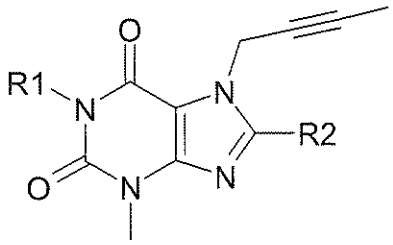
Claims

1. Use of A a DPP-4 inhibitor

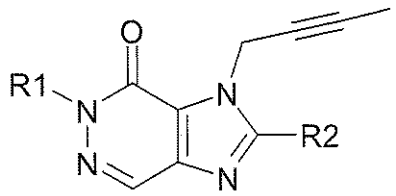
either, in a first embodiment (embodiment **A**),

of formula (I)



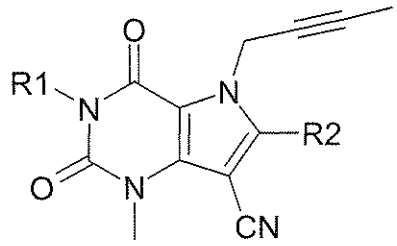
(I)

or of formula (II)



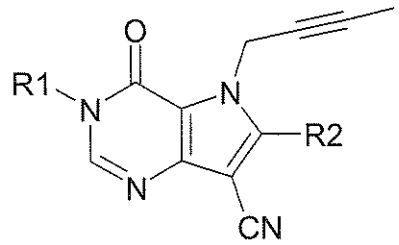
(II)

or of formula (III)



(III)

or of formula (IV)



(IV)

wherein **R1** denotes ([1,5]naphthyridin-2-yl)methyl, (quinazolin-2-yl)methyl, (quinoxalin-6-yl)methyl, (4-methyl-quinazolin-2-yl)methyl, 2-cyano-benzyl, (3-cyano-quinolin-2-yl)methyl,

(3-cyano-pyridin-2-yl)methyl, (4-methyl-pyrimidin-2-yl)methyl, or (4,6-dimethyl-pyrimidin-2-yl)methyl and **R2** denotes 3-(*R*)-amino-piperidin-1-yl, (2-amino-2-methyl-propyl)-methylamino or (2-(*S*)-amino-propyl)-methylamino,
or its pharmaceutically acceptable salt,
in a daily oral amount of 5 mg;

or, in a second embodiment (embodiment **B**),
selected from the group consisting of
sitagliptin, vildagliptin, saxagliptin, alogliptin,
(2*S*)-1-{[2-(5-Methyl-2-phenyl-oxazol-4-yl)-ethylamino]-acetyl}-pyrrolidine-2-carbonitrile,
(2*S*)-1-{[1,1,-Dimethyl-3-(4-pyridin-3-yl-imidazol-1-yl)-propylamino]-acetyl}-pyrrolidine-2-carbonitrile,
(*S*)-1-((2*S*,3*S*,11b*S*)-2-Amino-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-3-yl)-4-fluoromethyl-pyrrolidin-2-one,
(3,3-Difluoropyrrolidin-1-yl)-((2S,4S)-4-(4-(pyrimidin-2-yl)piperazin-1-yl)pyrrolidin-2-yl)methanone,
(1((3S,4S)-4-amino-1-(4-(3,3-difluoropyrrolidin-1-yl)-1,3,5-triazin-2-yl)pyrrolidin-3-yl)-5,5-difluoropiperidin-2-one,
(2S,4S)-1-{2-[(3S,1R)-3-(1H-1,2,4-Triazol-1-ylmethyl)cyclopentylamino]-acetyl}-4-fluoropyrrolidine-2-carbonitrile,
(R)-2-[6-(3-Amino-piperidin-1-yl)-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl]-4-fluoro-benzonitrile, and
5-{(S)-2-[2-((S)-2-Cyano-pyrrolidin-1-yl)-2-oxo-ethylamino]-propyl}-5-(1H-tetrazol-5-yl)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene-2,8-dicarboxylic acid bis-dimethylamide,
or its pharmaceutically acceptable salt;

for preparing a medicament for use in the treatment and/or prevention of non alcoholic fatty liver disease (NAFLD).

2. Use ~~The~~ of the DPP-4 inhibitor according to claim 1 for preparing a medicament for use in the treatment and/or prevention of non alcoholic fatty liver disease (NAFLD), wherein said DPP-4 inhibitor is selected from the group consisting of
1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine,
1-[([1,5]naphthyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,
1-[(quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

2-((R)-3-amino-piperidin-1-yl)-3-(but-2-ynyl)-5-(4-methyl-quinazolin-2-ylmethyl)-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one,

1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(2-amino-2-methyl-propyl)-methylamino]-xanthine,

1-[(3-cyano-quinolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

1-(2-cyano-benzyl)-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-[(*S*)-(2-amino-propyl)-methylamino]-xanthine,

1-[(3-cyano-pyridin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

1-[(4-methyl-pyrimidin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

1-[(4,6-dimethyl-pyrimidin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine and

1-[(quinoxalin-6-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-((*R*)-3-amino-piperidin-1-yl)-xanthine,

or a pharmaceutically acceptable salt thereof,

and wherein said DPP-4 inhibitor is administered in a daily oral amount of 5 mg.

3. ~~The~~ Use of the DPP-4 inhibitor according to claim 1 for preparing a medicament for use in the treatment and/or prevention of non alcoholic fatty liver disease (NAFLD), wherein said DPP-4 inhibitor is selected from the group consisting of

sitagliptin, vildagliptin, saxagliptin, alogliptin,

(2*S*)-1-{[2-(5-Methyl-2-phenyl-oxazol-4-yl)-ethylamino]-acetyl}-pyrrolidine-2-carbonitrile,

(2*S*)-1-{[1,1,-Dimethyl-3-(4-pyridin-3-yl-imidazol-1-yl)-propylamino]-acetyl}-pyrrolidine-2-carbonitrile,

(*S*)-1-((2*S*,3*S*,11b*S*)-2-Amino-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2H-pyrido[2,1-a]isoquinolin-3-yl)-4-fluoromethyl-pyrrolidin-2-one,

(3,3-Difluoropyrrolidin-1-yl)-((2S,4S)-4-(4-(pyrimidin-2-yl)piperazin-1-yl)pyrrolidin-2-yl)methanone,

(1((3S,4S)-4-amino-1-(4-(3,3-difluoropyrrolidin-1-yl)-1,3,5-triazin-2-yl)pyrrolidin-3-yl)-5,5-difluoropiperidin-2-one,

(2S,4S)-1-{2-[(3S,1R)-3-(1H-1,2,4-Triazol-1-ylmethyl)cyclopentylamino]-acetyl}-4-fluoropyrrolidine-2-carbonitrile, and

(R)-2-[6-(3-Amino-piperidin-1-yl)-3-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-ylmethyl]-4-fluoro-benzonitrile,

or a pharmaceutically acceptable salt thereof.

4. ~~The~~ Use of the DPP-4 inhibitor according to claim 1 for preparing a medicament for use in the treatment and/or prevention of non alcoholic fatty liver disease (NAFLD), wherein said DPP-4 inhibitor is
1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine, in an daily oral amount of 5 mg.

5. Use of ~~The~~ the DPP-4 inhibitor according to any of the claims 1 to 4, wherein the medicament is for use in the treatment and/or prevention of non alcoholic fatty liver disease (NAFLD), wherein said non alcoholic fatty liver disease (NAFLD) is selected from the group consisting of hepatic steatosis, non-alcoholic steatohepatitis (NASH) and liver fibrosis.

6. Use of ~~The~~ the DPP-4 inhibitor according to any of the claims 1 to 4 wherein the medicament is for use in the treatment and/or prevention of hepatic steatosis.

7. Use of ~~The~~ the DPP-4 inhibitor according to any of the claims 1 to 4 wherein the medicament is for use in the treatment and/or prevention of non-alcoholic steatohepatitis (NASH).

8. Use of ~~The~~ the DPP-4 inhibitor according to any of the claims 1 to 4 wherein the medicament is for use in the treatment and/or prevention of liver fibrosis.

9. Use of ~~A~~ a pharmaceutical composition for preparing a medicament for use in the treatment and/or prevention of non alcoholic fatty liver disease (NAFLD) including hepatic steatosis, non-alcoholic steatohepatitis (NASH) and/or liver fibrosis, said pharmaceutical composition comprising a DPP-4 inhibitor ~~according to~~as defined in any of the claims 1 to 4.

10. The ~~pharmaceutical composition~~use according to claim 9, ~~for use in the treatment and/or prevention of non alcoholic fatty liver disease (NAFLD) including hepatic steatosis, non-alcoholic steatohepatitis (NASH) and/or liver fibrosis, said~~wherein the pharmaceutical composition further ~~comprising~~ comprises metformin.

11. The ~~pharmaceutical composition~~use according to claim 9, ~~for use in the treatment and/or prevention of non alcoholic fatty liver disease (NAFLD) including hepatic steatosis, non-alcoholic steatohepatitis (NASH) and/or liver fibrosis, said~~wherein the pharmaceutical composition further ~~comprising~~ comprises pioglitazone.

12. Use of a DPP-4 inhibitor as defined in any of the claims 1 to 4 for the manufacture of a pharmaceutical composition for treatment and/or prevention of diabetic non alcoholic fatty liver disease (~~particularly~~ diabetic NAFLD) including hepatic steatosis, non-alcoholic steatohepatitis (NASH) and/or liver fibrosis.

13. Use of a DPP-4 inhibitor as defined in any of the claims 1 to 4 for the manufacture of a pharmaceutical composition for treating and/or preventing non alcoholic fatty liver disease (NAFLD)/non-alcoholic steatohepatitis (NASH), particularly NAFLD/NASH associated with diabetes.

14. The use according to claim 12 or 13, wherein the pharmaceutical composition further comprises one or more other active substances selected from the group consisting of antidiabetic substances, including active substances used to lower the blood sugar level, active substances used to lower the lipid level in the blood, active substances used to raise the HDL level in the blood, active substances used to lower blood pressure, active substances used for treating atherosclerosis, active substances used for treating obesity, antioxidants, and anti-inflammatory agents, such as e.g. for separate, sequential, simultaneous, concurrent or chronologically staggered use of the active ingredients.

15. Use of a DPP-4 inhibitor as defined in any of the claims 1 to 4 for the manufacture of a pharmaceutical composition for treatment and/or prevention of non alcoholic fatty liver disease (NAFLD), including hepatic steatosis, non-alcoholic steatohepatitis (NASH) and/or liver fibrosis, in combination with one or more other active substances selected from the group consisting of antidiabetic substances, including active substances used to lower the blood sugar level, active substances used to lower the lipid level in the blood, active substances used to raise the HDL level in the blood, active substances used to lower blood pressure, active substances used for treating atherosclerosis, active substances used for treating obesity, antioxidants, and anti-inflammatory agents.

16. The use according to claim 14 or 15, wherein said other active substances are selected from the group consisting of biguanides including metformin, thiazolidinones including pioglitazone, statines including atorvastatin, and ARBs including telmisartan.

17. A pharmaceutical package containing a pharmaceutical composition comprising a DPP-4 inhibitor ~~according to~~as defined in any of the claims 1 to 4, beside instructions for treating and/or preventing non alcoholic fatty liver disease (NAFLD) including hepatic steatosis, non-alcoholic steatohepatitis (NASH) and/or liver fibrosis, optionally in combination with one, two or more other active substances selected from the group consisting of antidiabetic substances, including active substances used to lower the blood sugar level, active substances used to lower the lipid level in the blood, active substances used to raise the HDL level in the blood, active substances used to lower blood pressure, active substances used for treating atherosclerosis, active substances used for treating obesity, antioxidants, anti-inflammatory agents, and vascular endothelial protecting agents.

18. Use of a DPP-4 inhibitor according to any of the claims 1 to 4 wherein the medicament is for use in treating and/or preventing NAFLD/NASH and/or diseases or disorders related or associated therewith, in patients having one or more disorders selected from NAFLD, metabolic syndrome, insulin resistance, IGT, IFG, overweight, obesity (particularly visceral and/or abdominal obesity), dyslipidemia (e.g. hyperlipidemia, hypertriglyceridemia and/or hypoHDLemia), diabetes (particularly type 2 diabetes), hypertension, hyperglycemia, hyperinsulinemia, hyperuricemia, severe sleep apnoe, polycystic ovary syndrome, and chronic hepatitis C infection.

19. Use of the DPP-4 inhibitor as defined in any of the claims 1 to 4 for preparing a medicament for use in reducing liver fat.

20. Use of a DPP-4 inhibitor as defined in any of the claims 1 to 4 for preparing a medicament for use in the treatment and/or prevention of fibrosis, such as e.g. fibrosis of the liver, lung, skin, heart or kidney.

21. Use of a DPP-4 inhibitor according to any of the preceding claims, wherein 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(*R*)-amino-piperidin-1-yl)-xanthine is administered in a daily oral amount of 5 mg.