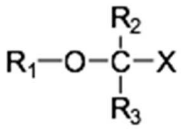
Claims

1. Use of a compound of Formula (II)



(II)

wherein R_1 is selected from a C_{10}-C_{22} alkenyl having 3-6 double bonds;

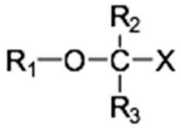
R_2 and R_3 are the same or different and are selected from the group of a hydrogen atom, a hydroxy group, an alkyl group, a halogen atom, an alkoxy group, an acyloxy group, an acyl group, an alkenyl group, an alkynyl group, an aryl group, an alkylthio group, an alkoxycarbonyl group, a carboxy group, an alkylsulfinyl group, an alkylsulfonyl group, an amino group, and an alkylamino group; wherein R_2 and R_3 can be connected in order to form a cycloalkane like cyclopropane, cyclobutane, cyclopentane, or cyclohexane;

X is a carboxylic acid or a derivative thereof, wherein the derivative is a carboxylate, such as a carboxylic ester; a glyceride; an anhydride; a carboxamide; a phospholipid; or a hydroxymethyl; or a prodrug thereof;

or a pharmaceutically acceptable salt, solvate, or solvate of such a salt thereof,

in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of non-alcoholic steatohepatitis (NASH), wherein the medicament is co-administered with at least one additional active agent chosen from a glucagon-like peptide 1 (GLP-1) receptor agonist, an acetyl-CoA carboxylase (ACC) inhibitor, and a farnesoid X receptor (FXR) agonist.

2. Use of a compound of Formula (II)



(II)

wherein R_1 is selected from a C_{10}-C_{22} alkenyl having 3-6 double bonds;

R_2 and R_3 are the same or different and are selected from the group of a hydrogen atom, a hydroxy group, an alkyl group, a halogen atom, an alkoxy group, an acyloxy group, an acyl group, an alkenyl group, an alkynyl group, an aryl group, an alkylthio group, an alkoxycarbonyl group, a carboxy group, an alkylsulfinyl group, an alkylsulfonyl group, an amino group, and an

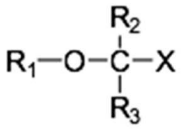
alkylamino group; wherein R_2 and R_3 can be connected in order to form a cycloalkane like cyclopropane, cyclobutane, cyclopentane, or cyclohexane;

X is a carboxylic acid or a derivative thereof, wherein the derivative is a carboxylate, such as a carboxylic ester; a glyceride; an anhydride; a carboxamide; a phospholipid; or a hydroxymethyl; or a prodrug thereof;

or a pharmaceutically acceptable salt, solvate, or solvate of such a salt thereof,

in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of alcoholic steatohepatitis (ASH), wherein the medicament is co-administered with at least one additional active agent chosen from a glucagon-like peptide 1 (GLP-1) receptor agonist, an acetyl-CoA carboxylase (ACC) inhibitor, and a farnesoid X receptor (FXR) agonist.

3. Use of a compound of Formula (II)



(II)

wherein R_1 is selected from a C_{10}-C_{22} alkenyl having 3-6 double bonds;

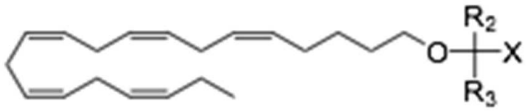
R_2 and R_3 are the same or different and are selected from the group of a hydrogen atom, a hydroxy group, an alkyl group, a halogen atom, an alkoxy group, an acyloxy group, an acyl group, an alkenyl group, an alkynyl group, an aryl group, an alkylthio group, an alkoxycarbonyl group, a carboxy group, an alkylsulfinyl group, an alkylsulfonyl group, an amino group, and an alkylamino group; wherein R_2 and R_3 can be connected in order to form a cycloalkane like cyclopropane, cyclobutane, cyclopentane, or cyclohexane;

X is a carboxylic acid or a derivative thereof, wherein the derivative is a carboxylate, such as a carboxylic ester; a glyceride; an anhydride; a carboxamide; a phospholipid; or a hydroxymethyl; or a prodrug thereof;

or a pharmaceutically acceptable salt, solvate, or solvate of such a salt thereof,

in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of fatty liver disease, wherein the medicament is co-administered with at least one additional active agent chosen from a glucagon-like peptide 1 (GLP-1) receptor agonist, an acetyl-CoA carboxylase (ACC) inhibitor, and a farnesoid X receptor (FXR) agonist.

4. The use of any one of claims 1 to 3, wherein the compound is of Formula (I), and R_2, R_3, and X are as defined for Formula (II)



(I).

5. The use according to any one of claims 1 to 4,

wherein R_2 and R_3 are independently chosen from a hydrogen atom or linear, branched, and/or cyclic C_1-C_6 alkyl groups;

X is a carboxylic acid or a derivative thereof, wherein the derivative is a carboxylate, such as a carboxylic ester; a glyceride; an anhydride; a carboxamide; a phospholipid; or a hydroxymethyl; or a prodrug thereof;

or a pharmaceutically acceptable salt, solvate, or solvate of such salt thereof.

6. The use of any one of claims 1 to 5, wherein R_2 and R_3 are independently chosen from a hydrogen atom, a methyl group, an ethyl group, a n-propyl group, and an isopropyl group.

7. The use of any one of claims 1 to 5, wherein R_2 and R_3 are both independently C_1-C_6 alkyl groups.

8. The use of any one of claims 1 to 6, wherein one of R_2 and R_3 is a hydrogen atom and the other is an ethyl group.

9. The use of any one of claims 1 to 8, wherein X is a carboxylic acid.

10. The use of any one of claims 1 to 8, wherein X is a C_1-C_6 alkyl ester.

11. The use of claim 10, wherein X is chosen from a methyl ester, an ethyl ester, an isopropyl ester, a *n*-butyl ester, and a *tert*-butyl ester.

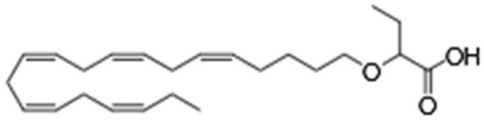
12. The use of any one of claims 1 to 3, 10, or 11, wherein X is selected from the group of a methyl ester and an ethyl ester.

13. The use of any one of claims 1 to 8, wherein X is a glyceride chosen from a triglyceride, a 1,2-diglyceride, a 1,3-diglyceride, a 1-monoglyceride, and a 2-monoglyceride.

14. The use of any one of claims 1 to 13, wherein the compound is present in the form of an enantiomer, a diastereomer, or a mixture thereof.

15. The use of claim 14, wherein the first compound is present in its R form, in its S form, or in racemic form.

16. The use of any one of claims 1 to 4, wherein the first compound is 2-(((5Z,8Z,11Z,14Z,17Z)-icosa-5,8,11,14,17-pentaen-1-yl)oxy)butanoic acid (Compound A), or a pharmaceutically acceptable salt or ester thereof, and the formula is



(Compound A).

17. The use of any one of claims 1 to 16, wherein the compound is administered in a dose of between about 5 mg to about 4 g per dose.

18. The use of any one of claims 1 to 17, wherein the compound is administered once daily.

19. The use of any one of claims 1 to 18, wherein the additional active agent is chosen from semaglutide, firsocostat, and obeticholic acid (OCA).

20. The use of any one of claims 1 to 19, wherein the additional active agent is semaglutide.

21. The use of any one of claims 1 to 20, wherein the additional active agent is firsocostat.

22. The use of any one of claims 1 or 4 to 21, wherein the use treats or reverses NASH.

23. The use of any one of claims 1 or 4 to 22, wherein

a) the use reduces the development of hepatic fibrosis or reduces existing hepatic fibrosis in a subject with NASH;

b) the use reduces the development of hepatic inflammation or reduces existing hepatic inflammation in a subject with NASH; and/or

c) the use reduces the development of steatohepatitis or reduces existing steatohepatitis in a subject with NASH.

24. The use of any one of claims 2 or 4 to 21, wherein the use treats or reverses ASH.

25. The use of any one of claims 2, 4 to 21, or 24, wherein

a) the use reduces the development of hepatic fibrosis or reduces existing hepatic fibrosis in a subject with ASH;

b) the use reduces the development of hepatic inflammation or reduces existing hepatic inflammation in a subject with ASH; and/or

c) the use reduces the development of steatohepatitis or reduces existing steatohepatitis in a subject with ASH.

26. The use of any one of claims 3 to 21, wherein the use treats or reverses fatty liver disease.

27. The use of any one of claims 3 to 21 or 26, wherein the use reduces or reverses steatosis.

28. The use of any one of claims 3 to 21, 26, or 27, wherein the fatty liver disease is

a) non-alcoholic fatty liver disease (NAFLD); or

b) alcoholic fatty liver disease (ALD).

29. The use of any one of claims 3 to 21 or 26 to 28, wherein the fatty liver disease is not accompanied by an inflammatory response and cellular damage.

30. The use of any one of claims 1 to 29, wherein the compound is formulated in a composition.

31. The use of claim 30, wherein the composition is formulated for oral administration.

32. The use of claim 30 or claim 31, wherein the composition further comprises at least one binder, excipient, diluent, or antioxidant, or any combinations thereof.

33. The use of any one of claims 1 to 32, wherein the compound is administered at a dosage of about 600 mg daily.

34. The use of any one of claims 1 to 32, wherein the compound is administered at a dosage of about 300 mg daily.

35. The use of any one of claims 1, 2, 4 to 25, or 30 to 34, wherein

a) hepatic inflammatory cells are reduced by 30-50% or by 60-80%;

b) the liver hydroxyproline content is decreased by 20-40%; and/or

c) the hepatic fibrotic area as determined by picrosirius red staining is decreased by 30-50%.

36. The use of any one of claims 1 to 35, wherein

a) hepatic steatosis area is reduced by 70-90%;

b) the percentage of hepatocytes with lipid droplets is reduced by 70-90%;

c) the NAFLD activity (NAS) score is reduced; and/or

d) the steatosis score is reduced.