

CLAIMS

1. Saponin derivative based on a saponin comprising a triterpene aglycone core structure and at least one of a first saccharide chain and a second saccharide chain linked to the aglycone core structure, wherein:
- 5 i. the saponin derivative comprises an aglycone core structure comprising an aldehyde group which has been derivatised; or
- ii. the saponin derivative comprises the first saccharide chain wherein the first saccharide chain comprises a carboxyl group, preferably a carboxyl group of a glucuronic acid moiety, which has been derivatised; or
- 10 iii. the saponin derivative comprises the second saccharide chain wherein the second saccharide chain comprises at least one acetoxy (Me(CO)O-) group which has been derivatised; or
- iv. the saponin derivative comprises any combination of derivatisations i., ii. and iii., preferably any combinations of two derivatisations i., ii. and iii.;
- 15 wherein the first saccharide chain and the second saccharide chain are independently selected from a monosaccharide, a linear oligosaccharide and a branched oligosaccharide.
2. Saponin derivative according to claim 1, wherein the saponin derivative is a monodesmosidic triterpene glycoside or a bidesmosidic triterpene glycoside, more preferably a bidesmosidic triterpene glycoside.
- 20 3. Saponin derivative according to claim 1 or 2, wherein the saponin derivative comprises the first saccharide chain wherein the first saccharide chain comprises a carboxyl group, preferably a carboxyl group of a glucuronic acid moiety, which has been derivatised, and/or wherein the saponin derivative comprises the second saccharide chain wherein the second saccharide chain comprises at least one acetoxy (Me(CO)O-) group which has been derivatised,
- 25 preferably the saponin derivative comprises both of said first saccharide chain which has been derivatised and said second saccharide chain which has been derivatised,
- more preferably, the saponin derivative comprises both of said first saccharide chain which has been derivatised and said second saccharide chain which has been derivatised and the saponin derivative comprises an aglycone core structure comprising an aldehyde group or an aldehyde group which has been derivatised,
- 30 most preferably, the saponin derivative comprises both of said first saccharide chain which has been derivatised and said second saccharide chain which has been derivatised and the saponin derivative comprises an aglycone core structure comprising an aldehyde group.
- 35 4. Saponin derivative according to any one of claims 1-3, wherein the saponin derivative comprises an aglycone core structure selected from the group consisting of:
- 2alpha-hydroxy oleanolic acid;
- 40 16alpha-hydroxy oleanolic acid;

- hederagenin (23-hydroxy oleanolic acid);
 16 α ,23-dihydroxy oleanolic acid;
 gypsogenin;
 quillaic acid;
 5 protoaescigenin-21(2-methylbut-2-enoate)-22-acetate;
 23-oxo-barringtogenol C-21,22-bis(2-methylbut-2-enoate);
 23-oxo-barringtogenol C-21(2-methylbut-2-enoate)-16,22-diacetate;
 digitogenin;
 3,16,28-trihydroxy oleanan-12-en;
 10 gypsogenic acid,
 and
 derivatives thereof,
 preferably the saponin derivative comprises an aglycone core structure selected from quillaic acid and
 gypsogenin or derivatives thereof, more preferably the saponin derivative aglycone core structure is
 15 quillaic acid or a derivative thereof.

5. Saponin derivative according to any one of the claims 1-4, wherein the saponin derivative comprises
 an aglycone core structure selected from the group consisting of quillaic acid, gypsogenin, and
 derivatives thereof, preferably the saponin derivative comprises an aglycone core structure selected
 20 from the group consisting of quillaic acid and derivatives thereof, wherein the first saccharide chain,
 when present, is linked to the C₃ atom or the C₂₈ atom of the aglycone core structure, preferably to the
 C₃ atom, and/or wherein the second saccharide chain, when present, is linked to the C₂₈ atom of the
 aglycone core structure.

25 6. Saponin derivative according to any one of the claims 1-5, wherein the first saccharide chain, if
 present, is selected from:

- GlcA-,
 Glc-,
 Gal-,
 30 Rha-(1→2)-Ara-,
 Gal-(1→2)-[Xyl-(1→3)]-GlcA-,
 Glc-(1→2)-[Glc-(1→4)]-GlcA-,
 Glc-(1→2)-Ara-(1→3)-[Gal-(1→2)]-GlcA-,
 Xyl-(1→2)-Ara-(1→3)-[Gal-(1→2)]-GlcA-,
 35 Glc-(1→3)-Gal-(1→2)-[Xyl-(1→3)]-Glc-(1→4)-Gal-,
 Rha-(1→2)-Gal-(1→3)-[Glc-(1→2)]-GlcA-,
 Ara-(1→4)-Rha-(1→2)-Glc-(1→2)-Rha-(1→2)-GlcA-,
 Ara-(1→4)-Fuc-(1→2)-Glc-(1→2)-Rha-(1→2)-GlcA-,
 Ara-(1→4)-Rha-(1→2)-Gal-(1→2)-Rha-(1→2)-GlcA-,
 40 Ara-(1→4)-Fuc-(1→2)-Gal-(1→2)-Rha-(1→2)-GlcA-,

- Ara-(1→4)-Rha-(1→2)-Glc-(1→2)-Fuc-(1→2)-GlcA-,
 Ara-(1→4)-Fuc-(1→2)-Glc-(1→2)-Fuc-(1→2)-GlcA-,
 Ara-(1→4)-Rha-(1→2)-Gal-(1→2)-Fuc-(1→2)-GlcA-,
 Ara-(1→4)-Fuc-(1→2)-Gal-(1→2)-Fuc-(1→2)-GlcA-,
 5 Xyl-(1→4)-Rha-(1→2)-Glc-(1→2)-Rha-(1→2)-GlcA-,
 Xyl-(1→4)-Fuc-(1→2)-Glc-(1→2)-Rha-(1→2)-GlcA-,
 Xyl-(1→4)-Rha-(1→2)-Gal-(1→2)-Rha-(1→2)-GlcA-,
 Xyl-(1→4)-Fuc-(1→2)-Gal-(1→2)-Rha-(1→2)-GlcA-,
 Xyl-(1→4)-Rha-(1→2)-Glc-(1→2)-Fuc-(1→2)-GlcA-,
 10 Xyl-(1→4)-Fuc-(1→2)-Glc-(1→2)-Fuc-(1→2)-GlcA-,
 Xyl-(1→4)-Rha-(1→2)-Gal-(1→2)-Fuc-(1→2)-GlcA-,
 Xyl-(1→4)-Fuc-(1→2)-Gal-(1→2)-Fuc-(1→2)-GlcA-, and
 derivatives thereof,
 and/or wherein the second saccharide chain, if present, is selected from:
- 15 Glc-,
 Gal-,
 Rha-(1→2)-[Xyl-(1→4)]-Rha-,
 Rha-(1→2)-[Ara-(1→3)-Xyl-(1→4)]-Rha-,
 Ara-,
 20 Xyl-,
 Xyl-(1→4)-Rha-(1→2)-[R1-(→4)]-Fuc- wherein R1 is 4E-Methoxycinnamic acid,
 Xyl-(1→4)-Rha-(1→2)-[R2-(→4)]-Fuc- wherein R2 is 4Z-Methoxycinnamic acid,
 Xyl-(1→4)-[Gal-(1→3)]-Rha-(1→2)-4-OAc-Fuc-,
 Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-3,4-di-OAc-Fuc-,
 25 Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R3-(→4)]-3-OAc-Fuc- wherein R3 is 4E-Methoxycinnamic acid,
 Glc-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-4-OAc-Fuc-,
 Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-4-OAc-Fuc-,
 (Ara- or Xyl-)(1→3)-(Ara- or Xyl-)(1→4)-(Rha- or Fuc-)(1→2)-[4-OAc-(Rha- or Fuc-)(1→4)]-(Rha- or
 Fuc-),
 30 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Qui-(1→4)]-Fuc-,
 Api-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-Fuc-,
 Xyl-(1→4)-[Gal-(1→3)]-Rha-(1→2)-Fuc-,
 Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-Fuc-,
 Ara/Xyl-(1→4)-Rha/Fuc-(1→4)-[Glc/Gal-(1→2)]-Fuc-,
 35 Api-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R4-(→4)]-Fuc- wherein R4 is 5-O-[5-O-Ara/Api-3,5-
 dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid),
 Api-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R5-(→4)]-Fuc- wherein R5 is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-
 methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid),
 Api-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Rha-(1→3)]-4-OAc-Fuc-,
 40 Api-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[Rha-(1→3)]-4-OAc-Fuc-,

- 6-OAc-Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-[3-OAc-Rha-(1→3)]-Fuc-,
 Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-[3-OAc-Rha-(1→3)]-Fuc-,
 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Qui-(1→4)]-Fuc-,
 Glc-(1→3)-[Xyl-(1→4)]-Rha-(1→2)-[Qui-(1→4)]-Fuc-,
 5 Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Xyl-(1→3)-4-OAc-Qui-(1→4)]-Fuc-,
 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[3,4-di-OAc-Qui-(1→4)]-Fuc-,
 Glc-(1→3)-[Xyl-(1→4)]-Rha-(1→2)-Fuc-,
 6-OAc-Glc-(1→3)-[Xyl-(1→4)]-Rha-(1→2)-Fuc-,
 Glc-(1→3)-[Xyl-(1→3)-Xyl-(1→4)]-Rha-(1→2)-Fuc-,
 10 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Xyl-(1→3)-4-OAc-Qui-(1→4)]-Fuc-,
 Api/Xyl-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[Rha-(1→3)]-4OAc-Fuc-,
 Api-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[Rha-(1→3)]-4OAc-Fuc-,
 Api/Xyl-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R6-(→4)]-Fuc- wherein R6 is 5-O-[5-O-Rha-(1→2)-
 Ara/Api-3,5-dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid),
 15 Api/Xyl-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R7-(→4)]-Fuc- wherein R7 is 5-O-[5-O-Ara/Api-3,5-
 dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid),
 Api/Xyl-(1→3)-Xyl-(1→4)-[Glc-(1→3)]-Rha-(1→2)-[R8-(→4)]-Fuc- wherein R8 is 5-O-[5-O-Ara/Api-3,5-
 dihydroxy-6-methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid),
 Api-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R9-(→4)]-Fuc- wherein R9 is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-
 20 methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid),
 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R10-(→4)]-Fuc- wherein R10 is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-
 methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid),
 Api-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R11-(→3)]-Fuc- wherein R11 is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-
 methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid),
 25 Xyl-(1→3)-Xyl-(1→4)-Rha-(1→2)-[R12-(→3)]-Fuc- wherein R12 is 5-O-[5-O-Ara/Api-3,5-dihydroxy-6-
 methyl-octanoyl]-3,5-dihydroxy-6-methyl-octanoic acid)
 Glc-(1→3)-[Glc-(1→6)]-Gal-, and
 derivatives thereof.
- 30 7. Saponin derivative according to any one of the claims 1-6, wherein the saponin derivative comprises
 the first saccharide chain and comprises the second saccharide chain, wherein the first saccharide chain
 comprises more than one saccharide moiety and the second saccharide chain comprises more than
 one saccharide moiety, and wherein the aglycone core structure is quillaic acid or gypsogenin, wherein
 one, two or three, preferably one or two, of:
- 35 i. an aldehyde group in the aglycone core structure has been derivatised,
 ii. the first saccharide chain comprises a carboxyl group of a glucuronic acid moiety which has
 been derivatised, and
 iii. the second saccharide chain comprises at least one acetoxyl (Me(CO)O-) group which has been
 derivatised.

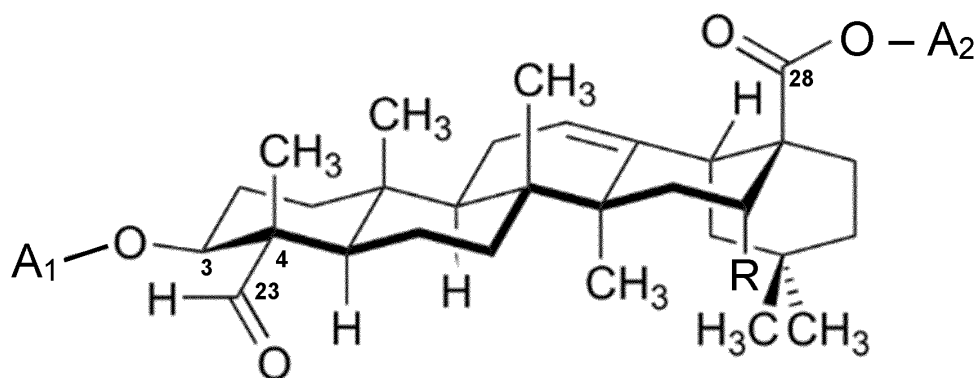
8. Saponin derivative according to any one of the claims 1-7, wherein the saponin derivative is a derivative of a saponin selected from the group of saponins consisting of: *Quillaja* bark saponin, dipsacaside B, saikosaponin A, saikosaponin D, macranthoidin A, esculentoside A, phytolaccagenin, aescinate, AS6.2, NP-005236, AMA-1, AMR, alpha-Hederin, NP-012672, NP-017777, NP-017778, NP-017774, NP-018110, NP-017772, NP-018109, NP-017888, NP-017889, NP-018108, SA1641, AE X55, NP-017674, NP-017810, AG1, NP-003881, NP-017676, NP-017677, NP-017706, NP-017705, NP-017773, NP-017775, SA1657, AG2, SO1861, GE1741, SO1542, SO1584, SO1658, SO1674, SO1832, SO1904, SO1862, QS-7, QS1861, QS-7 api, QS1862, QS-17, QS-18, QS-21 A-apio, QS-21 A-xylo, QS-21 B-apio, QS-21 B-xylo, beta-Aescin, Aescin Ia, Teaseed saponin I, Teaseedsaponin J, Assamsaponin F, Digitonin, Primula acid 1 and AS64R, stereoisomers thereof and combinations thereof, preferably the saponin derivative is selected from the group consisting of a QS-21 derivative, a SO1861 derivative, a SA1641 derivative and a GE1741 derivative, more preferably the saponin derivative is selected from the group consisting of a QS-21 derivative and a SO1861 derivative, most preferably the saponin derivative is SO1861 derivative.

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9. Saponin derivative according to any one of the claims 1-8, wherein the saponin derivative is a saponin derivative of the quillaic acid saponin or gypsogenin saponin of claim 4 which is represented by Molecule 1:

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(Molecule 1)

wherein

the first saccharide chain A_1 represents hydrogen, a monosaccharide or a linear or branched oligosaccharide, preferably A_1 represents a saccharide chain as defined in claim 6, more preferably A_1 represents a saccharide chain as defined in claim 6 and A_1 comprises or consists of a glucuronic acid moiety;

the second saccharide chain A_2 represents hydrogen, a monosaccharide or a linear or branched oligosaccharide, preferably A_2 represents a saccharide chain as defined in claim 6, more preferably A_2 represents a saccharide chain as defined in claim 6 and A_2 comprises at least one

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acetoxy (Me(CO)O-) group, such as one, two, three or four acetoxy groups, wherein at least one of A₁ and A₂ is not hydrogen, preferably both A₁ and A₂ are an oligosaccharide chain; and R is hydrogen in gypsogenin or hydroxyl in quillaic acid;

wherein the saponin derivative corresponds to the saponin represented by Molecule 1 wherein at least one of the following derivatisations is present:

- i. the aldehyde group at position C₂₃ of the quillaic acid or gypsogenin has been derivatised;
- ii. the carboxyl group of a glucuronic acid moiety of A₁, when A₁ represents a saccharide chain as defined in claim 6 and A₁ comprises or consists of a glucuronic acid moiety, has been derivatised; and
- 10 iii. one or more, preferably all, of acetoxy group(s) of one saccharide moiety or of two or more saccharide moieties of A₂, when A₂ represents a saccharide chain as defined in claim 6 and A₂ comprises at least one acetoxy group, has/have been derivatised.

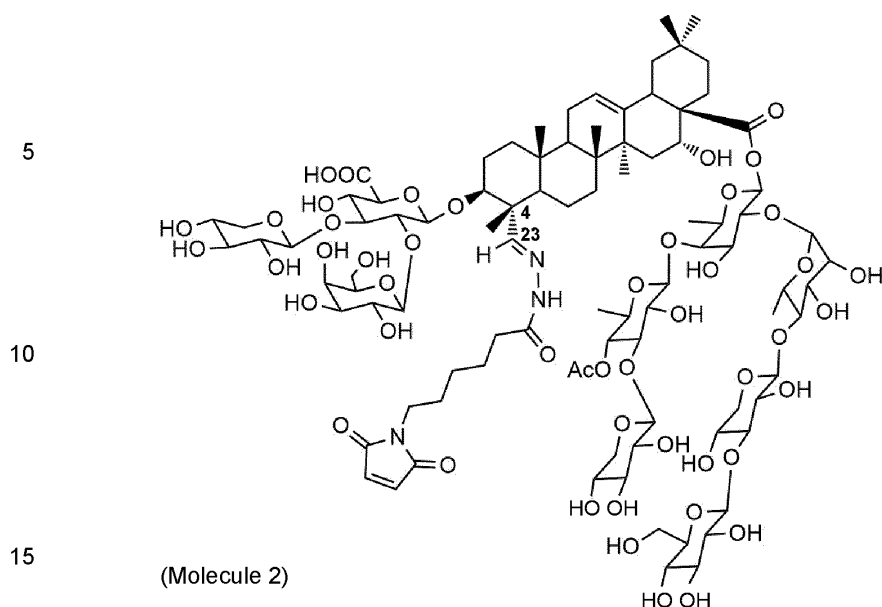
10. Saponin derivative according to claim 9, wherein A₁ represents a saccharide chain as defined in claim 6 and comprises or consists of a glucuronic acid moiety and wherein the carboxyl group of a glucuronic acid moiety of A₁ has been derivatised and/or wherein A₂ represents a saccharide chain as defined in claim 6 and A₂ comprises at least one acetoxy group and wherein at least one acetoxy group of A₂ has been derivatised.

20 11. Saponin derivative according to claim 9 or 10, wherein the saponin represented by Molecule 1 is a bidesmosidic triterpene saponin.

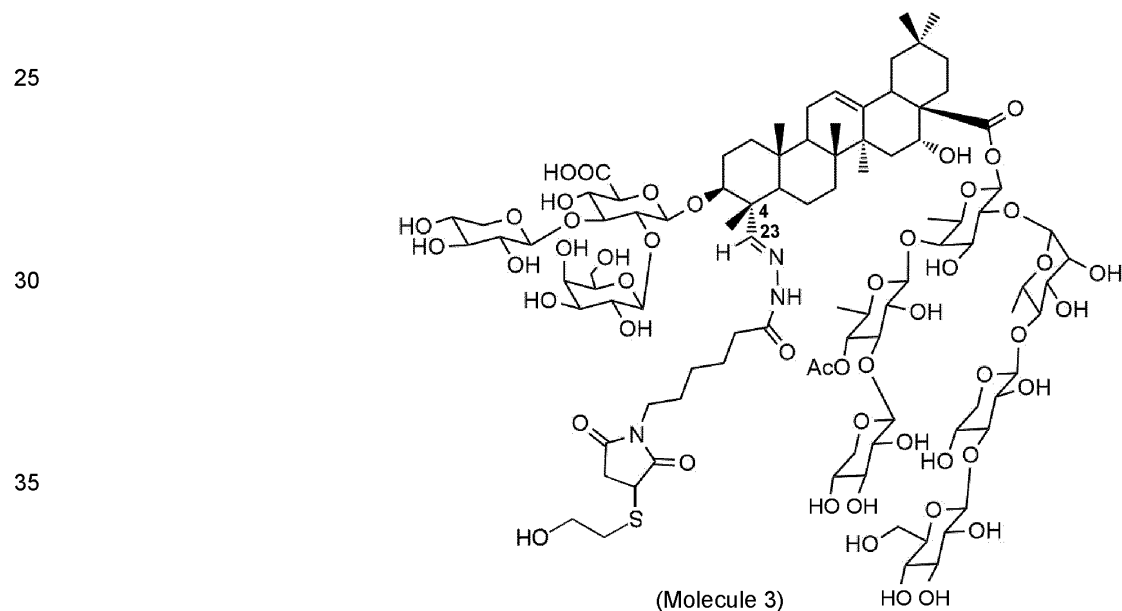
25 12. Saponin derivative according to any one of the claims 9-11, wherein the saponin derivative corresponds to the saponin represented by Molecule 1 wherein at least one of the following derivatisations is present, preferably one or two of the following derivatisations is present:

- i. the aldehyde group at position C₂₃ of the quillaic acid or gypsogenin has been derivatised by;
 - reduction to an alcohol;
 - transformation into a hydrazone bond through reaction with N-ε-maleimidocaproic acid hydrazide (EMCH), therewith providing a saponin-Ald-EMCH such as a SO1861-Ald-EMCH or a QS-21-Ald-EMCH, wherein the maleimide group of the EMCH is optionally derivatised by formation of a thioether bond with mercaptoethanol;
 - transformation into a hydrazone bond through reaction with N-[β-maleimidopropionic acid] hydrazide (BMPH) wherein the maleimide group of the BMPH is optionally derivatised by formation of a thioether bond with mercaptoethanol; or
 - transformation into a hydrazone bond through reaction with N-[κ-maleimidoundecanoic acid] hydrazide (KMUH) wherein the maleimide group of the KMUH is optionally derivatised by formation of a thioether bond with mercaptoethanol;
- ii. the carboxyl group of a glucuronic acid moiety of A₁, when A₁ represents a saccharide chain as defined in claim 6 and A₁ comprises or consists of a glucuronic acid moiety, has been

- derivatised by transformation into an amide bond through reaction with 2-amino-2-methyl-1,3-propanediol (AMPD) or *N*-(2-aminoethyl)maleimide (AEM), therewith providing a saponin-Glu-AMPD such as a QS-21-Glu-AMPD or a SO1861-Glu-AMPD or a saponin-Glu-AEM such as a QS-21-Glu-AEM or a SO1861-Glu-AEM; and
- 5 iii. one or more, preferably all, of acetoxy group(s) of one saccharide moiety or of two or more saccharide moieties of A₂, when A₂ represents a saccharide chain as defined in claim 6 and A₂ comprises at least one acetoxy group, has/have been derivatised by transformation into a hydroxyl group (HO-) by deacetylation.
- 10 13. Saponin derivative according to any one of the claims 9-12, wherein A₁ is Gal-(1→2)-[Xyl-(1→3)]-GlcA and/or A₂ is Glc-(1→3)-Xyl-(1→4)-Rha-(1→2)-[Xyl-(1→3)-4-OAc-Qui-(1→4)]-Fuc, preferably the saponin represented by Molecule 1 is 3-O-beta-D-galactopyranosyl-(1→2)-[beta-D-xylopyranosyl-(1→3)]-beta-D-glucuronopyranosyl quillaic acid 28-O-beta-D-glucopyranosyl-(1→3)-beta-D-xylopyranosyl-(1→4)-alpha-L-rhamnopyranosyl-(1→2)-[beta-D-xylopyranosyl-(1→3)-4OAc-beta-D-
- 15 quinovopyranosyl-(1→4)]-beta-D-fucopyranoside, more preferably SO1861, GE1741, SA1641 and/or QS-21, most preferably SO1861.
14. Saponin derivative of any one of the claims 1-13, wherein the saponin derivative is selected from the group consisting of derivatives of: SO1861, SA1657, GE1741, SA1641, QS-21, QS-21A, QS-21 A-api, QS-21 A-xyl, QS-21B, QS-21 B-api, QS-21 B-xyl, QS-7-xyl, QS-7-api, QS-17-api, QS-17-xyl, QS1861, QS1862, Quillajasaponin, Saponinum album, QS-18, Quil-A, Gyp1, gypsoside A, AG1, AG2, SO1542, SO1584, SO1658, SO1674, SO1832, SO1862, SO1904, stereoisomers thereof and combinations thereof, preferably the saponin derivative is selected from the group consisting of a SO1861 derivative, a GE1741 derivative, a SA1641 derivative, a QS-21 derivative, and a combination
- 20 thereof, more preferably the saponin derivative is a SO1861 derivative or a QS21 derivative, most preferably, the saponin derivative is a SO1861 derivative.
15. Saponin derivative of any one of the claims 1-14, wherein the saponin derivative is a SO1861 derivative comprising a single derivatisation, wherein the single derivatisation is transformation of a carboxyl group of a glucuronic acid moiety of SO1861 by binding 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (HATU) to the carboxyl group of the glucuronic acid moiety of SO1861 or by binding (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP) to the carboxyl group of the glucuronic moiety of SO1861, or wherein the saponin derivative is a SO1861 derivative represented by Molecule 2, which represents a SO1861
- 30 derivative comprising an aldehyde group at indicated position C₂₃ of the quillaic acid aglycone core structure which has been derivatised by transformation into a hydrazone bond through reaction with *N*-ε-maleimidocaproic acid hydrazide (EMCH):



or wherein the saponin derivative is a SO1861 derivative represented by Molecule 3, which represents a SO1861 derivative comprising an aldehyde group at indicated position C₂₃ of the quillaic acid aglycone core structure which has been derivatised by transformation into a hydrazone bond through reaction with N-ε-maleimidocaproic acid hydrazide (EMCH) wherein the maleimide group of the EMCH is derivatised with mercaptoethanol therewith forming a thioether bond:

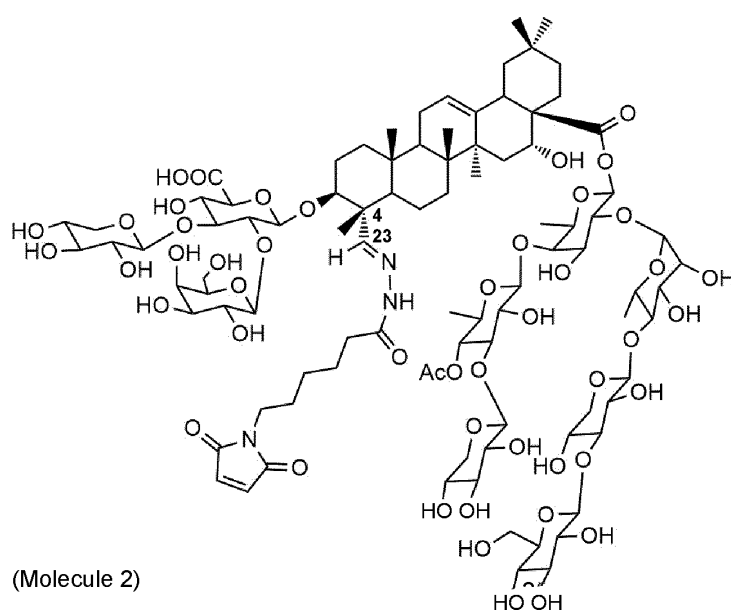


16. Saponin derivative according to any one of the claims 1-14, with the proviso that the saponin derivative is not a SO1861 derivative comprising a single derivatisation, wherein the single derivatisation is transformation of the carboxyl group of a glucuronic acid moiety of SO1861 by reaction of 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (HATU) with the carboxyl group of the glucuronic acid moiety of SO1861, or wherein the saponin derivative is a SO1861 derivative represented by Molecule 2, which represents a SO1861 derivative comprising an aldehyde group at indicated position C₂₃ of the quillaic acid aglycone core structure which has been derivatised by transformation into a hydrazone bond through reaction with N-ε-maleimidocaproic acid hydrazide (EMCH):

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17. Saponin derivative according to any one of the claims 1-16, wherein

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- i. the saponin derivative comprises an aglycone core structure wherein the aglycone core structure comprises an aldehyde group which has been derivatised by:

- reduction to an alcohol;
- transformation into a hydrazone bond through reaction with N-ε-maleimidocaproic acid hydrazide (EMCH) wherein the maleimide group of the EMCH is optionally derivatised by formation of a thioether bond with mercaptoethanol;
- transformation into a hydrazone bond through reaction with N-[β-maleimidopropionic acid] hydrazide (BMPH) wherein the maleimide group of the BMPH is optionally derivatised by formation of a thioether bond with mercaptoethanol; or

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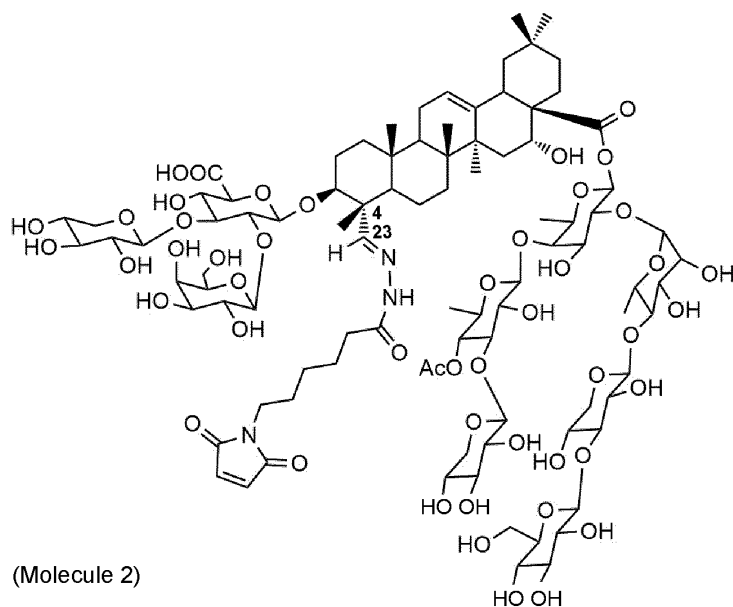
- transformation into a hydrazone bond through reaction with N-[κ -maleimidoundecanoic acid] hydrazide (KMUH) wherein the maleimide group of the KMUH is optionally derivatised by formation of a thioether bond with mercaptoethanol;
- ii. the first saccharide chain comprises a carboxyl group, preferably a carboxyl group of a glucuronic acid moiety, which has been derivatised by transformation into an amide bond through reaction with 2-amino-2-methyl-1,3-propanediol (AMPD) or *N*-(2-aminoethyl)maleimide (AEM);
- iii. the second saccharide chain comprises an acetoxy group (Me(CO)O-) which has been derivatised by transformation into a hydroxyl group (HO-) by deacetylation; or
- iv. the saponin derivative comprises any combination of two or three derivatisations i., ii. and iii., preferably any combination of two derivatisations i., ii. and iii.;
- preferably, the saponin derivative comprises an aglycone core structure wherein the aglycone core structure comprises an aldehyde group which has been derivatised by transformation into a hydrazone bond through reaction with EMCH wherein the maleimide group of the EMCH is optionally derivatised by formation of a thioether bond with mercaptoethanol.
18. Saponin derivative according to claim 17, wherein the saponin derivative comprises an aglycone core structure wherein the aglycone core structure comprises an aldehyde group and wherein the first saccharide chain comprises a carboxyl group, preferably a carboxyl group of a glucuronic acid moiety, which has been derivatised by transformation into an amide bond through reaction with *N*-(2-aminoethyl)maleimide (AEM).
19. Saponin derivative according to claim 17, with the proviso that when the aldehyde group in the aglycone core structure is derivatised by transformation into a hydrazone bond through reaction with ϵ -maleimidocaproic acid hydrazide (EMCH) and the saponin is SO1861, at least one of the glucuronic acid and the acetoxy group (Me(CO)O-) is also derivatised, and with the proviso that when the saponin is SO1861 and the carboxyl group of the glucuronic acid moiety of SO1861 is derivatised by reaction of 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (HATU) with the carboxyl group of the glucuronic acid moiety of SO1861, at least one of the aldehyde group and the acetoxy group (Me(CO)O-) is also modified.
20. Saponin derivative of claim 19, with the proviso that when the aldehyde group in the aglycone core structure of the saponin derivative is derivatised through reaction with EMCH and the saponin is SO1861, at least one of the glucuronic acid and the acetoxy group (Me(CO)O-) is also derivatised, and with the proviso that when the saponin is SO1861 and the carboxyl group of the glucuronic acid moiety of SO1861 is derivatised by bound HATU, at least one of the aldehyde group and the acetoxy group (Me(CO)O-) is also derivatised.
21. First pharmaceutical composition comprising the saponin derivative according to any one of the claims 1-20 and optionally a pharmaceutically acceptable excipient and/or diluent.

22. First pharmaceutical composition of claim 21, wherein the saponin derivative is the saponin derivative represented by Molecule 2:

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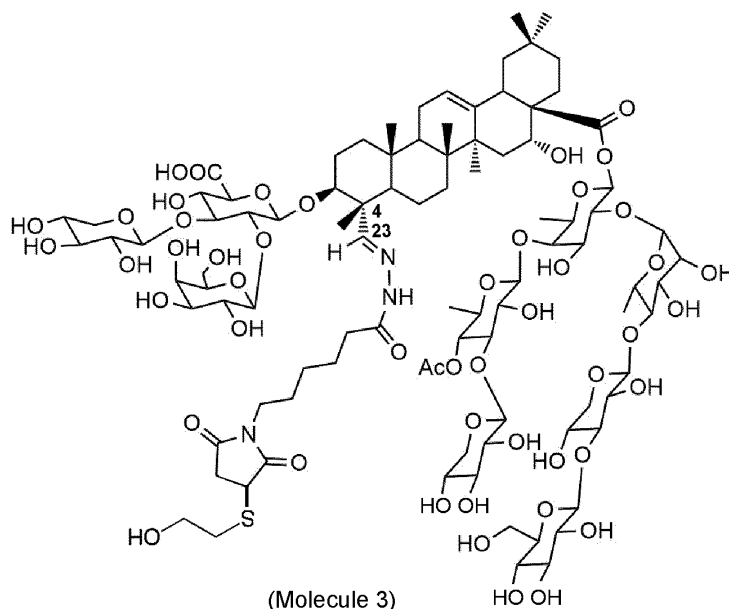


or SO1861 derivative comprising a single derivatisation, wherein the single derivatisation is transformation of the carboxyl group of the glucuronic acid moiety of SO1861 by reaction of 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (HATU) with the carboxyl group of the glucuronic acid moiety of SO1861, or the saponin derivative is the saponin derivative represented by Molecule 3:

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23. Pharmaceutical combination comprising:

- the first pharmaceutical composition of claim 21 or 22; and
- a second pharmaceutical composition comprising any one or more of an antibody-toxin conjugate, a receptor-ligand – toxin conjugate, an antibody-drug conjugate, a receptor-ligand – drug conjugate, an antibody-oligonucleotide conjugate or a receptor-ligand – oligonucleotide conjugate, and optionally comprising a pharmaceutically acceptable excipient and/or diluent.

24. Third pharmaceutical composition comprising the saponin derivative of any one of the claims 1-20 and further comprising any one or more of: an antibody-toxin conjugate, a receptor-ligand – toxin conjugate, an antibody-drug conjugate, a receptor-ligand – drug conjugate, an antibody-nucleic acid conjugate or a receptor-ligand – nucleic acid conjugate, and optionally comprising a pharmaceutically acceptable excipient and/or diluent.

25. Pharmaceutical combination of claim 23 or the third pharmaceutical composition of claim 24, wherein the second pharmaceutical composition or the third pharmaceutical composition comprises any one or more of an antibody-drug conjugate, a receptor-ligand – drug conjugate, an antibody-oligonucleotide conjugate or a receptor-ligand – oligonucleotide conjugate, wherein the drug is for example a toxin such as saporin and dianthin, and wherein the oligonucleotide is for example an siRNA or a BNA, for example for gene silencing of apolipoprotein B or HSP27.

26. Pharmaceutical combination of claim 23 or claim 25 or the third pharmaceutical composition of claim 24 or 25, wherein the saponin derivative is a saponin derivative according to claim 14, preferably the saponin derivative represented by Molecule 2 or Molecule 3.

27. First pharmaceutical composition of claim 21 or 22, pharmaceutical combination of any one of the claims 23 or 25-26 or the third pharmaceutical composition of any one of the claims 24-25, for use as a medicament.

28. First pharmaceutical composition of claim 21 or 22, pharmaceutical combination of any one of the claims 23 or 25-26 or the third pharmaceutical composition of any one of the claims 24-25, for use in the treatment or prophylaxis of a cancer, an infectious disease, viral infection, hypercholesterolemia, primary hyperoxaluria, haemophilia A, haemophilia B, alpha-1 antitrypsin related liver disease, acute hepatic porphyria, transthyretin-mediated amyloidosis, or an auto-immune disease.

29. *In vitro* or *ex vivo* method for transferring a molecule from outside a cell to inside said cell, preferably into the cytosol of said cell, comprising the steps of:

- a) providing a cell;
- b) providing the molecule for transferring from outside the cell into the cell provided in step a);

- c) providing a saponin derivative according to any one of the claims 1-20;
- d) contacting the cell of step a) *in vitro* or *ex vivo* with the molecule of step b) and the saponin derivative of step c), therewith establishing the transfer of the molecule from outside the cell into said cell.

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30. The method of claim 29, wherein the cell is a human cell such as a T-cell, an NK-cell, a tumor cell and/or wherein the saponin derivative is the saponin derivative of any one of the claims 13-20, and/or wherein the molecule of step b) is any one of: an antibody-drug conjugate, a receptor-ligand – drug conjugate, an antibody-oligonucleotide conjugate or a receptor-ligand – oligonucleotide conjugate, wherein the drug is for example a toxin and wherein the oligonucleotide is for example an siRNA or a BNA.

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