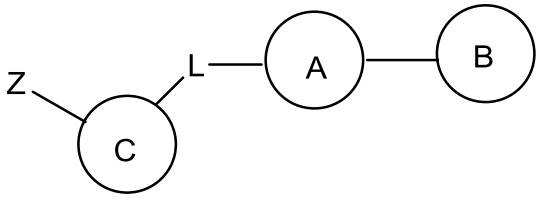
WE CLAIM:

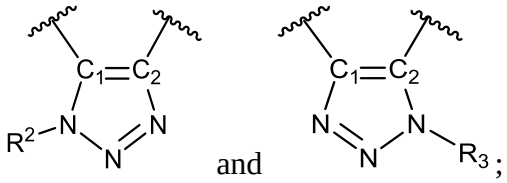
1. A compound of Formula (XII):



(XII)

wherein:

ring C is selected from:



;

wherein the wavy lines ( ) indicate the points of attachment of the C_1 carbon to Z, and the C_2 carbon to L;

L is a CH_2, CF_2, O, NR^L, S, S(=O), C(=O), CH_2-Q, or Q-CH_2; wherein Q is O, NR^L, or S;

Z is -C(=O)H or -CH_2OY;

Y is hydrogen or W;

W is methylene substituted with

R^4; -C(=O)R^5; -C(=O)OR^5; -C(=O)NR^5R^6; -C(=O)SR^5; -S(O)R^5; -$S(O)_2R^5$; -S(O)(OR^5); -$S(O)_2$(OR^5); –$SO_2N R^5R^6$; -$P(=O)(OR^7)_2$; -$P(=O)(O^-)_2$; -P(=O)(OR^7)(O^-); or -P(=O)(X) wherein X is -$O(C(R^8)_2)_mO$-;

R^L is hydrogen, C_{1-4} alkyl, C_{3-6} cycloalkyl, phenyl, or benzyl; wherein the C_{1-4} alkyl is optionally substituted with hydroxycarbonyl, alkoxycarbonyl, hydroxycarbonylalkyl, or alkylcarbonyloxy; and the phenyl group alone or as a part of the benzyl group is optionally substituted with one or two groups selected from halo and haloalkoxy;

Ring A is cycloalkyl, C_{8-11} spirocycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

Ring B is present or not present; wherein:

when Ring B is present, then Ring A is optionally substituted with 1 or 2 R^{A1} groups;

each R^{A1} is independently selected from halo, alkyl, alkoxy, cyano, nitro, hydroxy, hydroxyalkyl, haloalkyl, haloalkoxy, (cycloalkyl)alkyl, (cycloalkyl)alkoxy, and cycloalkyl;

when Ring B is not present, then Ring A is optionally substituted with 1, 2, or 3 R^{A2} groups;

Ring B, when present, is cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each is optionally substituted with 1, 2, or 3 R^{B} groups;

each R^{A2} and R^{B} is independently halo; cyano; alkyl; hydroxyalkyl; alkylsulfonyl; aminosulfonyl; alkylaminosulfonyl; dialkylaminosulfonyl; haloalkyl; alkoxy; aminoalkoxy; alkylaminoalkoxy; dialkylaminoalkoxy; hydroxyalkoxy; haloalkoxy; alkylcarbonyl; alkoxyalkoxy; aminocarbonyl; alkylaminocarbonyl; dialkylaminocarbonyl; alkylcarbonylaminoalkoxy; cycloalkyl; (cycloalkyl)alkyl; cycloalkyloxy; (cycloalkyl)alkoxy wherein the cycloalkyl group is optionally substituted with hydroxyalkyl; cycloalkylcarbonyl; cycloalkylcarbonyloxy; heterocycloalkyl optionally substituted with one or two groups independently selected from halo, alkyl, and alkylcarbonyl; (5-6-membered heterocycloalkyl-one)alkyl; 5-6-membered heterocycloalkyl-one; (heterocycloalkyl)alkyl; heterocycloalkylcarbonyl; or 5-6-membered heteroaryl optionally substituted with one group selected from alkyl, hydroxyalkyl, (hydroxycycloalkyl)alkyl, alkoxyalkyl, and hydroxycycloalkyl;

each R^{2} and R^{3} is independently hydrogen, alkyl, phenyl, benzyl, or alkoxy-substituted benzyl; wherein the alkyl is optionally substituted with halo, alkoxy, haloalkoxy, alkylcarbonyloxy, cycloalkylcarbonyloxy, or heterocycloalkylcarbonyloxy optionally substituted with alkoxycarbonyl;

R^{4} is alkylcarbonyloxy, phenylcarbonyloxy, cycloalkylcarbonyloxy, heterocycloalkylcarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkoxycarbonyloxy, $-N(R^{10})C(O)R^{11}$, $-N(R^{10})C(O)OR^{11}$, $-N(R^{10})C(O)NR^{12}R^{13}$, $-O-P(=O)(O^{-})_2$, $-O-P(=O)(OR^{7})(O^{-})$, or -O-P(=O)(X) wherein X is $-O(C(R^{8})_2)_mO-$;

each R^{8} is independently hydrogen, halo, $-CN$, $-OR^{9}$, $-C(=O)R^{9}$, $-C(=O)OR^{9}$, $-C(=O)N(R^{9})_2$, $-N(R^{9})_2$, $-SR^{9}$, $-S(O)R^{9}$, $-S(O)_2R^{9}$, $-OC(=O)R^{9}$, $-OC(=O)OR^{9}$, $-OC(=O)(N(R^{9})_2)$, $-N(R^{9})C(=O)R^{14}$, $-N(R^{9})C(=O)OR^{14}$, $-SO_2N(R^{9})_2$, alkyl, aryl, cycloalkyl, heterocycloalkyl, or heteroaryl;

each R^{5}, R^{6}, R^{7}, R^{9}, R^{10}, R^{11}, R^{12}, R^{13}, and R^{14} is independently hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, heterocycloalkyl, or heteroaryl; and

m is 1, 2, or 3; and

provided:

i. the compound represented by Formula (XII) is exclusive of:
    a. 4-(phenylamino)-1H-1,2,3-triazole-5-carbaldehyde;
    b. 4-(((tetrahydro-2H-pyran-2-yl)oxy)methyl)-1H-1,2,3-triazole-5-carbaldehyde;
    c. ethyl hydrogen (((5-((5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)methyl)phosphonate;
    d. diethyl (((5-((5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)methyl)phosphonate; and
    e. 1-((4-(hydroxymethyl)-1H-1,2,3-triazol-5-yl)methyl)-5-methylpyrimidine-2,4(1H,3H)-dione;
ii. when Z is -C(=O)H, L is NR^L, R^L is hydrogen, and Ring A is phenyl, then Ring B is present and/or the phenyl Ring A is substituted with 1, 2, or 3 R^{A2} groups;
iii. when Z is -C(=O)H, L is CH_2, and Ring A is cyclopropyl, phenyl, indole, or thiophene, then Ring B is present;
iv. when Z is -C(=O)H, L is CH_2-O, and Ring A is phenyl, then Ring B is present;
v. when Z is $-CH_2OY$, Y is W, W is $-P(=O)(OR^7)_2$ or $-P(=O)(OR^7)(O^-)$, R^7 is ethyl, L is CH_2, and Ring A is pyrimidine-2,4-dione, then Ring B is present and/or the pyrimidine-2,4-dione Ring A is unsubstituted or substituted with 2 R^{A2}; and
vi. when Z is $-CH_2OY$, Y is hydrogen, L is CH_2, and Ring A is pyrimidine-2,4-dione, then Ring B is present and/or the pyrimidine-2,4-dione Ring A is unsubstituted or substituted with 2 R^{A2}; and

optionally a single stereoisomer or mixture of stereoisomers thereof and additionally optionally a pharmaceutically acceptable salt thereof.

2. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of claim 1, wherein
L is a CF_2, O, S, S(=O), C(=O), CH_2-NR^L, CH_2-S, or Q-CH_2; wherein Q is O, NR^L, or S.

3. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of claim 1, wherein

L is a CH_2, CF_2, O, NR^L, S, S(=O), C(=O), CH_2-Q, or Q-CH_2; wherein Q is O, NR^L, or S; and

Z is -CH_2OY.

4. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of claim 1, wherein

L is a CF_2, O, NR^L, S, S(=O), C(=O), CH_2-Q, or Q-CH_2; wherein Q is O, NR^L, or S; and

Z is -CH_2OY.

5. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of claim 1, wherein

L is a CF_2, O, S, S(=O), C(=O), CH_2-NR^L, CH_2-S, or Q-CH_2; wherein Q is O, NR^L, or S; and

Z is -C(=O)H.

6. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-2, wherein Z is -C(=O)H.

7. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-2, wherein Z is -CH_2OY.

8. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-4 or 7, wherein Y is hydrogen.

9. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-4 or 7, wherein Y is W.

10. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of claim 9, wherein W is methylene substituted with R^4; -C(=O)R^5; -C(=O)OR^5; -C(=O)NR^5R^6; -C(=O)SR^5; -S(O)R^5; -$S(O)_2R^5$; -S(O)(OR^5); -$S(O)_2$(OR^5); or –$SO_2NR^5R^6$.

11. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of claim 9, wherein W is methylene substituted with R^4; -$P(=O)(OR^7)_2$; -$P(=O)(O^-)_2$; -$P(=O)(OR^7)(O^-)$; or -P(=O)(X) wherein X is -$O(C(R^8)_2)_mO$-.

12. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1 or 3-11, wherein L is a CF_2, O, NR^L, S, S(=O), C(=O), CH_2-O, or O-CH_2.

13. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1 or 3-11, wherein L is a CF_2, O, S, S(=O), C(=O), CH_2-O, or O-CH_2.

14. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1 or 3-11, wherein L is O, NR^L, or S.

15. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1 or 3-11, wherein L is O, NH, or S.

16. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-15, wherein L is O or S.

17. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-16, wherein L is O.

18. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-17, wherein Ring A is C_{3-7} cycloalkyl, 5-6 membered heterocycloalkyl, or phenyl.

19. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-18, wherein Ring A is C_{3-7} cycloalkyl.

20. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-18, wherein Ring A is 5-6 membered heterocycloalkyl.

21. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-18, wherein Ring A is phenyl.

22. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-21, wherein Ring B is present.

23. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-22, wherein Ring B is 5-6 membered heterocycloalkyl, aryl, or heteroaryl.

24. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-23, wherein Ring B is 5-6 membered heterocycloalkyl.

25. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-23, wherein Ring B is phenyl.

26. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-23, wherein Ring B is heteroaryl.

27. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-26, wherein Ring B is independently substituted with 1 R^B group.

28. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-26, wherein Ring B is independently substituted with 2 R^B groups.

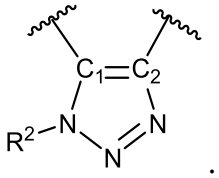
29. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-28, wherein R^B is independently halo, C_{1-4}

alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{3-7} cycloalkoxy, piperidinyl, piperidinylalkyl, or piperidinylcarbonyl.

30. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-29, wherein R^B is independently chloro, bromo, fluoro, methyl, trifluoromethyl, methoxy, isopropoxy, trifluoromethoxy, cyclopropoxy, cyclopentoxy, piperidinyl, piperidinylalkyl, or piperidinylcarbonyl.

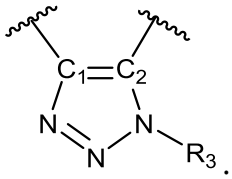
31. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-30, wherein R^2 and R^3 are independently hydrogen.

32. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-31, wherein ring C is:



.

33. The compound, single stereoisomer or mixture of stereoisomers or pharmaceutically acceptable salt of any one of claims 1-31, wherein ring C is:



.

34. A compound selected from the group consisting of compounds 487, 488, 489, 490, 491, 492, 493-1, 493-2, 494, 495, 496, and 497, or a single stereoisomer or mixture of stereoisomers thereof and additionally optionally as a pharmaceutically acceptable salt thereof.

35. A pharmaceutical composition comprising a compound of any one of claims 1-34, optionally as a single stereosiomer, or mixtures of stereoisomers, and a pharmaceutically acceptable excipient.

36. Use of a compound or pharmaceutically acceptable salt thereof of any one of claims 1-34 or the pharmaceutical composition of claim 35 in the manufacture of a medicament for a method of treating a disease or disorder associated with a defect in glyoxylate metabolism, the medicament is to be administered to a patient suffering from such disease or disorder..

37. Use of a compound or pharmaceutically acceptable salt thereof of any one of claims 1-34 or the pharmaceutical composition of claim 35 in the manufacture of a medicament for a method of treating a disease or disorder associated with the enzyme glycolate oxidase (GO) or alterations in oxalate metabolism, the medicament is to be administered to a patient suffering from such disease or disorder.

38. The use of claim 36 or 37, wherein the disease or disorder is characterized by high oxalate content in the urine.

39. The use of claim 36 or 37, wherein the disease or disorder is characterized by a deficiency in the enzyme alanine: glyoxylate aminotransferase (AGT).

40. The use of claim 36 or 37, wherein the disease or disorder is selected from the group consisting of: hyperoxaluria, genetic or environmental vitamin B6 deficiency, genetic or environmental abnormal calcium metabolism, abnormal collagen metabolism, abnormal function of oxalate transporters, and genetic kidney disease.

41. The use of claim 40, wherein the hyperoxaluria is a primary hyperoxaluria ("PH") or is a secondary hyperoxaluria.

42. The use of claim 41, wherein the primary hyperoxaluria ("PH") is selected from the group consisting of: Primary hyperoxaluria type 1 ("PH1"), Primary hyperoxaluria type 2 ("PH2"), and Primary hyperoxaluria type 3 ("PH3").

43. The use of claim 40, wherein the genetic or environmental abnormal calcium metabolism is hypercalciuria or hyperparathyroidism.

44. The use of claim 40, wherein the genetic kidney disease is Hirschsprung's disease.

45. The use of claim 36 or 37, wherein the disease or disorder is an enteric hyperoxaluria.

46. The use of claim 45, wherein the enteric hyperoxaluria is selected from the group consisting of: fat malabsorption, steatorrhea, inflammatory bowel disease ("IBD"), pancreatic insufficiency, biliary cirrhosis, short-bowel syndrome, bariatric surgery, jejunoileal bypass, Crohn's disease, ulcerative colitis, cystic fibrosis, high blood pressure, diabetes, obesity, absence of the gastrointestinal tract-dwelling bacterium Oxalobacter formigenes, and ileal dysfunction.

47. The use of claim 36 or 37, wherein the disease or disorder is a dietary hyperoxaluria.

48. The use of claim 47, wherein the dietary hyperoxaluria is associated with and/or the result of one or more of a high oxalate diet, a high protein diet, a high oxalate precursor diet, and a low calcium diet.

49. The use of claim 36 or 37, wherein the disease or disorder is an idiopathic hyperoxaluria.

50. The use of claim 36 or 37, wherein the disease or disorder is a kidney disease.

51. The use of claim 50, wherein the kidney disease is selected from the group consisting of: primary hyperoxaluria, dietary hyperoxaluria, kidney stones (nephrolithiasis), recurrent kidney stones, progressive kidney failure, nephrocalcinosis, urinary tract infections, end stage renal disease, chronic kidney disease ("CKD"), end-stage kidney disease ("ESKD"), hypertension, diabetes, urolithiasis, and systemic oxalosis.

52. The use of claim 50, wherein the kidney disease is chronic kidney disease ("CKD") or end-stage kidney disease ("ESKD").

53. The use of claim 36 or 37, wherein the disease or disorder is oxalate nephropathy or chronic calcium-oxalate nephropathy.

54. The use of claim 36 or 37, wherein the disease or disorder is calcium oxalate (CaOx) stone disease, calcium oxalate (CaOx) nephrolithiasis, or renal failure.

55. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-34 or the pharmaceutical composition of claim 35, for use as a medicament.

56. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-34 or the pharmaceutical composition of claim 35, for use in a method of treating a disease or disorder associated with a defect in glyoxylate metabolism.

57. The compound or pharmaceutically acceptable salt thereof for use or the pharmaceutical composition for use of claim 56, wherein the disease of disorder is primary hyperoxaluria.

58. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-34 or the pharmaceutical composition of claim 35, for use in a method of treating a disease or disorder associated with the enzyme glycolate oxidase (GO) or alterations in oxalate metabolism.