CLAIMS

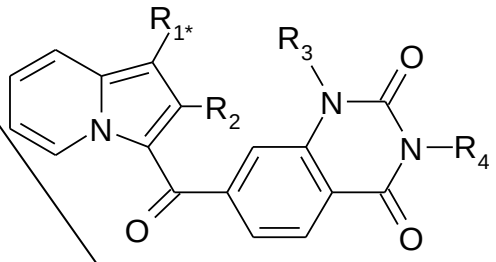
1. A compound of the formula:

M_1-L-M_2

in which M_1 and M_2, which may be identical or different, each represent, independently of one another, a monomer unit M and

L represents a linker group which links M_1 and M_2 covalently, wherein

monomer unit M is of formula (M):



(M)

in which,

* indicates the site of linkage between the monomer unit M and the linker L,

- **R_1** represents

. a group –NHCOPhO*, such that the *-labeled oxygen atom is covalently bonded to linker L;

or

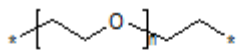
. an aryl or a heteroaryl group, said group being substituted with a group chosen from a divalent oxygen atom, such that the oxygen atom is covalently bonded to the linker L, and an amide group -CONH*-, such that the *-labeled nitrogen atom is covalently bonded to the linker L,

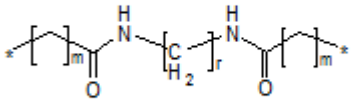
- **R_2** represents an alkyl group,

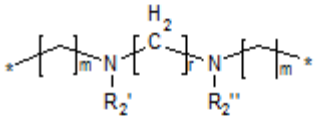
- **R_3** represents a hydrogen atom or a linear, branched, or cyclic alkyl group, and

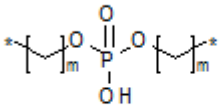
- **R_4** represents a hydrogen atom, an alkyl or -alkyl-$COOR_5$ group, with R_5 representing a hydrogen atom or an alkyl group; and

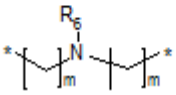
linker L is chosen from formula (A), formula (B), formula (C), formula (D) or formula (E):


(A)


(B)


(C)


(D)


(E)

wherein

* indicates the atom for connecting L with R_1,

n represents 0, 1, 2, 3, 4, or 5,

m represents 1, 2, 3, 4, or 5,

r represents 1, 2, 3, 4, 5, or 6,

R_2' and **R_2''**, which may be identical or different, represent a linear alkyl radical having from 1 to 5 carbon atoms, and which can be optionally linked to form a ring,

R_6 represents a (C_1-C_4)alkyl group optionally substituted with one or more substituents independently selected from:

- an aryl or heteroaryl group, each optionally substituted with hydroxyl or $NR_6'R_6''$, wherein **R_6'** and **R_6''** are independently chosen from a hydrogen atom or a linear, branched or cyclic (C_1-C_4)alkyl group,

- a heterocycloalkyl group comprising at least one heteroatom chosen from a nitrogen atom and an oxygen atom, wherein the heterocycloalkyl group is optionally substituted with a linear or branched alkyl group,

- an $NR_6'R_6''$ group where **R_6'** and **R_6''** are independently chosen from a hydrogen atom or a linear, branched or cyclic (C_1-C_4)alkyl group, and

- an -O-(C_1-C_4)alkyl group optionally substituted with a hydroxy group, or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, wherein **R_1** represents a group -NHCO-PhO*, -Ph-O* or -Ph-NHCO*, or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 1, wherein **R_2** represents a methyl group, or a pharmaceutically acceptable salt thereof.

4. The compound according to claim 1, wherein:
R_3 represents a hydrogen atom,
R_4 represents an -alkyl-$COOR_5$ group, wherein R_5 represents a hydrogen atom or an alkyl group, or a pharmaceutically acceptable salt thereof.

5. The compound according to claim 1, such that the monomer units M_1 and M_2 are identical.

6. The compound according to claim 1 chosen from the following compounds:

-2,2'-{oxybis[ethane-2,1-diyloxyethane-2,1-diyloxybenzene-3,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-6,3(2*H*)-diyl)]} diacetic acid;
-2,2'-{oxybis[ethane-2,1-diyloxyethane-2,1-diyloxybenzene-3,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-6,3(2*H*)-diyl)]} diacetic acid;
-2,2'-{ethane-1,2-diylbis[oxyethane-2,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-6,3(2*H*)-diyl)]} diacetic acid;
-2,2'-{hexane-1,6-diylbis[imino(2-oxoethane-2,1-diyl)oxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-6,3(2*H*)-diyl)]}diacetic acid;
-2,2'-{butane-1,4-diylbis[imino(2-oxoethane-2,1-diyl)oxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-6,3(2*H*)-diyl)]}diacetic acid;
-2,2'-{hexane-1,6-diylbis[imino(2-oxoethane-2,1-diyl)oxybenzene-3,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-6,3(2*H*)-diyl)]}diacetic acid;
2,2'-{butane-1,4-diylbis[imino(2-oxoethane-2,1-diyl)oxybenzene-3,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-6,3(2*H*)-diyl)]}diacetic acid;
2,2'-({[2-(2-hydroxyethoxy)ethyl]imino}bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-

7,3(2*H*)-diyl)])diacetic acid;
2,2'-{(ethylimino)bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]} diacetic acid;
2,2'-({[2-(morpholin-4-yl)ethyl]imino}bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)])diacetic acid;
2,2'-({[2-(4-methylpiperazin-1-yl)ethyl]imino}bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)])diacetic acid;
2,2'-{[(pyridin-4-ylmethyl)imino]bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]}diacetic acid;
2,2'-({[4-(dimethylamino)benzyl]imino}bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)])diacetic acid;
2,2'-({[2-(diethylamino)ethyl]imino}bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)])diacetic acid;
2,2'-{piperazine-1,4-diylbis[propane-3,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]}diacetic acid;
[7-({1-[4-({9-[4-(3-{[3-(carboxymethyl)-2,4-dioxo-1,4-dihydroquinazolin-7(2*H*)-yl]carbonyl}-2-methylindolizin-1-yl)phenyl]-4-hydroxy-4-oxido-9-oxo-3,5-dioxa-8-aza-4λ^5-phosphanon-1-yl}carbamoyl)phenyl]-2-methylindolizin-3-yl}carbonyl)-2,4-dioxo-1,4-dihydroquinazolin-3(2*H*)-yl]acetic acid;
2,2'-{ethane-1,2-diylbis[oxyethane-2,1-diylcarbamoylbenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]}diacetic acid;
2,2'-{ethane-1,2-diylbis[oxyethane-2,1-diylcarbamoylbenzene-3,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]}diacetic acid;
[7-({1-[3-({9-[3-(3-{[3-(carboxymethyl)-2,4-dioxo-1,4-dihydroquinazolin-7(2*H*)-yl]carbonyl}-2-methylindolizin-1-yl)phenyl]-4-hydroxy-4-oxido-9-oxo-3,5-dioxa-8-aza-4λ^5-phosphanon-1-yl}carbamoyl)phenyl]-2-methylindolizin-3-yl}carbonyl)-2,4-dioxo-1,4-dihydroquinazolin-3(2*H*)-yl]acetic acid;

2,2'-{ethane-1,2-diylbis[imino(2-oxoethane-2,1-diyl)oxybenzene-3,1-diylcarbonylimino(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]}diacetic acid; and

a pharmaceutically acceptable salt thereof.

7. A pharmaceutical composition comprising a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

8. A method of activating fibroblast growth factor receptor in a patient, comprising administering to the patient a compound according to claim 1.

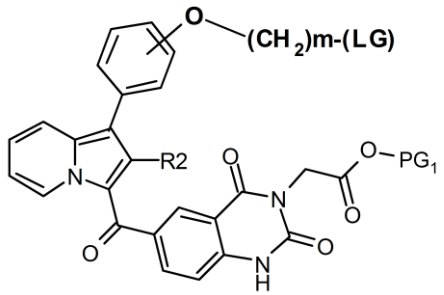
9. The method according to claim 8, wherein the patient suffers from cardiac ischaemia, arteritis, arteriosclerosis, angina pectoris, obesity, diabetes, thromboangitis obliterans, post-angioplasty restenosis, post-endoarterectomy restenosis, muscle injury, muscular dystrophy, myoblast survival, sarcopenia, nociception, chronic pain, peripheral neuropathy, bioartificial pancreatic graft survival, graft revascularization, retinal degeneration, pigmentary retinitis, osteoarthritis, osteoporosis, pre-eclampsia, vascular lesions, acute respiratory distress syndrome or alopecia.

10. A method of promoting angiogenesis in a patient, comprising administering to the patient a compound according to claim 1.

11. A process for preparing a compound according to claim 1, wherein:

(a)

a compound of formula **(IX)**

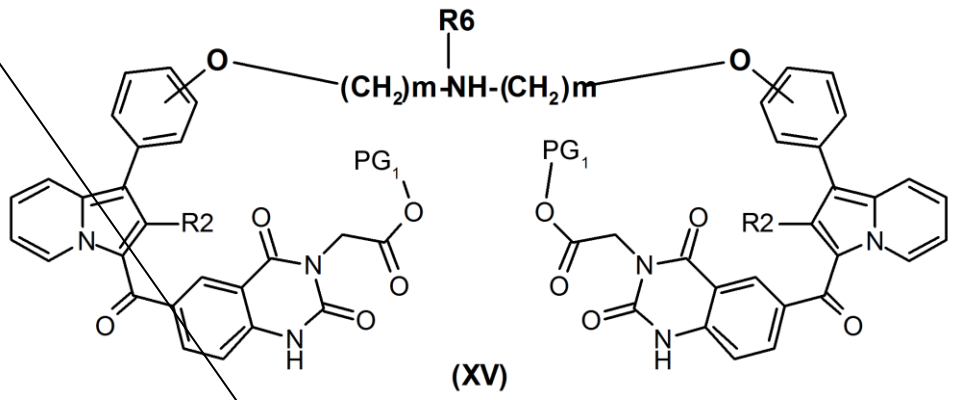


(IX)

in which **m** represents 1, 2, 3, 4, or 5, $\mathbf{R_2}$ represents an alkyl group, PG_1 represents

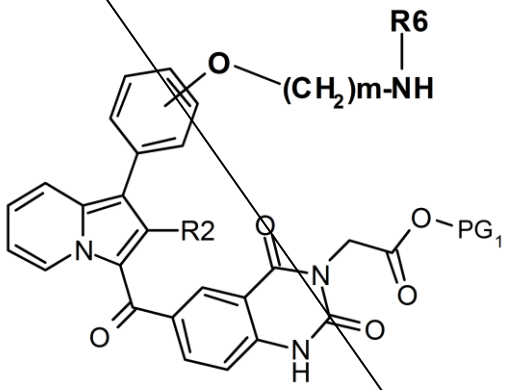
an alkyl group and LG represents a halogen atom or an activated hydroxy group,

reacts with an amine R_6-NH_2 in the presence of a base to give a dimer of formula **(XV)**



(XV)

(b) an amine of formula **(XVI)**



(XVI)

wherein **R_6** represents a (C_1-C_4)alkyl group optionally substituted with one or more substituents independently chosen from:

- an aryl or heteroaryl group, each optionally substituted with hydroxyl or $NR_6'R_6''$ group, wherein **R_6'** and **R_6''** are independently chosen from a hydrogen atom and a linear, branched or cyclic (C_1-C_4)alkyl group,
- a heterocycloalkyl group comprising at least one heteroatom chosen from a nitrogen atom and an oxygen atom optionally substituted with a linear or branched alkyl group,
- an $NR_6'R_6''$ group where **R_6'** and **R_6''** are independently chosen from a hydrogen atom and a linear, branched or cyclic (C_1-C_4)alkyl group, and
- an -O-(C_1-C_4)alkyl group optionally substituted with a hydroxy group, or a

pharmaceutically acceptable salt thereof;

when present in excess, reacts with a stoichiometric amount of the compound of formula (IX) to give the dimer of formula (XV), and

- the dimer of formula **(XV)** is saponified.

CLAIMS

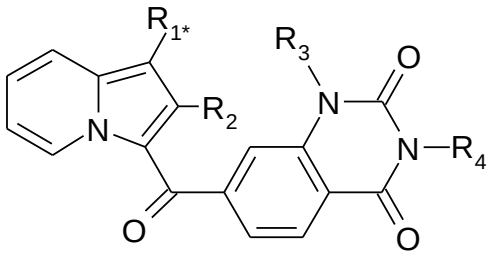
1. A compound of the formula:

$$M_1\text{-}L\text{-}M_2$$

in which M_1 and M_2, which may be identical or different, each represent, independently of one another, a monomer unit M and

L represents a linker group which links M_1 and M_2 covalently, wherein

monomer unit M is of formula (M):



(M)

in which,

* indicates the site of linkage between the monomer unit M and the linker L,

- **R_1** represents

. a group –NHCOPhO*, such that the *-labeled oxygen atom is covalently bonded to linker L;

or

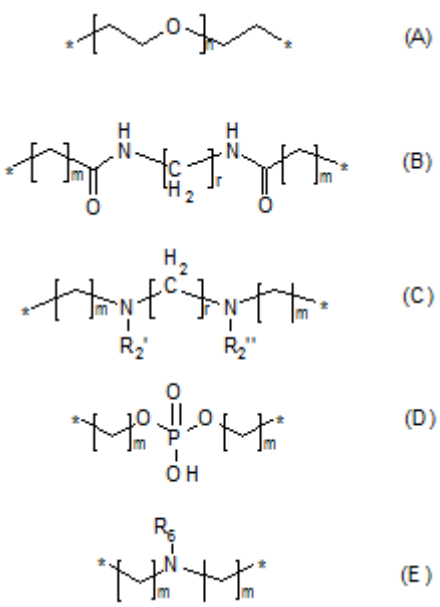
. an aryl or a heteroaryl group, said group being substituted with a group chosen from a divalent oxygen atom, such that the oxygen atom is covalently bonded to the linker L, and an amide group -CONH*-, such that the *-labeled nitrogen atom is covalently bonded to the linker L,

- **R_2** represents an alkyl group,

- **R_3** represents a hydrogen atom or a linear, branched, or cyclic alkyl group, and

- **R_4** represents a hydrogen atom, an alkyl or -alkyl-$COOR_5$ group, with R_5 representing a hydrogen atom or an alkyl group; and

linker L is chosen from formula (A), formula (B), formula (C), formula (D) or formula (E):



wherein

* indicates the atom for connecting L with R_1,

n represents 0, 1, 2, 3, 4, or 5,

m represents 1, 2, 3, 4, or 5,

r represents 1, 2, 3, 4, 5, or 6,

R_2' and **R_2''**, which may be identical or different, represent a linear alkyl radical having from 1 to 5 carbon atoms, and which can be optionally linked to form a ring,

R_6 represents a (C_1-C_4)alkyl group optionally substituted with one or more substituents independently selected from:

- an aryl or heteroaryl group, each optionally substituted with hydroxyl or $NR_6'R_6''$, wherein **R_6'** and **R_6''** are independently chosen from a hydrogen atom or a linear, branched or cyclic (C_1-C_4)alkyl group,

- a heterocycloalkyl group comprising at least one heteroatom chosen from a nitrogen atom and an oxygen atom, wherein the heterocycloalkyl group is optionally substituted with a linear or branched alkyl group,

- an $NR_6'R_6''$ group where **R_6'** and **R_6''** are independently chosen from a hydrogen atom or a linear, branched or cyclic (C_1-C_4)alkyl group, and

- an -O-(C_1-C_4)alkyl group optionally substituted with a hydroxy group, or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, wherein **R_1** represents a group -NHCO-PhO*, -Ph-O* or -Ph-NHCO*, or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 1, wherein $\mathbf{R_2}$ represents a methyl group, or a pharmaceutically acceptable salt thereof.

4. The compound according to claim 1, wherein:
$\mathbf{R_3}$ represents a hydrogen atom,
$\mathbf{R_4}$ represents an -alkyl-$COOR_5$ group, wherein R_5 represents a hydrogen atom or an alkyl group, or a pharmaceutically acceptable salt thereof.

5. The compound according to claim 1, such that the monomer units M_1 and M_2 are identical.

6. The compound according to claim 1 chosen from the following compounds:

2,2'-({[2-(2-hydroxyethoxy)ethyl]imino}bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)])diacetic acid;
2,2'-{(ethylimino)bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]} diacetic acid;
2,2'-({[2-(morpholin-4-yl)ethyl]imino}bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)])diacetic acid;
2,2'-({[2-(4-methylpiperazin-1-yl)ethyl]imino}bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)])diacetic acid;
2,2'-{[(pyridin-4-ylmethyl)imino]bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]}diacetic acid;
2,2'-({[4-(dimethylamino)benzyl]imino}bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)])diacetic acid;
2,2'-({[2-(diethylamino)ethyl]imino}bis[pentane-5,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)])diacetic acid;
2,2'-{piperazine-1,4-diylbis[propane-3,1-diyloxybenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-

diyl)]}diacetic acid;

[7-({1-[4-({9-[4-(3-{[3-(carboxymethyl)-2,4-dioxo-1,4-dihydroquinazolin-7(2*H*)-yl]carbonyl}-2-methylindolizin-1-yl)phenyl]-4-hydroxy-4-oxido-9-oxo-3,5-dioxa-8-aza-4λ^5-phosphanon-1-yl}carbamoyl)phenyl]-2-methylindolizin-3-yl}carbonyl)-2,4-dioxo-1,4-dihydroquinazolin-3(2*H*)-yl]acetic acid;

2,2'-{ethane-1,2-diylbis[oxyethane-2,1-diylcarbamoylbenzene-4,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]}diacetic acid;

2,2'-{ethane-1,2-diylbis[oxyethane-2,1-diylcarbamoylbenzene-3,1-diyl(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]}diacetic acid;

[7-({1-[3-({9-[3-(3-{[3-(carboxymethyl)-2,4-dioxo-1,4-dihydroquinazolin-7(2*H*)-yl]carbonyl}-2-methylindolizin-1-yl)phenyl]-4-hydroxy-4-oxido-9-oxo-3,5-dioxa-8-aza-4λ^5-phosphanon-1-yl}carbamoyl)phenyl]-2-methylindolizin-3-yl}carbonyl)-2,4-dioxo-1,4-dihydroquinazolin-3(2*H*)-yl]acetic acid;

2,2'-{ethane-1,2-diylbis[imino(2-oxoethane-2,1-diyl)oxybenzene-3,1-diylcarbonylimino(2-methylindolizine-1,3-diyl)carbonyl(2,4-dioxo-1,4-dihydroquinazoline-7,3(2*H*)-diyl)]}diacetic acid; and

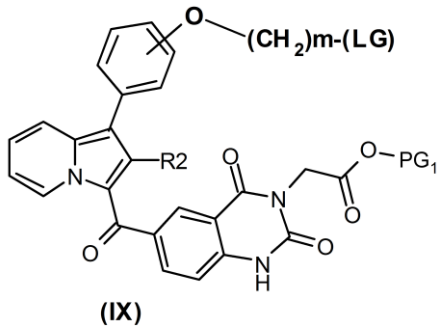
a pharmaceutically acceptable salt thereof.

7. A pharmaceutical composition comprising a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

8. A process for preparing a compound according to claim 1, wherein:

(a)

a compound of formula **(IX)**

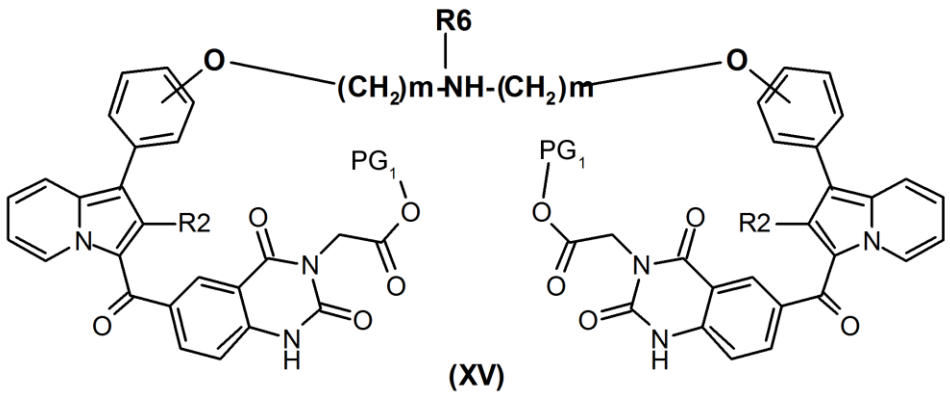


(IX)

in which **m** represents 1, 2, 3, 4, or 5, $\mathbf{R_2}$ represents an alkyl group, PG_1 represents

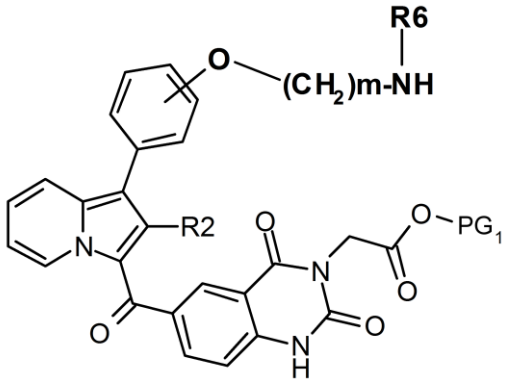
an alkyl group and LG represents a halogen atom or an activated hydroxy group,

reacts with an amine R_6-NH_2 in the presence of a base to give a dimer of formula **(XV)**



(XV)

(b) an amine of formula **(XVI)**



(XVI)

wherein **R_6** represents a (C_1-C_4)alkyl group optionally substituted with one or more substituents independently chosen from:

- an aryl or heteroaryl group, each optionally substituted with hydroxyl or $NR_6'R_6''$ group, wherein **R_6'** and **R_6''** are independently chosen from a hydrogen atom and a linear, branched or cyclic (C_1-C_4)alkyl group,

- a heterocycloalkyl group comprising at least one heteroatom chosen from a nitrogen atom and an oxygen atom optionally substituted with a linear or branched alkyl group,

- an $NR_6'R_6''$ group where **R_6'** and **R_6''** are independently chosen from a hydrogen atom and a linear, branched or cyclic (C_1-C_4)alkyl group, and

- an -O-(C_1-C_4)alkyl group optionally substituted with a hydroxy group, or a

pharmaceutically acceptable salt thereof;

when present in excess, reacts with a stoichiometric amount of the compound of formula (IX) to give the dimer of formula (XV), and

- the dimer of formula **(XV)** is saponified.