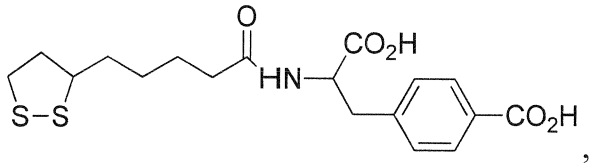
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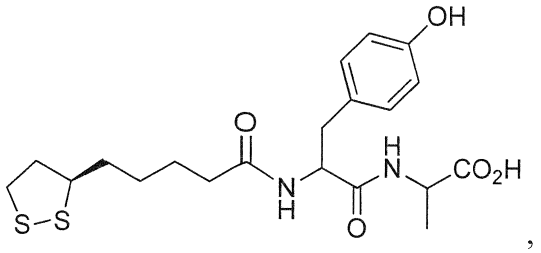
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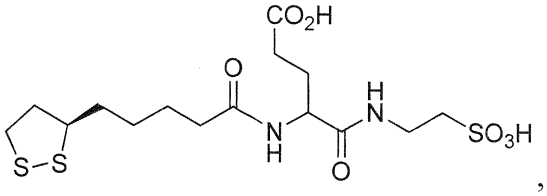
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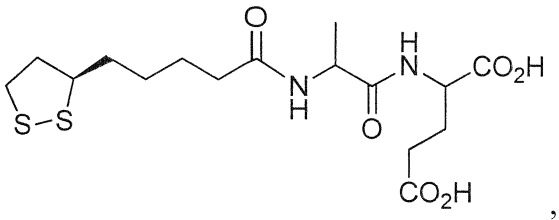
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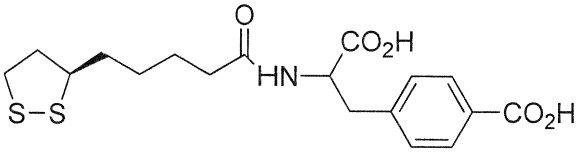
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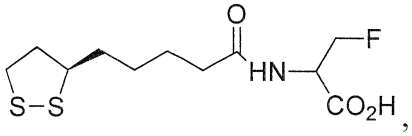
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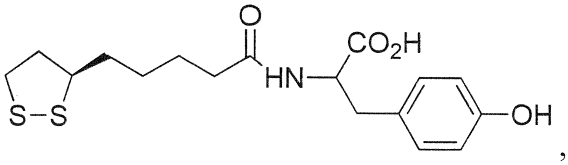
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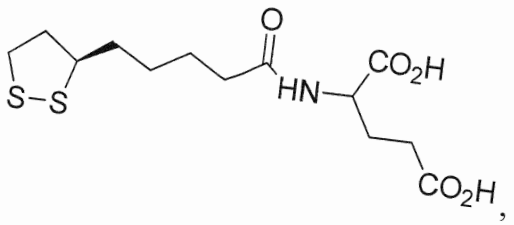
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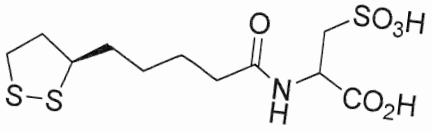
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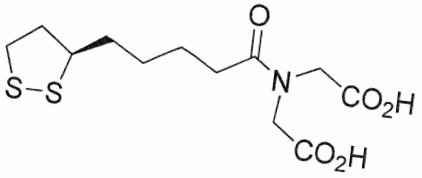
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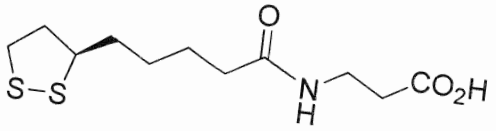
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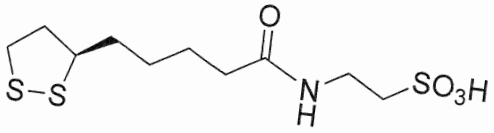
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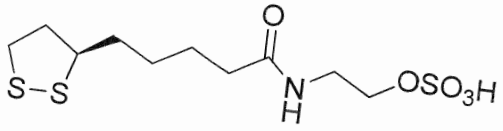
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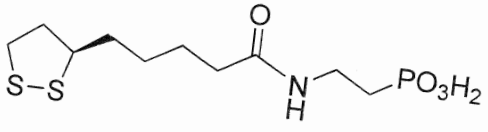
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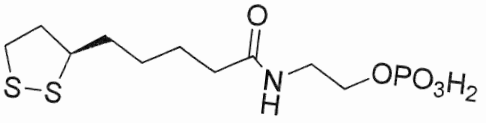
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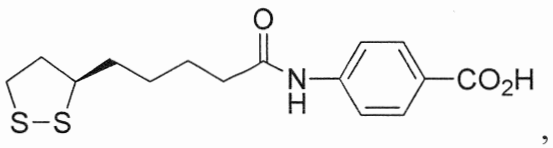
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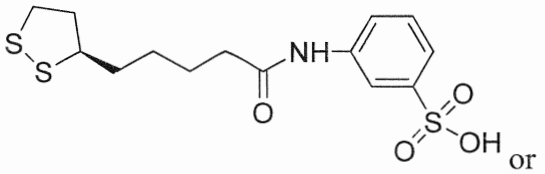
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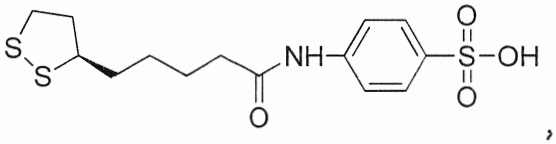
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or



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or a pharmaceutically acceptable salt thereof.

15. The use of any one of Claims 11 to 14 wherein:

the ischemia-reperfusion injury is selected from the group consisting of a cerebrovascular ischemia-reperfusion injury, a renal ischemia-reperfusion injury, a hepatic ischemia-reperfusion injury, an ischemia-reperfusion cardiomyopathy, a cutaneous ischemia-reperfusion injury, a bowel ischemia-reperfusion injury, an intestinal ischemia-reperfusion injury, a gastric ischemia-reperfusion injury, a pulmonary ischemia-reperfusion injury, a pancreatic ischemia-reperfusion injury, a skeletal muscle ischemia-reperfusion injury, an abdominal muscle ischemia-reperfusion injury, a limb ischemia-reperfusion injury, ischemia-reperfusion colitis, a mesenteric ischemia-reperfusion injury and a silent ischemia-reperfusion injury; or

the ischemic injury is a myocardial ischemic injury; or the ischemic injury is consequent to an ischemia selected from the group consisting of a cardiovascular ischemia, a cerebrovascular ischemia, a renal ischemia, a hepatic ischemia, a ischemia-reperfusion cardiomyopathy, a cutaneous ischemia, a bowel ischemia, an intestinal ischemia, a gastric ischemia, a pulmonary ischemia, a pancreatic ischemia, a skeletal muscle ischemia, an abdominal muscle ischemia, a limb ischemia, an ischemia-reperfusion colitis, a mesenteric ischemia and a silent ischemia; or

the ischemia-reperfusion injury is a myocardial ischemia-reperfusion injury; or

the ischemic injury or ischemia-reperfusion injury includes peri-operative cardiac damage; or

the ischemia-reperfusion injury is a renal ischemia-reperfusion injury; or

the ischemic injury or ischemia-reperfusion injury is consequent to a therapeutic intervention, such as a therapeutic intervention selected from the group consisting of a coronary artery bypass graft surgery, a coronary angioplasty surgery, a transplant surgery and a cardiopulmonary bypass surgery.