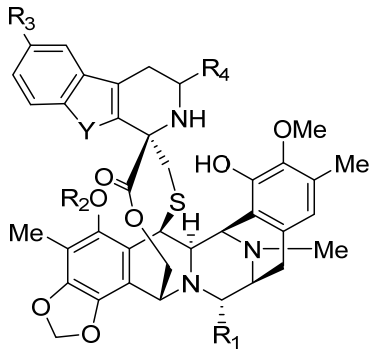
Claims

1. A drug conjugate comprising a drug moiety covalently attached to the rest of the drug conjugate, the drug conjugate having formula $[D\text{-}(X)_b\text{-}(AA)_w\text{-}(T)_g\text{-}(L)\text{-}]_n\text{-}Ab$ wherein:

D is a drug moiety having the following formula (I) or a pharmaceutically acceptable salt, ester, solvate, tautomer or stereoisomer thereof,



(I)

wherein:

D is covalently attached via a hydroxy or amine group to $(X)_b$ if any, or $(AA)_w$ if any, or to $(T)_g$ if any, or (L);

Y is -NH- or -O-;

R_1 is -OH or -CN;

R_2 is a $-C(=O)R_a$ group;

R_3 is hydrogen or a $-OR_b$ group;

R_4 is selected from $-CH_2O-$ and $-CH_2NH-$;

R_a is selected from hydrogen, substituted or unsubstituted C_1-C_{12} alkyl, substituted or unsubstituted C_2-C_{12} alkenyl, and substituted or unsubstituted C_2-C_{12} alkynyl;

R_b is selected from substituted or unsubstituted C_1-C_{12} alkyl, substituted or unsubstituted C_2-C_{12} alkenyl, and substituted or unsubstituted C_2-C_{12} alkynyl;

X and T are extending groups that may be the same or different;

each AA is independently an amino acid unit;

L is a linker group;

w is an integer ranging from 0 to 12;

b is an integer of 0 or 1;

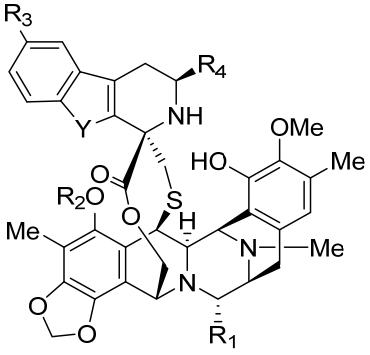
g is an integer of 0 or 1;

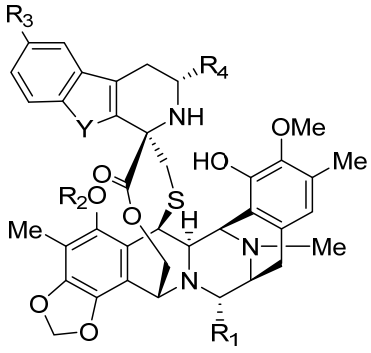
Ab is a moiety comprising at least one antigen binding site; and

n is the ratio of the group $[D\text{-}(X)_b\text{-}(AA)_w\text{-}(T)_g\text{-}(L)\text{-}]$ to the moiety comprising at least one antigen binding site and is in the range from 1 to 20;

wherein the drug moiety D is conjugated via the R_4 position.

2. The drug conjugate according to claim 1, wherein D is selected from formula Ia or Ib, or a pharmaceutically acceptable salt or ester thereof:


Ia


Ib

wherein:

Y is -NH- or -O-;

R_1 is -OH or -CN;

R_2 is a -C(=O) R_a group;

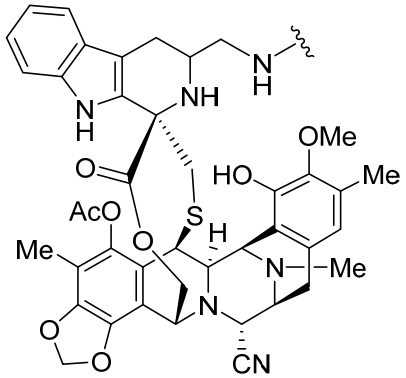
R_3 is hydrogen or a $–OR_b$ group;

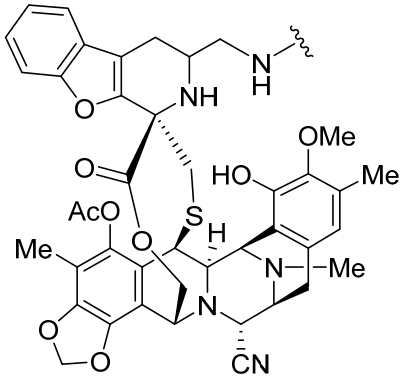
R_4 is selected from $-CH_2O-$ and $-CH_2NH-$;

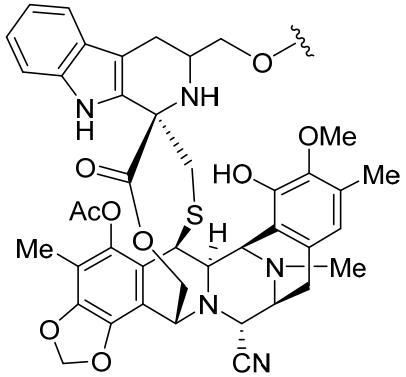
R_a is selected from hydrogen, substituted or unsubstituted C_1-C_{12} alkyl, substituted or unsubstituted C_2-C_{12} alkenyl, and substituted or unsubstituted C_2-C_{12} alkynyl; and

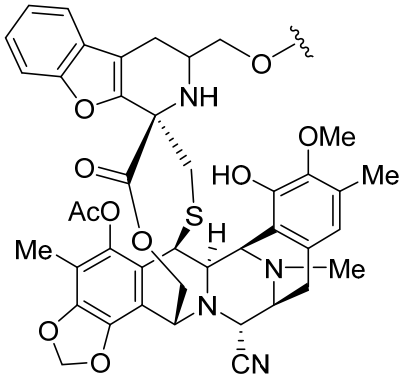
R_b is selected from substituted or unsubstituted C_1-C_{12} alkyl, substituted or unsubstituted C_2-C_{12} alkenyl, and substituted or unsubstituted C_2-C_{12} alkynyl.

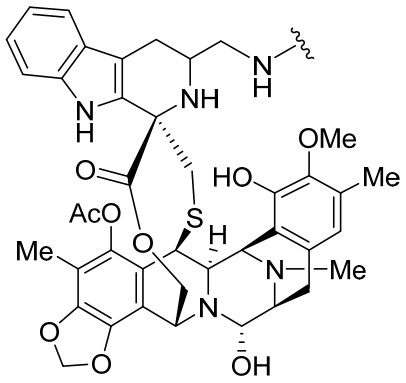
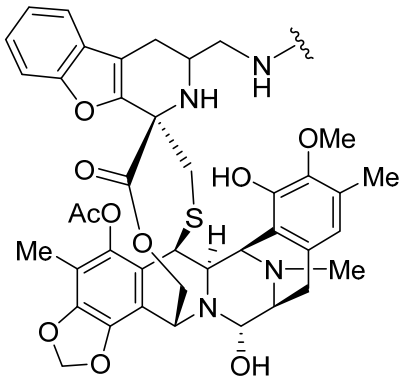
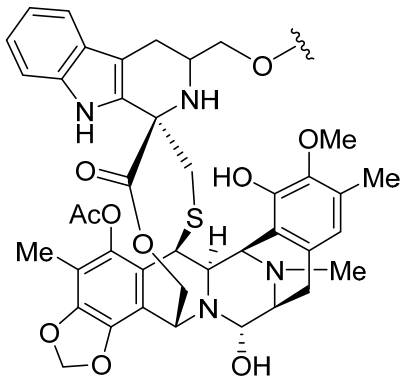
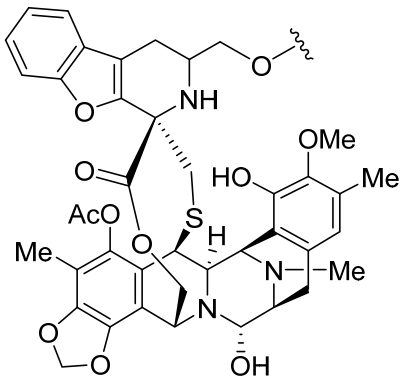
3. The drug conjugate according to claim 1, wherein D is a compound of formula:


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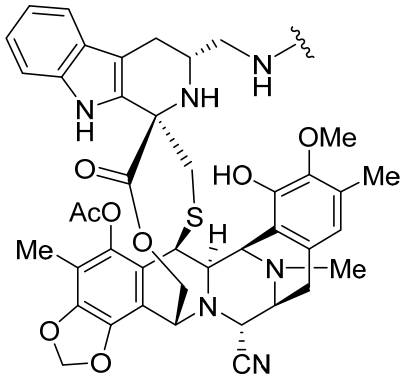
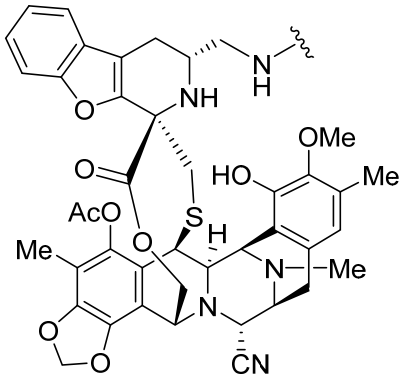
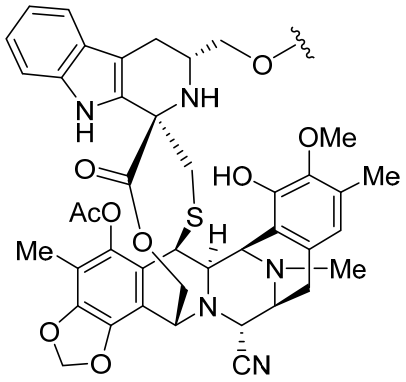
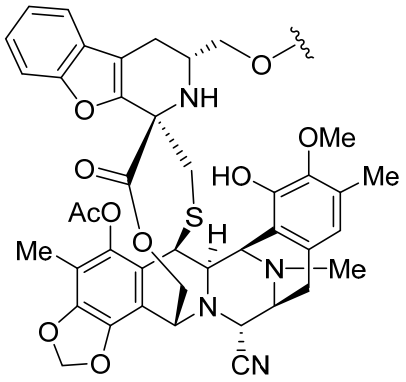

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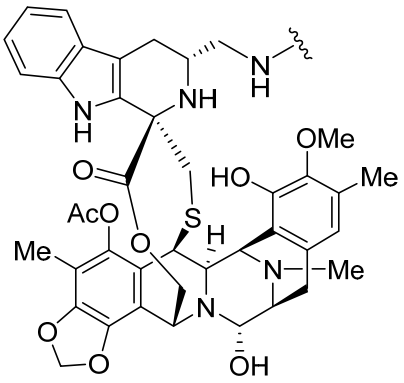
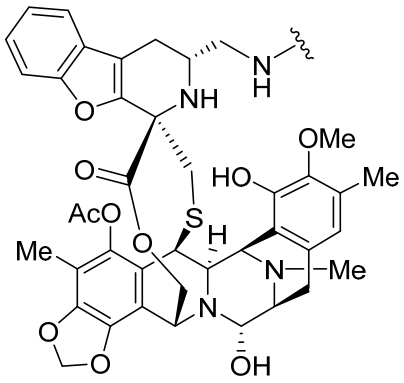
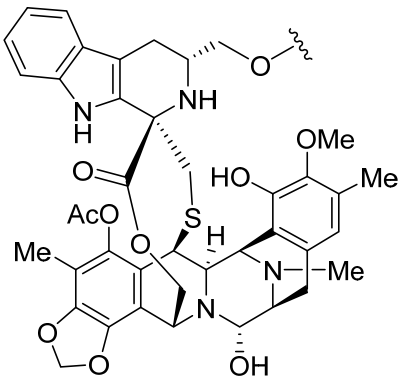
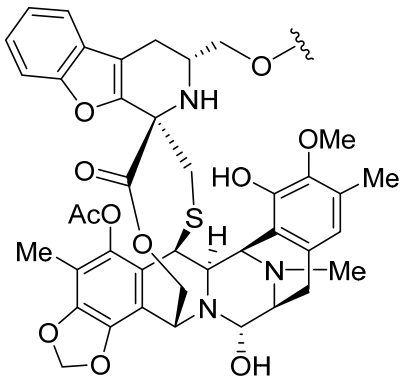
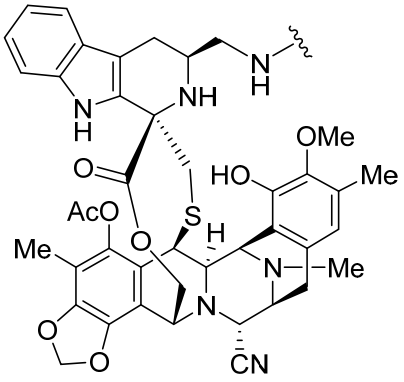
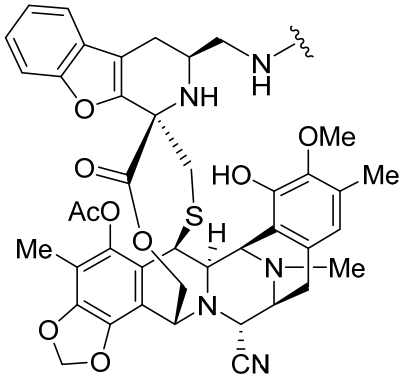
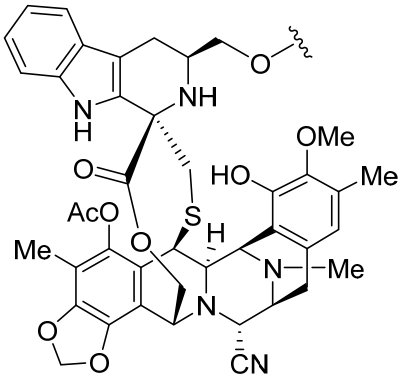
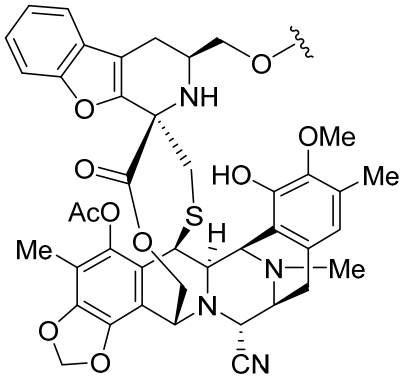

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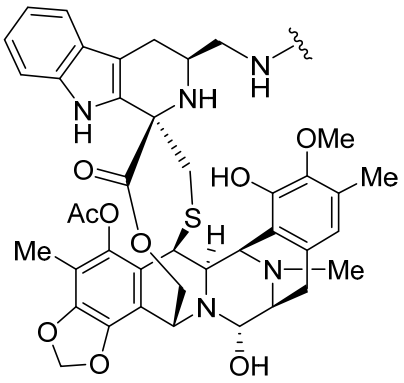
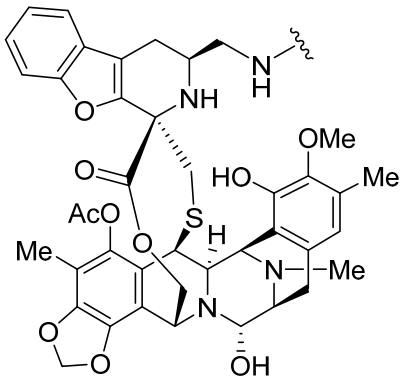
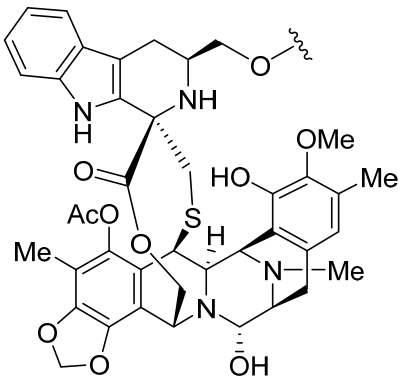
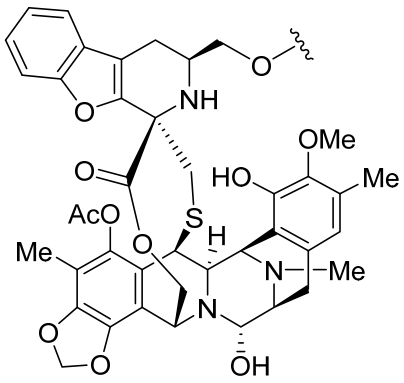
or a pharmaceutically acceptable salt or ester thereof;

wherein the wavy line indicates the point of covalent attachment to $(X)_b$ if any, or $(AA)_w$ if any, or to $(T)_g$ if any, or (L);

preferably of formula:

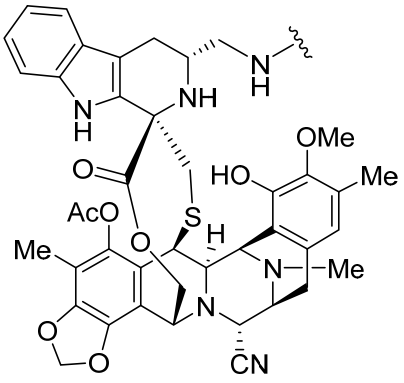
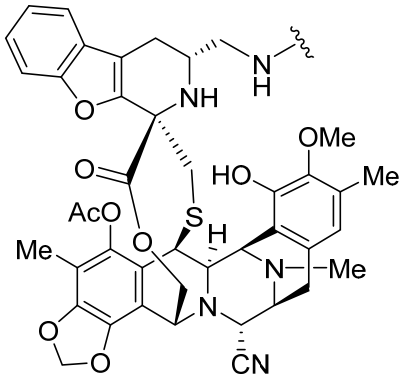
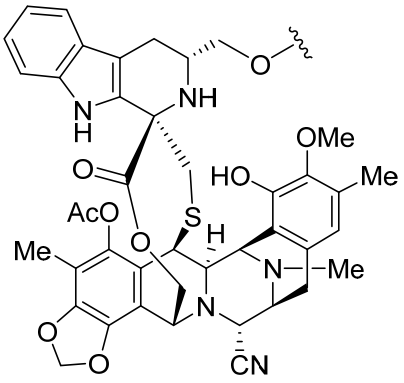
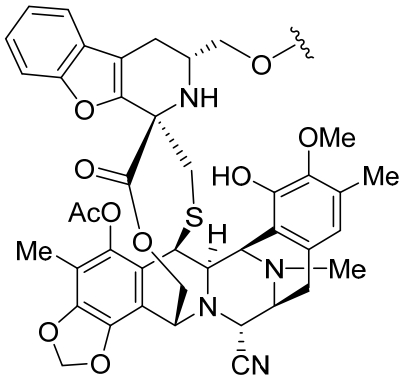

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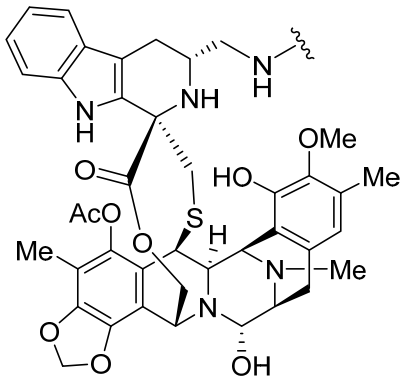
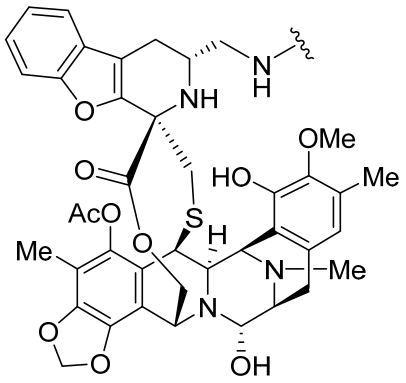
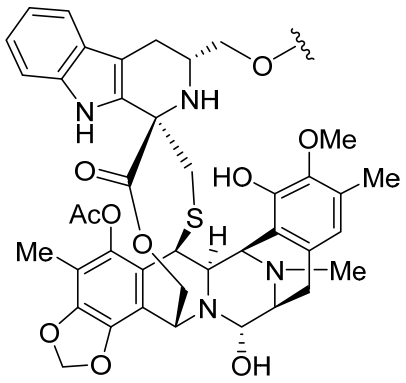
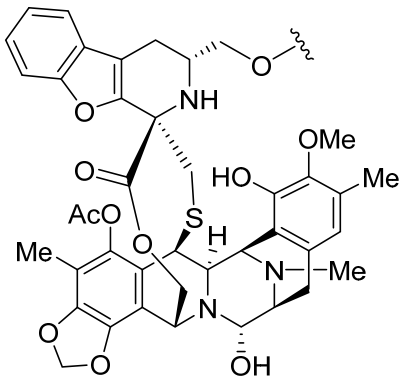

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or a pharmaceutically acceptable salt or ester thereof;

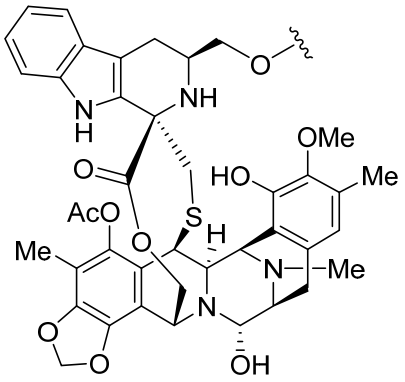
preferably of formula:


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or a pharmaceutically acceptable salt or ester thereof.

4. The drug conjugate according to claim 1, wherein D is a compound of formula:

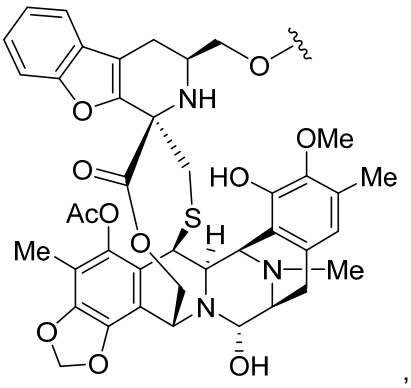

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or a pharmaceutically acceptable salt or ester thereof;

wherein the wavy line indicates the point of covalent attachment to $(X)_b$ if any, or $(AA)_w$ if any, or to $(T)_g$ if any, or (L);

or

wherein D is a compound of formula:



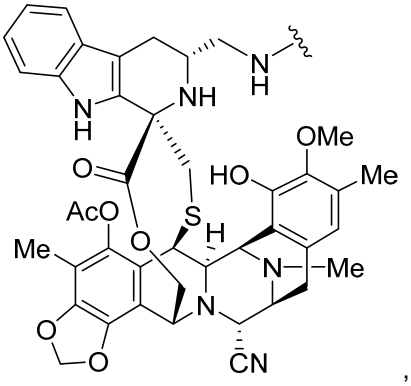
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or a pharmaceutically acceptable salt or ester thereof;

wherein the wavy line indicates the point of covalent attachment to $(X)_b$ if any, or $(AA)_w$ if any, or to $(T)_g$ if any, or (L);

or

wherein D is a compound of formula:



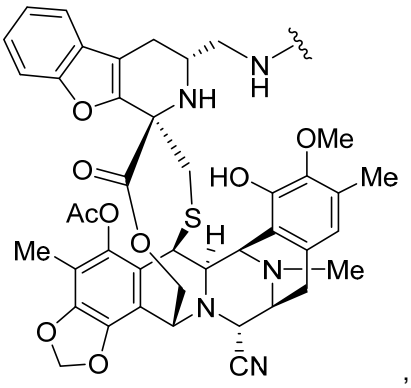
,

or a pharmaceutically acceptable salt or ester thereof;

wherein the wavy line indicates the point of covalent attachment to $(X)_b$ if any, or $(AA)_w$ if any, or to $(T)_g$ if any, or (L);

or

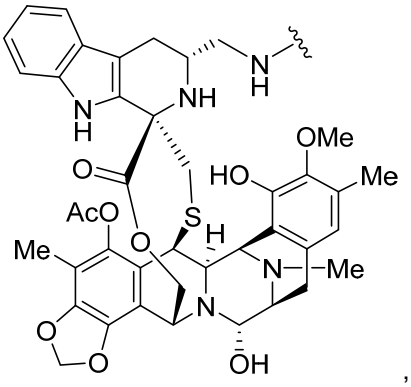
wherein D is a compound of formula:



or a pharmaceutically acceptable salt or ester thereof;

wherein the wavy line indicates the point of covalent attachment to $(X)_b$ if any, or $(AA)_w$ if any, or to $(T)_g$ if any, or (L); or

wherein D is a compound of formula:

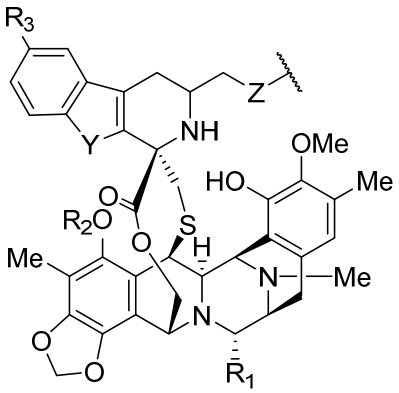


or a pharmaceutically acceptable salt or ester thereof;

wherein the wavy line indicates the point of covalent attachment to $(X)_b$ if any, or $(AA)_w$ if any, or to $(T)_g$ if any, or (L).

5. A drug conjugate comprising a drug moiety covalently attached to the rest of the drug conjugate, the drug conjugate having formula $[D-(X)_b-(AA)_w-(T)_g-(L)-]_n$-Ab wherein:

D is a drug moiety having the following formula (IH) or a pharmaceutically acceptable salt, ester, solvate, tautomer or stereoisomer thereof:



(IH)

wherein:

the wavy line indicates the point of covalent attachment to $(X)_b$ if any, or $(AA)_w$ if any, or to $(T)_g$ if any, or (L);

each Y and Z is independently selected from -NH- and -O-;

R_1 is -OH or -CN;

R_2 is a $-C(=O)R_a$ group;

R_3 is hydrogen or a $-OR_b$ group;

R_a is selected from hydrogen, substituted or unsubstituted C_1-C_{12} alkyl, substituted or unsubstituted C_2-C_{12} alkenyl, and substituted or unsubstituted C_2-C_{12} alkynyl, wherein the optional substituents are one or more substituents R_x; and

R_b is selected from substituted or unsubstituted C_1-C_{12} alkyl, substituted or unsubstituted C_2-C_{12} alkenyl, and substituted or unsubstituted C_2-C_{12} alkynyl, wherein the optional substituents are one or more substituents R_x;

substituents R_x are selected from the group consisting of C_1-C_{12} alkyl groups which may be optionally substituted with at least one group R_y, C_2-C_{12} alkenyl groups which may be optionally substituted with at least one group R_y, C_2-C_{12} alkynyl groups which may be optionally substituted with at least one group R_y, halogen atoms, oxo groups, thio groups, cyano groups, nitro groups, OR_y, $OCOR_y$, $OCOOR_y$, COR_y, $COOR_y$, $OCONR_yR_z$, $CONR_yR_z$, $S(O)R_y$, SO_2R_y, $P(O)(R_y)OR_z$, NR_yR_z, NR_yCOR_z, $NR_yC(=O)NR_yR_z$, $NR_yC(=NR_y)NR_yR_z$, aryl groups having from 6 to 18 carbon atoms in one or more rings which may optionally be substituted with one or more substituents which may be the same or different selected from the group consisting of R_y, OR_y, $OCOR_y$, $OCOOR_y$, NR_yR_z, NR_yCOR_z, and $NR_yC(=NR_y)NR_yR_z$, aralkyl groups comprising an alkyl group having from 1 to 12 carbon atoms substituted with an optionally substituted aryl group as defined above, aralkyloxy groups comprising an alkoxy group having from 1 to 12 carbon atoms substituted with an optionally substituted aryl group as defined above, and a 5-

to 14- membered saturated or unsaturated heterocyclic group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s), said heterocyclic group optionally being substituted with one or more substituents R_y, and where there is more than one optional substituents on any given group the optional substituents R_y may be the same or different;

each R_y and R_z is independently selected from the group consisting of hydrogen, C_1-C_{12} alkyl groups, C_1-C_{12} alkyl groups that are substituted with at least one halogen atom, aralkyl groups comprising a C_1-C_{12} alkyl group that is substituted with an aryl group having from 6 to 18 carbon atoms in one or more rings and heterocycloalkyl groups comprising a C_1-C_{12} alkyl group that is substituted with a 5- to 14- membered saturated or unsaturated heterocyclic group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s);

X and T are extending groups that may be the same or different;

each AA is independently an amino acid unit;

L is a linker group;

w is an integer ranging from 0 to 12;

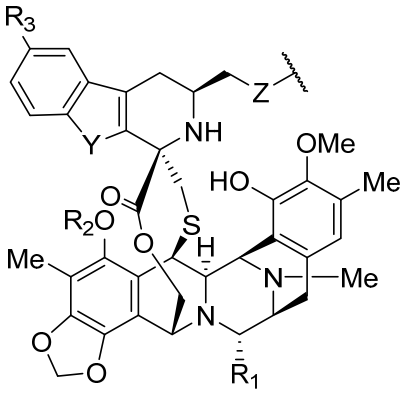
b is an integer of 0 or 1;

g is an integer of 0 or 1;

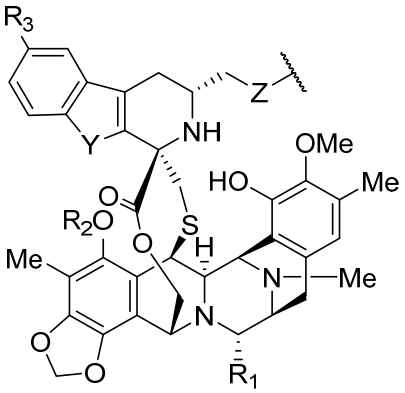
Ab is a moiety comprising at least one antigen binding site; and

n is the ratio of the group $[D\text{-}(X)_b\text{-}(AA)_w\text{-}(T)_g\text{-}(L)\text{-}]$ to the moiety comprising at least one antigen binding site and is in the range from 1 to 20.

6. A drug conjugate according to claim 5, or a pharmaceutically acceptable salt, ester, solvate, tautomer or stereoisomer thereof, wherein D is a drug moiety selected from formulas (IHa) and (IHb):



(IHa)

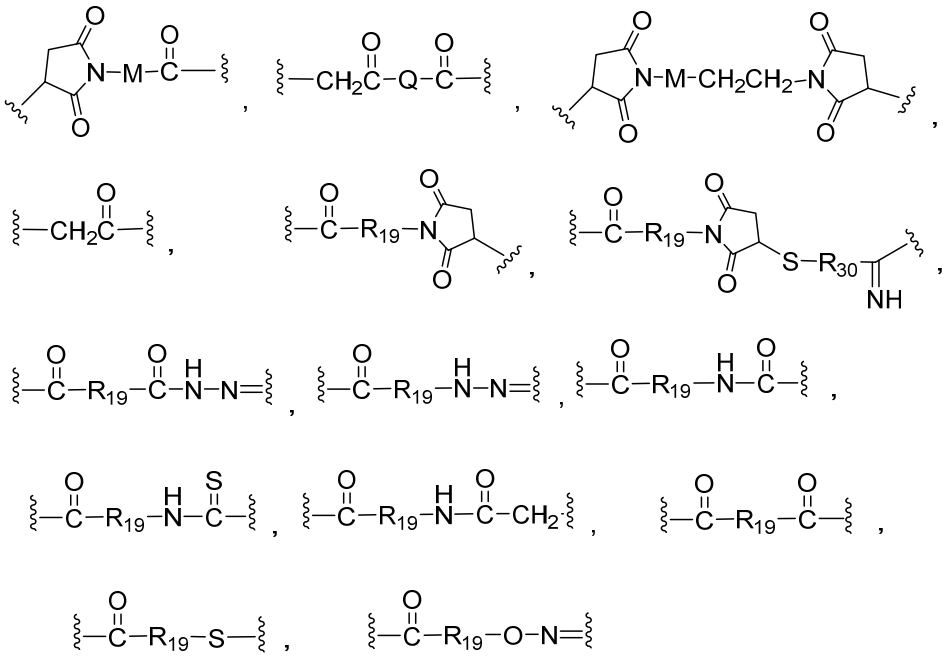


(IHb)

where the wavy lines, R_1, R_2, R_3, Y, and Z are as defined for formula (IH).

7. The drug conjugate according to any one of claims 1 to 6, wherein the salt is selected from hydrochloride, hydrobromide, hydroiodide, sulfate, nitrate, phosphate, acetate, trifluoroacetate, maleate, fumarate, citrate, oxalate, succinate, tartrate, malate, mandelate, methanesulfonate, *p*-toluenesulfonate, sodium, potassium, calcium, ammonium, ethylenediamine, ethanolamine, *N*,*N*-dialkylenethanolamine, triethanolamine and basic aminoacids.

8. A drug conjugate according to any one of the preceding claims, wherein L is a linker group selected from the group consisting of:



wherein

the wavy lines indicate the point of covalent attachments to an Ab (the wavy line to the right) and to $(T)_g$ if any, or $(AA)_w$ if any, or $(X)_b$ if any, or D (the wavy line to the left);

R_{19} is selected from -C_1-C_{12} alkylene-, -C_3-C_8 carbocyclo, -O-(C_1-C_{12} alkylene), -C_6-C_{18} arylene in one or more rings which may optionally be substituted with one or more substituents R_x, -C_1-C_{12} alkylene-C_6-C_{18} arylene- wherein the arylene group is in one or more rings which may optionally be substituted with one or more substituents R_x, -C_6-C_{18} arylene-C_1-C_{12} alkylene- wherein the arylene group is in one or more rings which may optionally be substituted with one or more substituents R_x, -C_1-C_{12} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{12} alkylene-, -C_5-C_{14} heterocyclo- wherein said heterocyclo group may be a saturated or unsaturated group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s), said group optionally being substituted with one or more substituents R_x, -C_1-C_{12} alkylene-(C_5-C_{14} heterocyclo)- wherein said heterocyclo group may be a saturated or unsaturated group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s), said group optionally being substituted with one or more substituents R_x, -(C_5-C_{14} heterocyclo)-C_1-C_{12} alkylene- wherein said heterocyclo group may be a saturated or unsaturated group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s), said group optionally being substituted with one or more substituents R_x, -$(OCH_2CH_2)_r$- and -CH_2-$(OCH_2CH_2)_r$-, wherein each of the above alkylene substituents whether alone or attached to another moiety the carbon chain may optionally be substituted by one or more substituents R_x;

R_{30} is a -C_1-C_6 alkylene- group;

M is selected from the group consisting of -C_1-C_6 alkylene-, -C_1-C_6 alkylene-(C_3-C_8 carbocyclo)-, -$(CH_2CH_2O)_s$-, -C_1-C_6 alkylene-(C_3-C_8 carbocyclo)-CON(H or C_1-C_6 alkyl)-C_1-C_6 alkylene-, phenylene which may optionally be substituted with one or more substituents R_x, phenylene-C_1-C_6 alkylene- wherein the phenylene moiety may optionally be substituted with one or more substituents R_x and -C_1-C_6 alkylene-CON(H or C_1-C_6 alkyl)C_1-C_6 alkylene-;

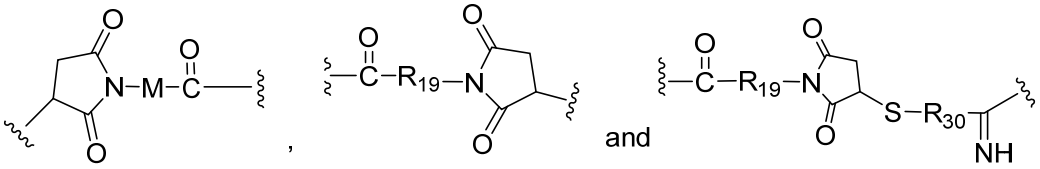
Q is selected from the group consisting of -N(H or C_1-C_6 alkyl)phenylene- and -N(H or C_1-C_6 alkyl)-$(CH_2)_s$;

r is an integer ranging from 1 to 10; and

s is an integer ranging from 1 to 10;

or

wherein L is a linker group selected from the group consisting of:



wherein:

the wavy lines indicate the point of covalent attachments to an Ab (the wavy line to the right) and to $(T)_g$ if any, or $(AA)_w$ if any, or to $(X)_b$ (the wavy line to the left);

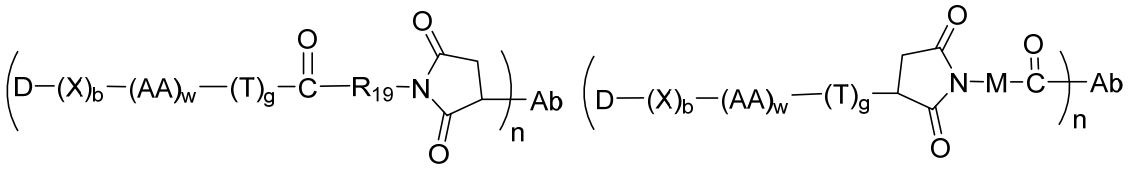
R_{19} is selected from -C_1-C_{12} alkylene-, -O-(C_1-C_{12} alkylene), -C_6-C_{12} arylene in one or more rings which may optionally be substituted with one or more substituents R_x, -C_1-C_{12} alkylene-C_6-C_{12} arylene- wherein the arylene group is in one or more rings which may optionally be substituted with one or more substituents R_x, -C_6-C_{12} arylene-C_1-C_{12} alkylene- wherein the arylene group is in one or more rings which may optionally be substituted with one or more substituents R_x, -C_5-C_{12} heterocyclo- wherein said heterocyclo group may be a saturated or unsaturated group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s), said group optionally being substituted with one or more substituents R_x, -C_1-C_{12} alkylene-(C_5-C_{12} heterocyclo)- wherein said heterocyclo group may be a saturated or unsaturated group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s), said group optionally being substituted with one or more substituents R_x, -(C_5-C_{12} heterocyclo)-C_1-C_{12} alkylene- wherein said heterocyclo group may be a saturated or unsaturated group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s), said group optionally being substituted with one or more substituents R_x, -$(OCH_2CH_2)_r$- and -CH_2-$(OCH_2CH_2)_r$-, wherein each of the above alkylene substituents whether alone or attached to another moiety the carbon chain may optionally be substituted by one or more substituents R_x;

R_{30} is a -C_1-C_6 alkylene- group;

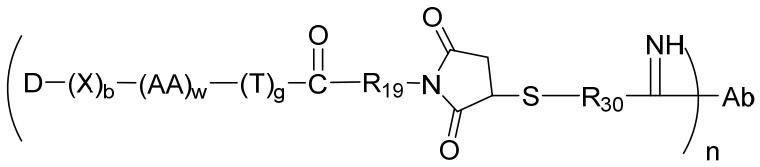
M is selected from the group consisting of -C_1-C_6 alkylene-, -C_1-C_6 alkylene-(C_3-C_8 carbocyclo)- and phenylene which may optionally be substituted with one or more substituents R_x; and

r is an integer ranging from 1-6.

9. A drug conjugate according to any one of claims 1 to 8, selected from the formulas (IV), (V) and (VI):



(IV) (V)



(VI)

wherein:

X and T are extending groups that may be the same or different;

each AA is independently an amino acid unit;

w is an integer ranging from 0 to 12;

b is an integer of 0 or 1;

g is an integer of 0 or 1;

D is a drug moiety;

Ab is a moiety comprising at least one antigen binding site;

n is the ratio of the group [D-$(X)_b$-$(AA)_w$-$(T)_g$-(L)-] wherein L is as defined in formula (IV), (V) or (VI) to the moiety comprising at least one antigen binding site and is in the range from 1 to 20;

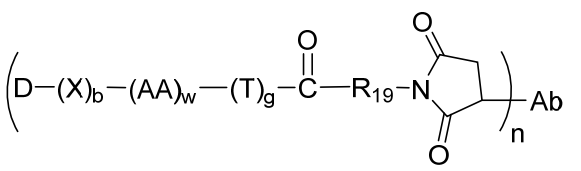
R_{19} is selected from -C_1-C_8 alkylene-, -O-(C_1-C_8 alkylene), -C_1-C_8 alkylene-C_6-C_{12} arylene- wherein the arylene group is in one or more rings which may optionally be substituted with one or more substituents R_x, and -C_6-C_{12} arylene-C_1-C_8 alkylene- wherein the arylene group is in one or more rings which may optionally be substituted with one or more substituents R_x, wherein each of the above alkylene substituents whether alone or attached to another moiety the carbon chain may optionally be substituted by one or more substituents R_x;

R_{30} is a –C_2-C_4 alkylene- group; and

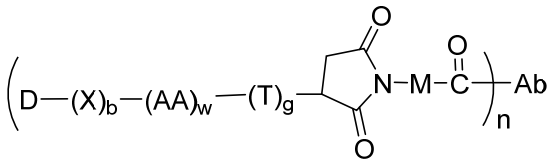
M is selected from the group consisting of -C_1-C_3 alkylene- and -C_1-C_3 alkylene-(C_5-C_7 carbocyclo)-;

or

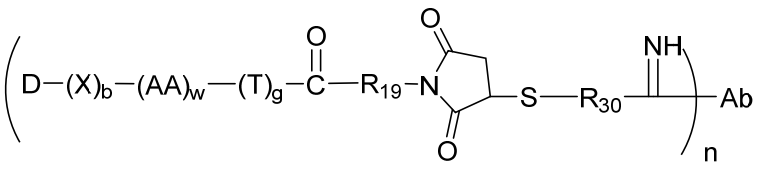
selected from the formulas (IV), (V) and (VI):



(IV)



(V)



(VI)

wherein:

X and T are extending groups that may be the same or different;

each AA is independently an amino acid unit;

w is an integer ranging from 0 to 12;

b is an integer of 0 or 1;

g is an integer of 0 or 1;

D is a drug moiety;

Ab is a moiety comprising at least one antigen binding site;

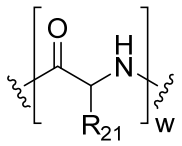
n is the ratio of the group [D-$(X)_b$-$(AA)_w$-$(T)_g$-(L)-] wherein L is as defined in (IV), (V) or (VI) to the moiety comprising at least one antigen binding site and is in the range from 1 to 20;

R_{19} is selected from -C_1-C_6 alkylene-, phenylene-C_1-C_6 alkylene- wherein the phenylene group may optionally be substituted with one or more substituents R_x selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, halogen atoms, nitro groups and cyano groups, wherein each of the above alkylene substituents whether alone or attached to another moiety in the carbon chain may optionally be substituted by one or more substituents R_x selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, aryl groups having from 6 to 12 carbon atoms, halogen atoms, nitro groups and cyano groups, and preferably R_{19} is a -C_1-C_6 alkylene group;

R_{30} is a –C_2-C_4 alkylene- group; and

M is -C_1-C_3 alkylene-(C_5-C_7 carbocyclo)-.

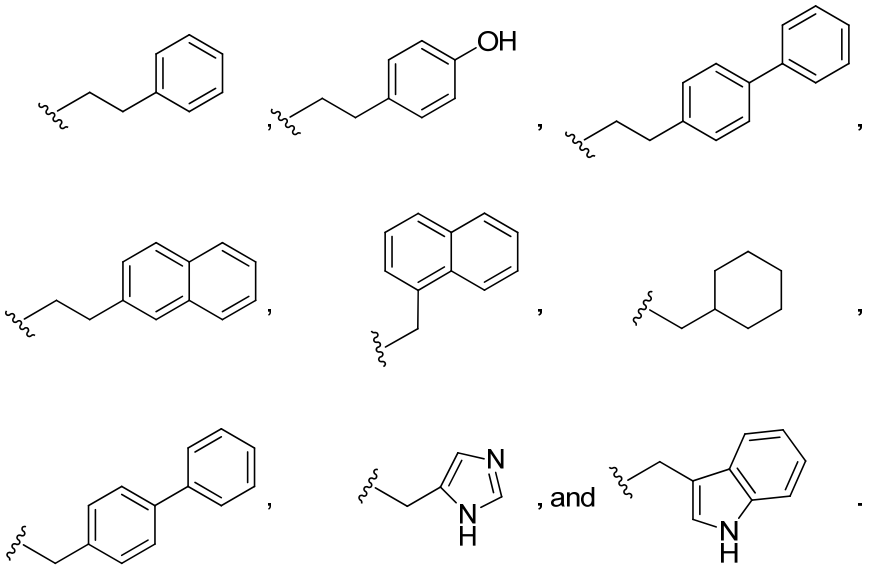
10. A drug conjugate according to any one of claims 1 to 9, wherein $(AA)_w$ is of formula (II):



(II)

wherein the wavy lines indicate the point of covalent attachments to $(X)_b$ if any, or to the drug moiety (the wavy line to the left) and to $(T)_g$ if any, or to the linker (the wavy line to the right); and

R_{21} is, at each occurrence, selected from the group consisting of hydrogen, methyl, isopropyl, isobutyl, sec-butyl, benzyl, p-hydroxybenzyl, $-CH_2OH$, $-CH(OH)CH_3$, $-CH_2CH_2SCH_3$, $-CH_2CONH_2$, $-CH_2COOH$, $-CH_2CH_2CONH_2$, $-CH_2CH_2COOH$, $-(CH_2)_3NHC(=NH)NH_2$, $-(CH_2)_3NH_2$, $-(CH_2)_3NHCOCH_3$, $-(CH_2)_3NHCHO$, $-(CH_2)_4NHC(=NH)NH_2$, $-(CH_2)_4NH_2$, $-(CH_2)_4NHCOCH_3$, $-(CH_2)_4NHCHO$, $-(CH_2)_3NHCONH_2$, $-(CH_2)_4NHCONH_2$, $-CH_2CH_2CH(OH)CH_2NH_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-, phenyl, cyclohexyl,



and w is an integer ranging from 0 to 12;

or

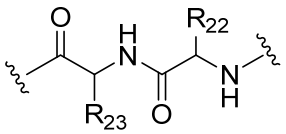
wherein $(AA)_w$ is of formula (II) wherein:

R_{21} is selected, at each occurrence, from the group consisting of hydrogen, methyl, isopropyl, sec-butyl, benzyl, indolylmethyl, $-(CH_2)_3NHCONH_2$, $-(CH_2)_4NH_2$, $-(CH_2)_3NHC(=NH)NH_2$ and $-(CH_2)_4NHC(=NH)NH_2$; and

w is an integer ranging from 0 to 6;

or

wherein w is 0 or 2, and where w is 2, then $(AA)_w$ is of formula (III):



(III)

wherein:

the wavy lines indicate the point of covalent attachments to $(X)_b$ if any, or to the drug moiety (the wavy line to the left) and to $(T)_g$ if any, or to the linker (the wavy line to the right);

R_{22} is selected from methyl, benzyl, isopropyl, *sec*-butyl and indolylmethyl; and

R_{23} is selected from methyl, $-(CH_2)_4NH_2$, $-(CH_2)_3NHCONH_2$ and $-(CH_2)_3NHC(=NH)NH_2$.

11. A drug conjugate according to any one of claims 1 to 10, wherein X is an extending group selected from:
where D is covalently attached via an amine group (for example where Z is -NH-):

-COO-(C_1-C_6 alkylene)NH-;

-COO-CH_2-(phenylene which may optionally be substituted with one or more substituents R_x)-NH-;

-COO-(C_1-C_6 alkylene)NH-COO-CH_2-(phenylene which may optionally be substituted with one or more substituents R_x)-NH-;

-$COCH_2NH$-$COCH_2$-NH-;

-$COCH_2NH$-;

-COO-(C_1-C_6 alkylene)S-;

-COO-(C_1-C_6 alkylene)NHCO(C_1-C_6 alkylene)S-; and

where D is covalently attached via an hydroxy group (for example where Z is -O-):

-CONH-(C_1-C_6 alkylene)NH-;

-COO-CH_2-(phenylene which may optionally be substituted with one or more substituents R_x)-NH-;

-CONH-(C_1-C_6 alkylene)NH-COO-CH_2-(phenylene which may optionally be substituted with one or more substituents R_x)-NH-;

-$COCH_2NH$-$COCH_2$-NH-;

-$COCH_2NH$-;

-CONH-(C_1-C_6 alkylene)S-;

-CONH-(C_1-C_6 alkylene)NHCO(C_1-C_6 alkylene)S-; and

b is 0 or 1, preferably 1;

or

wherein X is an extending group selected from the group consisting of:

where D is covalently attached via an amine group (for example where Z is -NH-):

-COO-(C_2-C_4 alkylene)NH-;

-COO-CH_2-phenylene-NH-, wherein said phenylene group may optionally be substituted with from one to four substituents R_x selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, halogen atoms, nitro groups and cyano groups;

-COO-(C_2-C_4 alkylene)NH-COO-CH_2-(phenylene which may optionally be substituted with from one to four substituents R_x selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, halogen atoms, nitro groups and cyano groups)-NH-;

-$COCH_2NH$-$COCH_2$-NH-;

-COO-(C_2-C_4 alkylene)S-;

-COO-(C_2-C_4 alkylene)NHCO(C_1-C_3 alkylene)S-; or

where D is covalently attached via an hydroxy group (for example where Z is -O-):

-CONH-(C_2-C_4 alkylene)NH-;

-COO-CH_2-phenylene-NH-, wherein said phenylene group may optionally be substituted with from one to four substituents R_x selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, halogen atoms, nitro groups and cyano groups;

-CONH-(C_2-C_4 alkylene)NH-COO-CH_2-(phenylene which may optionally be substituted with from one to four substituents R_x selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, halogen atoms, nitro groups and cyano groups)-NH-;

-$COCH_2NH$-$COCH_2$-NH-;

-CONH-(C_2-C_4 alkylene)S-;

-CONH-(C_2-C_4 alkylene)NHCO(C_1-C_3 alkylene)S-; and

b is 0 or 1, preferably 1;

or

wherein X is an extending group selected from the group consisting of:

where D is covalently attached via an amine group (for example where Z is -NH-):

-COO-CH_2-phenylene-NH-

-$COO(CH_2)_3NHCOOCH_2$-phenylene-NH-;

-$COO(CH_2)_3$NH-;

-$COO(CH_2)_3$-S-;

-$COO(CH_2)_3NHCO(CH_2)_2$S-; or

where D is covalently attached via an hydroxy group (for example where Z is -O-):

-COO-CH_2-phenylene-NH-

-$CONH(CH_2)_3NHCOOCH_2$-phenylene-NH-;

-$CONH(CH_2)_3$NH-;

-$CONH(CH_2)_3$-S-;

-$CONH(CH_2)_3NHCO(CH_2)_2$S-; and

b is 0 or 1, preferably 1.

12. A drug conjugate according to any one of claims 1 to 11, wherein T is an extending group selected from the group consisting of -CO-(C_1-C_6 alkylene)-NH-,-CO-(C_1-C_6 alkylene)-

[O-(C_2-C_6 alkylene)]$_j$-NH-, -COO-(C_1-C_6 alkylene)-[O-(C_2-C_6 alkylene)]$_j$-NH-; where j is an integer from 1 to 25, and g is 0 or 1;
or

wherein T is an extending group selected from the group consisting of -CO-(C_1-C_4 alkylene)NH-, -CO-(C_1-C_4 alkylene)-[O-(C_2-C_4 alkylene)]$_j$-NH-, -COO-(C_1-C_4 alkylene)-[O-(C_2-C_4 alkylene)]$_j$-NH-,where j is an integer from 1 to 10; and g is 0 or 1;

or

wherein T is an extending group selected from the group consisting of -CO-(C_1-C_4 alkylene)NH-, -CO-(C_1-C_4 alkylene)-[O-(C_2-C_4 alkylene)]$_j$-NH-, -COO-(C_1-C_4 alkylene)-[O-(C_2-C_4 alkylene)]$_j$-NH-; where j is an integer from 1 to 5; and g is 0 or 1.

13. A drug conjugate according to any one of claims 5 to 12, wherein D is a drug moiety of formula (IHa) or formula (IHb) or a pharmaceutically acceptable salt, ester, solvate, tautomer or stereoisomer thereof, wherein:
R_1 is CN or OH;

R_2 is C(=O)R_a, wherein R_a is selected from hydrogen and substituted or unsubstituted C_1-C_6 alkyl, wherein the optional substituents are one or more substituents R_x;

R_3 is hydrogen or a -OR_b group wherein R_b is a substituted or unsubstituted C_1-C_6 alkyl group, wherein the optional substituents are one or more substituents R_x,

Y is -NH- or -O-; and

Z is -NH- or -O-;

or

wherein D is a drug moiety of formula (IHa) or formula (IHb) or a pharmaceutically acceptable salt, ester, solvate, tautomer or stereoisomer thereof, wherein:

R_1 is CN or OH;

R_2 is acetyl;

R_3 is hydrogen or methoxy, more preferably hydrogen;

Y is -NH- or -O-; and

Z is -NH- or -O-;

or

wherein D is a drug moiety of formula (IHa) or formula (IHb), or a pharmaceutically acceptable salt, ester, solvate, tautomer or stereoisomer thereof wherein:

R_1 is CN;

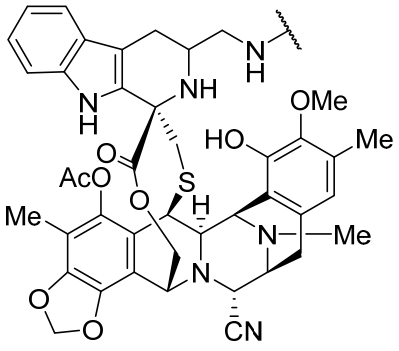
R_2 is acetyl:

R_3 is hydrogen;

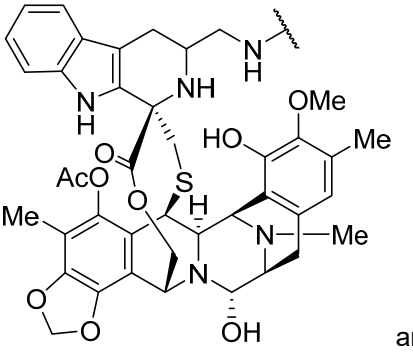
Y is -NH- or –O-; and

Z is -NH-.

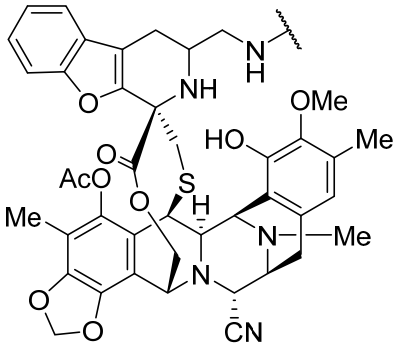
14. A drug conjugate according to any one of claims 1, 2, or 5 to 13, wherein D is selected from:



,



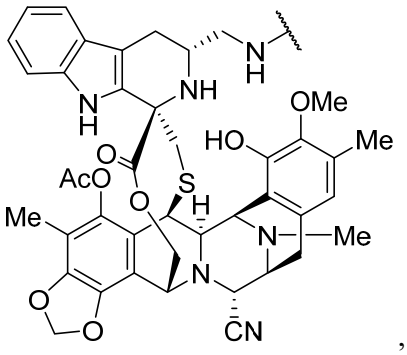
and



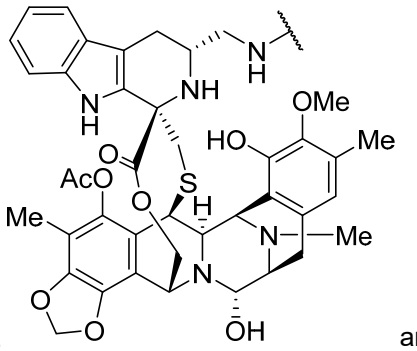
or a pharmaceutically acceptable salt, ester, solvate, tautomer or stereoisomer thereof, wherein the wavy line indicates the point of covalent attachment to $(X)_b$ if any, or $(AA)_w$ if any, or to $(T)_g$ if any, or to (L);

or

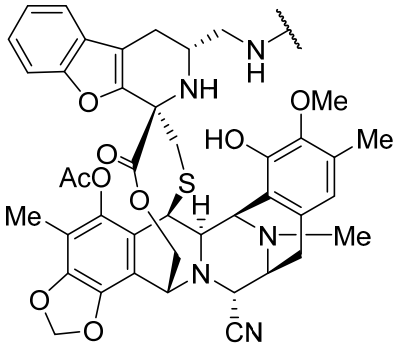
wherein D is



,



and



or a pharmaceutically acceptable salt, ester, solvate, tautomer or stereoisomer thereof, wherein the wavy line indicates the point of covalent attachment to $(X)_b$ if any, or $(AA)_w$ if any, or to $(T)_g$ if any, or to (L).

15. A drug conjugate according to any one of claims 1 to 14, wherein the moiety Ab comprising at least one antigen binding site is an antigen-binding peptide;
optionally

wherein the moiety Ab comprising at least one antigen binding site is an antibody, a single domain antibody or an antigen-binding fragment thereof;

optionally

wherein the moiety Ab comprising at least one antigen binding site is a monoclonal antibody, polyclonal antibody or bispecific antibody and wherein the antibody or an antigen-binding fragment thereof is derived from any species, preferably a human, mouse or rabbit;

optionally

wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of a human antibody, an antigen-binding fragment of a human antibody, a humanized antibody, an antigen-binding fragment of a humanized antibody, a chimeric antibody, an antigen-binding fragment of a chimeric antibody, a glycosylated antibody and a glycosylated antigen binding fragment;

optionally

wherein the antibody or antigen-binding fragment thereof is an antigen-binding fragment selected from the group consisting of an Fab fragment, an Fab' fragment, an F(ab')2 fragment and an Fv fragment;

optionally

wherein the antibody or antigen-binding fragment thereof is a monoclonal antibody which immunospecifically binds to cancer cell antigens, viral antigens, antigens of cells that produce autoimmune antibodies associated with autoimmune disease, microbial antigens, and preferably a monoclonal antibody which immunospecifically binds to cancer cell antigens;

optionally

wherein the moiety Ab comprising at least one antigen binding site is an antibody selected from the group consisting of Abciximab, Alemtuzumab, Anetumab, Atezolizumab, Avelumab, Basiliximab, Bevacizumab, Blinatomumab, Brentuximab, Catumaxomab, Cetuximab, Coltuximab, Daclizumab, Daratumumab, Denintuzumab, Denosumab, Depatuxizumab, Dinutuximab, Durvalumab, Elotuzumab, Enfortumab, Glembatumumab, Gemtuzumab, Ibritumomab, Indatuximab, Indusatumab, Inotuzumab, Ipilimumab, Labetuzumab, Ladiratuzumab, Laprituximab, Lifastuzumab, Lorvotuzumab, Milatuzumab, Mirvetuximab, Naratuximab, Necitumumab, Nimotuzumab, Nivolumab, Obinutuzumab, Ofatumumab, Olaratumab, Omalizumab, Palivizumab, Panitumumab, Pembrolizumab, Pertuzumab, Pinatuzumab, Polatuzumab, Ramucirumab, Rovalpituzumab, Sacituzumab, Siltuximab, Sirtratumab, Sofituzumab, Vadastuximab, Vorsetuzumab, Trastuzumab, an anti-CD4 antibody, an anti-CD5 antibody, an anti-CD13 antibody and an anti-CD 30 antibody, or an antigen-binding fragment or an immunologically active portion thereof;

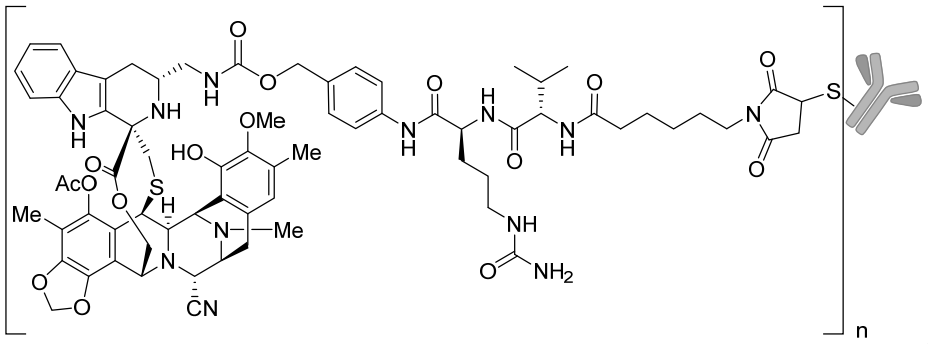
optionally

wherein the moiety Ab comprising at least one antigen binding site is an antibody selected from the group consisting of Abciximab, Alemtuzumab, Anetumab, Atezolizumab, Avelumab, Basiliximab, Bevacizumab, Blinatomumab, Brentuximab, Catumaxomab, Cetuximab, Daclizumab, Daratumumab, Denintuzumab, Denosumab, Depatuxizumab, Dinutuximab, Durvalumab, Elotuzumab, Enfortumab, Glembatumumab, Gemtuzumab, Ibritumomab, Indatuximab, Indusatumab, Inotuzumab, Ipilimumab, Labetuzumab, Ladiratuzumab, Laprituximab, Mirvetuximab, Naratuximab, Necitumumab, Nimotuzumab, Nivolumab, Obinutuzumab, Ofatumumab, Olaratumab, Omalizumab, Palivizumab, Panitumumab, Pembrolizumab, Pertuzumab, Polatuzumab, Ramucirumab, Rovalpituzumab, Sacituzumab, Siltuximab, Sirtratumab, Vadastuximab, Vorsetuzumab, Trastuzumab, an anti-CD4 antibody, an anti-CD5 antibody, an anti-CD13 antibody and an anti-CD 30 antibody, or an antigen-binding fragment or an immunologically active portion thereof;

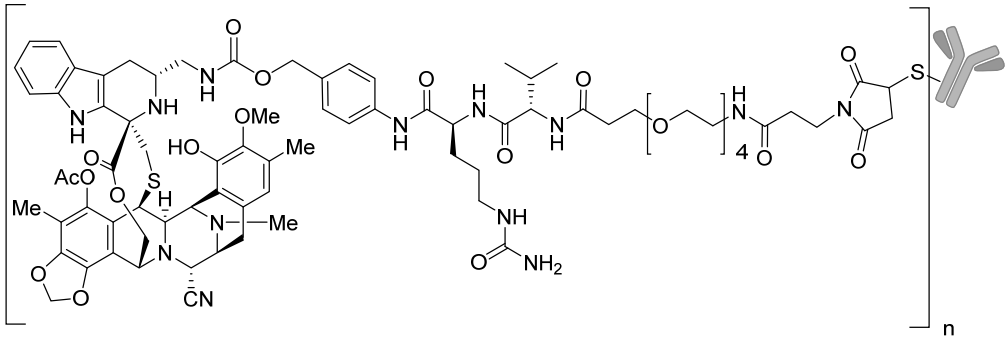
optionally

wherein the moiety Ab comprising at least one antigen binding site is an antibody selected from the group consisting of Abciximab, Alemtuzumab, Atezolizumab, Avelumab, Basiliximab, Bevacizumab, Blinatomumab, Brentuximab, Catumaxomab, Cetuximab, Daclizumab, Daratumumab, Denosumab, Dinutuximab, Durvalumab, Elotuzumab, Gemtuzumab, Ibritumomab, Inotuzumab, Ipilimumab, Labetuzumab, Necitumumab, Nimotuzumab, Nivolumab, Obinutuzumab, Ofatumumab, Olaratumab, Omalizumab, Palivizumab, Panitumumab, Pembrolizumab, Pertuzumab, Ramucirumab, Rovalpituzumab, Siltuximab, Trastuzumab, an anti-CD4 antibody, an anti-CD5 antibody, an anti-CD13 antibody and an anti-CD 30 antibody, or an antigen-binding fragment or an immunologically active portion thereof, more preferably Brentuximab, Gemtuzumab, Inozutumab, Rovalpituzumab, Trastuzumab, an anti-CD4 antibody, an anti-CD5 antibody, an anti-CD13 antibody and an anti-CD 30 antibody, or an antigen-binding fragment or an immunologicallly active portion thereof, preferably Trastuzumab and anti-CD13 antibody or an antigen-binding fragment or an immunologically active portion thereof, more preferably Trastuzumab or an antigen-binding fragment or an immunologically active portion thereof.

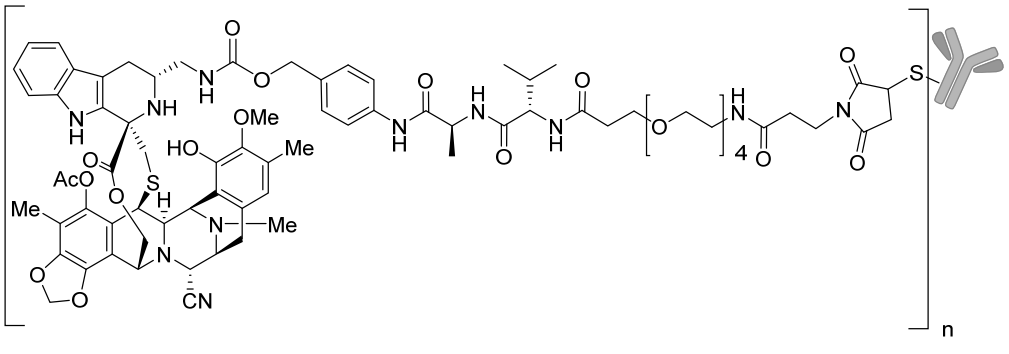
16. A drug conjugate according to claim 1, that is an antibody drug conjugate, selected from the group consisting of:



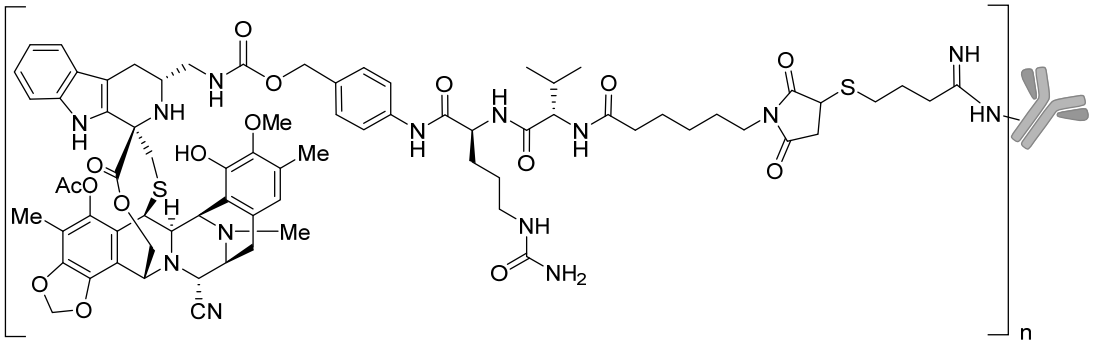
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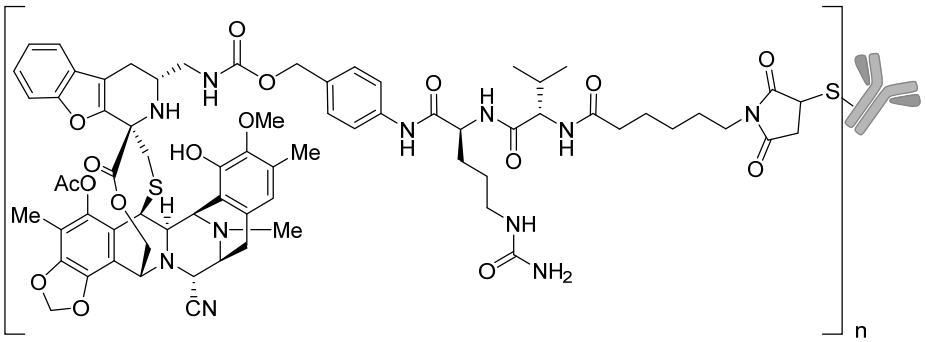
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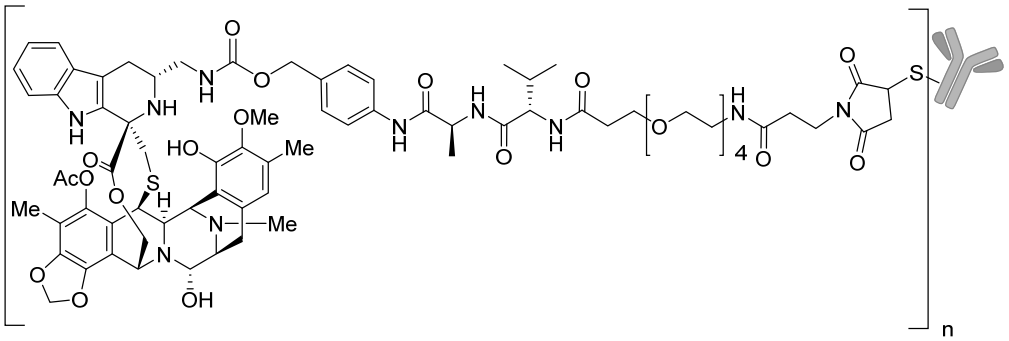
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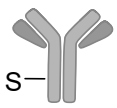
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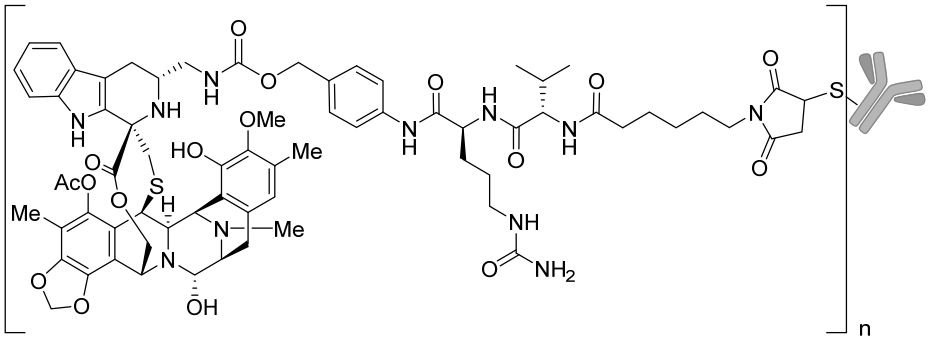
,

wherein n is from 2 to 6, more preferably 3, 4, or 5 and each  and  is independently selected from is independently selected from Brentuximab, Gemtuzumab, Inozutumab, Rovalpituzumab, Trastuzumab, an anti-CD4 antibody, an anti-CD5 antibody, an anti-CD13 antibody and an anti-CD 30 antibody, or an antigen-binding fragment or an

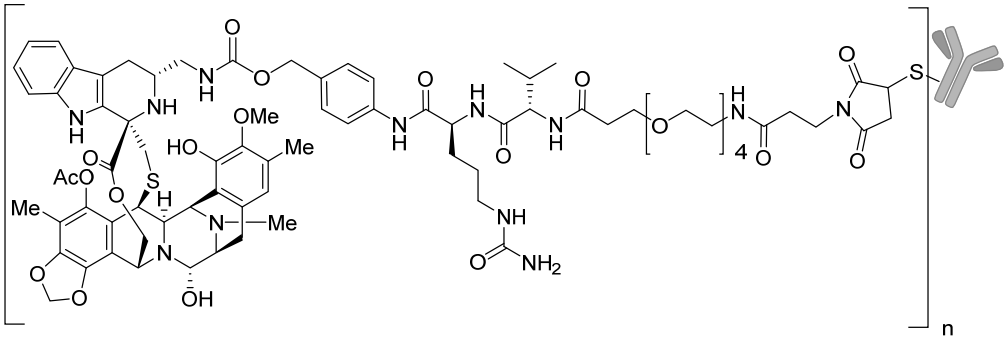
immunologically active portion thereof, and more preferably its is selected from Trastuzumab and anti-CD13 antibody or an antigen-binding fragment or an immunologically active portion thereof, particularly Trastuzumab or an antigen-binding fragment or an immunologically active portion thereof;

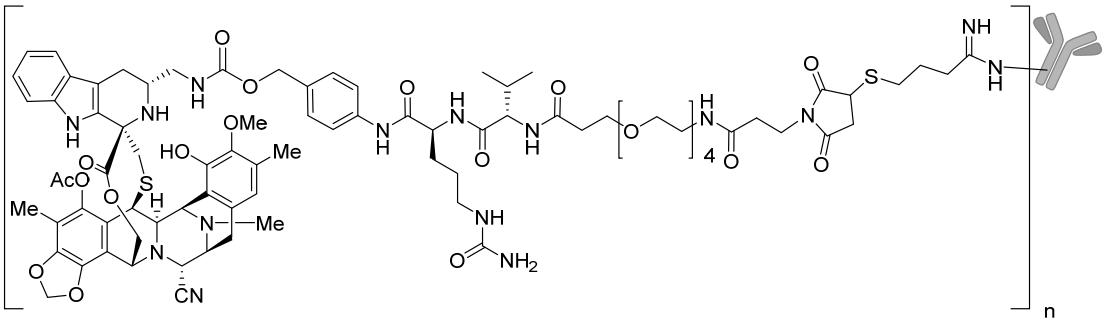
or

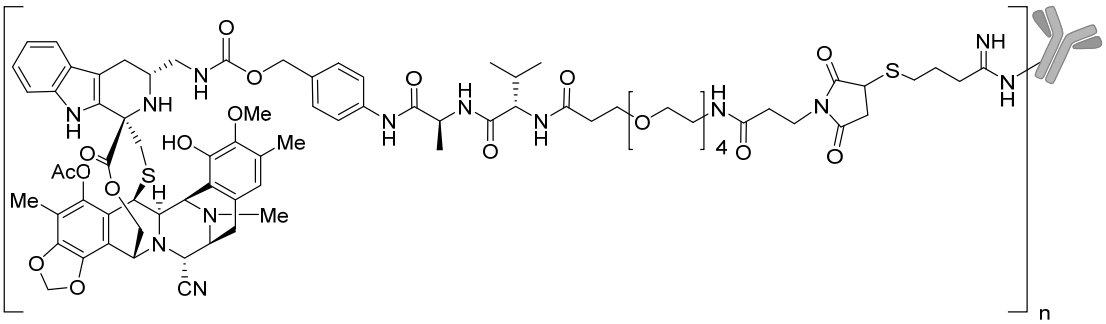
a drug conjugate, that is an antibody drug conjugate, selected from the group consisting of:

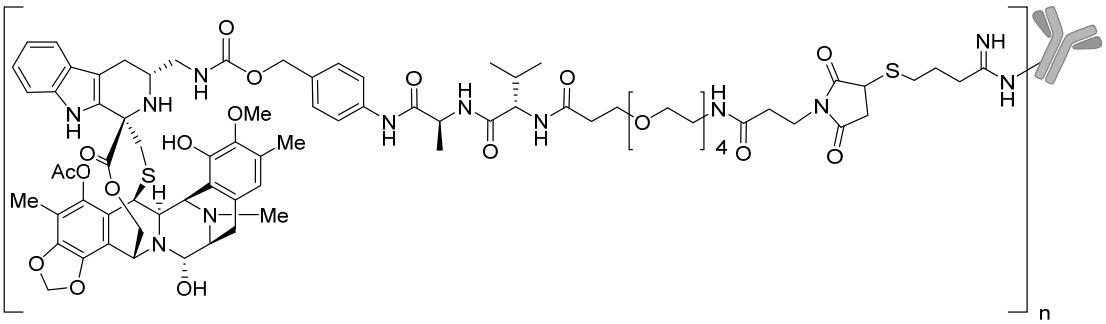


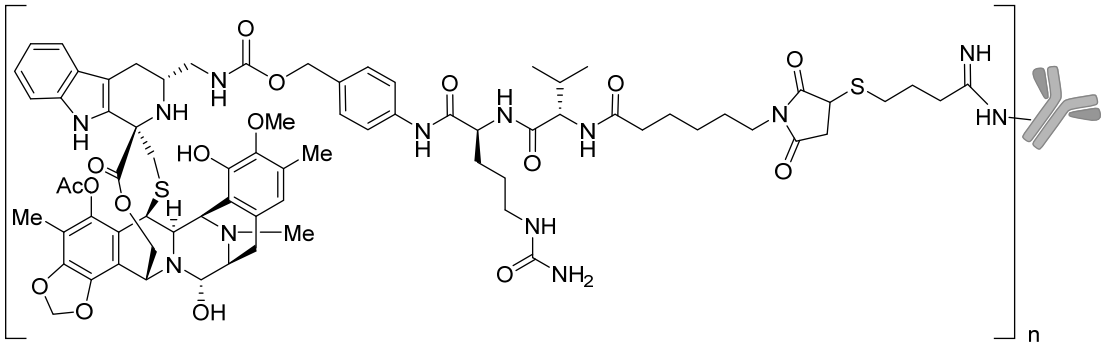
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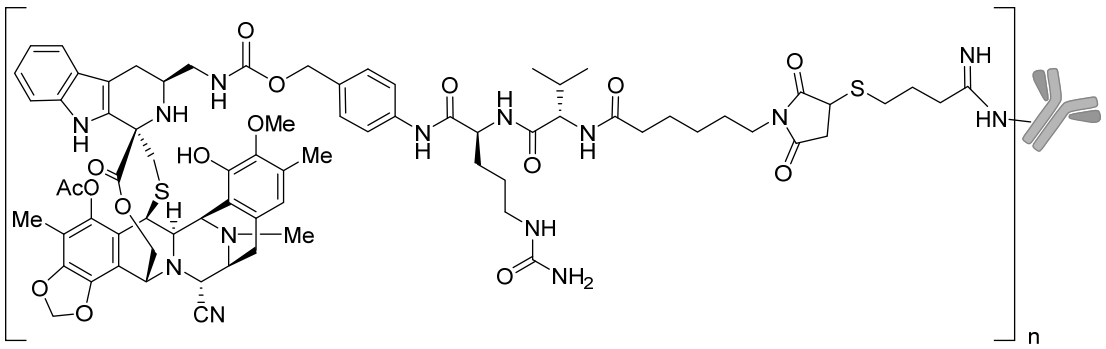


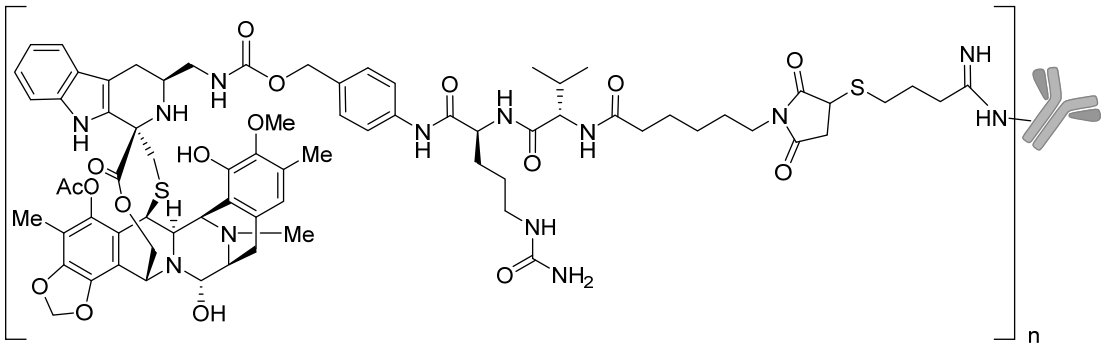


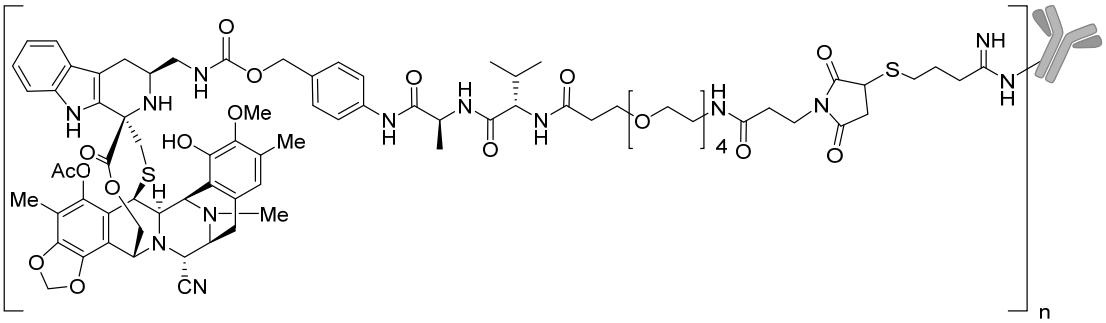


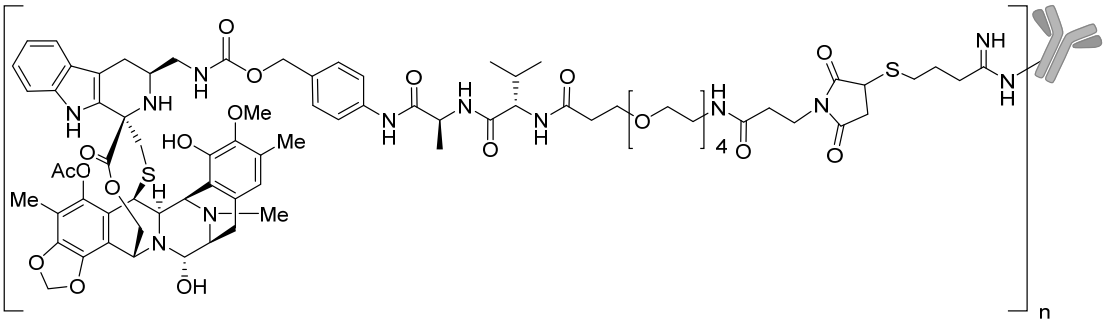


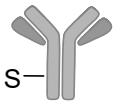


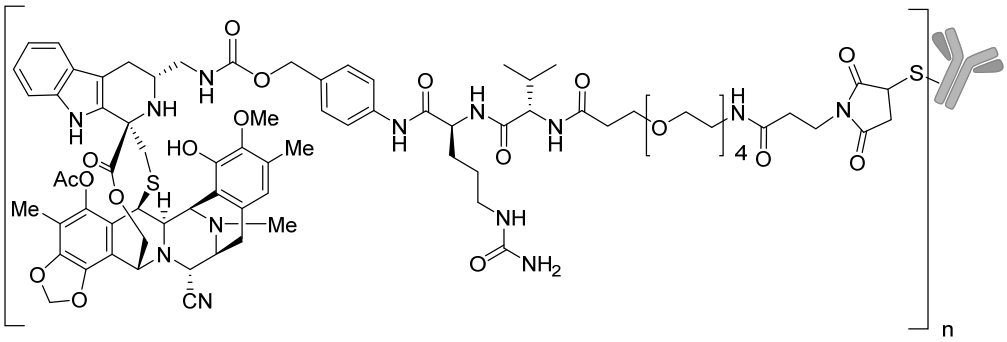


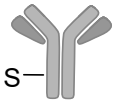






wherein n is from 2 to 6, more preferably 3, 4, or 5 and each  and  is independently selected from Brentuximab, Gemtuzumab, Inozutumab, Rovalpituzumab, Trastuzumab, an anti-CD4 antibody, an anti-CD5 antibody, an anti-CD13 antibody and an anti-CD 30 antibody, or an antigen-binding fragment or an immunologically active portion thereof, and more preferably its is selected from Trastuzumab and anti-CD13 antibody or an antigen-binding fragment or an immunologically active portion thereof, particularly Trastuzumab or an antigen-binding fragment or an immunologically active portion thereof; or a drug conjugate of formula



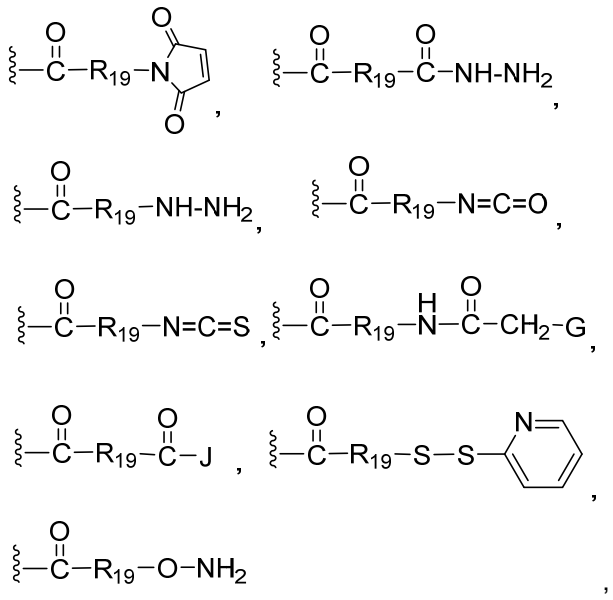
wherein n is from 2 to 6, more preferably 3, 4, or 5 and  is an anti-CD13 antibody or an antigen-binding fragment or an immunologically active portion thereof.

17. A drug conjugate according to claim 16, wherein the moiety Ab comprising at least one antigen binding site is selected from Trastuzumab and anti-CD13 antibody or an antigen-binding fragment or an immunologically active portion thereof;
or

wherein the moiety Ab comprising at least one antigen binding site is selected from Trastuzumab or an antigen-binding fragment or an immunologically active portion thereof.

18. A drug conjugate according to any one of claims 1 to 17 that is an antibody drug conjugate in isolated or purified form.

19. A compound of formula D-$(X)_b$-$(AA)_w$-$(T)_g$-L_1, wherein:
L_1 is a linker selected from the group of formulas consisting of:



wherein each of the the wavy lines indicates the point of covalent attachment to $(T)_g$ if any, or $(AA)_w$ if any, or to $(X)_b$ if any or to D;

G is selected from halo, -*O*-mesyl and -*O*-tosyl;

J is selected from halo, hydroxy, -*N*-succinimidoxy, -*O*-(4-nitrophenyl), -*O*-pentafluorophenyl, -*O*-tetrafluorophenyl and -O-C(O)-OR_{20};

R_{19} is selected from -C_1-C_{12} alkylene-, -C_3-C_8 carbocyclo, -O-(C_1-C_{12} alkylene), -C_6-C_{18} arylene in one or more rings which may optionally be substituted with one or more substituents R_x, -C_1-C_{12} alkylene-C_6-C_{18} arylene- wherein the arylene group is in one or more rings which may optionally be substituted with one or more substituents R_x, -C_6-C_{18} arylene-C_1-C_{12} alkylene- wherein the arylene group is in one or more rings which may optionally be substituted with one or more substituents R_x, -C_1-C_{12} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{12} alkylene-, -C_5-C_{14} heterocyclo- wherein said heterocyclo group may be a saturated or unsaturated group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s), said group optionally being substituted with one or more substituents R_x, -C_1-C_{12} alkylene-(C_5-C_{14} heterocyclo)- wherein said heterocyclo group may be a saturated or unsaturated group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s), said group optionally being substituted with one or more substituents R_x, -(C_5-C_{14} heterocyclo)-C_1-C_{12} alkylene-, wherein said heterocyclo group may be a saturated or unsaturated group having one or more rings and comprising at least one oxygen, nitrogen or sulphur atom in said ring(s), said group optionally being substituted with one or more substituents R_x, -$(OCH_2CH_2)_r$- and -CH_2-$(OCH_2CH_2)_r$-, wherein each of the above alkylene substituents whether alone or attached to another moiety the carbon chain may optionally be substituted by one or more substituents R_x;

R_{20} is a C_1-C_{12} alkyl or an aryl group having from 6 to 18 carbon atoms in one or more aromatic rings, said aryl groups optionally being substituted with one or more substituents R_x;

r is an integer ranging from 1-10;

b is an integer of 0 or 1;

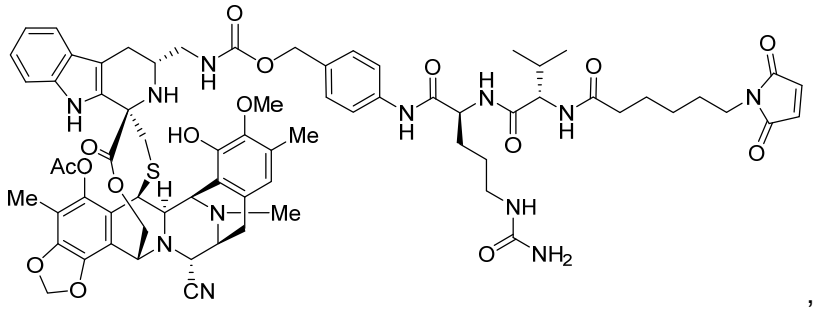
g is an integer of 0 or 1;

w is an integer ranging from 0 to 12;

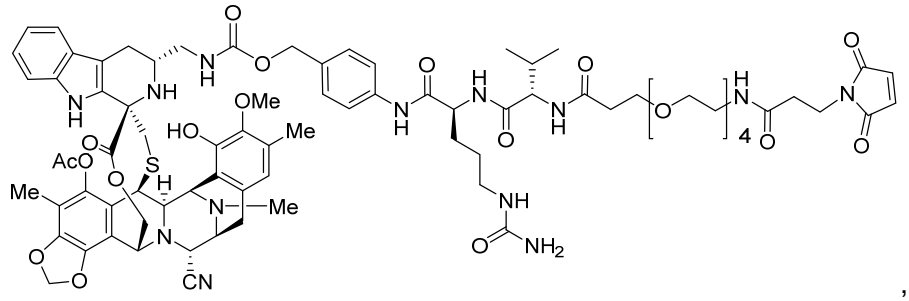
each of D, R_x, X, T, and AA is as defined in any one of claims 1 to 18;

optionally

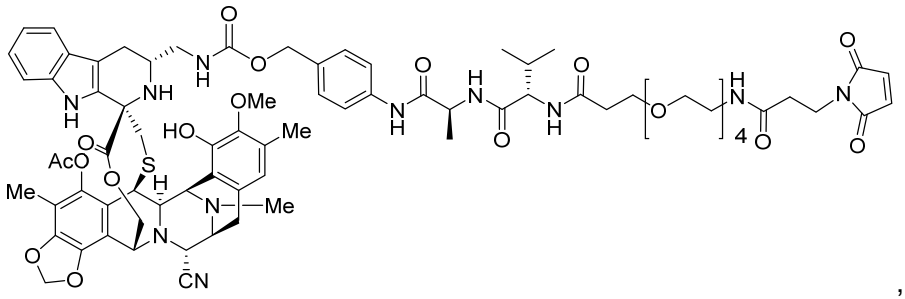
wherein the compound of formula D-X-$(AA)_w$-$(T)_g$-L_1 is selected from:



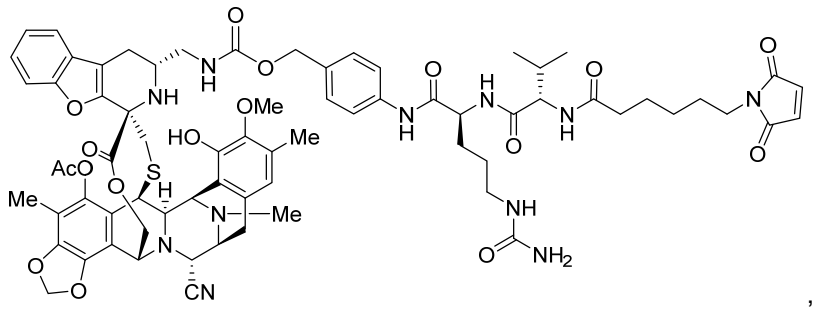
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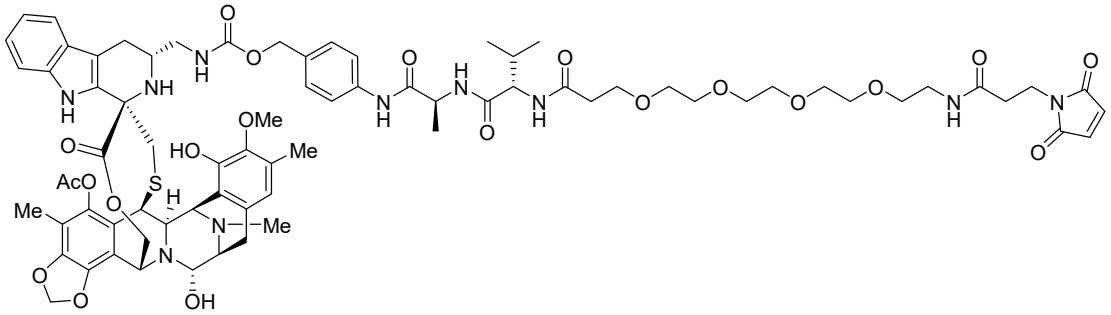


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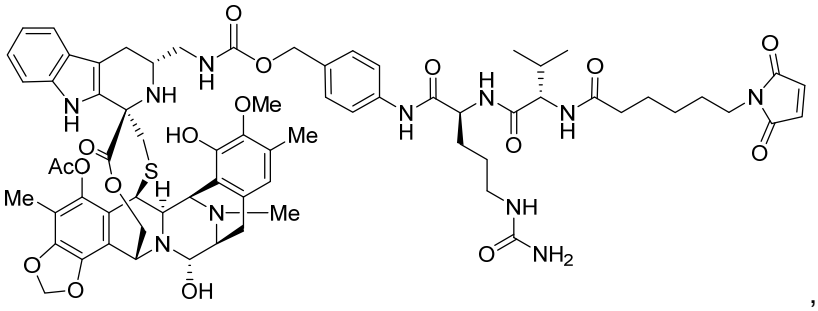


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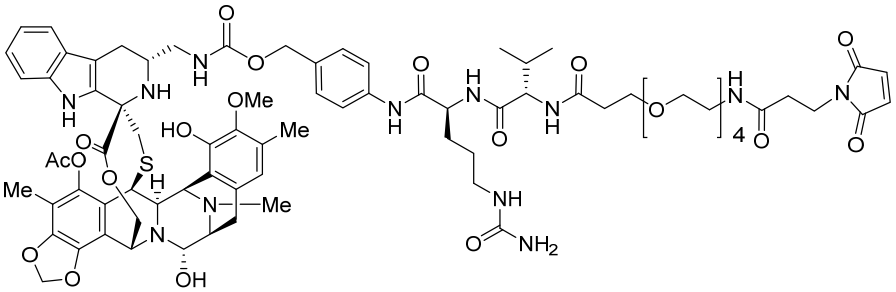
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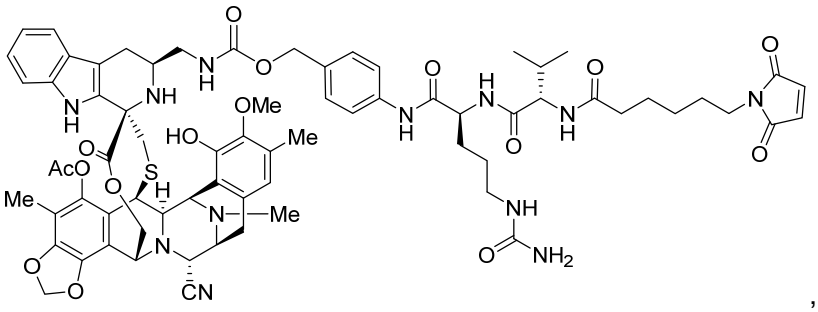
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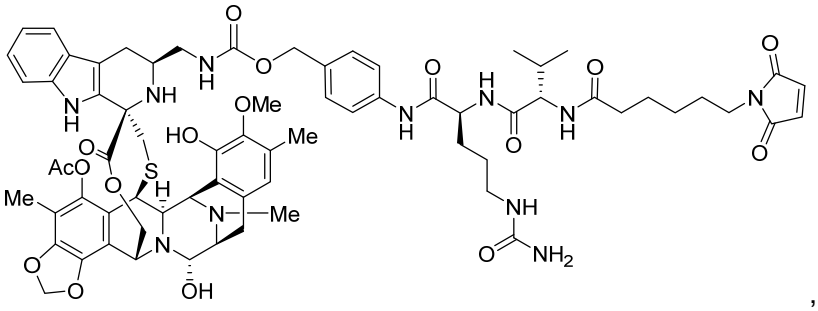
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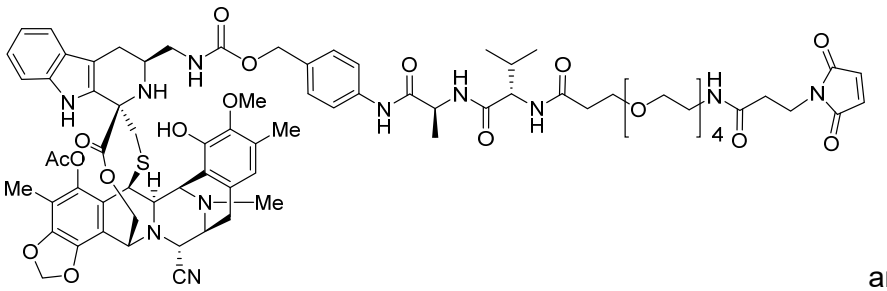
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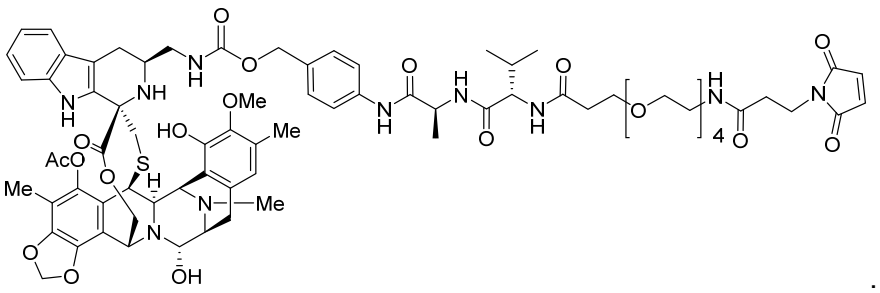
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5 and



20. A compound of formula D-$(X)_b$-$(AA)_w$-$(T)_g$-L_1, wherein each of D, X, AA, T, L_1, b, g and w are as defined in any one of claims 1 to 17.

21. A drug conjugate according to any one of claims 1 to 18, or a compound according to any one of claims 19 to 20, wherein b+g+w is not 0;

or

wherein b+w is not 0;

or

wherein when w is not 0, then b is 1.

22. Use of a drug moiety as described in any one of claims 1 to 7, as a payload in an antibody drug conjugate.

23. Use of a drug moiety as described in any one of claims 1 to 7, in the manufacture of a antibody drug conjugate.

24. A drug conjugate according to any one of claims 1 to 18, for use as a medicament.

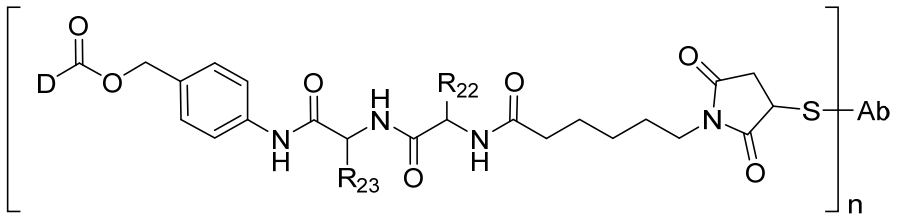
25. A pharmaceutical composition comprising a drug conjugate according to any one of claims 1 to 18 and a pharmaceutically acceptable carrier.

26. A kit comprising a therapeutically effective amount of a drug conjugate according to any one of claims 1 to 18 and a pharmaceutically acceptable carrier.

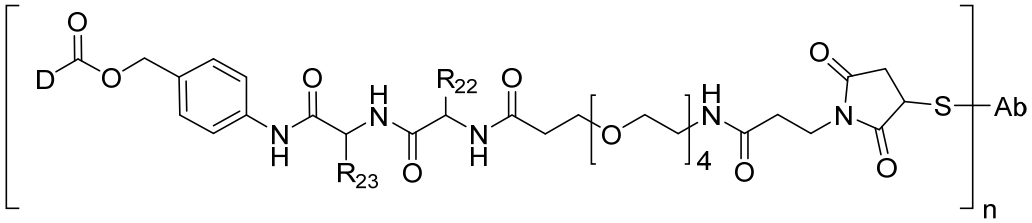
27. The kit according to claim 26 for use in the treatment of cancer, and more preferably a cancer selected from lung cancer, colorectal cancer, breast cancer, pancreas carcinoma, kidney cancer, leukaemia, multiple myeloma, lymphoma, gastric and ovarian cancer.

28. The drug conjugate according to any one of claims 1 to 15, wherein n is in the range of from 1-12, 1-8, 3-8, 3-6, 3-5, 1, 2, 3, 4, 5 or 6; preferably 3, 4 or 5 or more preferably 4.

29. A process for the preparation of a drug antibody conjugate according to any one of claims 1 to 18, comprising conjugating a moiety Ab comprising at least one antigen binding site and a drug D, Ab and D being as defined in any one of claims 1 to 18;
optionally wherein the preparation of a drug antibody conjugate of formula (G) or (G'):



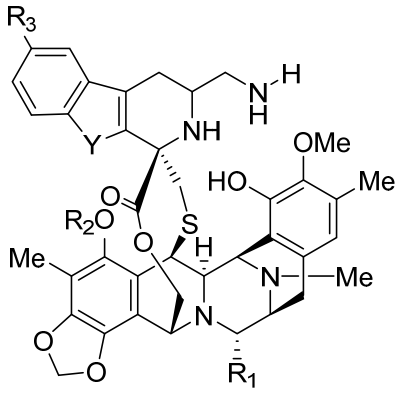
(G)



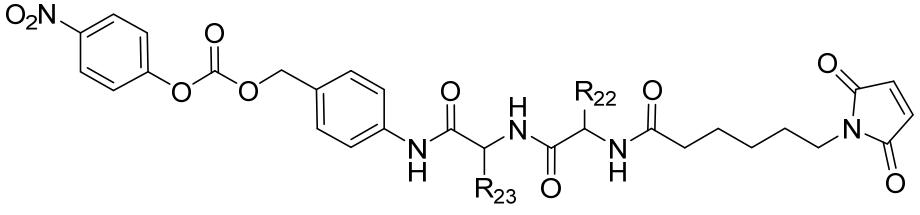
(G')

comprising the following steps:

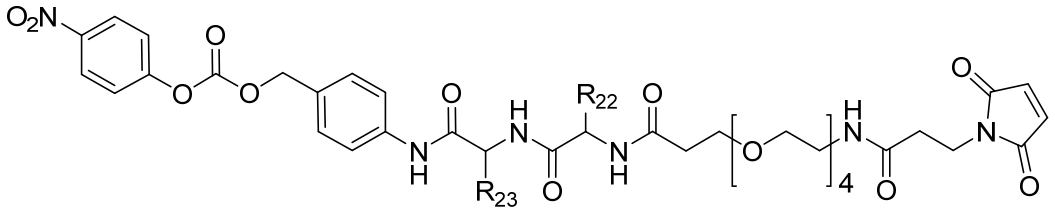
(i) reacting a drug D-H of formula (IH)-H:



wherein the substituents in the definitions of (IH)-H are as defined in any one of claims 1 to 18, with a compound of formula (D') or (E):

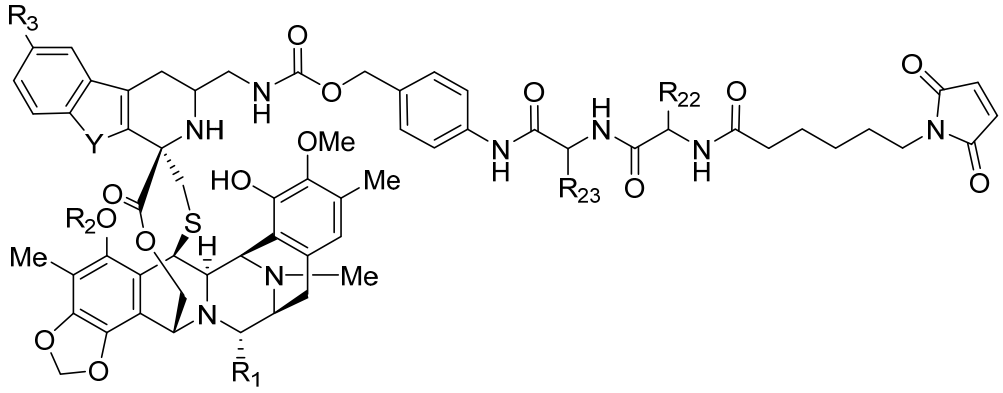


(D')

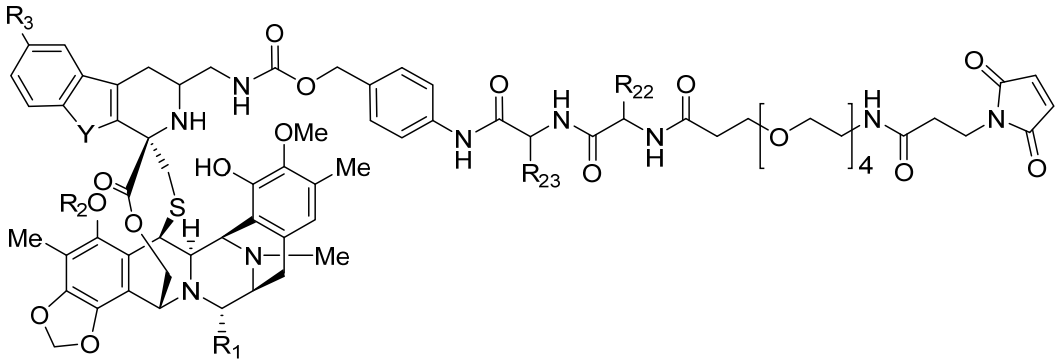


(E)

to give a compound of formula (F) or (F'),respectively:

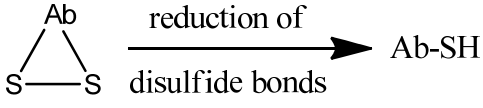


(F)



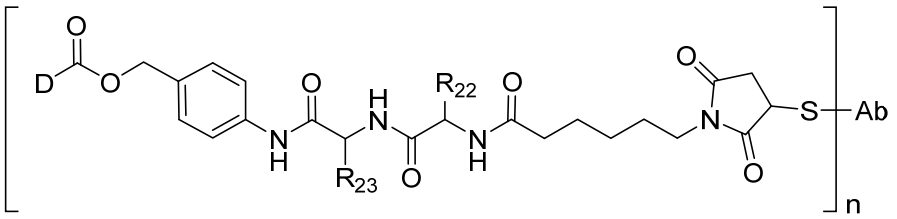
(F')

(ii)partial reduction of one or more disulfide bonds in the antibody to be conjugated to give a reduced antibody Ab-SH having free thiol groups:

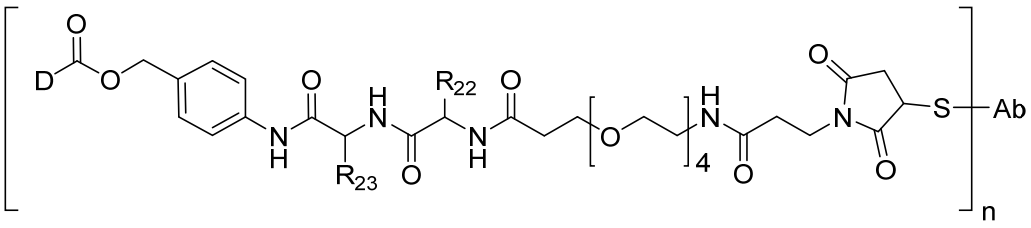


; and

(iii) reaction of the partially reduced antibody Ab-SH having free thiol groups with the compound of formula (F) or (F') produced in step (i) to give the desired drug antibody conjugate of formula (G) or (G') respectively:



(G)



(G')