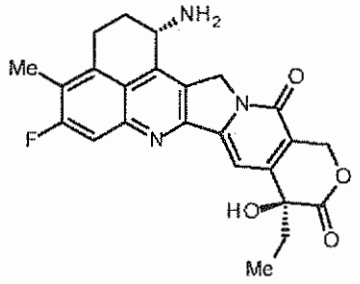
antibody-drug conjugate in which the antibody and exatecan are conjugated to each other via the linker, and confirmed an excellent antitumor effect exhibited by the conjugate to thereby complete the present disclosure.

[0011]

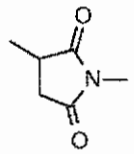
Specifically, the present invention relates to the followings.

In one aspect, the present invention refers to an antibody-drug conjugate wherein an antitumor compound represented by the following formula:



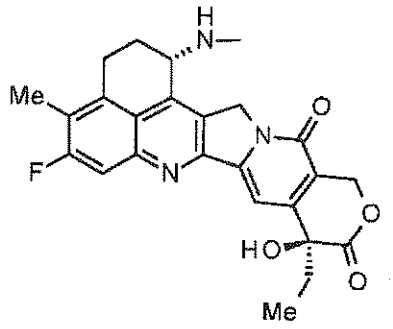
is conjugated to an antibody via a drug-linker having a structure represented by the following formula:

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX), wherein -(Succinimid-3-yl-N)- has a structure represented by the following formula:



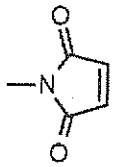
which is connected to the antibody at position 3 thereof via a thioether bond and connected to a methylene group in the linker structure containing this structure on the

nitrogen atom at position 1, and -(NH-DX) represents a group represented by the following formula:

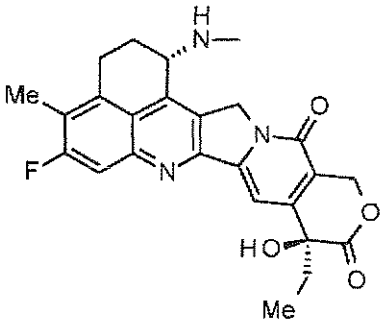


wherein the nitrogen atom of the amino group at position 1 is a connecting position. In another aspect, the present invention refers to a drug containing the antibody-drug conjugate according to the present invention, or a salt thereof. In still another aspect, the present invention refers to an antitumor drug and/or anticancer drug containing the antibody-drug conjugate according to the present invention, or a salt thereof. In another aspect, the present invention refers to a pharmaceutical composition containing the antibody-drug conjugate according to the present invention, or a salt thereof as an active component, and a pharmaceutically acceptable formulation component. Furthermore, the present invention refers to a compound of the following:

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX), wherein (maleimid-N-yl)- is a group represented by the following formula:

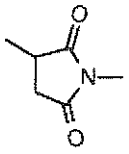


wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:

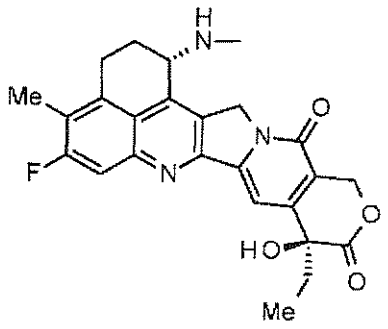


wherein the nitrogen atom of the amino group at position 1 is a connecting position. The present invention also refers to a linker having the following formula: -(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-

wherein -(Succinimid-3-yl-N)- has a structure represented by the following formula:

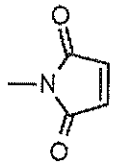


which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1. The present invention also refers to a compound of HO-CH_2-C(=O)-(NH-DX), wherein -(NH-DX) is a group represented by the following formula:

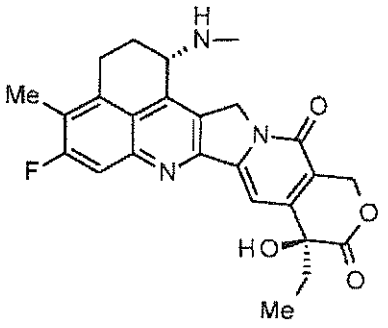


wherein the nitrogen atom of the amino group at position 1 is a connecting position. In another aspect, the present invention refers to a method for preparing an antibody-drug conjugate, wherein the antibody is treated in a reducing condition and thereafter reacted with a compound having following formula:

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX) wherein, (maleimid-N-yl)- is a group represented by the following formula:



wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:

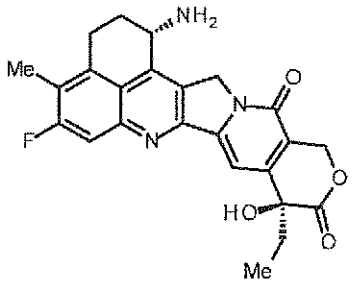


wherein the nitrogen atom of the amino group at position 1 is a connceting position.

[0011a]Also disclosed is:

[1] An antibody-drug conjugate wherein an antitumor compound represented by the following formula:

[Formula 2]



is conjugated to an antibody via a linker having a structure represented by the following formula:

$-L^1-L^2-L^P-NH-(CH_2)n^1-L^a-L^b-L^c-$.

[0012]

Here, the antibody is connected to the terminal of L^1, the antitumor compound is connected to the terminal of L^c with the nitrogen atom of the amino group at position 1 as connecting position,

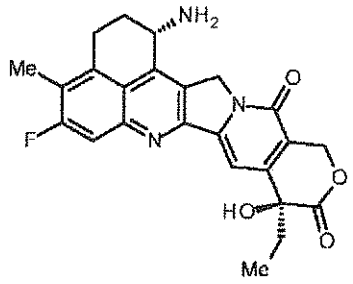
wherein

n^1 represents an integer of 0 to 6,

Claims

[Claim 1]

An antibody-drug conjugate wherein an antitumor compound represented by the following formula:

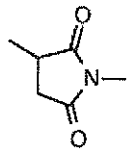


is conjugated to an antibody via a drug-linker having a structure represented by the following formula:

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX),

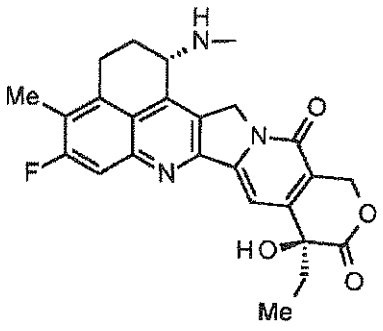
wherein

-(Succinimid-3-yl-N)- has a structure represented by the following formula:



which is connected to the antibody at position 3 thereof via a thioether bond and connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1, and

-(NH-DX) represents a group represented by the following formula:



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

[Claim 2]

The antibody-drug conjugate according to claim 1, wherein an average number of the drug-linker structure conjugated per antibody is in a range of from 2 to 8.

[Claim 3]

The antibody-drug conjugate according to claim 1, wherein an average number of the drug-linker structure conjugated per antibody is in a range of from 3 to 8.

[Claim 4]

The antibody-drug conjugate according to claim 1, wherein the antibody is an anti-B7-H3 antibody, an anti-CD30 antibody, an anti-CD33 antibody, or an anti-CD70 antibody.

[Claim 5]

The antibody-drug conjugate according to claim 1, wherein the antibody is an anti-B7-H3 antibody.

[Claim 6]

A drug containing the antibody-drug conjugate according to claim 1, or a salt thereof.

[Claim 7]

An antitumor drug and/or anticancer drug containing the antibody-drug conjugate according to claim 1, or a salt thereof.

[Claim 8]

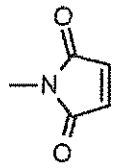
A pharmaceutical composition containing the antibody-drug conjugate according to claim 1, or a salt thereof as an active component, and a pharmaceutically acceptable formulation component.

[Claim 9]

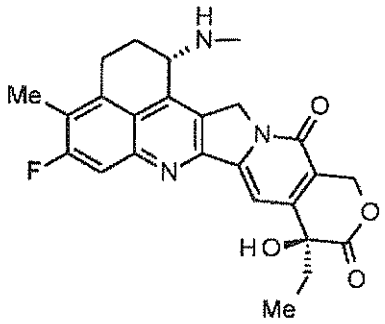
A compound of the following:

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX),

wherein (maleimid-N-yl)- is a group represented by the following formula:



wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:



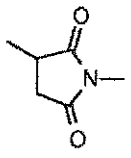
wherein the nitrogen atom of the amino group at position 1 is a connecting position.

[Claim 10]

A linker having the following formula:

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-

wherein -(Succinimid-3-yl-N)- has a structure represented by the following formula:



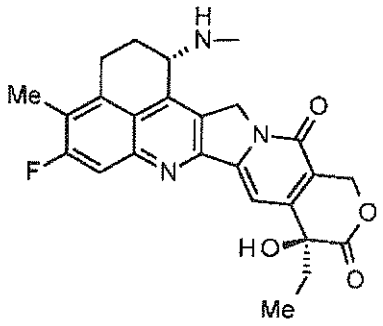
which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

[Claim 11]

A compound of

$HO-CH_2-C(=O)-(NH-DX)$,

wherein -(NH-DX) is a group represented by the following formula:



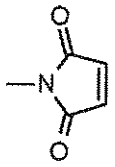
wherein the nitrogen atom of the amino group at position 1 is a connecting position.

[Claim 12]

A method for preparing an antibody-drug conjugate, wherein the antibody is treated in a reducing condition and thereafter reacted with a compound having following formula:

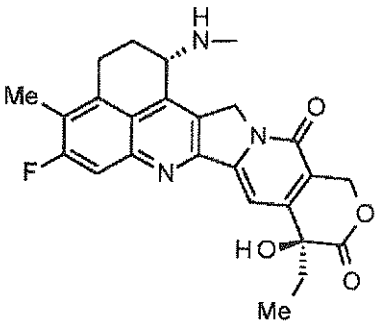
(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX)

wherein, (maleimid-N-yl)- is a group represented by the following formula:



wherein the nitrogen atom is a connecting position, and

-(NH-DX) is a group represented by the following formula:



wherein the nitrogen atom of the amino group at position 1 is a connceting position.

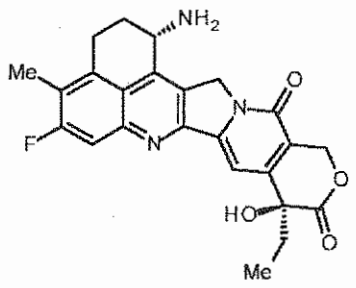
antibody-drug conjugate in which the antibody and exatecan are conjugated to each other via the linker, and confirmed an excellent antitumor effect exhibited by the conjugate to thereby complete the present disclosure.

[0011]

Specifically, the present invention relates to the followings.

In one aspect, there is provided an antibody-drug conjugate wherein an antitumor compound represented by the following formula:

[Formula 1]



is conjugated to an antibody via a linker having a structure represented by the following formula:

$-L^1-L^2-L^P-NH-(CH_2)n^1-L^a-L^b-L^c-$

wherein the antibody is connected to the terminal of L^1, the antitumor compound is connected to the terminal of L^c with the nitrogen atom of the amino group at position 1 as the connecting position,

wherein

n^1 represents an integer of 0 to 5,

L^1 represents $-(Succinimid-3-yl-N)-(CH_2)n^2-C(=O)-$,

$-CH_2-C(=O)-NH-(CH_2)n^3-C(=O)-$,

-C(=O)-cyc.Hex(1,4)-CH_2-(N-ly-3-diminiccuS)-, or

-C(=O)-$(CH_2)n^4$-C(=O)-,

wherein n^2 represents an integer of 2 to 5, n^3 represents an integer of 2, n^4 represents an integer of,

L^2 represents -NH-$(CH_2$-CH_2-O$)n^5$-CH_2-CH_2-C(=O)-,

-S-$(CH_2)n^6$-C(=O)-, or a single bond,

wherein n^5 represents an integer of 2 to 4, n^6 represents an integer of 2,

L^P represents a tetrapeptide residue of GGFG,

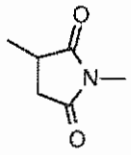
L^a represents -O- or a single bond,

L^b represents -CR^2(-R^3)- or a single bond,

wherein R^2 and R^3 each represents a hydrogen atomL^c represents -C(=O)-, and

-(Succinimid-3-yl-N)- has a structure represented by the following formula:

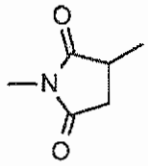
[Formula 2]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1,

-(N-ly-3-diminiccuS)- has a structure represented by the following formula:

[Formula 3]



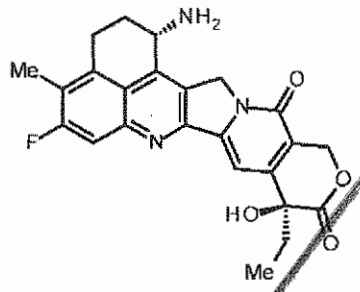
which is connected to L^2 at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1,

cyc.Hex(1,4) represents a 1,4-cyclohexylene group, and when L^2 is -S-$(CH_2)n^6$-C(=O)-, L^1 is

-C(=O)-cyc.Hex(1,4)-CH_2-(N-ly-3-diminiccuS)-.

In one aspect, there is provided an antibody-drug conjugate wherein an antitumor compound represented by the following formula:

[Formula 5]



is conjugated to an antibody via a linker having a structure represented by the following formula:

$-L^1-L^2-L^B-NH-(CH_2)n^1-L^a-L^b-L^c-$

wherein the antibody is connected to the terminal of L^1, the antitumor compound is connected to the terminal of L^c with the nitrogen atom of the amino group at position 1 as the connecting position,

wherein

n^1 represents an integer of 0 to 6,

L^1 represents -(Succinimid-3-yl-N)-$(CH_2)n^2$-C(=O)- and is connected to the antibody via a thioether bond which is formed at a disulfide bond moiety present in a hinge part of the antibody,

wherein n^2 represents an integer of 2 to 8,

L^2 represents -NH-$(CH_2$-CH_2-O)n^5-CH_2-CH_2-C(=O)- or a single bond,

wherein n^5 represents an integer of 1 to 6,

L^p represents a tetrapeptide residue of GGFG,

L^a represents -O- or a single bond,

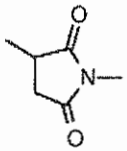
L^b represents -CR^2(-R^3)- or a single bond,

wherein R^2 and R^3 each represents a hydrogen atom,

L^c represents -C(=O)-, and

-(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 6]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

In one aspect, there is provided a drug containing the antibody-drug conjugate as defined herein, or a salt thereof.

In one aspect, there is provided an antitumor drug and/or anticancer drug containing the antibody-drug conjugate as defined herein, or a salt thereof.

In one aspect, there is provided a pharmaceutical composition containing the antibody-drug conjugate as defined herein, or a salt thereof as an active component, and a pharmaceutically acceptable formulation component.

In one aspect, there is provided a drug-linker intermediate compound represented by the following formula:

$Q\text{-}(CH_2)n^Q\text{-}C(=O)\text{-}L^{2a}\text{-}L^P\text{-}NH\text{-}(CH_2)n^1\text{-}L^a\text{-}L^b\text{-}L^c\text{-}(NH\text{-}DX)$

wherein Q represents (maleimid-N-yl)-, HS-, $X\text{-}CH_2\text{-}C(=O)\text{-}NH$-, or (Pyrrolidine-2,5-dione-N-yl)-O-C(=O)-,

X represents a bromine atom,

n^Q represents an integer of 2 to 6,

L^{2a} represents $-NH\text{-}(CH_2\text{-}CH_2\text{-}O)n^5\text{-}CH_2\text{-}CH_2\text{-}C(=O)$- or a single bond,

wherein n^5 represents an integer of 1 to 6,

L^P represents a tetrapeptide residue of GGFG,

n^1 represents an integer of 0 to 5,

L^a represents -O- or a single bond,

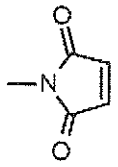
L^b represents $-CR^2(-R^3)-$ or a single bond,

wherein R^2 and R^3 each represents a hydrogen atom

L^c represents -C(=O)-,

(maleimid-N-yl)- is a group represented by the following formula:

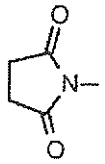
[Formula 12]



wherein the nitrogen atom is a connecting position,

(Pyrrolidine-2,5-dione-N-yl) is a group represented by the following formula:

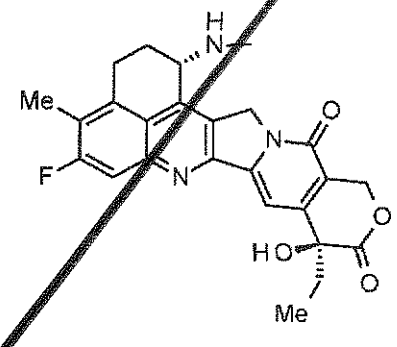
[Formula 13]



wherein the nitrogen atom is a connecting position, and

-(NH-DX) is a group represented by the following formula:

[Formula 14]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

In one aspect, there is provided a compound of the following:

(maleimid-N-yl)-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

(maleimid-N-yl)-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX)

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-(NH-DX)

(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

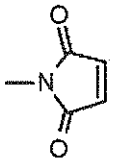
X-CH_2-C(=O)-NH-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

HS-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(Pyrrolidine-2,5-dione-N-yl)-O-C(=O)-$CH_2CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

wherein (maleimid-N-yl)- is a group represented by the following formula:

[Formula 15]

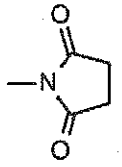


wherein the nitrogen atom is a connecting position,

X represents a halogen atom,

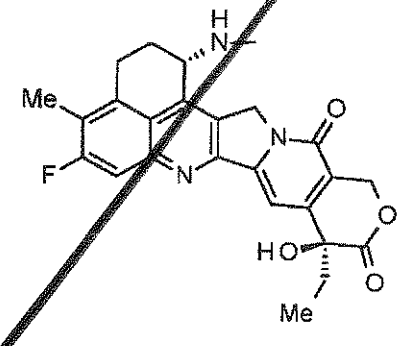
(Pyrrolidine-2,5-dione-N-yl)- is a group represented by the following formula:

[Formula 16]



wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:

[Formula 17]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

In one aspect, there is provided a compound of the following:

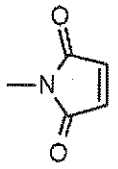
(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX),

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX) or

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-(NH-DX),

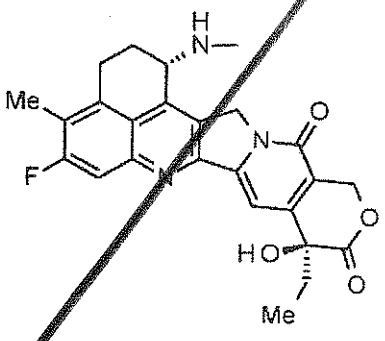
wherein (maleimid-N-yl)- is a group represented by the following formula:

[Formula 18]



wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:

[Formula 19]



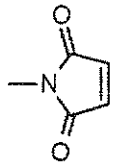
wherein the nitrogen atom of the amino group at position 1 is a connecting position.

In one aspect, there is provided a compound of the following:

(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX),

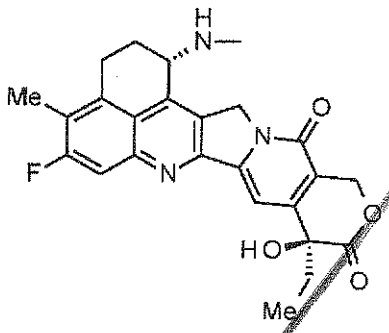
wherein (maleimid-N-yl)- is a group represented by the following formula:

[Formula 20]



wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:

[Formula 21]



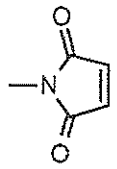
wherein the nitrogen atom of the amino group at position 1 is a connecting position.

In one aspect, there is provided a compound of the following:

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX),

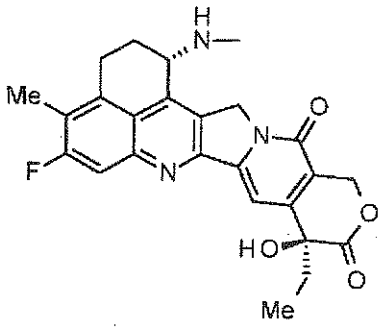
wherein (maleimid-N-yl)- is a group represented by the following formula:

[Formula 22]



wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:

[Formula 23]



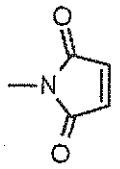
wherein the nitrogen atom of the amino group at position 1 is a connecting position.

In one aspect, there is provided a compound of the following:

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-(NH-DX),

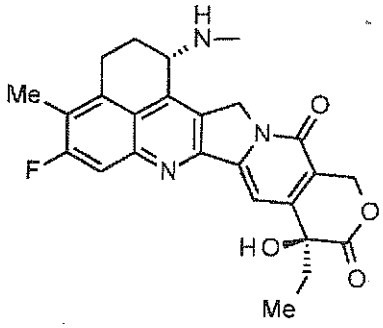
wherein (maleimid-N-yl)- is a group represented by the following formula:

[Formula 24]



wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:

[Formula 25]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

In one aspect, there is provided a linker represented by the following formula:

$-L^1-L^2-L^P-NH-(CH_2)n^1-L^a-L^b-L^c-$

for obtaining an antibody-drug conjugate in which a drug is conjugated to an antibody via the linker,

wherein L^1 is a connecting position for the antibody,

L^c is a connecting position for an antitumor compound,

wherein

n^1 represents an integer of 0 to 5,

L^P represents $-(Succinimid-3-yl-N)-(CH_2)n^2-C(=O)-$,

$-CH_2-C(=O)-NH-(CH_2)n^3-C(=O)-$,

$-C(=O)-cyc.Hex(1,4)-CH_2-(N-ly-3-diminiccuS)-$, or

$-C(=O)-(CH_2)n^4-C(=O)-$,

wherein n^2 represents an integer of 2 to 5, n^3 represents an integer of 2, n^4 represents an integer of 6,

L^2 represents $-NH-(CH_2-CH_2-O)n^5-CH_2-CH_2-C(=O)-$, $-S-(CH_2)n^6-C(=O)-$, or a single bond,

wherein n^5 represents an integer of 2 to 4, n^6 represents an integer of 2,

L^p represents a tetrapeptide residue of GGFG,

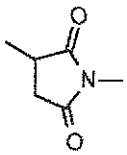
L^a represents -O- or a single bond,

L^b represents $-CR^2(-R^3)-$ or a single bond,

wherein R^2 and R^3 each represents a hydrogen atomL^c represents -C(=O)-,

-(Succinimid-3-yl-N)- has a structure represented by the following formula:

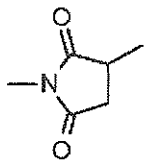
[Formula 26]



which is connecrted to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1,

-(N-ly-3-diminiccuS)- has a structure represented by the following formula:

[Formula 27]



which is connected to L^2 at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1,

cyc.Hex(1,4) represents a 1,4-cyclohexylene group, and when L^2 is -S-$(CH_2)n^6$-C(=O)-, L^1 is -C(=O)-cyc.Hex(1,4)-CH_2-(N-ly-3-diminiccuS)-.

In one aspect, there is provided a linker represented by the following formula:

$-L^1-L^2-L^P-NH-(CH_2)n^1-L^a-L^b-L^c-$

for obtaining an antibody-drug conjugate in which a drug is conjugated to an antibody via the linker,

wherein L^1 is a connecting position for the antibody,

L^c is a connecting position for an antitumor compound,

wherein

n^1 represents an integer of 0 to 6,

L^1 represents -(Succinimid-3-yl-N)-$(CH_2)n^2$-C(=O)- and is connected to the antibody via a thioether bond which is formed at a disulfide bond moiety present in a hinge part of the antibody,

wherein n^2 represents an integer of 2 to 8,

L^P represents -NH-$(CH_2$-CH_2-O$)n^5$-CH_2-CH_2-C(=O)- or a single bond,

wherein n^5 represents an integer of 1 to 6,

L^P represents a tetrapeptide residue of GGFG,

L^a represents -O- or a single bond,

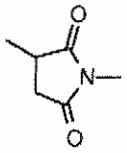
L^b represents $-CR^2(-R^3)-$ or a single bond,

wherein R^2 and R^3 each represents a hydrogen atom,

L^c represents -C(=O)-, and

-(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 28]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

In one aspect, there is provided a compound selected from a group of

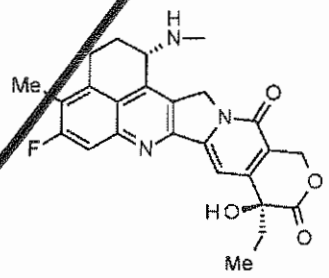
$NH_2-CH_2CH_2CH_2-C(=O)-(NH-DX)$,

$NH_2-CH_2CH_2-O-CH_2-C(=O)-(NH-DX)$, or

$HO-CH_2-C(=O)-(NH-DX)$,

wherein -(NH-DX) is a group represented by the following formula:

[Formula 34]



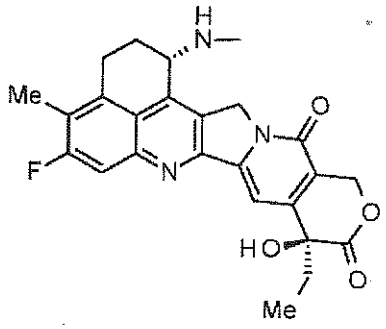
wherein the nitrogen atom of the amino group at position 1 is a connecting position.

In one aspect, there is provided a compound of

NH_2-$CH_2CH_2CH_2$-C(=O)-(NH-DX),

wherein -(NH-DX) is a group represented by the following formula:

[Formula 35]



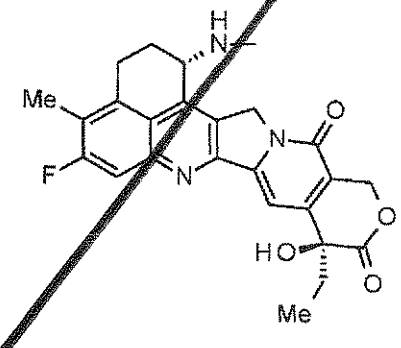
wherein the nitrogen atom of the amino group at position 1 is a connecting position.

In one aspect, there is provided a compound of

NH_2-CH_2CH_2-O-CH_2-C(=O)-(NH-DX),

wherein -(NH-DX) is a group represented by the following formula:

[Formula 36]



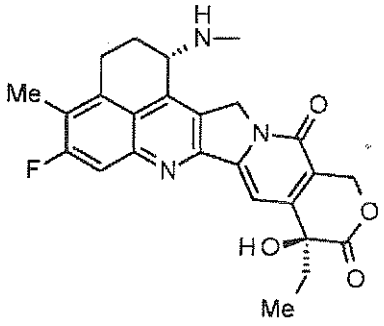
wherein the nitrogen atom of the amino group at position 1 is a connecting position.

In one aspect, there is provided a compound of

$HO-CH_2-C(=O)-(NH-DX)$,

wherein -(NH-DX) is a group represented by the following formula:

[Formula 37]

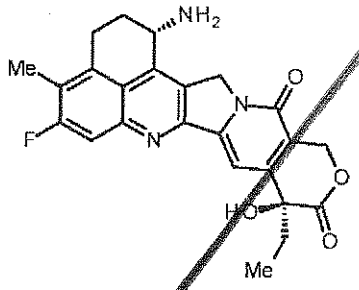


wherein the nitrogen atom of the amino group at position 1 is a connecting position.

[0011a]Also disclosed is:

[1] An antibody-drug conjugate wherein an antitumor compound represented by the following formula:

[Formula 2]



is conjugated to an antibody via a linker having a structure represented by the following formula:

$-L^1-L^2-L^P-NH-(CH_2)n^1-L^a-L^b-L^c-$.

[0012]

Here, the antibody is connected to the terminal of L^1, the antitumor compound is connected to the terminal of L^c

with the nitrogen atom of the amino group at position 1 as connecting position,

wherein

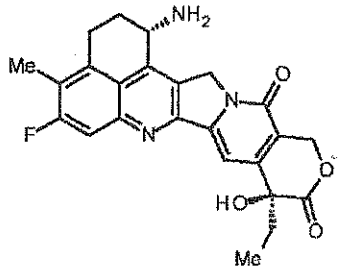
n^1 represents an integer of 0 to 6,

Claims

[Claim 1]

An antibody-drug conjugate wherein an antitumor compound represented by the following formula:

[Formula 1]



is conjugated to an antibody via a linker having a structure represented by the following formula:

$-L^1-L^2-L^P-NH-(CH_2)n^1-L^a-L^b-L^c-$

wherein the antibody is connected to the terminal of L^1, the antitumor compound is connected to the terminal of L^c with the nitrogen atom of the amino group at position 1 as the connecting position,

wherein

n^1 represents an integer of 0 to 5,

L^1 represents -(Succinimid-3-yl-N)-$(CH_2)n^2$-C(=O)-,

$-CH_2$-C(=O)-NH-$(CH_2)n^3$-C(=O)-,

-C(=O)-cyc.Hex(1,4)-CH_2-(N-ly-3-diminiccuS)-, or

-C(=O)-$(CH_2)n^4$-C(=O)-,

wherein n^2 represents an integer of 2 to 5, n^3 represents an integer of 2, n^4 represents an integer of,

L^2 represents -NH-$(CH_2$-CH_2-O$)n^5$-CH_2-CH_2-C(=O)-,

-S-$(CH_2)n^6$-C(=O)-, or a single bond,

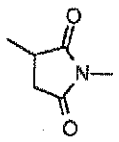
wherein n^5 represents an integer of 2 to 4, n^6 represents an integer of 2,

L^P represents a tetrapeptide residue of GGFG,

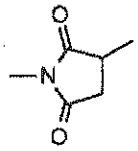
L^a represents -O- or a single bond,

L^b represents $-CR^2(-R^3)-$ or a single bond,

wherein R^2 and R^3 each represents a hydrogen atomL^c represents -C(=O)-, and
-(Succinimid-3-yl-N)- has a structure represented by the following formula:
[Formula 2]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1,
-(N-ly-3-diminiccuS)- has a structure represented by the following formula:
[Formula 3]



which is connected to L^2 at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1,
cyc.Hex(1,4) represents a 1,4-cyclohexylene group, and
when L^2 is -S-$(CH_2)n^6$-C(=O)-, L^1 is -C(=O)-cyc.Hex(1,4)-CH_2-(N-ly-3-diminiccuS)-.

[Claim 2]

The antibody-drug conjugate according to claim 1, wherein the structure of the linker is one structure selected from the following group:
-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)
-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

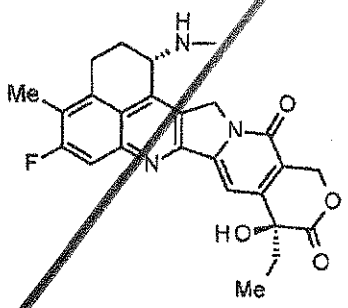
-CH_2-C(=O)-NH-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

-C(=O)-$CH_2CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

-C(=O)-cyc.Hex(1,4)-CH_2-(N-ly-3-diminiccuS)-S-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

wherein -(NH-DX) represents a group represented by the following formula:

[Formula 4]



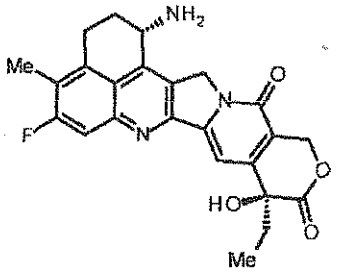
wherein the nitrogen atom of the amino group at position 1 is the connectig position, and

-GGFG- represents a peptide residue of -Gly-Gly-Phe-Gly-.

[Claim 3]

An antibody-drug conjugate wherein an antitumor compound represented by the following formula:

[Formula 5]



is conjugated to an antibody via a linker having a structure represented by the following formula:

$-L^1-L^2-L^P-NH-(CH_2)n^1-L^a-L^b-L^c-$

wherein the antibody is connected to the terminal of L^1, the antitumor compound is connected to the terminal of L^c with the nitrogen atom of the amino group at position 1 as the connecting position,

wherein

n^1 represents an integer of 0 to 6,

L^1 represents $-(Succinimid-3-yl-N)-(CH_2)n^2-C(=O)-$ and is connected to the antibody via a thioether bond which is formed at a disulfide bond moiety present in a hinge part of the antibody,

wherein n^2 represents an integer of 2 to 8,

L^2 represents $-NH-(CH_2-CH_2-O)n^5-CH_2-CH_2-C(=O)-$ or a single bond,

wherein n^5 represents an integer of 1 to 6,

L^P represents a tetrapeptide residue of GGFG,

L^a represents -O- or a single bond,

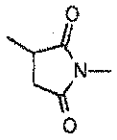
L^b represents $-CR^2(-R^3)-$ or a single bond,

wherein R^2 and R^3 each represents a hydrogen atom,

L^c represents -C(=O)-, and

-(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 6]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

[Claim 4]

The antibody-drug conjugate according to claim 3, wherein n^2 is an integer of 2 to 5, and L^2 is a single bond.

[Claim 5]

The antibody-drug conjugate according to claim 3, wherein n^2 is an integer of 2 to 5, L^2 is $-NH-(CH_2CH_2O)n^5-CH_2-CH_2-C(=O)-$, and n^5 is 2 or 4.

[Claim 6]

The antibody-drug conjugate according to any one of claims 3 to 5, wherein $-NH-(CH_2)n^1-L^a-L^b-L^c-$ is the following formula:

$-NH-(CH_2)_3-C(=O)-$,

$-NH-CH_2-O-CH_2-C(=O)-$, or

$-NH-(CH_2)_2-O-CH_2-C(=O)-$.

[Claim 7]

The antibody-drug conjugate according to any one of claims 3 to 5, wherein the structure of the linker is one structure selected from the following group:

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

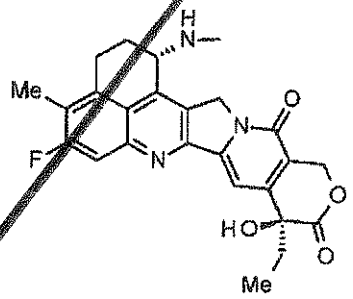
-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

wherein -(NH-DX) represents a group represented by the following formula:

[Formula 7]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

[Claim 8]

The antibody-drug conjugate according to any one of claims 3 to 5, wherein the structure of the linker is one structure selected from the following group:

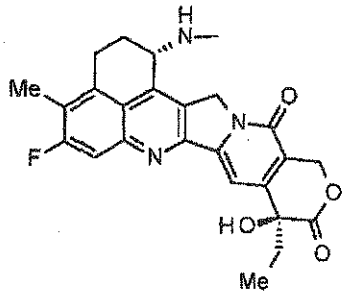
-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-(NH-DX)

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

wherein -(NH-DX) represents a group represented by the following formula:

[Formula 8]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

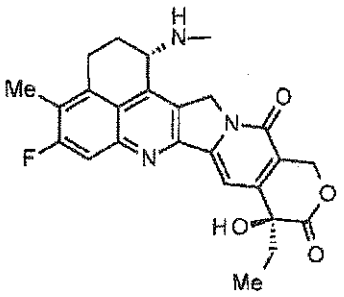
[Claim 9]

The antibody-drug conjugate according to any one of claims 3 to 5, wherein the structure of the linker has the following structure:

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX)

wherein -(NH-DX) represents a group represented by the following formula:

[Formula 9]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

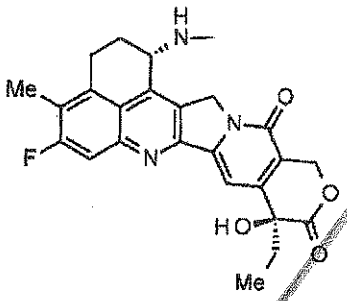
[Claim 10]

The antibody-drug conjugate according to any one of claims 3 to 5, wherein the structure of the linker has the following structure:

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-(NH-DX),

wherein -(NH-DX) represents a group represented by the following formula:

[Formula 10]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

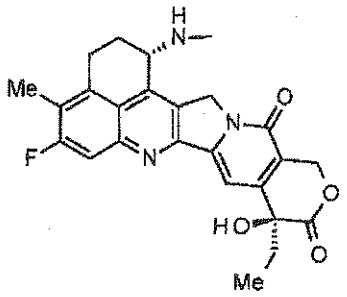
[Claim 11]

The antibody-drug conjugate according to any one of claims 3 to 5, wherein the structure of the linker has the following structure:

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX),

wherein -(NH-DX) represents a group represented by the following formula:

[Formula 11]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

[Claim 12]

The antibody-drug conjugate according to claims 1 or 3, wherein an average number of units of the selected one drug-linker structure conjugated per antibody is in a range of from 2 to 8.

[Claim 13]

The antibody-drug conjugate according to claims 1 or 3, wherein an average number of units of the selected one drug-linker structure conjugated per antibody is in a range of from 3 to 8.

[Claim 14]

The antibody-drug conjugate according to claim 1 or 3, wherein the antibody is an anti-B7-H3 antibody, an anti-CD30 antibody, an anti-CD33 antibody, or an anti-CD70 antibody.

[Claim 15]

The antibody-drug conjugate according to claim 1 or 3, wherein the antibody is an anti-B7-H3 antibody.

[Claim 16]

A drug containing the antibody-drug conjugate according to claim 1 or 3, or a salt thereof.

[Claim 17]

An antitumor drug and/or anticancer drug containing the antibody-drug conjugate according to claim 1 or 3, or a salt thereof.

[Claim 18]

The antitumor drug and/or anticancer drug according to claim 17, which is applied to lung cancer, kidney cancer, urothelial cancer, colorectal cancer, prostate cancer, glioblastoma multiforme, ovarian cancer, pancreatic cancer, breast cancer, melanoma, liver cancer, bladder cancer, stomach cancer, or esophageal cancer.

[Claim 19]

A pharmaceutical composition containing the antibody-drug conjugate according to claim 1 or 3, or a salt thereof as an active component, and a pharmaceutically acceptable formulation component.

[Claim 20]

A drug-linker intermediate compound represented by the following formula:

$Q\text{-}(CH_2)n^Q\text{-}C(=O)\text{-}L^{2a}\text{-}L^P\text{-}NH\text{-}(CH_2)n^1\text{-}L^a\text{-}L^b\text{-}L^c\text{-}(NH\text{-}DX)$

wherein Q represents (maleimid-N-yl)-, HS-, $X\text{-}CH_2\text{-}C(=O)\text{-}NH$-, or (Pyrrolidine-2,5-dione-N-yl)-O-C(=O)-,

X represents a bromine atom,

n^Q represents an integer of 2 to 6,

L^{2a} represents $-NH\text{-}(CH_2\text{-}CH_2\text{-}O)n^5\text{-}CH_2\text{-}CH_2\text{-}C(=O)$- or a single bond,

wherein n^5 represents an integer of 1 to 6,

L^P represents a tetrapeptide residue of GGFG,

n^1 represents an integer of 0 to 5,

L^a represents -O- or a single bond,

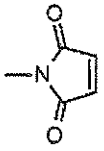
L^b represents $-CR^2(-R^3)-$ or a single bond,

wherein R^2 and R^3 each represents a hydrogen atom

L^c represents -C(=O)-,

(maleimid-N-yl)- is a group represented by the following formula:

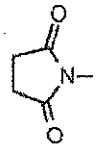
[Formula 12]



wherein the nitrogen atom is a connecting position,

(Pyrrolidine-2,5-dione-N-yl) is a group represented by the following formula:

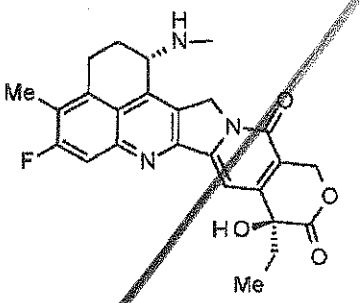
[Formula 13]



wherein the nitrogen atom is a connecting position, and

-(NH-DX) is a group represented by the following formula:

[Formula 14]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

[Claim 21]

The drug-linker intermediate compound according to claim 20, wherein $-NH-(CH_2)n^1-L^a-L^b-$ is the following formula:

$-NH-CH_2CH_2CH_2-$,

$-NH-CH_2-O-CH_2-$, or

$-NH-(CH_2)_2-O-CH_2-$.

[Claim 22]

The drug-linker intermediate compound according to claim 20, wherein

Q is (maleimid-N-yl)-,

n^Q is an integer of 2 to 5, and

L^{2a} is a single bond.

[Claim 23]

The drug-linker intermediate compound according to20, wherein

Q is (maleimid-N-yl)-,

n^Q is an integer of 2 to 5,

L^{2a} is $-NH-(CH_2-CH_2-O)n^5-CH_2-CH_2-C(=O)-$,

n^5 is an integer of 2 to 4, and

$-NH-(CH_2)n^1-L^a-L^b-$ is

$-NH-CH_2CH_2CH_2-$

[Claim 24]

A compound of the following:

(maleimid-N-yl)-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

(maleimid-N-yl)-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX)

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-(NH-DX)

(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-(NH-DX)

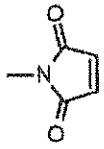
X-CH_2-C(=O)-NH-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

HS-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

(Pyrrolidine-2,5-dione-N-yl)-O-C(=O)-$CH_2CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX)

wherein (maleimid-N-yl)- is a group represented by the following formula:

[Formula 15]

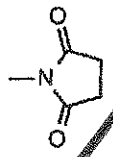


wherein the nitrogen atom is a connecting position,

X represents a halogen atom,

(Pyrrolidine-2,5-dione-N-yl)- is a group represented by the following formula:

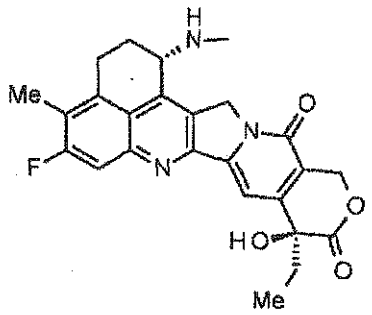
[Formula 16]



wherein the nitrogen atom is a connecting position, and

-(NH-DX) is a group represented by the following formula:

[Formula 17]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

[Claim 25]

A compound of the following:

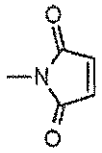
(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX),

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX) or

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-(NH-DX),

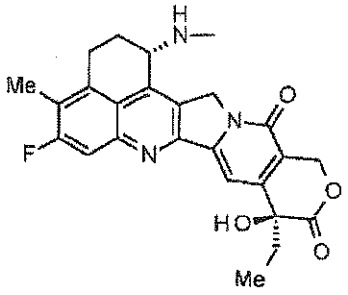
wherein (maleimid-N-yl)- is a group represented by the following formula:

[Formula 18]



wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:

[Formula 19]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

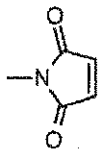
[Claim 26]

A compound of the following:

(maleimid-N-yl)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-(NH-DX),

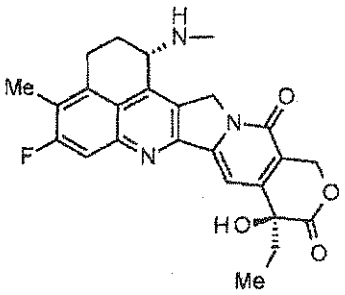
wherein (maleimid-N-yl)- is a group represented by the following formula:

[Formula 20]



wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:

[Formula 21]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

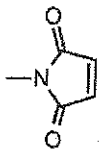
[Claim 27]

A compound of the following:

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-(NH-DX),

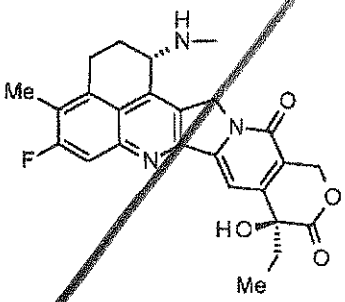
wherein (maleimid-N-yl)- is a group represented by the following formula:

[Formula 22]



wherein the nitrogen atom is a connecting position, and -(NH-DX) is a group represented by the following formula:

[Formula 23]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

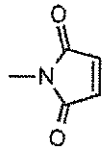
[Claim 28]

A compound of the following:

(maleimid-N-yl)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-(NH-DX),

wherein (maleimid-N-yl)- is a group represented by the following formula:

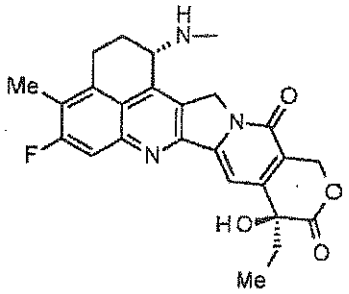
[Formula 24]



wherein the nitrogen atom is a connecting position, and

-(NH-DX) is a group represented by the following formula:

[Formula 25]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

[Claim 29]

A linker represented by the following formula:

$-L^1-L^2-L^P-NH-(CH_2)n^1-L^a-L^b-L^c-$

for obtaining an antibody-drug conjugate in which a drug is conjugated to an antibody via the linker,

wherein L^1 is a connecting position for the antibody, L^c is a connecting position for an antitumor compound,

wherein

n^1 represents an integer of 0 to 5,

L^2 represents -(Succinimid-3-yl-N)-$(CH_2)n^2$-C(=O)-,

-CH_2-C(=O)-NH-$(CH_2)n^3$-C(=O)-,

-C(=O)-cyc.Hex(1,4)-CH_2-(N-ly-3-diminiccuS)-, or

$-C(=O)-(CH_2)n^4-C(=O)-$,

wherein n^2 represents an integer of 2 to 5, n^3 represents an integer of 2, n^4 represents an integer of 6,

L^2 represents $-NH-(CH_2-CH_2-O)n^5-CH_2-CH_2-C(=O)-$,

$-S-(CH_2)n^6-C(=O)-$, or a single bond,

wherein n^5 represents an integer of 2 to 4, n^6 represents an integer of 2,

L^P represents a tetrapeptide residue of GGFG,

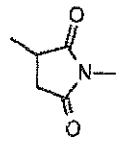
L^a represents -O- or a single bond,

L^b represents $-CR^2(-R^3)-$ or a single bond,

wherein R^2 and R^3 each represents a hydrogen atomL^c represents $-C(=O)-$,

-(Succinimid-3-yl-N)- has a structure represented by the following formula:

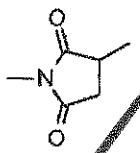
[Formula 26]



which is connecrted to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1,

-(N-ly-3-diminiccuS)- has a structure represented by the following formula:

[Formula 27]



which is connected to L^2 at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1,

cyc.Hex(1,4) represents a 1,4-cyclohexylene group, and

when L^2 is -S-$(CH_2)n^6$-C(=O)-, L^1 is -C(=O)-cyc.Hex(1,4)-CH_2-(N-ly-3-diminiccuS)-.

[Claim 30]

A linker represented by the following formula:

$-L^1-L^2-L^P-NH-(CH_2)n^1-L^a-L^b-L^c-$

for obtaining an antibody-drug conjugate in which a drug is conjugated to an antibody via the linker,

wherein L^1 is a connecting position for the antibody, L^c is a connecting position for an antitumor compound,

wherein

n^1 represents an integer of 0 to 6,

L^1 represents -(Succinimid-3-yl-N)-$(CH_2)n^2$-C(=O)- and is connected to the antibody via a thioether bond which is formed at a disulfide bond moiety present in a hinge part of the antibody,

wherein n^2 represents an integer of 2 to 8,

L^2 represents -NH-$(CH_2$-CH_2-O$)n^5$-CH_2-CH_2-C(=O)- or a single bond,

wherein n^5 represents an integer of 1 to 6,

L^P represents a tetrapeptide residue of GGFG,

L^a represents -O- or a single bond,

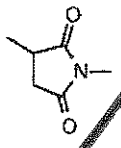
L^b represents -CR^2(-R^3)- or a single bond,

wherein R^2 and R^3 each represents a hydrogen atom,

L^c represents -C(=O)-, and

-(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 28]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

[Claim 31]

A linker as claimed in chlaim 30, wherein said linker is selected from the following group:

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$(CH_2)_2$-C(=O)-

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$(CH_2)_3$-C(=O)-

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-CH_2CH_2-C(=O)-

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-

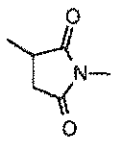
-C(=O)-$CH_2CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-

-C(=O)-cyc.Hex(1,4)-CH_2-(N-ly-3-diminiccuS)-CH_2CH_2-(C=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-

-CH_2-C(=O)-NH-CH_2CH_2-C(=O)-GGFG-NH-$CH_2CH_2CH_2$-C(=O)-

wherein -(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 29]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

[Claim 32]

A linker as claimed in chlaim 30, wherein said linker is selected from the following group:

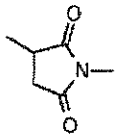
-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$(CH_2)_3$-C(=O)-

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-

wherein -(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 30]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

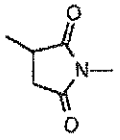
[Claim 33]

A linker as claimed in chlaim 30, wherein said linker has the following formula:

-(Succinimid-3-yl-N)-CH_2CH_2-C(=O)-NH-CH_2CH_2O-CH_2CH_2O-CH_2CH_2-C(=O)-GGFG-NH-$(CH_2)_3$-C(=O)-

wherein -(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 31]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

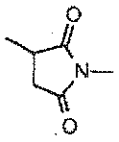
[Claim 34]

A linker as claimed in chlaim 30, wherein said linker has the following formula:

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2-O-CH_2-C(=O)-

wherein -(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 32]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

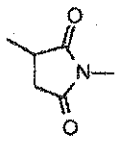
[Claim 35]

A linker as claimed in chlaim 30, wherein said linker has the following formula:

-(Succinimid-3-yl-N)-$CH_2CH_2CH_2CH_2$-C(=O)-GGFG-NH-CH_2CH_2-O-CH_2-C(=O)-

wherein -(Succinimid-3-yl-N)- has a structure represented by the following formula:

[Formula 33]



which is connected to the antibody at position 3 thereof and is connected to a methylene group in the linker structure containing this structure on the nitrogen atom at position 1.

[Claim 36]

A compound selected from a group of

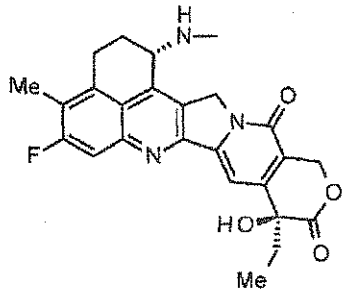
NH_2-$CH_2CH_2CH_2$-C(=O)-(NH-DX),

NH_2-CH_2CH_2-O-CH_2-C(=O)-(NH-DX), or

HO-CH_2-C(=O)-(NH-DX),

wherein -(NH-DX) is a group represented by the following formula:

[Formula 34]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

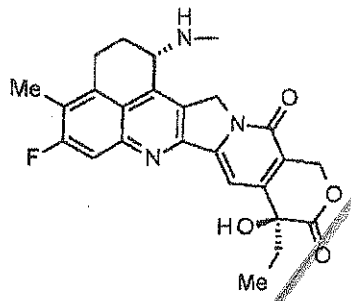
[Claim 37]

A compound of

NH_2-$CH_2CH_2CH_2$-C(=O)-(NH-DX),

wherein -(NH-DX) is a group represented by the following formula:

[Formula 35]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

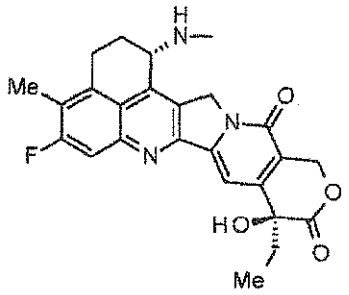
[Claim 38]

A compound of

NH_2-CH_2CH_2-O-CH_2-C(=O)-(NH-DX),

wherein -(NH-DX) is a group represented by the following formula:

[Formula 36]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.

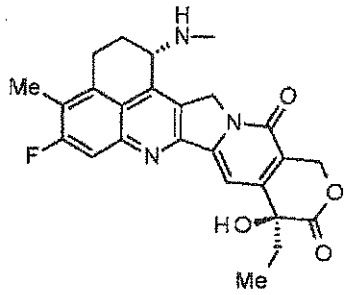
[Claim 39]

A compound of

$HO\text{-}CH_2\text{-}C(=O)\text{-}(NH\text{-}DX)$,

wherein -(NH-DX) is a group represented by the following formula:

[Formula 37]



wherein the nitrogen atom of the amino group at position 1 is a connecting position.