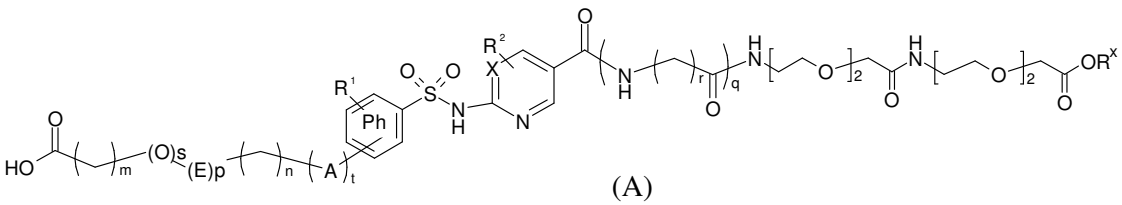
~~Claims~~

CLAIMS

1. A sulfonamide of formula (A)



(A)

wherein:

A is selected from the group consisting of oxygen atom, $-CH_2CH_2-$ group, $-OCH_2-$ group and $-CH_2O-$ group;

E represents a $-C_6H_3R-$ group with R being a hydrogen atom or a halogen atom, wherein the halogen atom is selected from the group consisting of fluorine, chlorine, bromine and iodine atom;

X represents a nitrogen atom or a -CH- group;

m is an integer in the range from 5 to 17;

n is zero or an integer in the range from 1 to 3;

p is zero or 1;

q is zero or 1;

r is an integer in the range from 1 to 6;

s is zero or 1;

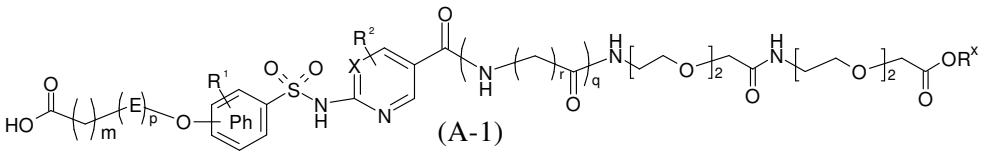
t is zero or 1;

R^1 represents at least one residue selected from the group of hydrogen atom, halogen atom, C1 to C3 alkyl group and halogenated C1 to C3 alkyl group;

R^2 represents at least one residue selected from the group of hydrogen atom, halogen atom, C1 to C3 alkyl group and halogenated C1 to C3 alkyl group;

R^x represents a hydrogen atom or an activation group.

2. The sulfonamide according to claim 1 having the formula (A-1)



(A-1)

wherein:

E represents a -C_6H_3R- group with R being a hydrogen atom or a halogen atom, wherein the halogen atom is selected from the group consisting of fluorine, chlorine, bromine and iodine atom;

X represents a nitrogen atom or a –CH- group;

p is zero or 1;

q is zero or 1;

r is an integer in the range from 1 to 6;

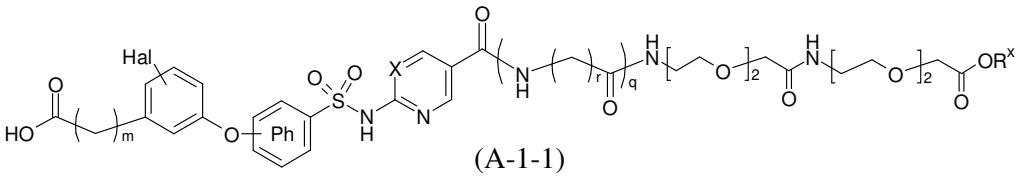
R^1 represents at least one residue selected from the group of hydrogen atom and halogen atom;

R^2 represents at least one residue selected from the group of hydrogen atom, C1 to C3 alkyl group and halogenated C1 to C3 alkyl group;

R^x represents a hydrogen atom or an activation group; and

with m being an integer in the range from 5 to 15 if p is zero, or m being an integer in the range from 7 to 15 if p is 1.

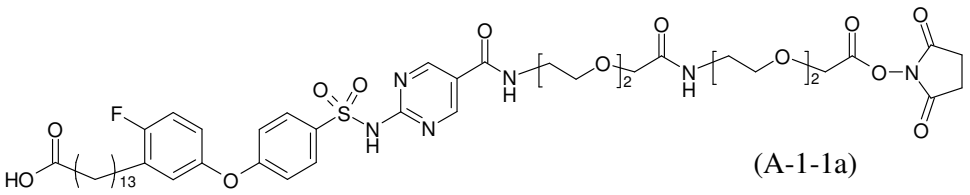
3. The sulfonamide according to claim 1 or 2, wherein the sulfonamide has the formula (A-1-1)



(A-1-1)

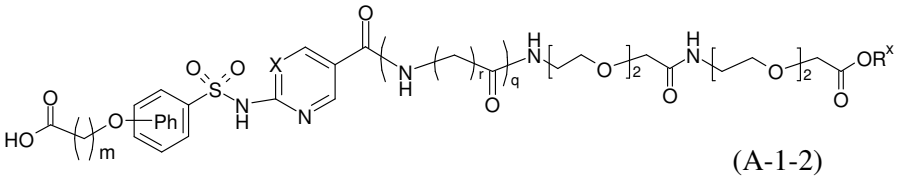
wherein X is a nitrogen atom or a –CH- group; m is an integer in the range from 7 to 15; r is an integer in the range from 1 to 6; q is zero or 1; Hal is a halogen atom selected from the group consisting of fluorine, chlorine, bromine and iodine atom; R^x represents a hydrogen atom or an activation group; and the HOOC-$(CH_2)_m$-C_6H_3Hal-O- group is situated in meta or para position on phenyl ring Ph with respect to the -$S(O)_2$- group.

4. The sulfonamide according to any of claims 1 to 3, wherein the sulfonamide has the formula (A-1-1a)



(A-1-1a)

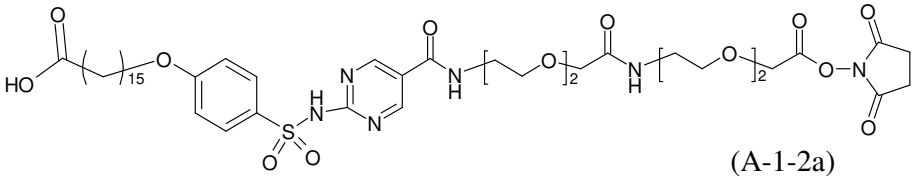
5. The sulfonamide according to claim 1 or 2, wherein the sulfonamide has the formula (A-1-2)



(A-1-2)

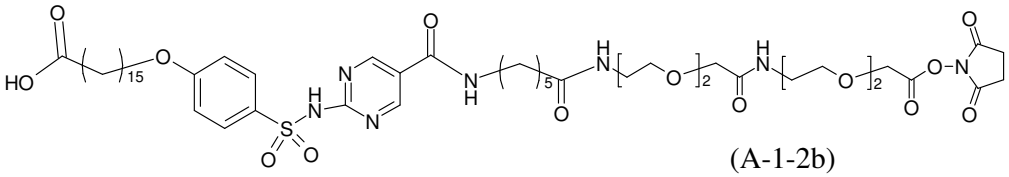
wherein X is a nitrogen atom or a -CH- group; m is an integer in the range from 5 to 15; r is an integer in the range from 1 to 6; q is zero or 1; and the $HOOC-(CH_2)_m-O-$ group is situated in meta or para position on phenyl ring Ph with respect to the $-S(O)_2-$ group.

6. The sulfonamide according to any of claims 1 to 2 or 5, wherein the sulfonamide has the formula (A-1-2a)



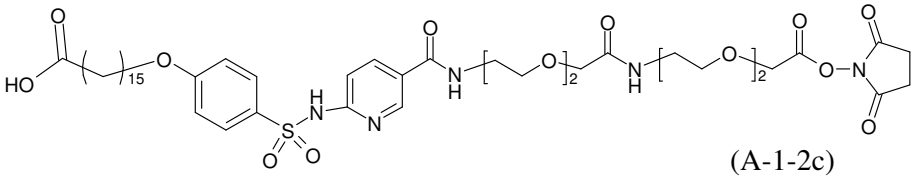
(A-1-2a) or

the formula (A-1-2b)



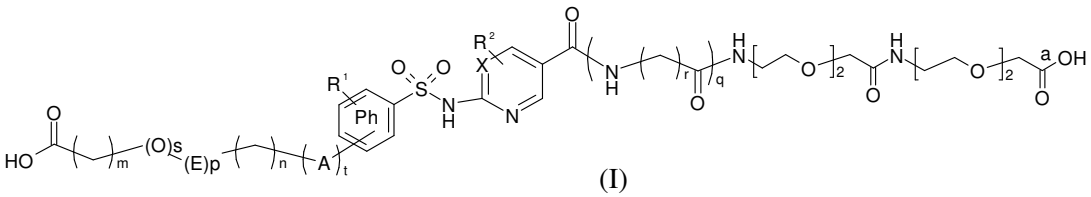
(A-1-2b) or

the formula (A-1-2c)



(A-1-2c)

7. A conjugate comprising a sulfonamide of formula (I) and an active pharmaceutical ingredient



(I)

wherein in the sulfonamide of formula (I):

A is selected from the group consisting of oxygen atom, -CH_2CH_2- group, -OCH_2-group and -CH_2O- group;

E represents a -C_6H_3R- group with R being a hydrogen atom or a halogen atom, wherein the halogen atom is selected from the group consisting of fluorine, chlorine, bromine and iodine atom;

X represents a nitrogen atom or a –CH- group;

m is an integer in the range from 5 to 17;

n is zero or an integer in the range from 1 to 3;

p is zero or 1;

q is zero or 1;

r is an integer in the range from 1 to 6;

s is zero or 1;

t is zero or 1;

R^1 represents at least one residue selected from the group of hydrogen atom, halogen atom, C1 to C3 alkyl group and halogenated C1 to C3 alkyl group;

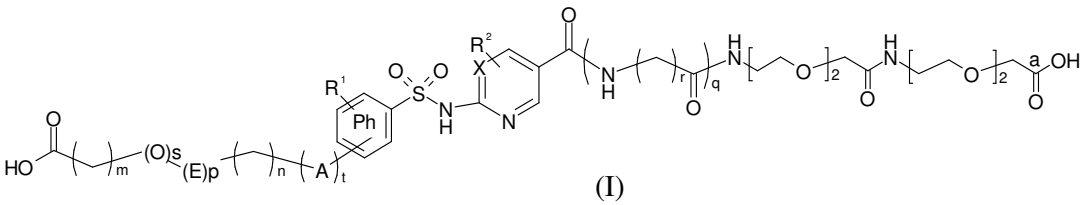
R^2 represents at least one residue selected from the group of hydrogen atom, halogen atom, C1 to C3 alkyl group and halogenated C1 to C3 alkyl group;

wherein the sulfonamide of formula (I) is covalently bound to the active pharmaceutical ingredient in that the terminal carboxy group “a” of the sulfonamide of formula (I) is covalently bound to an amino group of the pharmaceutically active agent.

8. The conjugate according to claim 7, wherein the active pharmaceutical ingredient is selected from the group consisting of insulin, insulin analog, GLP-1, and GLP-1 analog.

9. The conjugate according to claim 7 or 8, wherein the active pharmaceutical ingredient is insulin or an insulin analog, wherein the amino group of the peptide, to which the sulfonamide of formula (I) is covalently bound, is an epsilon amino group of a lysine present in the insulin or insulin analog or is the N-terminal amino group of the B chain of the insulin or insulin analog.

10. A process for preparing a conjugate comprising a sulfonamide of formula (I) and an active pharmaceutical ingredient



(I)

wherein in the sulfonamide of formula (I):

A is selected from the group consisting of oxygen atom, -CH_2CH_2- group, -OCH_2- group and –CH_2O- group;

E represents a -C_6H_3R- group with R being a hydrogen atom or a halogen atom, wherein the halogen atom is selected from the group consisting of fluorine, chlorine, bromine and iodine atom;

X represents a nitrogen atom or a –CH- group;

m is an integer in the range from 5 to 17;

n is zero or an integer in the range from 1 to 3;

p is zero or 1;

q is zero or 1;

r is an integer in the range from 1 to 6;

s is zero or 1;

t is zero or 1;

R^1 represents at least one residue selected from the group of hydrogen atom, halogen atom, C1 to C3 alkyl group and halogenated C1 to C3 alkyl group;

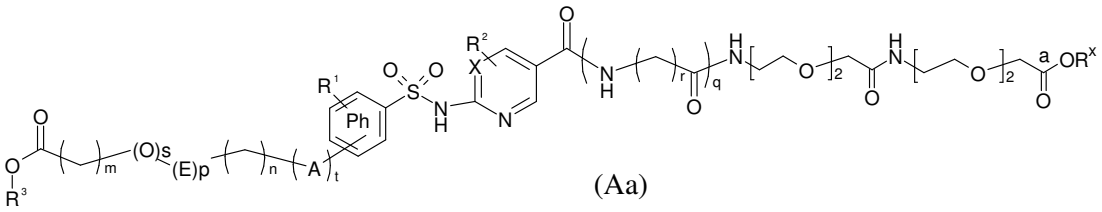
R^2 represents at least one residue selected from the group of hydrogen atom, halogen atom, C1 to C3 alkyl group and halogenated C1 to C3 alkyl group;

wherein the sulfonamide of formula (I) is covalently bound to the active pharmaceutical ingredient in that the terminal carboxy group “a” of the sulfonamide

of formula (I) is covalently bound to an amino group of the active pharmaceutical ingredient;

comprising:

(a) providing a sulfonamide of formula (Aa)



(Aa)

wherein X, Y, A, E, R^1, R^2 and the indices m, n, p, q, r, s, t have the meaning as defined in claim 1, R^x is a hydrogen atom or an activation group; and R^3 is a protective group or a hydrogen atom,; and a active pharmaceutical ingredient having a protected or unprotected C terminus;

(b) reacting the sulfonamide of formula (Aa) and the active pharmaceutical ingredient having a protected or unprotected C terminus under conditions suitable to form an amide bond between the free or activated carboxy group “a” of the sulfonamide of formula (Aa) and an amino group of the active pharmaceutical ingredient having a protected or unprotected C terminus;

(c) optionally removing one or both protection groups.

~~11. A conjugate comprising a sulfonamide of formula (I) and an active pharmaceutical ingredient obtained or obtainable from the process according to claim 10.~~

~~12~~

11. Pharmaceutical composition comprising in a pharmaceutically effective amount the conjugate comprising a sulfonamide of formula (I) and an active pharmaceutical ingredient according to any of claims 7 to 9 ~~or according to claim 11~~.

~~13~~12. The conjugate comprising a sulfonamide of formula (I) and an active pharmaceutical ingredient according to any of claims 7 to 9 ~~or according to claim 11~~ for use as a medicament.

~~14~~13. The conjugate comprising a sulfonamide of formula (I) and an active pharmaceutical ingredient according to any of claims 7 to 9 ~~or according to claim~~

11 for use as a medicament for treatment of a disease selected from the group consisting of gestational diabetes, diabetes mellitus type 1, diabetes mellitus type 2 and hyperglycemia and/or for lowering blood glucose levels.