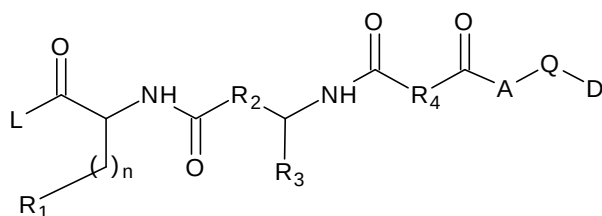


CLAIMS

1. A compound of Formula I



Formula I

or pharmaceutically acceptable salt, stereoisomer or isotope thereof,

wherein: n is 0, 1, 2, 3 or 4;

L is a ligand;

R₁ is selected from a 6 to 14 membered aryl or a 5 to 13 membered heteroaryl containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur;

R₁ is unsubstituted or substituted with one or more R₅;

R₅, at each occurrence, is independently selected from halogen, —C(O)NH₂, —C(O)OR₆, —C₁₋₃ alkyl, —OR₇, and a 6 to 10 membered aryl; wherein,

R₆ is hydrogen or C₁₋₃ alkyl;

R₇ is hydrogen or C₁₋₃ alkyl;

R₂ is absent or is selected from a 6 to 10 membered cycloalkyl or a 6 to 10 membered aryl;

R₃ is hydrogen or —C₁₋₅COOH;

R₄ is selected from a group consisting of —C₁₋₁₀ alkyl-, —C₂₋₆ alkenyl-, —C₁₋₃ alkyl-O-C₁₋₃ alkyl-, —C₂₋₆ alkyl-N(R₈)-, —C₂₋₆ alkyl(N(R₈)(R₈'))-, —N(R₈)-C₂₋₆ alkyl-, a 3 to 6 membered cycloalkyl and —C₁₋₂ alkyl-(-OC₂H₄)₁₋₈-OC₁₋₂ alkyl-; wherein,

R₈ and R₈' are independently selected from hydrogen, C₁₋₆ alkyl, -C(O)-C₁₋₄alkyl-aryl or -C(O)-(-C₂H₄O)₁₋₈-C₁₋₂ alkyl-N(R)(R'), wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl; wherein

R and R' are independently selected from hydrogen, -C₁₋₆ alkyl or -C(O)-C₁₋₄alkyl-aryl, wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl;

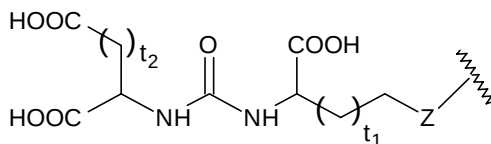
A is an amino acid or a peptide comprising 2-5 amino acids;

A is attached to Q through its C terminal;

Q is a self-immolative group; and

D is a cytotoxic agent or a therapeutic agent.

2. The compound as claimed in claim 1, wherein the ligand L is a ligand of Formula L₁:



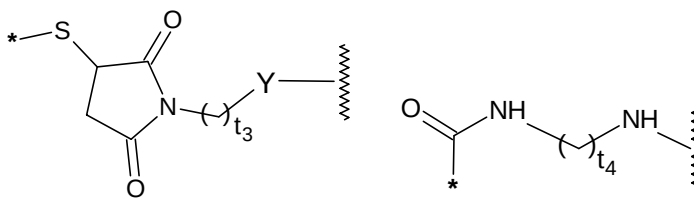
Formula L₁

wherein,

t₁ is 0, 1, 2, 3, or 4;

t₂ is 1, 2, 3 or 4;

Z is selected from the group consisting of N(R₉), Formula Z₁ and Formula Z₂:



Formula Z₁

Formula Z₂

wherein:

t₃ is selected from 1, 2, 3, 4, 5 or 6;

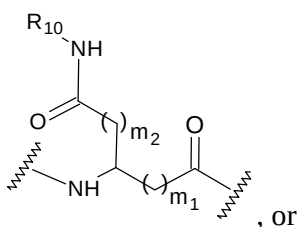
t₄ is selected from 1, 2, 3, 4, 5 or 6;

Y is -CH₂- or -NH- and

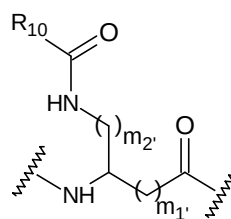
'www' indicates attachment of Formula L₁ to the rest of the compound of Formula I;

R₉ is selected from the group consisting of hydrogen, C₁₋₅ alkyl, a 6 to 10 membered aryl, a 5 to 10 membered heterocyclyl ring wherein the heterocyclyl ring contains one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur; and wherein R₉ is unsubstituted or substituted with halogen.

3. The compound as claimed in claim 1, wherein the amino acid in A at each occurrence is independently selected from the group consisting of alanine (ala), arginine (arg), aspartic acid (asp), cysteine (cys), glutamic acid (glu), glycine (gly), lysine (lys), phenylalanine (phe), serine (ser), threonine (thr), tryptophan (trp), valine (val), ornithine (orn), citrulline (cit), homocitrulline (hct), lanthionine (lan), homocysteine (hcy) or an amino acid having Formula A1 or Formula A2



Formula A₁



Formula A₂

wherein

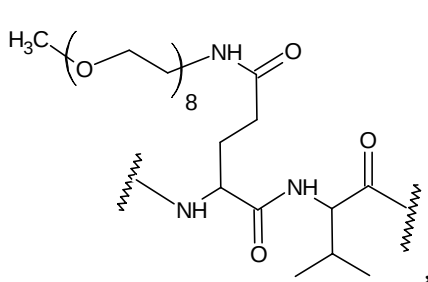
m_1 and m_1' are 0, 1, 2 or 3;

m_2 and m_2' are 0, 1, 2, 3 or 4;

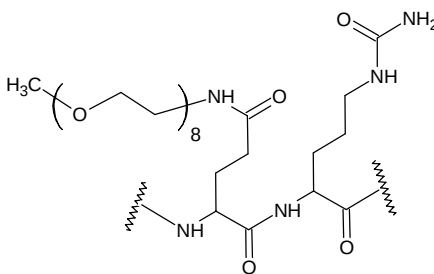
R_{10} is selected from $(-C_2H_4O)_{1-24}CH_3$, $(-C_2H_4O)_{1-24}C_{1-2}$ alkyl($N(R_{10'})$ ($R_{10''}$))—, C_{1-3} alkyl-aryl or — C_{1-3} alkyl-Het₁— $(-C_2H_4O)_{1-24}CH_3$, wherein Het₁ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur and wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}$ alkyl or $-OC_{1-3}$ alkyl; wherein

$R_{10'}$ and $R_{10''}$ are independently selected from hydrogen, C_{1-6} alkyl or $-C(O)-C_{1-4}$ alkyl-aryl wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}$ alkyl or $-OC_{1-3}$ alkyl.

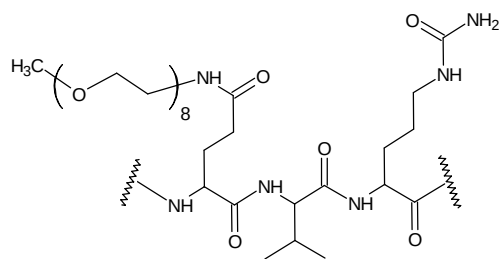
4. The compound as claimed in claim 1, wherein A is a peptide selected from the group consisting of ala-ala, ala-ala-ala, ala-phe, val-ala, val-cit, ala-val-cit, ala(beta)-val-cit, glu-val-cit, glu-cit, glu-val, gly-gly, gly-gly-phe, gly-gly-phe-gly, asp-cit, asp-val-cit and asp-val; or the peptide is selected from a group of compounds having following formula:



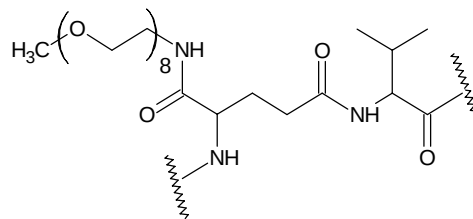
Formula P₁



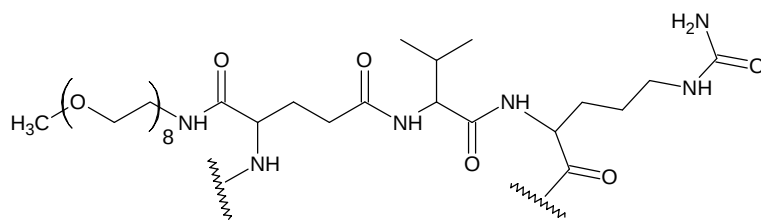
Formula P₂



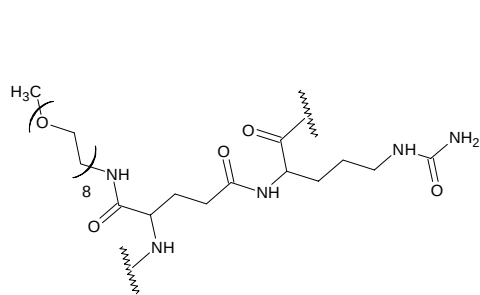
Formula P₃



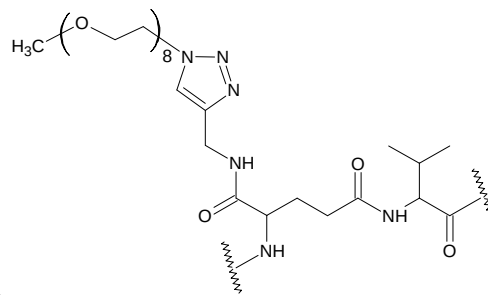
Formula P₄



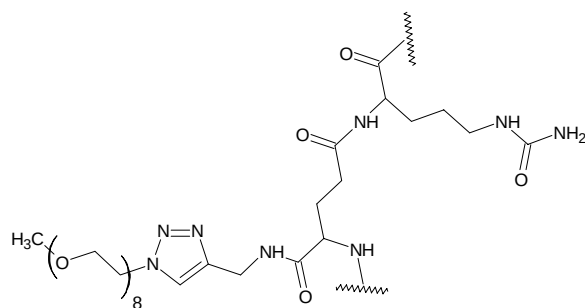
Formula P₅



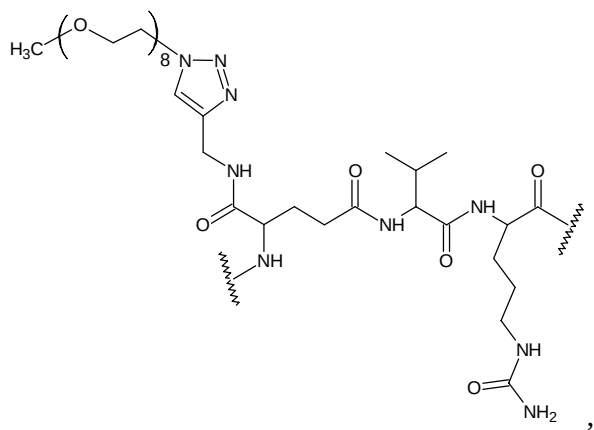
Formula P₆



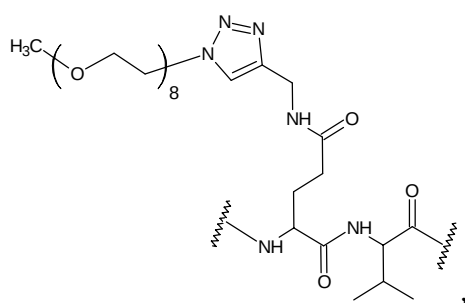
Formula P₇



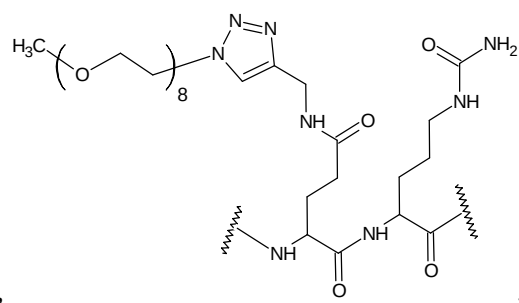
Formula P₈



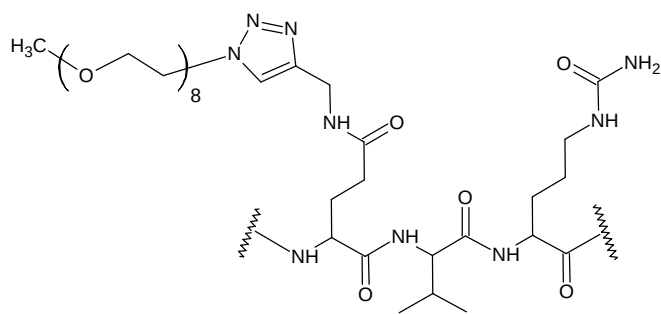
Formula P₉



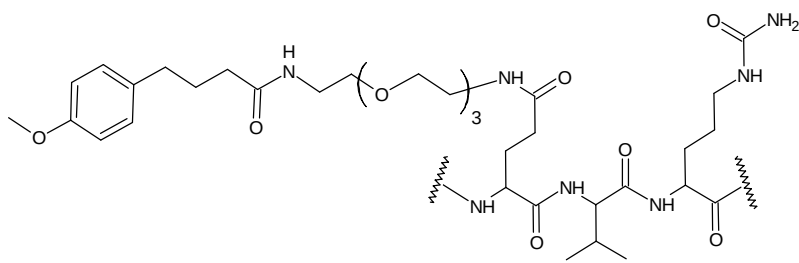
Formula P₁₀



Formula P₁₁



Formula P₁₂



Formula P₁₃



Formula P₁₄



Formula P₁₅



Formula P₁₆

5. The compound as claimed in claim 1, wherein the self-immolative group Q is of the Formula Q₁:



Formula Q₁

wherein,

R₁₁ is selected from a group consisting of —C₁₋₃ alkyl-OC(O)—**,

—C₁₋₃ alkyl-O-C(O)-N(R₁₉)-C₁₋₅ alkyl-N(R₁₉)-C(O)—**,

—C₁₋₃ alkyl-O-C(O)-N[C₁₋₅ alkyl-N(R₂₀R₂₁)]-C₁₋₃ alkyl—**, and

—C₁₋₃ alkyl-O-C(O)-Het₂-C₁₋₃ alkyl-N(R₁₉)-C(O)—**,

wherein

R₁₉ is selected from hydrogen, —C₁₋₃ alkyl or —C₁₋₃ alkyl-O-C₁₋₃ alkyl-OH;

R₂₀ is hydrogen or —C₁₋₃ alkyl;

R₂₁ is hydrogen or —C₁₋₃ alkyl; and

Het₂ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur;

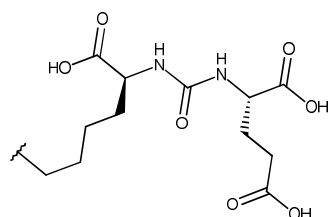
R₁₂ is selected from hydrogen, —C(O)N(R₁₃)(R₁₄) or —(OC₂H₄)₁₋₁₀-CH₃

R₁₃ is hydrogen;

R₁₄ is selected from —C₁₋₅ alkyl, —C₂₋₅ alkenyl, —C₂₋₅ alkynyl, —C₁₋₅ alkyl-N(R₁₅)(R₁₆),

—C₁₋₅ alkyl-O-C₁₋₃ alkyl, —(C₂H₄O)₁₋₁₀-C₂H₅, —(C₂H₄O)₁₋₁₀-C₂H₄-R₁₇, —C₁₋₃ alkyl-

Het₃-(C₂H₄O)₁₋₁₀-C₂H₄-R₁₈ or



; wherein:

R₁₅ is hydrogen or C1 to C3 alkyl;

R₁₆ is hydrogen or C1 to C3 alkyl; or

R₁₅ and R₁₆ along with the nitrogen atom to which they are attached form a 5 to 6 membered heterocyclic ring, wherein 1 or 2 carbon atoms in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur and wherein the 5 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, halogen or —OH;

R₁₇ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

R₁₈ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

Het₃ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen and sulfur;

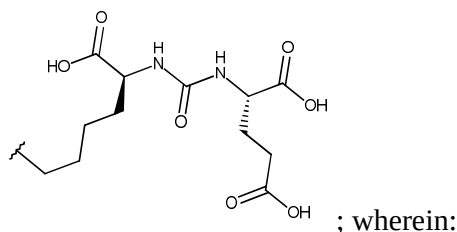
OR

R₁₃ and R₁₄ along with the nitrogen atom to which they are attached form a 4 to 6 membered heterocyclic ring, wherein 1 or 2 carbons in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the 4 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, —N(CH₃)₂ or —CH₂N(CH₃)₂;

R₂₂ is selected from hydrogen, —C(O)N(R₂₃)(R₂₄) or —(OC₂H₄)₁₋₁₀-CH₃

R₂₃ is hydrogen;

R₂₄ is selected from —C₁₋₅ alkyl, —C₂₋₅ alkenyl, —C₂₋₅ alkynyl, —C₁₋₅ alkyl-N(R₂₅)(R₂₆), —C₁₋₅ alkyl-O-C₁₋₃ alkyl, —(C₂H₄O)₁₋₁₀C₂H₅, —(C₂H₄O)₁₋₁₀-C₂H₄-R₂₇, —C₁₋₃ alkyl-Het₃-(C₂H₄O)₁₋₁₀-C₂H₄-R₂₈ or



R₂₅ is hydrogen or C1 to C3 alkyl;

R₂₆ is hydrogen or C1 to C3 alkyl; or

R₂₅ and R₂₆ along with the nitrogen atom to which they are attached form a 5 to 6 membered heterocyclic ring, wherein 1 or 2 carbon atoms in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur and wherein the 5 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, halogen or —OH;

R₂₇ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

R₂₈ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

Het₃ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen and sulfur;

OR

R₂₃ and R₂₄ along with the nitrogen atom to which they are attached form a 4 to 6 membered heterocyclic ring, wherein 1 or 2 carbons in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the 4 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, —N(CH₃)₂ or —CH₂N(CH₃)₂; and

' www ' indicates the point of attachment of Q to C terminal of A and ** indicates point of attachment of Q to D.

6. The compound as claimed in claim 1, wherein

R₁ is selected from 6 to 10 membered aryl or 5 to 10 membered heteroaryl containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur; or R₁ is unsubstituted or substituted with one or more R₅;

R₅ at each occurrence is independently selected from halogen, —OH, —OCH₃, —OC₂H₅ or 6 to 10 membered aryl;

R₂ is selected from a group consisting of 5 to 6 membered cycloalkyl and 6 to 10 membered aryl;

R₃ is hydrogen;

R₄ is selected from a group consisting of —C₁₋₁₀ alkyl-, —C₂₋₆ alkenyl-, —C₁₋₃ alkyl-O-C₁₋₃ alkyl-, —C₂₋₆ alkyl-N(R₈)—, —C₂₋₆ alkyl(N(R₈)(R₈'))—, —N(R₈)-C₂₋₆ alkyl—, a 3 to 6 membered cycloalkyl and —C₁₋₂ alkyl-(-OC₂H₄)₁₋₈-OC₁₋₂ alkyl—; wherein,

R₈ and R₈' are independently selected from hydrogen, C₁₋₆ alkyl, -C(O)-C₁₋₄alkyl-aryl or -C(O)-(-C₂H₄O)₁₋₈-C₁₋₂ alkyl-N(R)(R'), wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl; wherein

R and R' are independently selected from hydrogen, -C₁₋₆ alkyl or -C(O)-C₁₋₄alkyl-aryl, wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl;

A is selected from the group consisting of cit, ala-ala, ala-ala-ala, ala-phe, val-ala, val-cit, ala-val-cit, ala(beta)-val-cit, glu-val-cit, glu-cit, glu-val, gly-gly, gly-gly-phe, gly-gly-phe-gly, Formula P₃, Formula P₅, Formula P₉, Formula P₁₂, Formula P₁₃, Formula P₁₄, Formula P₁₅ and Formula P₁₆.

7. The compound as claimed in claim 1, wherein

n is 1;

R¹ is naphthyl;

R² is cyclohexyl or phenyl;

R³ is hydrogen;

R₄ is selected from a group consisting of —C₁₋₁₀ alkyl-, —C₂₋₆ alkenyl-, —C₁₋₃ alkyl-O-C₁₋₃ alkyl-, —C₂₋₆ alkyl-N(R₈)—, —C₂₋₆ alkyl(N(R₈)(R₈'))—, —N(R₈)-C₂₋₆ alkyl—, a 3 to 6 membered cycloalkyl and —C₁₋₂ alkyl-(-OC₂H₄)₁₋₈-OC₁₋₂ alkyl—; wherein,

R₈ and R₈' are independently selected from hydrogen, C₁₋₆ alkyl, -C(O)-C₁₋₄alkyl-aryl or -C(O)-(-C₂H₄O)₁₋₈-C₁₋₂ alkyl-N(R)(R'), wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl; wherein

R and R' are independently selected from hydrogen, -C₁₋₆ alkyl or -C(O)-C₁₋₄alkyl-aryl, wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl;

A is selected from the group consisting of cit, ala-ala, ala-ala-ala, ala-phe, val-ala, val-cit, ala-val-cit, ala(beta)-val-cit, glu-val-cit, glu-cit, glu-val, gly-gly, gly-gly-phe, gly-phe-gly, gly-gly-phe-gly, Formula P₃, Formula P₅, Formula P₉, Formula P₁₂, Formula P₁₃, Formula P₁₄, Formula P₁₅ and Formula P₁₆.

8. The compound as claimed in claim 1, wherein
n is 0, 1 or 2;

R¹ is selected from the group consisting of phenyl, indolyl, thiophenyl, quinoliny, and isoquinoliny; or R¹ is unsubstituted or substituted with one or more R⁵;

R⁵ is selected from halogen, —OH, or 6 to 10 membered aryl ring;

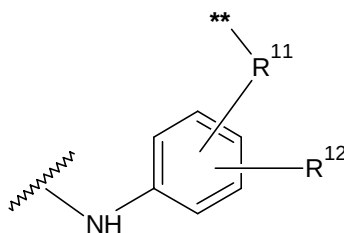
R² is cyclohexyl or phenyl;

R³ is hydrogen;

R⁴ is —C₁₋₁₀ alkyl;

A is val-cit; and

Q is a radical of Formula Q₁,



Formula Q₁

wherein

R¹¹ is —CH₂OC(O)—; and

R¹² is hydrogen.

9. The compound as claimed in claim 1, wherein

R¹ is selected from 6 to 10 membered aryl;

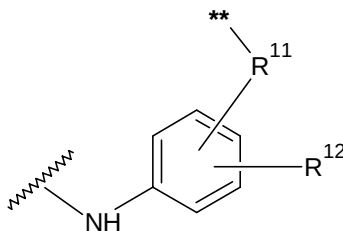
R² is absent;

R³ is —CH₂COOH, —CH₂CH₂COOH;

R⁴ is 3 to 6 membered cycloalkyl;

A is Cit;

Q is a radical of Formula Q₁,



Formula Q₁

wherein

R¹¹ is —CH₂-O-C(O)-N(CH₃)-C₂H₄-N(CH₃)-C(O)—; and

R¹² is hydrogen.

10. The compound as claimed in claim 1, wherein

n is 0, 1 or 2;

R₁ is selected from a 6 to 10 membered aryl;

R₂ is cyclohexyl or phenyl;

R₃ is hydrogen;

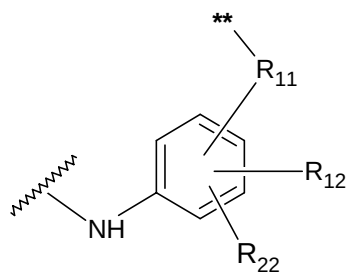
R₄ is selected from a group consisting of —C₁₋₁₀ alkyl- and —C₂₋₆ alkyl(N(R₈)(R₈'))—; wherein,

R₈ and R₈' are independently selected from hydrogen, C₁₋₆ alkyl, -C(O)-C₁₋₄alkyl-aryl or -C(O)-(-C₂H₄O)₁₋₈-C₁₋₂ alkyl-N(R)(R'), wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl; wherein

R and R' are independently selected from hydrogen, -C₁₋₆ alkyl or -C(O)-C₁₋₄alkyl-aryl, wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl;

A is selected from the group consisting of val-cit, gly-gly-phe-gly, Formula P₂, Formula P₁₃, Formula P₁₄, Formula P₁₅ and Formula P₁₆;

Q is of Formula Q₁,

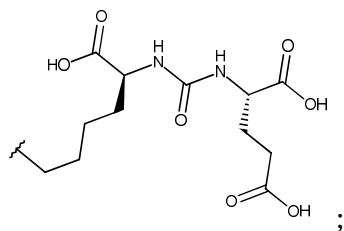


Formula Q₁

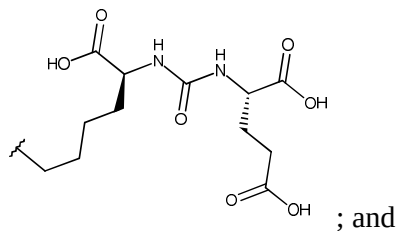
wherein:

R₁₁ is —CH₂-O-C(O)—; and

R₁₂ is selected from hydrogen or —C(O)N(R₁₃)(R₁₄), wherein R₁₃ is hydrogen and R₁₄ is selected from —C₁₋₅ alkyl-N(R₁₅)(R₁₆) or



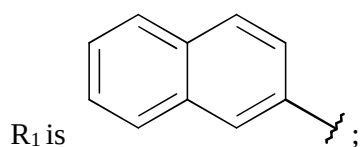
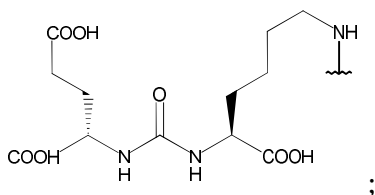
R₂₂ is selected from hydrogen or —C(O)N(R₂₃)(R₂₄), wherein R₂₃ is hydrogen and R₂₄ is selected from —C₁₋₅ alkyl-N(R₂₅)(R₂₆) or



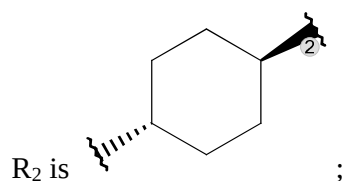
wherein at least one of R₁₂ and R₂₂ is hydrogen.

11. The compound as claimed in claim 1, wherein:

L is a ligand of formula:



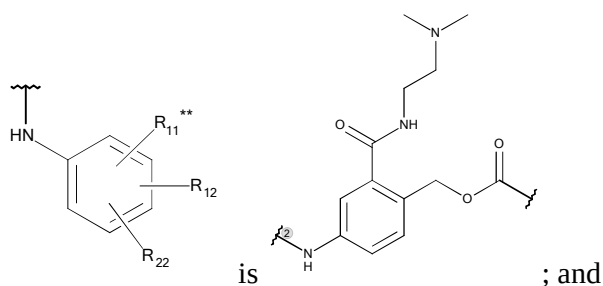
n is 1;



R₃ is hydrogen;

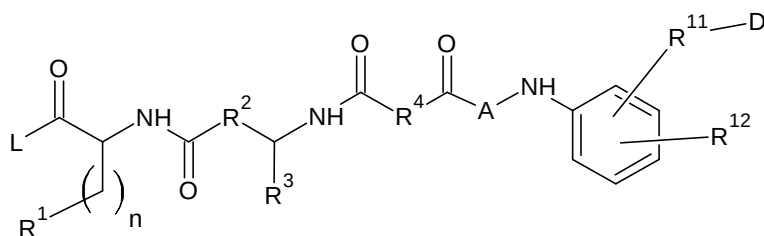
R₄ is -C₃H₆-;

A is val-cit;



D is Monomethyl auristatin E (MMAE).

12. A compound of Formula II:



Formula II

or pharmaceutically acceptable salt, solvate, stereoisomer or isotope thereof; wherein,

n is 0, 1, 2, 3 or 4;

L is a Ligand;

R₁ is selected from a 6 to 14 membered aryl or a 5 to 13 membered heteroaryl containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur;

R₁ is unsubstituted or substituted with one or more R₅;

R₅, at each occurrence, is independently selected from halogen, —C(O)NH₂, —C(O)OR₆, —C₁₋₃ alkyl, —OR₇, and a 6 to 10 membered aryl; wherein:

R₆ is hydrogen or C₁₋₃ alkyl;

R₇ is hydrogen or C₁₋₃ alkyl;

R₂ is absent or is selected from a 6 to 10 membered cycloalkyl or a 6 to 10 membered aryl;

R₃ is hydrogen, or —C₁-C₅COOH;

R₄ is selected from a group consisting of —C₁₋₁₀ alkyl-, —C₂₋₆ alkenyl-, —C₁₋₃ alkyl-O-C₁₋₃ alkyl-, —C₂₋₆ alkyl-N(R₈)—, —C₂₋₆ alkyl(N(R₈)(R₈'))—, —N(R₈)-C₂₋₆ alkyl—, a 3 to 6 membered cycloalkyl and —C₁₋₂ alkyl-(-OC₂H₄)₁₋₈-OC₁₋₂ alkyl—; wherein,

R₈ and R₈' are independently selected from hydrogen, C₁₋₆ alkyl, -C(O)-C₁₋₄alkyl-aryl or -C(O)-(-C₂H₄O)₁₋₈-C₁₋₂ alkyl-N(R)(R'), wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl; wherein

R and R' are independently selected from hydrogen, -C₁₋₆ alkyl or -C(O)-C₁₋₄alkyl-aryl, wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl;

A is an amino acid or a peptide comprising 2-5 amino acids;

A is attached to Q through its C terminal;

R₁₁ is selected from —C₁₋₃ alkyl-OC(O)—**,

—C₁₋₃ alkyl-O-C(O)-N(R₁₉)-C₁₋₅ alkyl-N(R₁₉)-C(O)—**,

—C₁₋₃ alkyl-O-C(O)-N[C₁₋₅ alkyl-N(R₂₀R₂₁)]-C₁₋₃ alkyl—**, or

—C₁₋₃ alkyl-O-C(O)-Het₂-C₁₋₃ alkyl-N(R₁₉)-C(O)—**,

wherein ** indicates point of attachment to D;

R₁₉ is selected from H, —C₁₋₃ alkyl or —C₁₋₃ alkyl-O-C₁₋₃ alkyl-OH;

R₂₀ is H or —C₁₋₃ alkyl;

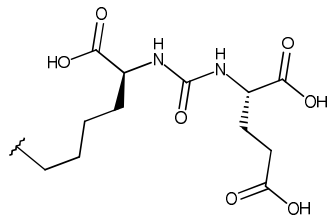
R₂₁ is H or —C₁₋₃ alkyl; and

Het₂ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur;

R₁₂ is selected from hydrogen, —C(O)N(R₁₃)(R₁₄) or —(-OC₂H₄)₁₋₁₀-CH₃;

R₁₃ is hydrogen;

R₁₄ is selected from —C₁₋₅ alkyl, —C₂₋₅ alkenyl, —C₂₋₅ alkynyl, —C₁₋₅ alkyl-N(R₁₅)(R₁₆), —C₁₋₅ alkyl-O-C₁₋₃ alkyl, —(-C₂H₄O)₁₋₁₀C₂H₅, —(-C₂H₄O)₁₋₁₀-C₂H₄-R₁₇ or —C₁₋₃ alkyl-Het₃-(-C₂H₄O)₁₋₁₀-C₂H₄-R₁₈ or



R₁₅ is hydrogen or C₁₋₃ alkyl;

R₁₆ is hydrogen or C₁₋₃ alkyl; or

R₁₅ and R₁₆ along with the nitrogen atom to which they are attached form a 5 to 6 membered heterocyclic ring, wherein 1 or 2 carbon atoms in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur and wherein the 5 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, halogen or -OH;

R₁₇ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

R₁₈ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

Het₃ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen and sulfur;

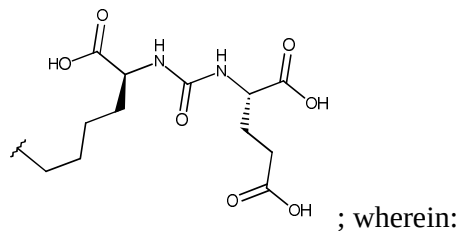
OR

R₁₃ and R₁₄ along with the nitrogen atom to which they are attached form a 4 to 6 membered heterocyclic ring, wherein 1 or 2 carbons in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the 4 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, —N(CH₃)₂ or —CH₂N(CH₃)₂;

R₂₂ is selected from hydrogen, —C(O)N(R₂₃)(R₂₄) or —(OC₂H₄)₁₋₁₀-CH₃, wherein:

R₂₃ is hydrogen;

R₂₄ is selected from —C₁₋₅ alkyl, —C₂₋₅ alkenyl, —C₂₋₅ alkynyl, —C₁₋₅ alkyl-N(R₂₅)(R₂₆), —C₁₋₅ alkyl-O-C₁₋₃ alkyl, —(C₂H₄O)₁₋₁₀-C₂H₅, —(C₂H₄O)₁₋₁₀-C₂H₄-R₂₇ or —C₁₋₃ alkyl-Het₃-(C₂H₄O)₁₋₁₀-C₂H₄-R₂₈ or



R₂₅ is hydrogen or C₁ to C₃ alkyl;

R₂₆ is hydrogen or C₁ to C₃ alkyl; or

R₂₅ and R₂₆ along with the nitrogen atom to which they are attached form a 5 to 6 membered heterocyclic ring, wherein 1 or 2 carbon atoms in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur and wherein the 5 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, halogen or -OH;

R₂₇ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

R₂₈ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

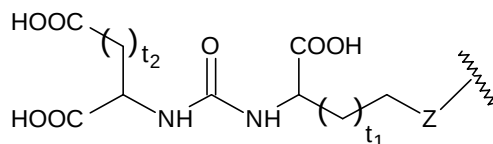
Het₃ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen and sulfur;

OR

R₂₃ and R₂₄ along with the nitrogen atom to which they are attached form a 4 to 6 membered heterocyclic ring, wherein 1 or 2 carbons in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the 4 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, —N(CH₃)₂ or —CH₂N(CH₃)₂; and

D is a cytotoxic agent or therapeutic agent.

13. The compound as claimed in claim 12, wherein the ligand L is a ligand of Formula L₁:



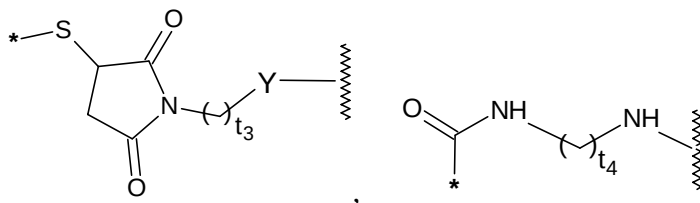
Formula L₁

wherein,

t₁ is 0, 1, 2, 3, or 4;

t₂ is 1, 2, 3 or 4;

Z is selected from the group consisting of N(R₉), Formula Z₁ and Formula Z₂:



Formula Z₁

Formula Z₂

wherein:

t₃ is selected from 1, 2, 3, 4, 5 or 6;

t₄ is selected from 1, 2, 3, 4, 5 or 6;

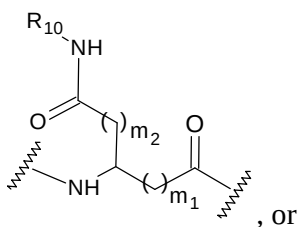
Y is —CH₂— or —NH— and

‘’ indicates attachment of Formula L₁ to the rest of the compound of Formula I;

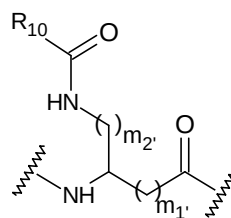
R₉ is selected from the group consisting of hydrogen, C₁₋₅ alkyl, a 6 to 10 membered aryl, a 5 to 10 membered heterocyclyl ring wherein the heterocyclyl ring contains one, two or three

heteroatoms independently selected from nitrogen, oxygen or sulfur; and wherein R₉ is unsubstituted or substituted with halogen.

14. The compound as claimed in claim 12, wherein the amino acid in A at each occurrence is independently selected from the group consisting of alanine (ala), arginine (arg), aspartic acid (asp), cysteine (cys), glutamic acid (glu), glycine (gly), lysine (lys), phenylalanine (phe), serine (ser), threonine (thr), tryptophan (trp), valine (val), ornithine (orn), citrulline (cit), homocitrulline (hct), lanthionine (lan), homocysteine (hcy) or an amino acid having Formula A₁ or Formula A₂



Formula A₁



Formula A₂

wherein

m₁ and m₁' are 0, 1, 2 or 3;

m₂ and m₂' are 0, 1, 2, 3 or 4;

R₁₀ is selected from (-C₂H₄O)₁₋₂₄CH₃, (-C₂H₄O)₁₋₂₄C₁₋₂ alkyl(N(R₁₀')(R₁₀''))—, C₁₋₃ alkyl-aryl or —C₁₋₃ alkyl-Het₁-(-C₂H₄O)₁₋₂₄CH₃, wherein Het₁ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur and wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl; wherein

R₁₀' and R₁₀' are independently selected from hydrogen, C₁₋₆ alkyl or -C(O)-C₁₋₄alkyl-aryl wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl.

15. The compound as claimed in claim 12, wherein

R₁ is naphthyl;

R₂ is a 6 to 10 membered cycloalkyl;

R₃ is hydrogen;

R₄ is selected from —C₁₋₁₀ alkyl- or —C₂₋₆ alkyl(N(R₈)(R₈'))—; wherein

R₈ and R₈' are independently selected from hydrogen, -C(O)-C₁₋₄alkyl-aryl or -C(O)-(-C₂H₄O)₁₋₈-C₁₋₂ alkyl-N(R)(R'), wherein said aryl is selected from 6 to 14 membered

aryl and is optionally substituted by $-C_{1-3}\text{alkyl}$ or $-OC_{1-3}\text{alkyl}$, wherein both R_8 and R_8' are not hydrogen; wherein

R and R' are independently selected from hydrogen or $-C(O)-C_{1-4}\text{alkyl-aryl}$, wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}\text{alkyl}$ or $-OC_{1-3}\text{alkyl}$, wherein both R and R' are not hydrogen;

R_{11} is selected from $-C_{1-3}\text{alkyl-OC(O)-**}$, wherein $**$ indicates point of attachment to D;

R_{12} is $-C(O)N(R_{13})(R_{14})$, wherein:

R_{13} is hydrogen; and

R_{14} is $-C_{1-5}\text{alkyl-N}(R_{15})(R_{16})$,

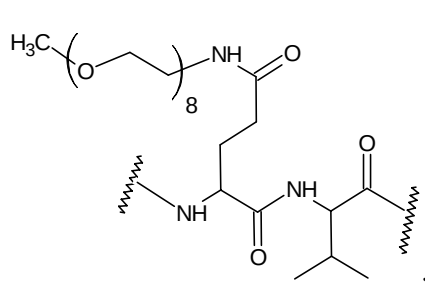
wherein:

R_{15} is C1 to C3 alkyl;

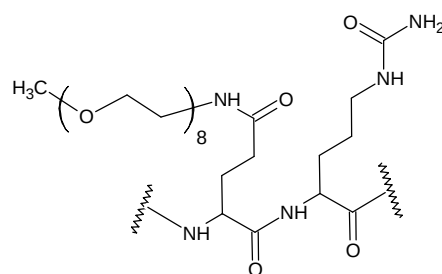
R_{16} is C1 to C3 alkyl; and

R_{22} is hydrogen.

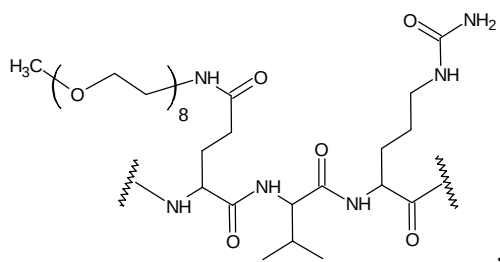
16. The compound as claimed in claim 12, wherein A is a peptide selected from the group consisting of ala-ala, ala-ala-ala, ala-phe, val-ala, val-cit, ala-val-cit, ala(beta)-val-cit, glu-val-cit, glu-cit, glu-val, gly-gly, gly-gly-phe, gly-phe-gly, gly-gly-phe-gly, asp-cit, asp-val-cit and asp-val; or the peptide is selected from a group of compounds having following formula:



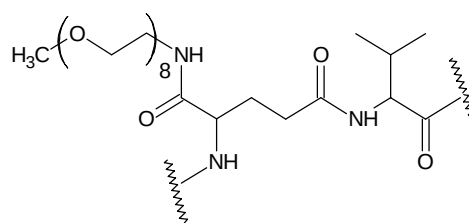
Formula P₁



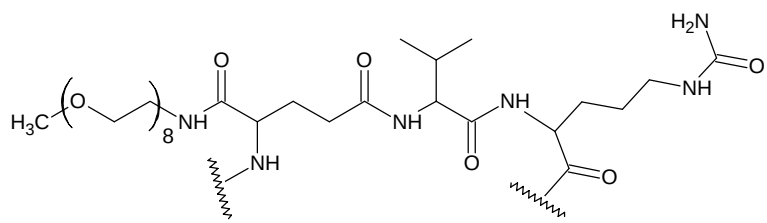
Formula P₂



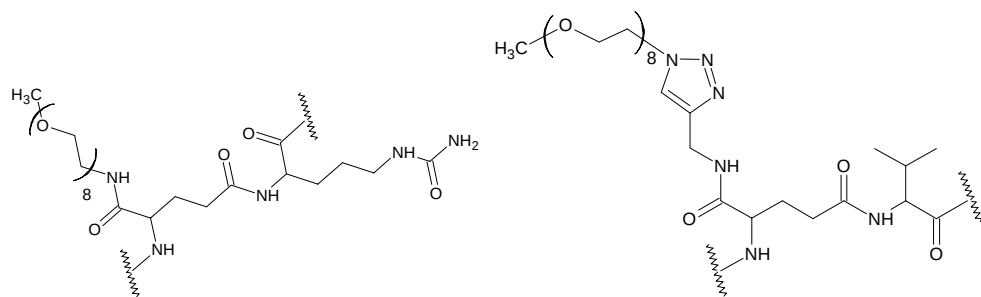
Formula P₃



Formula P₄

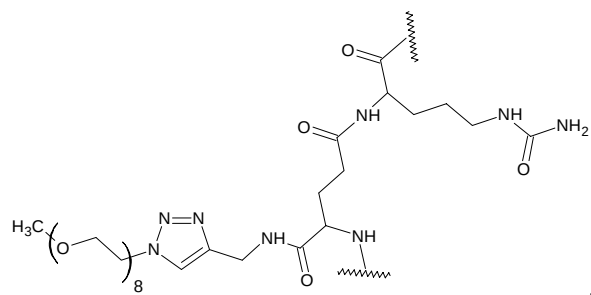


Formula P5

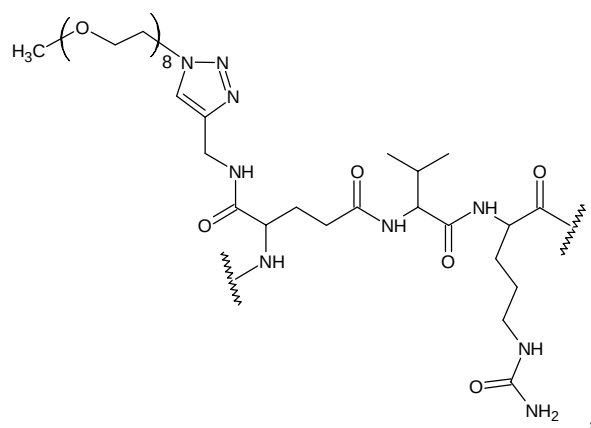


Formula P6

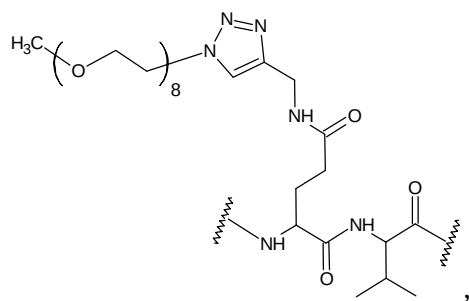
Formula P7

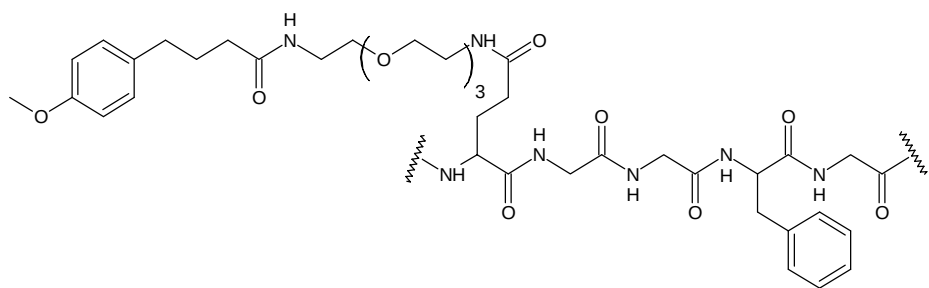


Formula P8



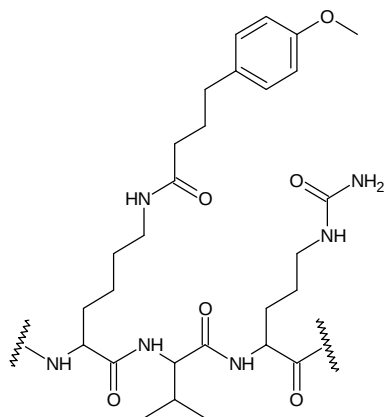
Formula P9





, and

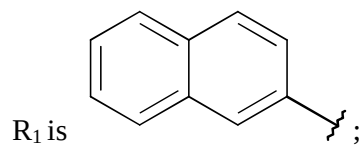
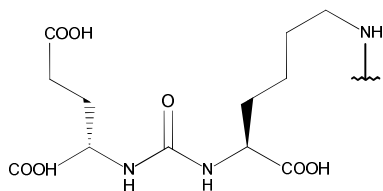
Formula P₁₅



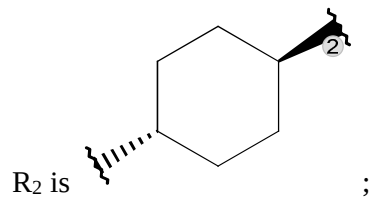
Formula P₁₆

17. The compound as claimed in claim 12, wherein:

L is a ligand of formula:



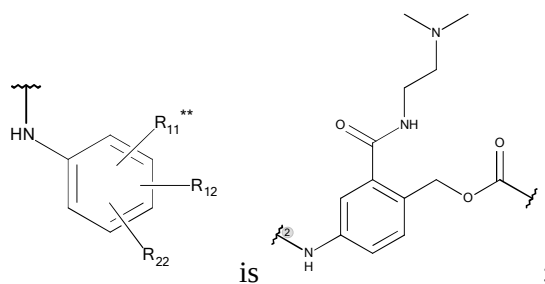
n is 1;



R₃ is hydrogen;

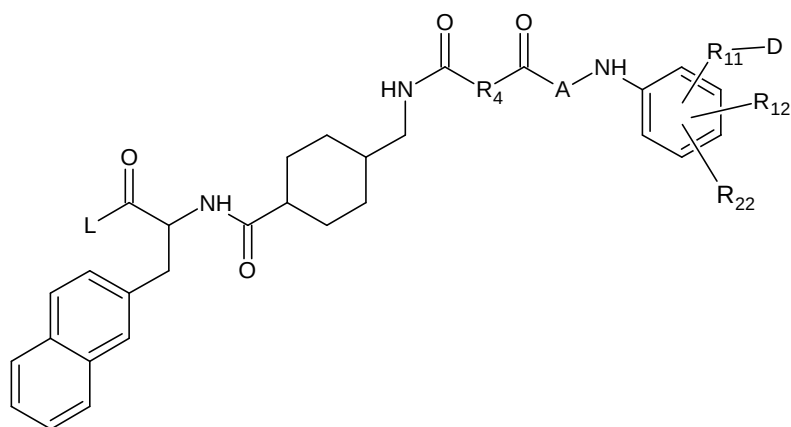
R₄ is -C₃H₆-;

A is val-cit;



D is Monomethyl auristatin E (MMAE).

18. A compound of Formula III:



Formula III

or pharmaceutically acceptable salt, solvate, stereoisomer or isotope thereof; wherein,

L is a Ligand;

R₄ is selected from a group consisting of —C₁₋₁₀ alkyl, —C₂₋₆ alkenyl, —C₁₋₃ alkyl-O-C₁₋₃ alkyl—, —C₂₋₆ alkyl-N(R₈)—, —C₂₋₆ alkyl(N(R₈)(R₈'))—, —N(R₈)-C₂₋₆ alkyl—, a 3 to 6 membered cycloalkyl and —C₁₋₂ alkyl (-OC₂H₄)₁₋₈-OC₁₋₂ alkyl—; wherein:

R₈ and R₈' are independently selected from hydrogen, C₁₋₆ alkyl, -C(O)-C₁₋₄alkyl-aryl or -C(O)-(-C₂H₄O)₁₋₈-C₁₋₂ alkyl-N(R)(R'), wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl; wherein

R and R' are independently selected from hydrogen, -C₁₋₆ alkyl or -C(O)-C₁₋₄alkyl-aryl, wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl;

A is an amino acid or a peptide comprising 2-5 amino acids;

R₁₁ is selected from —C₁₋₃ alkyl-OC(O)—**,

—C₁₋₃ alkyl-O-C(O)-N(R₁₉)-C₁₋₅ alkyl-N(R₁₉)-C(O)—**,
 —C₁₋₃ alkyl-O-C(O)-N[C₁₋₅ alkyl-N(R₂₀R₂₁)]-C₁₋₃ alkyl—**, or
 —C₁₋₃ alkyl-O-C(O)-Het₂-C₁₋₃ alkyl-N(R₁₉)-C(O)—**,

wherein ** indicates point of attachment to D;

R₁₉ is selected from H, CH₃ or —C₂H₄-O-C₂H₄-OH;

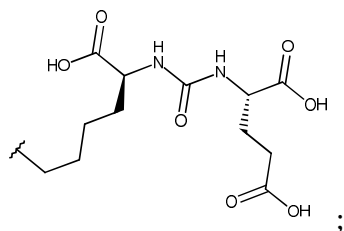
R₂₀ is CH₃; R₂₁ is CH₃; and

Het₂ is pyrrolidinyl.

R₁₂ is selected from hydrogen, —C(O)N(R₁₃)(R₁₄) or —(OC₂H₄)₁₋₁₀-CH₃;

R₁₃ is hydrogen;

R₁₄ is —CH₃, —CH₂-C≡CH, —C₁₋₃ alkyl-N(R₁₅)(R₁₆), —C₂H₄OCH₃, —(C₂H₄O)₃₋₈-C₂H₅, —(C₂H₄O)₅₋₁₀-C₂H₄-R₁₇, —CH₂-triazole-(C₂H₄O)₄-C₂H₄-R₁₈ or



R₁₅ is —CH₃ or —C₂H₅; R₁₆ is —CH₃ or —C₂H₅;

or

R₁₅ and R₁₆ along with the nitrogen atom to which they are attached form a 5 to 6 membered heterocyclic ring, wherein 1 or 2 carbon atoms in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur and wherein the 5 to 6 membered heterocyclic ring is unsubstituted or substituted with —CH₃;

R₁₇ is —C(O)NHC₂H₄N(CH₃)₂;

R₁₈ is —C(O)NHC₂H₄N(CH₃)₂;

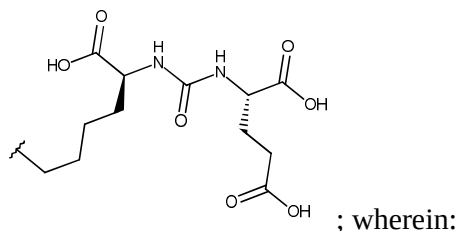
or

R₁₃ and R₁₄ along with the nitrogen atom to which they are attached form a 4 to 6 membered heterocyclic ring, wherein 1 or 2 carbons in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the 4 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, —N(CH₃)₂ or —CH₂N(CH₃)₂;

R₂₂ is selected from hydrogen, —C(O)N(R₂₃)(R₂₄) or —(OC₂H₄)₁₋₁₀-CH₃;

R₂₃ is hydrogen;

R₂₄ is selected from —CH₃, —CH₂-C≡CH, —C₁₋₃ alkyl-N(R₂₅)(R₂₆), —C₂H₄OCH₃, —(C₂H₄O)₃₋₈-C₂H₅, —(C₂H₄O)₅₋₁₀-C₂H₄-R₂₇, —CH₂-triazole-(C₂H₄O)₄-C₂H₄-R₂₈ or



R₂₅ is —CH₃ or —C₂H₅;

R₂₆ is —CH₃ or —C₂H₅; or

R₂₅ and R₂₆ along with the nitrogen atom to which they are attached form a 5 to 6 membered heterocyclic ring, wherein 1 or 2 carbon atoms in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur and wherein the 5 to 6 membered heterocyclic ring is unsubstituted or substituted with —CH₃;

R₂₇ is —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

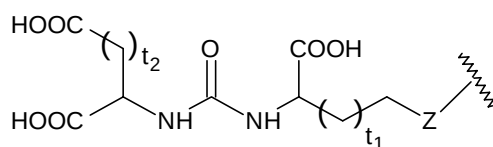
R₂₈ is —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

OR

R₂₃ and R₂₄ along with the nitrogen to which they are attached form a 4 to 6 membered heterocyclic ring, wherein 1 or 2 carbons in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the 4 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, —N(CH₃)₂ or —CH₂N(CH₃)₂; and D is a cytotoxic agent or therapeutic agent as defined above.

19. The compound as claimed in claim 18, wherein

the ligand L is of the Formula L₁:



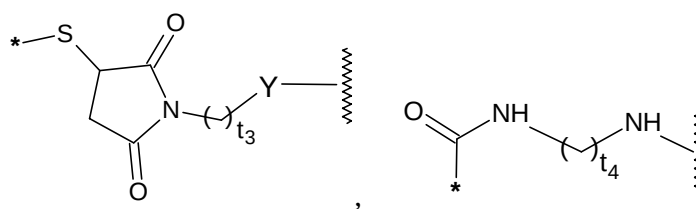
Formula L₁

wherein,

t₁ is 0, 1, 2, 3, or 4;

t₂ is 1, 2, 3 or 4;

Z is selected from the group consisting of N(R₉), Formula Z₁ and Formula Z₂:



Formula Z₁

Formula Z₂

wherein:

t₃ is selected from 1, 2, 3, 4, 5 or 6;

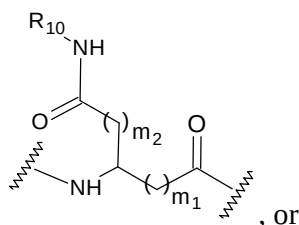
t₄ is selected from 1, 2, 3, 4, 5 or 6;

Y is -CH₂- or -NH- and

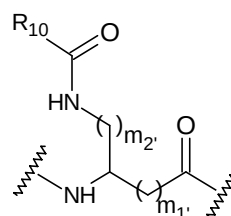
‘’ indicates attachment of Formula L₁ to the rest of the compound of Formula I;

R₉ is selected from the group consisting of hydrogen, C₁₋₅ alkyl, a 6 to 10 membered aryl, a 5 to 10 membered heterocyclyl ring wherein the heterocyclyl ring contains one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur; and wherein R₉ is unsubstituted or substituted with halogen.

20. The compound as claimed in claim 18, wherein the amino acid in A at each occurrence is independently selected from the group consisting of alanine (ala), arginine (arg), aspartic acid (asp), cysteine (cys), glutamic acid (glu), glycine (gly), lysine (lys), phenylalanine (phe), serine (ser), threonine (thr), tryptophan (trp), valine (val), ornithine (orn), citrulline (cit), homocitrulline (hct), lanthionine (lan), homocysteine (hcy) or an amino acid having Formula A₁ or Formula A₂



Formula A₁



Formula A₂

wherein

m₁ and m₁' are 0, 1, 2 or 3;

m₂ and m₂' are 0, 1, 2, 3 or 4;

R₁₀ is selected from (-C₂H₄O)₁₋₂₄CH₃, (-C₂H₄O)₁₋₂₄C₁₋₂ alkyl(N(R₁₀')(R₁₀''))—, C₁₋₃ alkyl-aryl or —C₁₋₃ alkyl-Het₁-(-C₂H₄O)₁₋₂₄CH₃, wherein Het₁ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from

nitrogen, oxygen or sulfur and wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}$ alkyl or $-OC_{1-3}$ alkyl; wherein

$R_{10'}$ and $R_{10''}$ are independently selected from hydrogen, C_{1-6} alkyl or $-C(O)-C_{1-4}$ alkyl-aryl wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}$ alkyl or $-OC_{1-3}$ alkyl.

21. The compound as claimed in claim 18, wherein

R_4 is selected from a group consisting of $-C_{1-10}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{1-3}$ alkyl-O- C_{1-3} alkyl—, $-C_{2-6}$ alkyl-N(R_8)—, $-C_{2-6}$ alkyl(N(R_8)($R_{8'}$))—, $-N(R_8)-C_{2-6}$ alkyl—, a 3 to 6 membered cycloalkyl and $-C_{1-2}$ alkyl $(-OC_2H_4)_{1-8}-OC_{1-2}$ alkyl—; wherein:

R_8 and $R_{8'}$ are independently selected from hydrogen, C_{1-6} alkyl, $-C(O)-C_{1-4}$ alkyl-aryl or $-C(O)-(-C_2H_4O)_{1-8}-C_{1-2}$ alkyl-N(R)(R'), wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}$ alkyl or $-OC_{1-3}$ alkyl; wherein

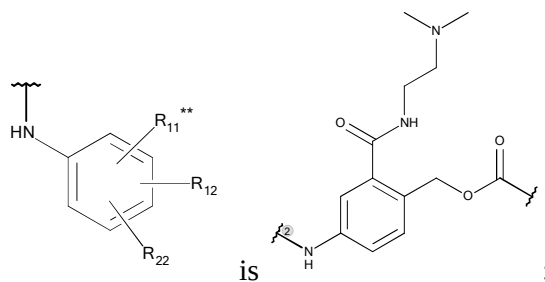
R and R' are independently selected from hydrogen, $-C_{1-6}$ alkyl or $-C(O)-C_{1-4}$ alkyl-aryl, wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}$ alkyl or $-OC_{1-3}$ alkyl;

22. The compound as claimed in claim 18, wherein:

wherein:

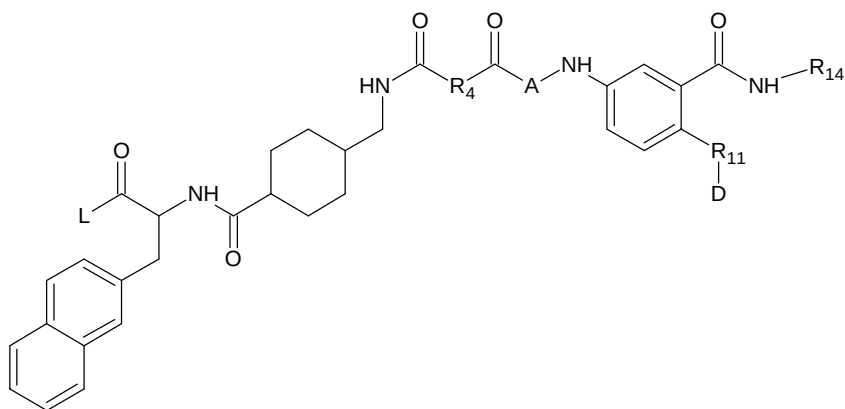
R_4 is $-C_3H_6-$;

A is val-cit;



D is Monomethyl auristatin E (MMAE).

23. A compound of Formula IV,



Formula IV

or pharmaceutically acceptable salt, solvate, stereoisomer or isotope thereof; wherein,

L is a Ligand; D is a cytotoxic or therapeutic agent as defined above;

R₄ is selected from a group consisting of —C₁₋₁₀ alkyl, —C₂₋₆ alkenyl, —C₁₋₃ alkyl-O-C₁₋₃ alkyl—, —C₂₋₆ alkyl-N(R₈)—, —C₂₋₆ alkyl(N(R₈)(R₈'))—, —N(R₈)-C₂₋₆ alkyl—, 3 to 6 membered cycloalkyl and —C₁₋₂ alkyl (-OC₂H₄)₁₋₈-OC₁₋₂ alkyl—; wherein:

R₈ and R₈' are independently selected from hydrogen, C₁₋₆ alkyl, -C(O)-C₁₋₄alkyl-aryl or -C(O)-(-C₂H₄O)₁₋₈-C₁₋₂ alkyl-N(R)(R'), wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl; wherein

R and R' are independently selected from hydrogen, -C₁₋₆ alkyl or -C(O)-C₁₋₄alkyl-aryl, wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl;

A is an amino acid or a peptide comprising 2-5 amino acids;

R₁₁ is selected from —C₁₋₃ alkyl-OC(O)—**,

—C₁₋₃ alkyl-O-C(O)-N(R₁₉)-C₁₋₅ alkyl-N(R₁₉)-C(O)—**,

—C₁₋₃ alkyl-O-C(O)-N[C₁₋₅ alkyl-N(R₂₀R₂₁)]-C₁₋₃ alkyl—**, or

—C₁₋₃ alkyl-O-C(O)-Het₂-C₁₋₃ alkyl-N(R₁₉)-C(O)—**,

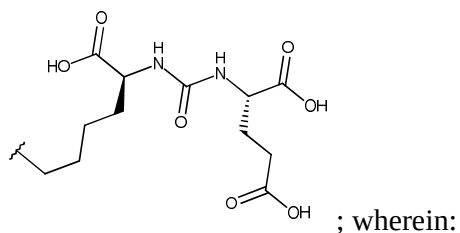
wherein ** indicates point of attachment to D and

R₁₉ is selected from H, -CH₃ or -C₂H₄-O-C₂H₄-OH;

R₂₀ is -CH₃; R₂₁ is -CH₃;

Het₂ is pyrrolidine;

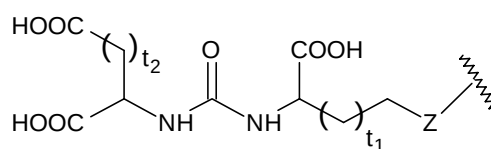
R₁₄ is selected from —C₁-C₅ alkyl, —C₁ to C₅ alkyl-N(R₁₅)(R₁₆), —C₁-C₅ alkyl-OCH₃, (-C₂H₄O)₁₋₁₀ CH₂-CH₃, or



R_{15} is C_{1-3} alkyl; and

R_{16} is C_{1-3} alkyl.

24. The compound as claimed in claim 23, wherein
the ligand L is of the Formula L₁:



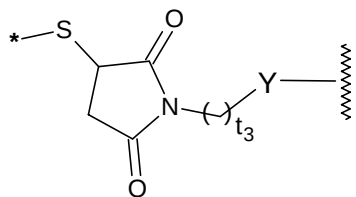
Formula L₁

wherein,

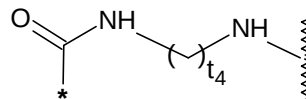
t_1 is 0, 1, 2, 3, or 4;

t_2 is 1, 2, 3 or 4;

Z is selected from the group consisting of $N(R_9)$, Formula Z₁ and Formula Z₂:



Formula Z₁



Formula Z₂

wherein:

t_3 is selected from 1, 2, 3, 4, 5 or 6;

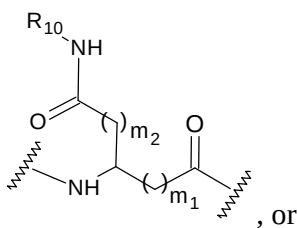
t_4 is selected from 1, 2, 3, 4, 5 or 6;

Y is $-CH_2-$ or $-NH-$ and

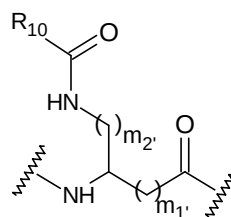
'www' indicates attachment of Formula L₁ to the rest of the compound of Formula I;

R_9 is selected from the group consisting of hydrogen, C_{1-5} alkyl, a 6 to 10 membered aryl, a 5 to 10 membered heterocyclyl ring wherein the heterocyclyl ring contains one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur; and wherein R_9 is unsubstituted or substituted with halogen.

25. The compound as claimed in claim 23, wherein the amino acid in A at each occurrence is independently selected from the group consisting of alanine (ala), arginine (arg), aspartic acid (asp), cysteine (cys), glutamic acid (glu), glycine (gly), lysine (lys), phenylalanine (phe), serine (ser), threonine (thr), tryptophan (trp), valine (val), ornithine (orn), citrulline (cit), homocitrulline (hct), lanthionine (lan), homocysteine (hcy) or an amino acid having Formula A₁ or Formula A₂



Formula A₁



Formula A₂

wherein

m_1 and m_1' are 0, 1, 2 or 3;

m_2 and m_2' are 0, 1, 2, 3 or 4;

R_{10} is selected from $(-C_2H_4O)_{1-24}CH_3$, $(-C_2H_4O)_{1-24}C_{1-2}$ alkyl($N(R_{10'})$ ($R_{10''}$))—, C_{1-3} alkyl-aryl or — C_{1-3} alkyl-Het₁- $(-C_2H_4O)_{1-24}CH_3$, wherein Het₁ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur and wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}$ alkyl or $-OC_{1-3}$ alkyl; wherein

$R_{10'}$ and $R_{10''}$ are independently selected from hydrogen, C_{1-6} alkyl or $-C(O)-C_{1-4}$ alkyl-aryl wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}$ alkyl or $-OC_{1-3}$ alkyl.

26. The compound as claimed in claim 23, wherein

R_{11} is — C_{1-3} alkyl-OC(O)—**

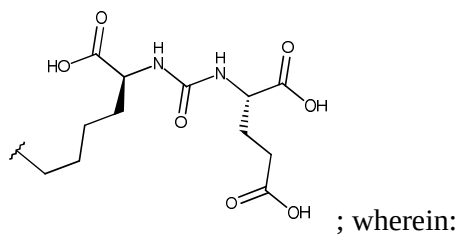
wherein ** indicates the point of attachment to D;

R_{12} is —C(O)N(R_{13})(R_{14}),

wherein:

R_{13} is hydrogen;

R_{14} is selected from — C_{1-5} alkyl-N(R_{15})(R_{16}) and



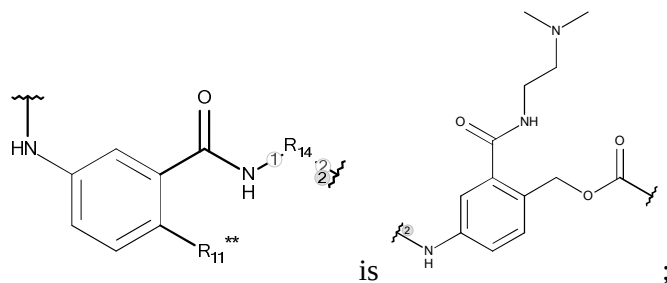
R_{15} is C_{1-3} alkyl; and

R_{16} is C_{1-3} alkyl.

27. The compound as claimed in claim 23, wherein:

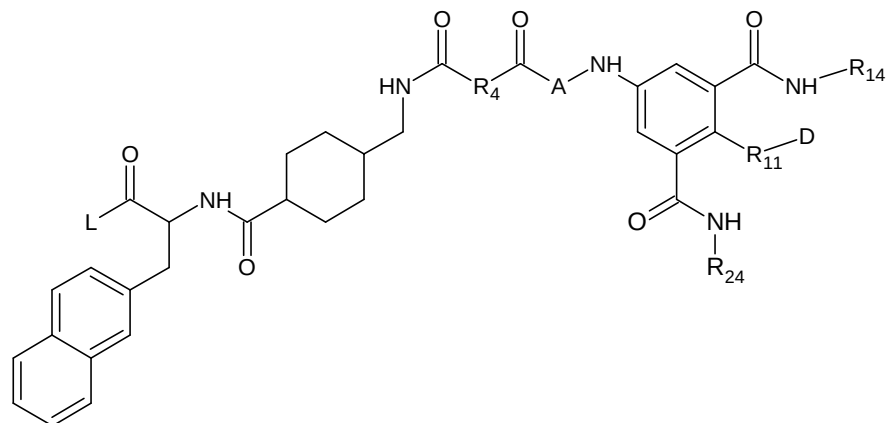
R_4 is $-C_3H_6-$;

A is val-cit;



D is Monomethyl auristatin E (MMAE).

28. A compound of Formula V,



Formula V

wherein

or pharmaceutically acceptable salt, solvate, stereoisomer or isotope thereof; wherein,

L is a Ligand;

A is an amino acid or a peptide comprising 2-5 amino acids;

R₄ is selected from a group consisting of —C₁₋₁₀ alkyl, —C₂₋₆ alkenyl, —C₁₋₃ alkyl-O-C₁₋₃ alkyl—, —C₂₋₆ alkyl-N(R₈)—, —N(R₈)-C₂₋₆ alkyl—, a 3 to 6 membered cycloalkyl and —C₁₋₂ alkyl (-OC₂H₄)₁₋₈-OC₁₋₂ alkyl—; wherein:

R₈ is hydrogen or C₁₋₆ alkyl;

R₁₁ is selected from —C₁₋₃ alkyl-OC(O)—**,

—C₁₋₃ alkyl-O-C(O)-N(R₁₉)-C₁₋₅ alkyl-N(R₁₉)-C(O)—**,

—C₁₋₃ alkyl-O-C(O)-N[C₁₋₅ alkyl-N(R₂₀R₂₁)]-C₁₋₃ alkyl—**, or

—C₁₋₃ alkyl-O-C(O)-Het₂-C₁₋₃ alkyl-N(R₁₉)-C(O)—**,

wherein ** indicates point of attachment to D;

R₁₉ is selected from H, -CH₃ or —C₂H₄-O-C₂H₄-OH;

R₂₀ is -CH₃; R₂₁ is -CH₃; and

Het₂ is pyrrolidinyl;

R₁₄ is selected from —C_{1-C5} alkyl, —C₁ to C₅ alkyl-N(R₁₅)(R₁₆), —C_{1-C5} alkyl-OCH₃, (-C₂H₄O)₁₋₁₀ CH₂-CH₃ wherein:

R₁₅ is C₁₋₃ alkyl;

R₁₆ is C₁₋₃ alkyl;

R₂₄ is selected from —C₁₋₅ alkyl, —C₁₋₅ alkyl-N(R₂₅)(R₂₆), —C₁₋₅ alkyl-OCH₃, (-C₂H₄O)₁₋₁₀CH₂-CH₃ wherein:

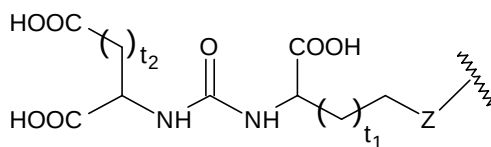
R₂₅ is hydrogen or C₁₋₃ alkyl; and

R₂₆ is hydrogen or C₁₋₃ alkyl

D is a cytotoxic agent or therapeutic agent.

29. The compound as claimed in claim 28, wherein

the ligand L is of the Formula L₁:



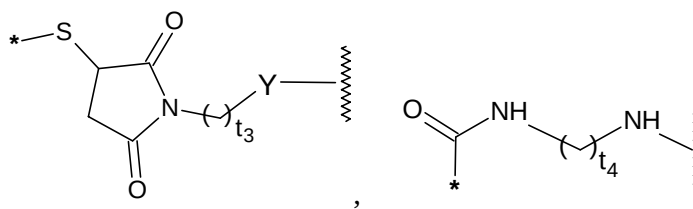
Formula L₁

wherein,

t₁ is 0, 1, 2, 3, or 4;

t₂ is 1, 2, 3 or 4;

Z is selected from the group consisting of N(R₉), Formula Z₁ and Formula Z₂:



Formula Z₁

Formula Z₂

wherein:

t₃ is selected from 1, 2, 3, 4, 5 or 6;

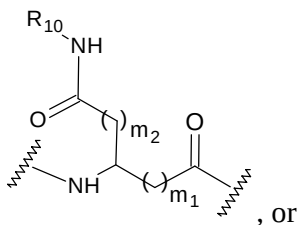
t₄ is selected from 1, 2, 3, 4, 5 or 6;

Y is -CH₂- or -NH- and

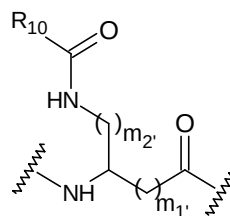
‘ wwww ’ indicates attachment of Formula L₁ to the rest of the compound of Formula I;

R₉ is selected from the group consisting of hydrogen, C₁₋₅ alkyl, a 6 to 10 membered aryl, a 5 to 10 membered heterocyclyl ring wherein the heterocyclyl ring contains one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur; and wherein R₉ is unsubstituted or substituted with halogen.

30. The compound as claimed in claim 28, wherein the amino acid in A at each occurrence is independently selected from the group consisting of alanine (ala), arginine (arg), aspartic acid (asp), cysteine (cys), glutamic acid (glu), glycine (gly), lysine (lys), phenylalanine (phe), serine (ser), threonine (thr), tryptophan (trp), valine (val), ornithine (orn), citrulline (cit), homocitrulline (hct), lanthionine (lan), homocysteine (hcy) or an amino acid having Formula A₁ or Formula A₂



Formula A₁



Formula A₂

wherein

m₁ and m₁' are 0, 1, 2 or 3;

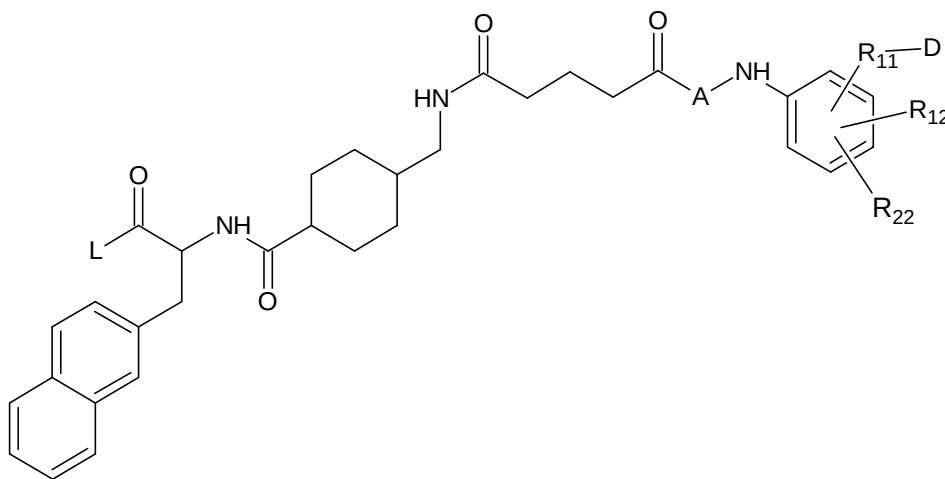
m₂ and m₂' are 0, 1, 2, 3 or 4;

R₁₀ is selected from (-C₂H₄O)₁₋₂₄CH₃, (-C₂H₄O)₁₋₂₄C₁₋₂ alkyl(N(R₁₀')(R₁₀''))—, C₁₋₃ alkyl-aryl or —C₁₋₃ alkyl-Het₁-(-C₂H₄O)₁₋₂₄CH₃, wherein Het₁ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from

nitrogen, oxygen or sulfur and wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}$ alkyl or $-OC_{1-3}$ alkyl; wherein

$R_{10'}$ and $R_{10''}$ are independently selected from hydrogen, C_{1-6} alkyl or $-C(O)-C_{1-4}$ alkyl-aryl wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by $-C_{1-3}$ alkyl or $-OC_{1-3}$ alkyl.

31. A compound of Formula VI,



Formula VI

or pharmaceutically acceptable salt, stereoisomer or isotope thereof; wherein:

L is a Ligand;

A is an amino acid or a peptide comprising 2-5 amino acids;

R_{11} is selected from $-C_{1-3}$ alkyl- $OC(O)-^{**}$,

$-C_{1-3}$ alkyl-O- $C(O)-N(R_{19})-C_{1-5}$ alkyl- $N(R_{19})-C(O)-^{**}$,

$-C_{1-3}$ alkyl-O- $C(O)-N[C_{1-5}$ alkyl- $N(R_{20}R_{21})]-C_{1-3}$ alkyl- ** , or

$-C_{1-3}$ alkyl-O- $C(O)-Het_2-C_{1-3}$ alkyl- $N(R_{19})-C(O)-^{**}$,

wherein ** indicates point of attachment to D;

R_{19} is selected from H, CH_3 or $-C_2H_4-O-C_2H_4-OH$;

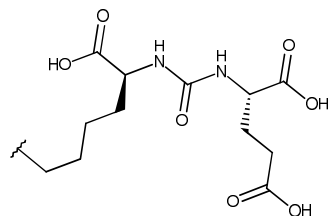
R_{20} is CH_3 ; R_{21} is CH_3 ; and

Het_2 is pyrrolidinyl;

R_{12} is selected from hydrogen, $-C(O)N(R_{13})(R_{14})$ or $-(OC_2H_4)_{1-10}-CH_3$;

R_{13} is hydrogen;

R_{14} is $-CH_3$, $-CH_2-C\equiv CH$, $-C_{1-3}$ alkyl- $N(R_{15})(R_{16})$, $-C_2H_4OCH_3$, $-(C_2H_4O)_{3-8}-C_2H_5$, $-(C_2H_4O)_{5-10}-C_2H_4-R_{17}$, $-CH_2$ -triazole- $-(C_2H_4O)_4-C_2H_4-R_{18}$ or



; wherein:

R₁₅ is —CH₃ or —C₂H₅;

R₁₆ is —CH₃ or —C₂H₅; or

R₁₅ and R₁₆ along with the nitrogen atom to which they are attached form a 5 to 6 membered heterocyclic ring, wherein 1 or 2 carbon atoms in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur and wherein the 5 to 6 membered heterocyclic ring is unsubstituted or substituted with —CH₃;

R₁₇ is —C(O)NHC₂H₄N(CH₃)₂;

R₁₈ is —C(O)NHC₂H₄N(CH₃)₂;

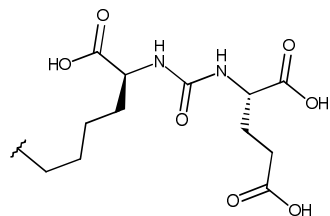
OR

R₁₃ and R₁₄ along with the nitrogen atom to which they are attached form a 4 to 6 membered heterocyclic ring, wherein 1 or 2 carbons in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the 4 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, —N(CH₃)₂ or —CH₂N(CH₃)₂;

R₂₂ is selected from hydrogen, —C(O)N(R₂₃)(R₂₄) or —(OC₂H₄)₁₋₁₀-CH₃;

R₂₃ is hydrogen;

R₂₄ is —CH₃, —CH₂-C≡CH, —C₁₋₃ alkyl-N(R₂₅)(R₂₆), —C₂H₄OCH₃, —(C₂H₄O)₃₋₈-C₂H₅, —(C₂H₄O)₅₋₁₀-C₂H₄-R₂₇, —CH₂-triazolyl-(C₂H₄O)₄-C₂H₄-R₂₈ or



; wherein:

R₂₅ is —CH₃ or —C₂H₅;

R₂₆ is —CH₃ or —C₂H₅; or

R₂₅ and R₂₆ along with the nitrogen atom to which they are attached form a 5 to 6 membered heterocyclic ring, wherein 1 or 2 carbon atoms in the heterocyclic ring

are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur and wherein the 5 to 6 membered heterocyclic ring is unsubstituted or substituted with —CH_3 ;

R_{27} is $\text{—C(O)NHC}_2\text{H}_4\text{N(CH}_3)_2$;

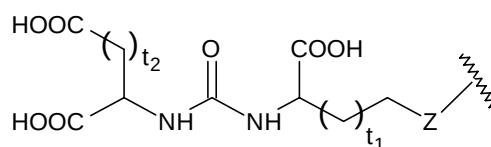
R_{28} is $\text{—C(O)NHC}_2\text{H}_4\text{N(CH}_3)_2$;

OR

R_{23} and R_{24} along with the nitrogen atom to which they are attached form a 4 to 6 membered heterocyclic ring, wherein 1 or 2 carbons in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the 4 to 6 membered heterocyclic ring is unsubstituted or substituted with C_{1-3} alkyl, $\text{—N(CH}_3)_2$ or $\text{—CH}_2\text{N(CH}_3)_2$; and

D is a cytotoxic agent or therapeutic agent.

32. The compound as claimed in claim 31, wherein the ligand L is of the Formula L₁:



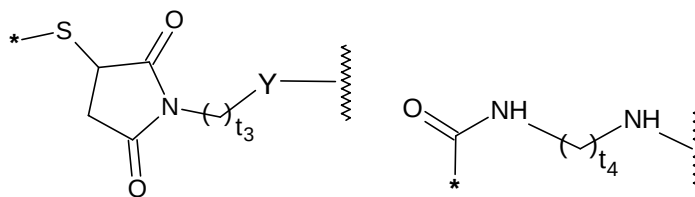
Formula L₁

wherein,

t_1 is 0, 1, 2, 3, or 4;

t_2 is 1, 2, 3 or 4;

Z is selected from the group consisting of $\text{N(R}_9\text{)}$, Formula Z₁ and Formula Z₂:



Formula Z₁

Formula Z₂

wherein:

t_3 is selected from 1, 2, 3, 4, 5 or 6;

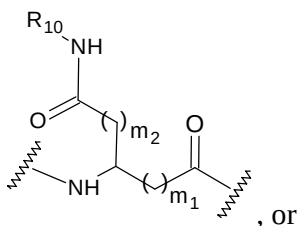
t_4 is selected from 1, 2, 3, 4, 5 or 6;

Y is $\text{—CH}_2\text{—}$ or —NH— and

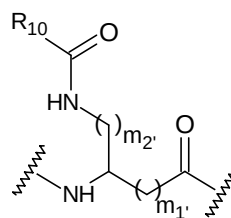
'~~~~~' indicates attachment of Formula L₁ to the rest of the compound of Formula I;

R₉ is selected from the group consisting of hydrogen, C₁₋₅ alkyl, a 6 to 10 membered aryl, a 5 to 10 membered heterocyclyl ring wherein the heterocyclyl ring contains one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur; and wherein R₉ is unsubstituted or substituted with halogen.

33. The compound as claimed in claim 31, wherein the amino acid in A at each occurrence is independently selected from the group consisting of alanine (ala), arginine (arg), aspartic acid (asp), cysteine (cys), glutamic acid (glu), glycine (gly), lysine (lys), phenylalanine (phe), serine (ser), threonine (thr), tryptophan (trp), valine (val), ornithine (orn), citrulline (cit), homocitrulline (hct), lanthionine (lan), homocysteine (hcy) or an amino acid having Formula A₁ or Formula A₂



Formula A₁



Formula A₂

wherein

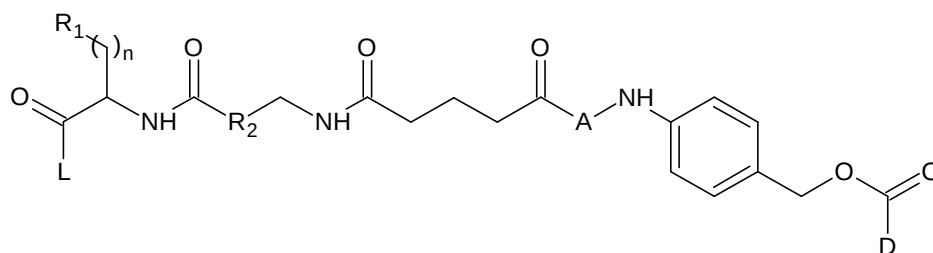
m₁ and m₁' are 0, 1, 2 or 3;

m₂ and m₂' are 0, 1, 2, 3 or 4;

R₁₀ is selected from (-C₂H₄O)₁₋₂₄CH₃, (-C₂H₄O)₁₋₂₄C₁₋₂ alkyl(N(R₁₀')(R₁₀''))—, C₁₋₃ alkyl-aryl or —C₁₋₃ alkyl-Het₁-(-C₂H₄O)₁₋₂₄CH₃, wherein Het₁ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur and wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl; wherein

R₁₀' and R₁₀' are independently selected from hydrogen, C₁₋₆ alkyl or -C(O)-C₁₋₄alkyl-aryl wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl.

34. A compound of Formula VII



Formula VII

or pharmaceutically acceptable salt, stereoisomer or isotope thereof;

wherein:

L is a Ligand;

n is 0, 1, or 2;

R₁ is selected from the group consisting of phenyl, indolyl, thiophenyl, quinolinyl and isoquinolinyl;

R₁ is unsubstituted or substituted with one or more R₅;

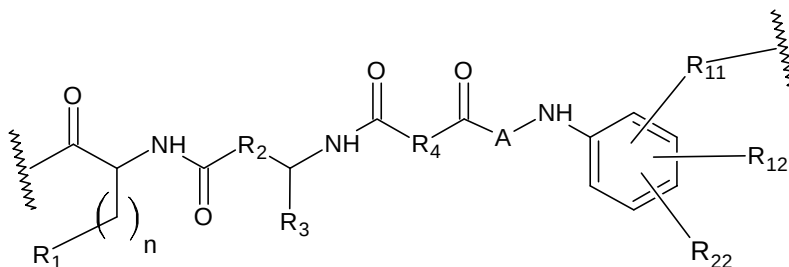
R₅ is selected from halogen, —OH, or a 6 to 10 membered aryl ring;

R₂ is cyclohexyl or phenyl;

A is a peptide val-cit; and

D is a cytotoxic agent or therapeutic agent.

35. The compound as claimed in any one of claims 1 to 34 for use in the treatment of cancer.
36. The compound as claimed in any one of claims 1 to 34 for use in the treatment of cancer that is positive for expression of PSMA.
37. Use of the compound as claimed in any one of claims 1 to 34 for the preparation of a medicament for the treatment of cancer.
38. A pharmaceutical composition comprising the compound as claimed in any one of claims 1 to 34, and a pharmaceutically acceptable carrier.
39. A ligand-drug conjugate, wherein the ligand L and the drug D is conjugated via linker of Formula VIII:



Formula VIII

wherein

n is 0, 1, 2, 3 or 4;

R₁ is selected from a 6 to 14 membered aryl or a 5 to 10 membered heteroaryl containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur;

R₁ is unsubstituted or substituted with one or more R₅;

R₅, at each occurrence, is independently selected from halogen, —C(O)NH₂, —C(O)OR₆, —C₁₋₃ alkyl, —OR₇, and a 6 to 10 membered aryl; wherein:

R₆ is hydrogen or C₁₋₃ alkyl;

R₇ is hydrogen or C₁₋₃ alkyl;

R₂ is absent or is selected from a 6 to 10 membered cycloalkyl or a 6 to 10 membered aryl;

R₃ is hydrogen or —C₁-C₅COOH;

R₄ is selected from a group consisting of —C₁₋₁₀ alkyl-, —C₂₋₆ alkenyl-, —C₁₋₃ alkyl-O-C₁₋₃ alkyl—, —C₂₋₆ alkyl-N(R₈)—, —C₂₋₆ alkyl(N(R₈)(R₈'))—, —N(R₈)-C₂₋₆ alkyl—, a 3 to 6 membered cycloalkyl and —C₁₋₂ alkyl-(-OC₂H₄)₁₋₈-OC₁₋₂ alkyl—; wherein:

R₈ and R₈' are independently selected from hydrogen, C₁₋₆ alkyl, -C(O)-C₁₋₄alkyl-aryl or -C(O)-(-C₂H₄O)₁₋₈-C₁₋₂ alkyl-N(R)(R'), wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl; wherein

R and R' are independently selected from hydrogen, -C₁₋₆ alkyl or -C(O)-C₁₋₄alkyl-aryl, wherein said aryl is selected from 6 to 14 membered aryl and is optionally substituted by -C₁₋₃alkyl or -OC₁₋₃alkyl;

A is an amino acid or a peptide comprising 2-5 amino acids;

A is attached to NH through its C terminal;

R₁₁ is selected from a group consisting of —C₁₋₃ alkyl-OC(O)—**,

—C₁₋₃ alkyl-O-C(O)-N(R₁₉)-C₁₋₅ alkyl-N(R₁₉)-C(O)—**,

—C₁₋₃ alkyl-O-C(O)-N[C₁₋₅ alkyl-N(R₂₀R₂₁)]-C₁₋₃ alkyl—**, and

—C₁₋₃ alkyl-O-C(O)-Het₂-C₁₋₃ alkyl-N(R₁₉)-C(O)—**,

wherein:

R₁₉ is selected from hydrogen, —C₁₋₃ alkyl or —C₁₋₃ alkyl-O-C₁₋₃ alkyl-OH;

R₂₀ is hydrogen or —C₁₋₃ alkyl;

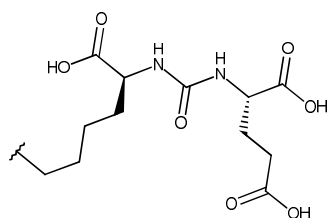
R₂₁ is hydrogen or —C₁₋₃ alkyl; and

Het₂ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen or sulfur;

R₁₂ is selected from hydrogen, —C(O)N(R₁₃)(R₁₄) or —(OC₂H₄)₁₋₁₀-CH₃;

R₁₃ is hydrogen;

R₁₄ is selected from —C₁₋₅ alkyl, —C₂₋₅ alkenyl, —C₂₋₅ alkynyl, —C₁₋₅ alkyl-N(R₁₅)(R₁₆), —C₁₋₅ alkyl-O-C₁₋₃ alkyl, —(C₂H₄O)₁₋₁₀C₂H₅, —(C₂H₄O)₁₋₁₀-C₂H₄-R₁₇ or —C₁₋₃ alkyl-Het₃-(C₂H₄O)₁₋₁₀-C₂H₄-R₁₈ or



; wherein:

R₁₅ is hydrogen or C1 to C3 alkyl;

R₁₆ is hydrogen or C1 to C3 alkyl; or

R₁₅ and R₁₆ along with the nitrogen atom to which they are attached form a 5 to 6 membered heterocyclic ring, wherein 1 or 2 carbon atoms in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur and wherein the 5 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, halogen or —OH;

R₁₇ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

R₁₈ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

Het₃ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen and sulfur;

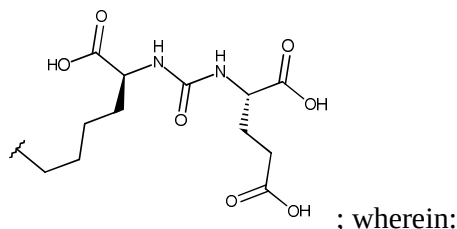
OR

R₁₃ and R₁₄ along with the nitrogen atom to which they are attached form a 4 to 6 membered heterocyclic ring, wherein 1 or 2 carbons in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the 4 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, —N(CH₃)₂ or —CH₂N(CH₃)₂;

R₂₂ is selected from hydrogen, —C(O)N(R₂₃)(R₂₄) or —(OC₂H₄)₁₋₁₀-CH₃;

R₂₃ is hydrogen;

R₂₄ is selected from —C₁₋₅ alkyl, —C₂₋₅ alkenyl, —C₂₋₅ alkynyl, —C₁₋₅ alkyl-N(R₂₅)(R₂₆), —C₁₋₅ alkyl-O-C₁₋₃ alkyl, —(C₂H₄O)₁₋₁₀C₂H₅, —(C₂H₄O)₁₋₁₀-C₂H₄-R₂₇ or —C₁₋₃ alkyl-Het₃-(C₂H₄O)₁₋₁₀-C₂H₄-R₂₈ or



R₂₅ is hydrogen or C₁ to C₃ alkyl;

R₂₆ is hydrogen or C₁ to C₃ alkyl; or

R₂₅ and R₂₆ along with the nitrogen atom to which they are attached form a 5 to 6 membered heterocyclic ring, wherein 1 or 2 carbon atoms in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur and wherein the 5 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, halogen or —OH;

R₂₇ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

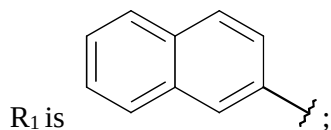
R₂₈ is selected from hydrogen or —C(O)NH-C₂₋₅ alkyl-N(CH₃)₂;

Het₃ is a 5 to 10 membered heterocyclic ring containing one, two or three heteroatoms independently selected from nitrogen, oxygen and sulfur;

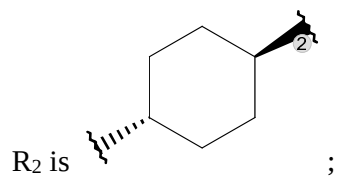
OR

R₂₃ and R₂₄ along with the nitrogen atom to which they are attached form a 4 to 6 membered heterocyclic ring, wherein 1 or 2 carbons in the heterocyclic ring are optionally replaced with additional heteroatoms independently selected from nitrogen, oxygen and sulfur, and wherein the 4 to 6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₃ alkyl, —N(CH₃)₂ or —CH₂N(CH₃)₂.

40. The compound as claimed in claim 39, wherein:



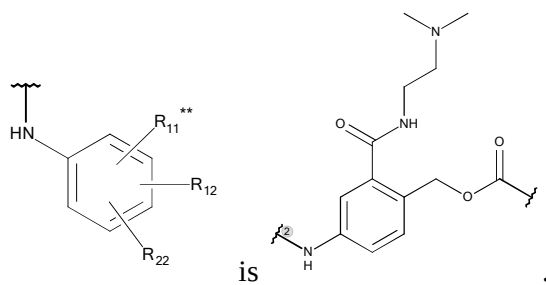
n is 1;



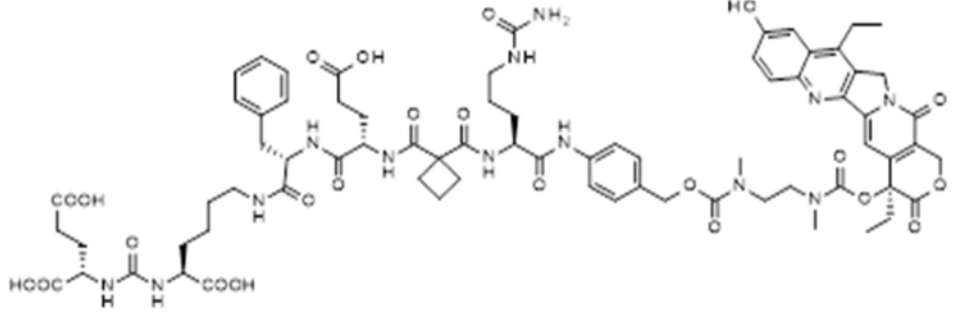
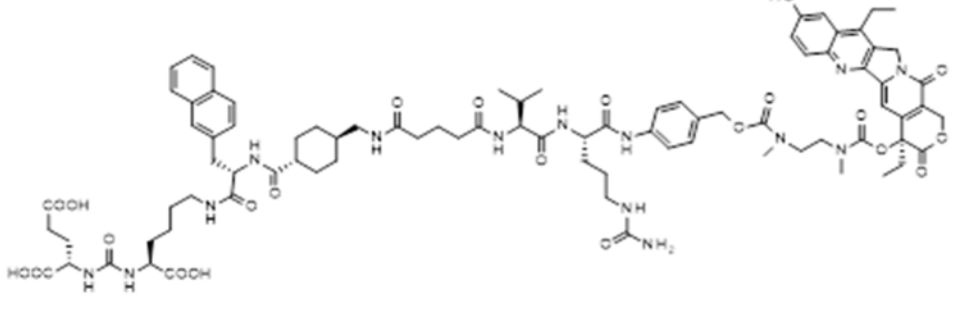
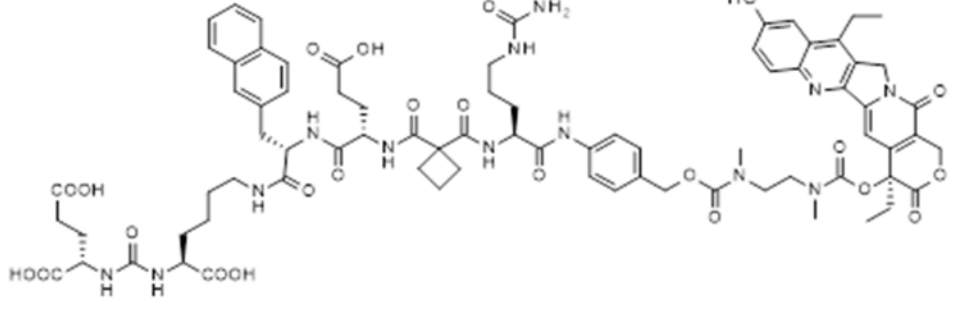
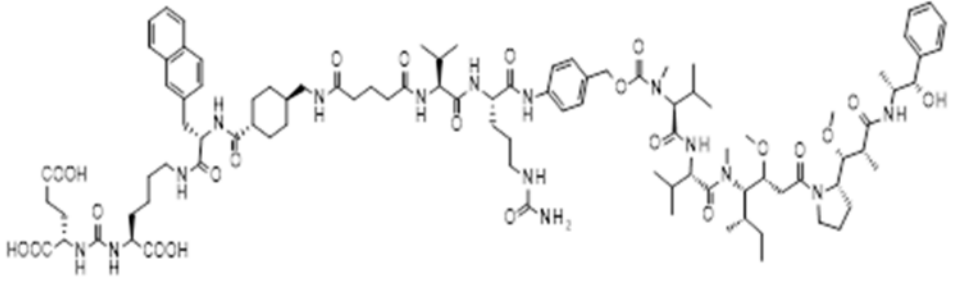
R₃ is hydrogen;

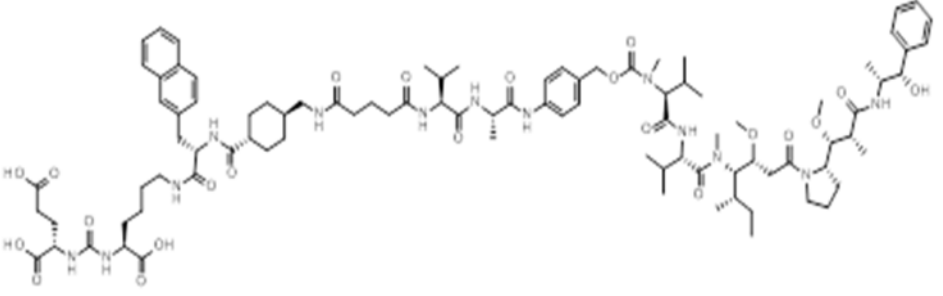
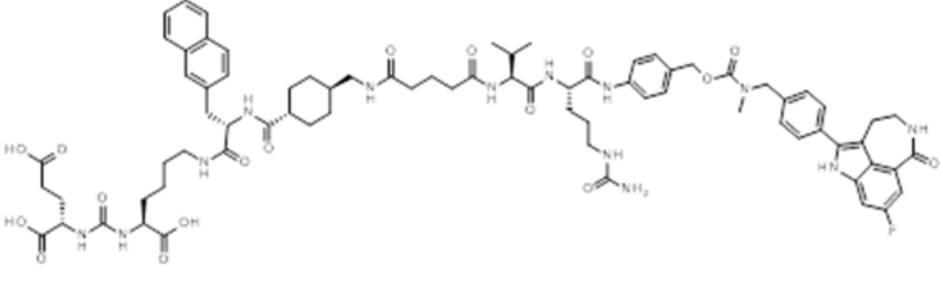
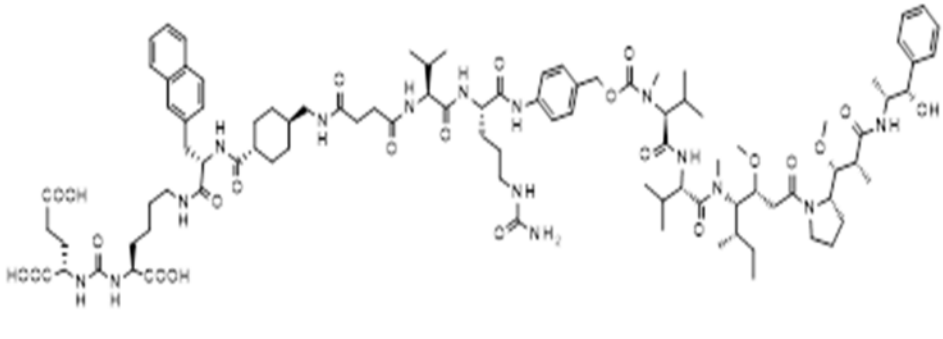
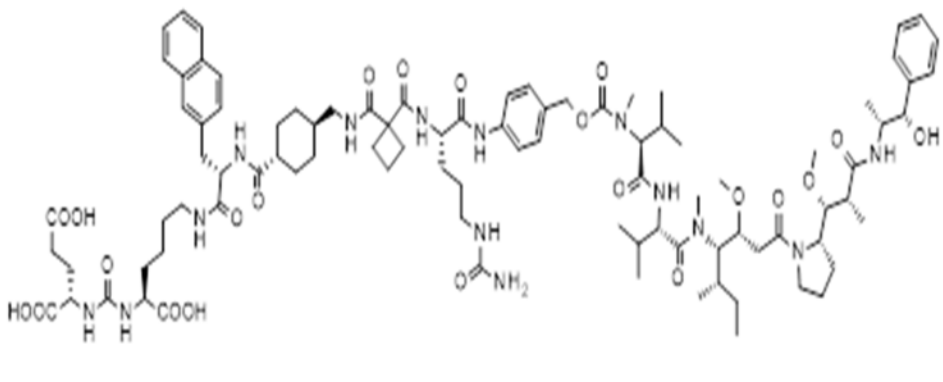
R₄ is -C₃H₆-;

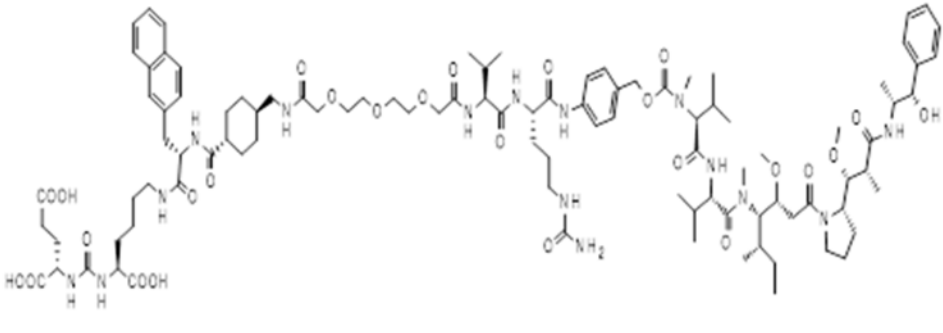
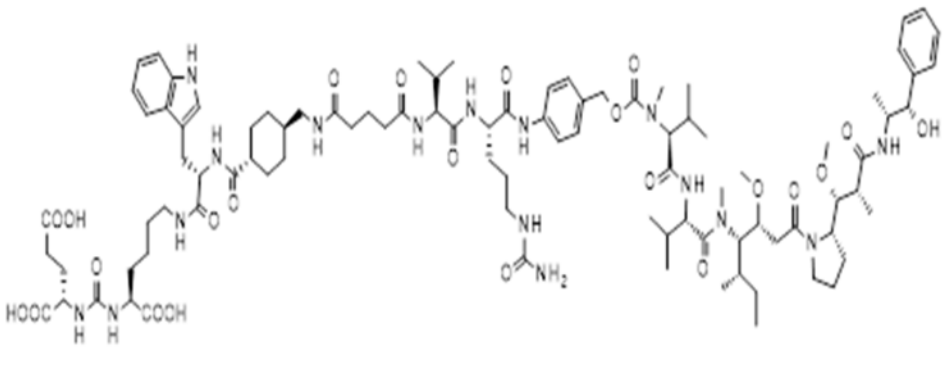
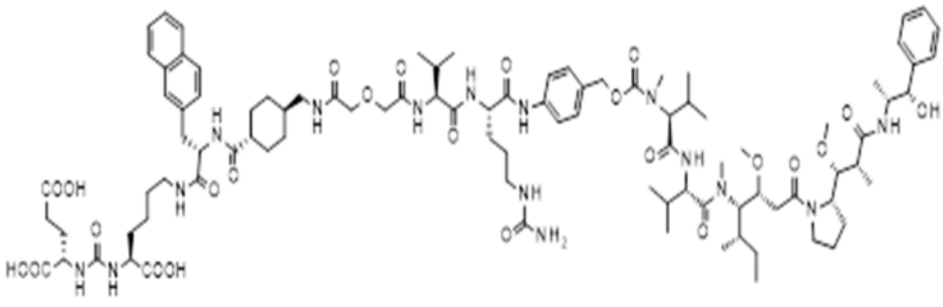
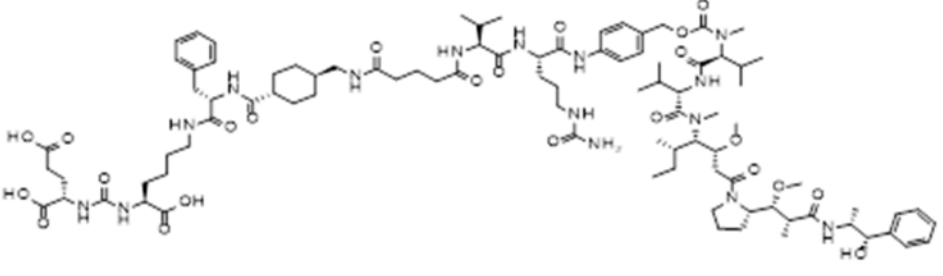
A is val-cit;

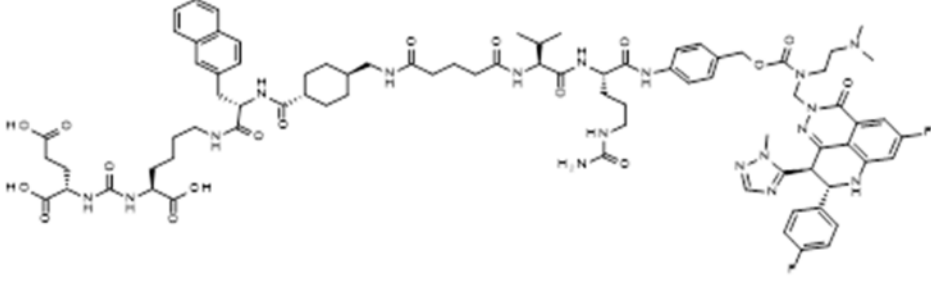
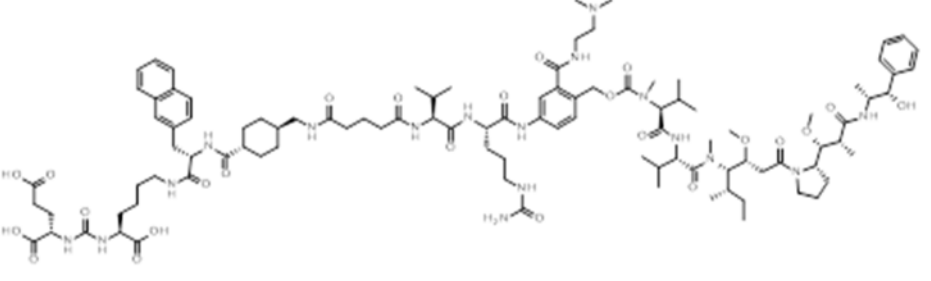
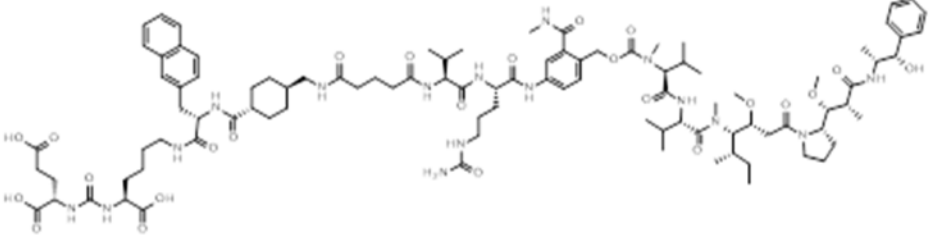
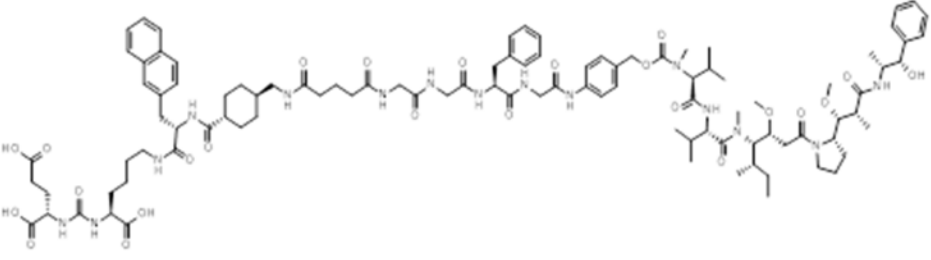
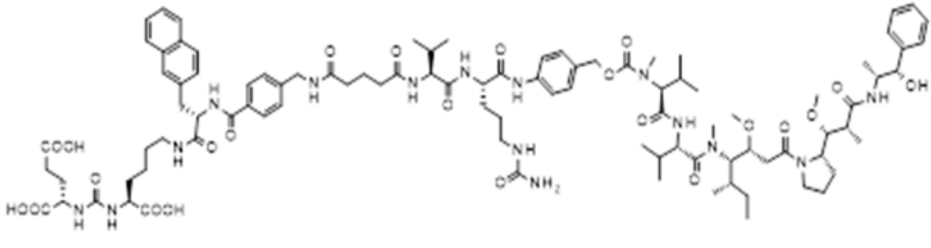


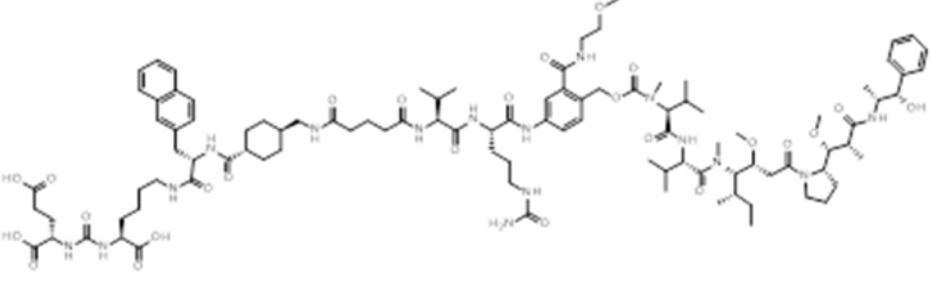
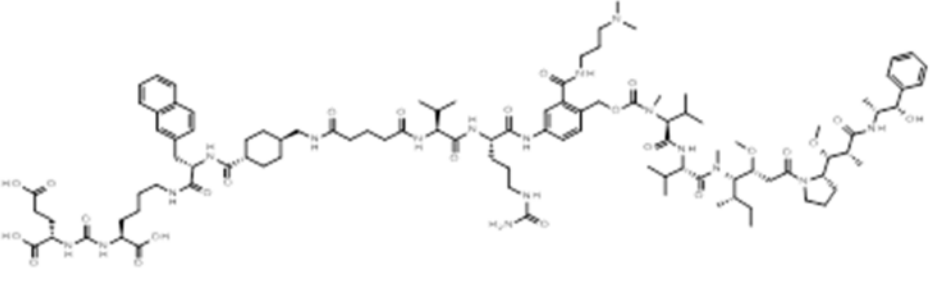
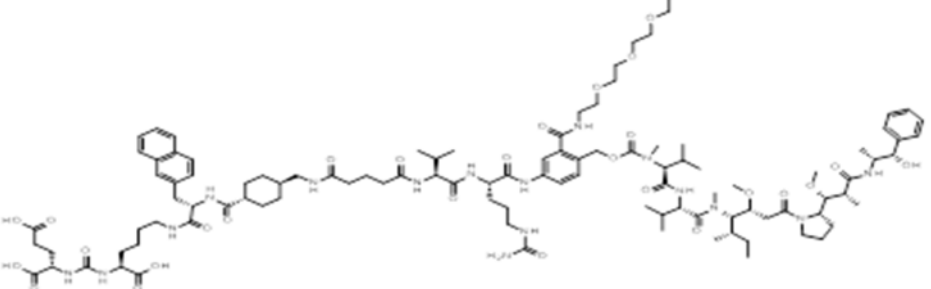
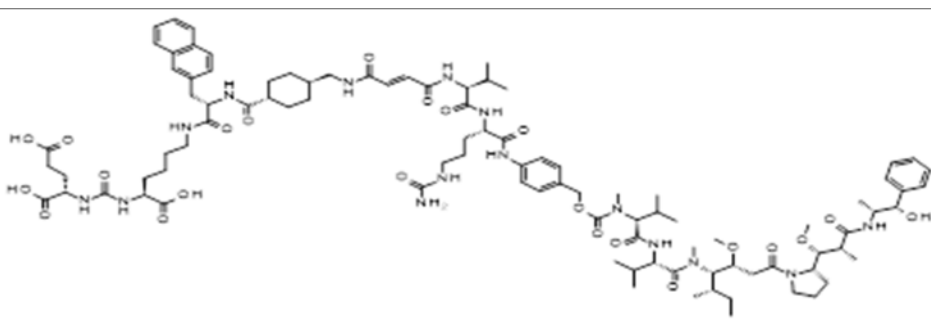
41. A compound selected from:

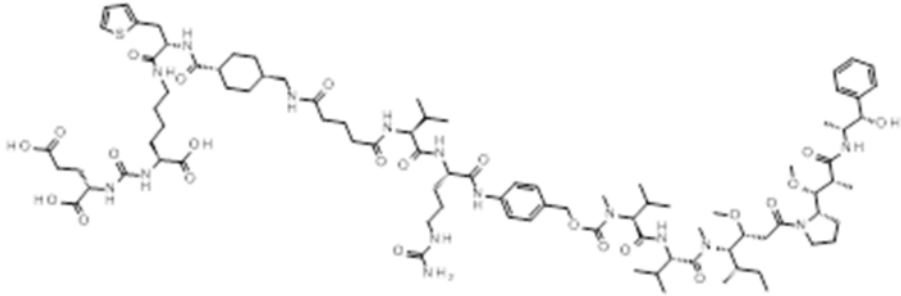
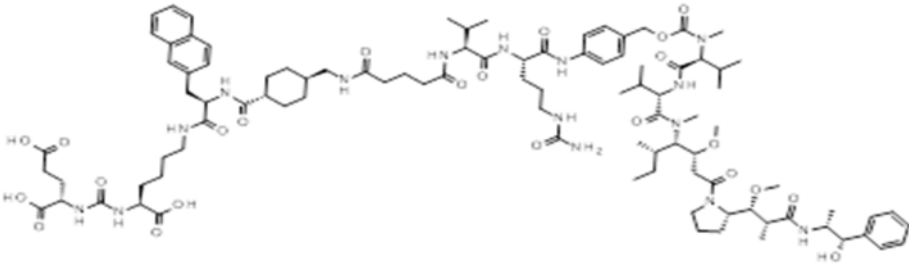
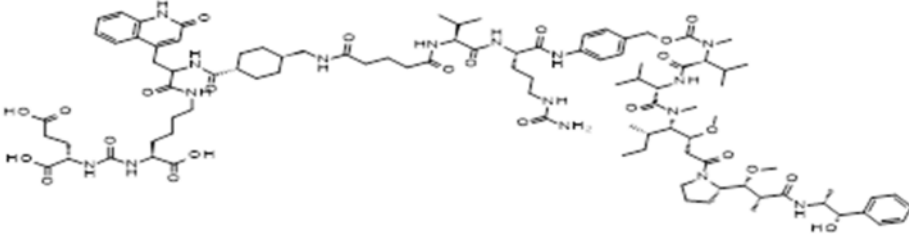
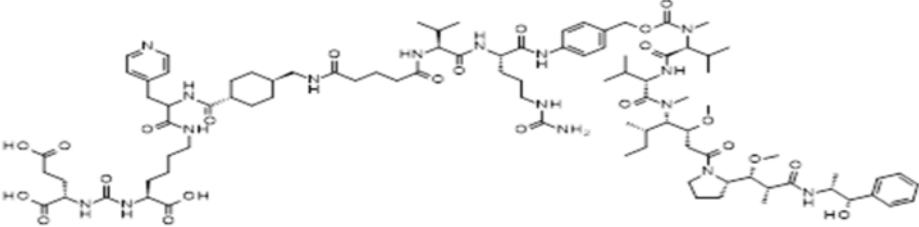
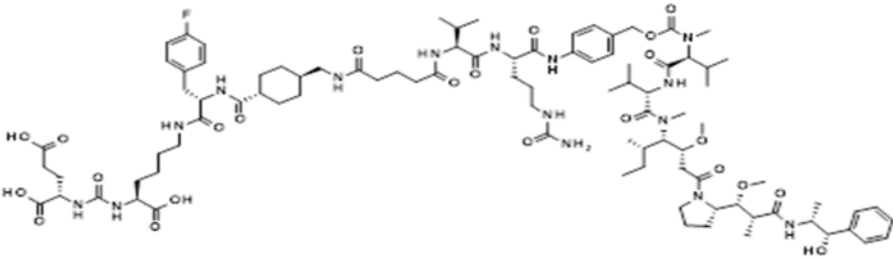
#	Structure/Name
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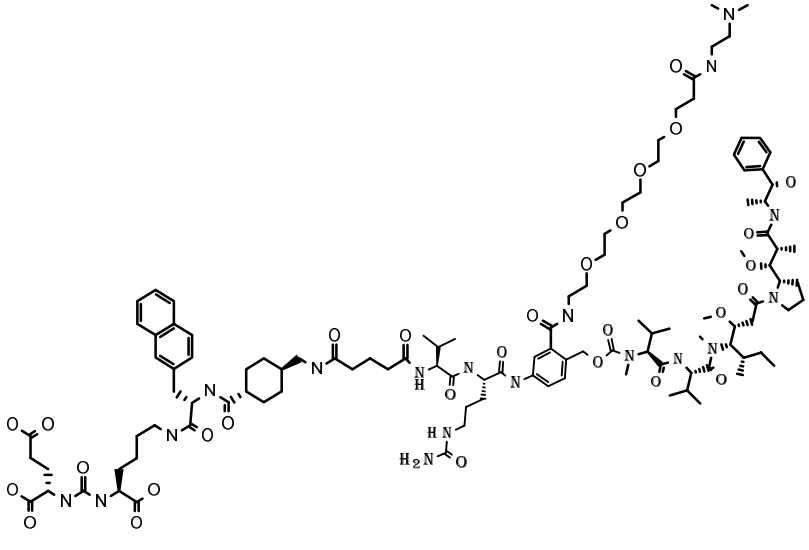
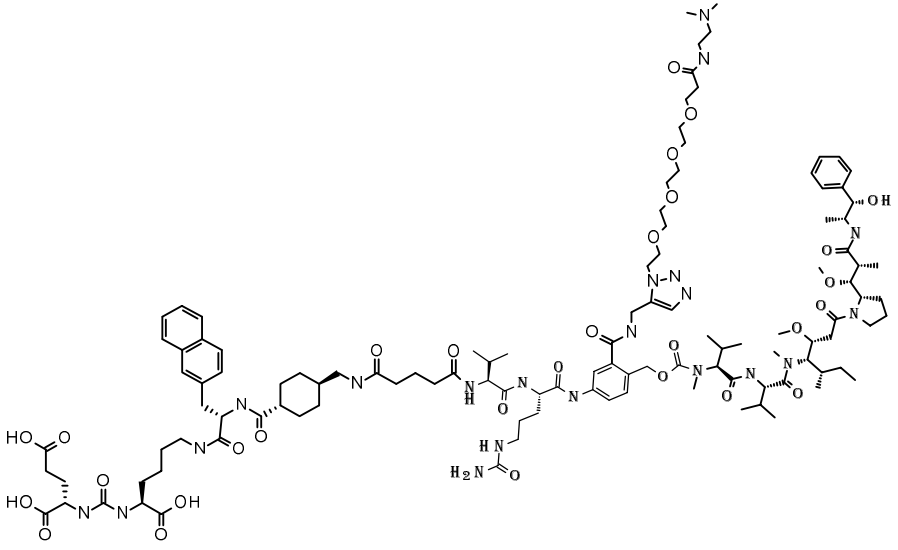
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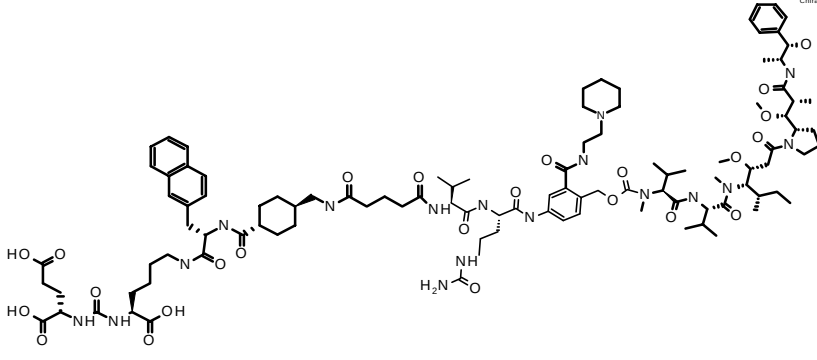
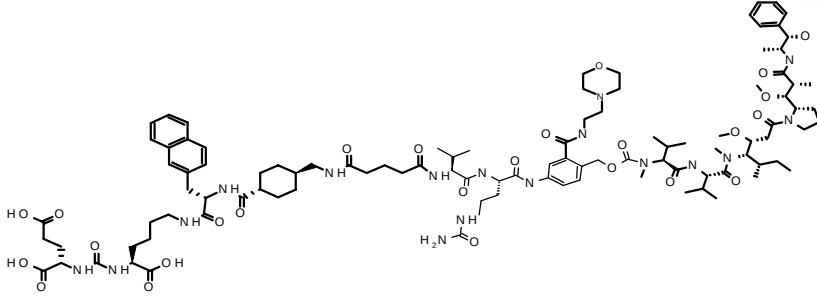
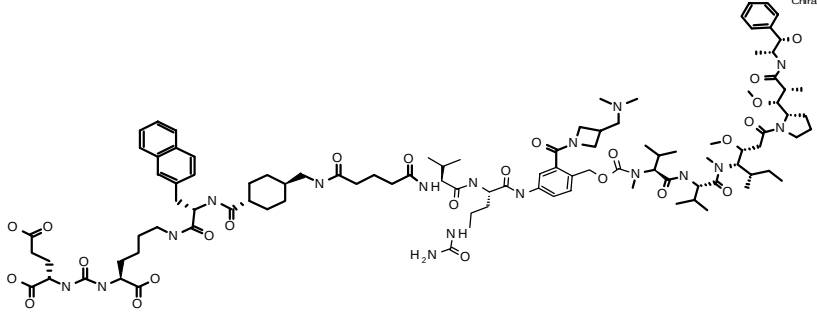
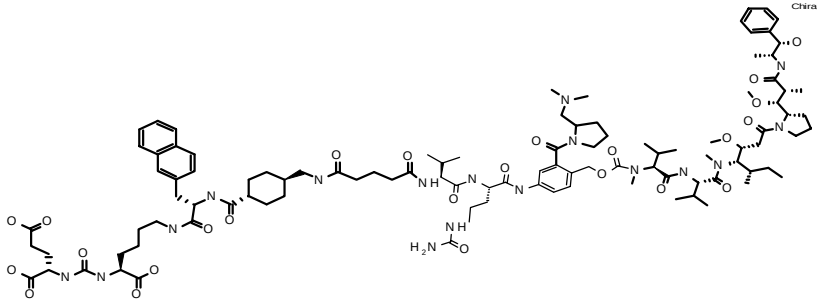
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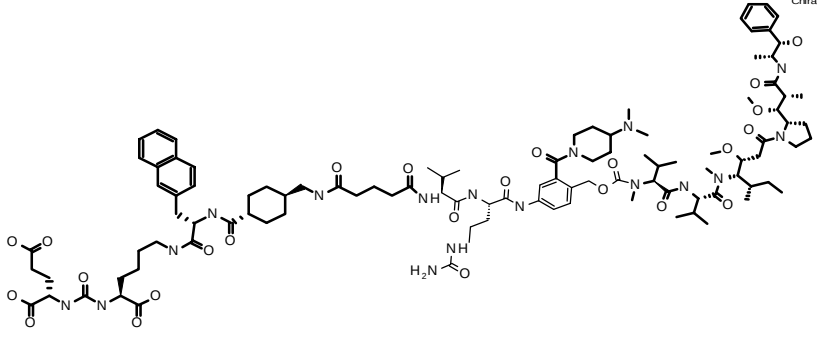
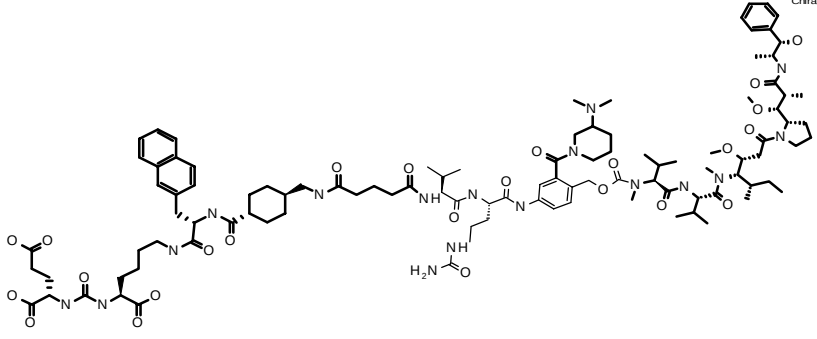
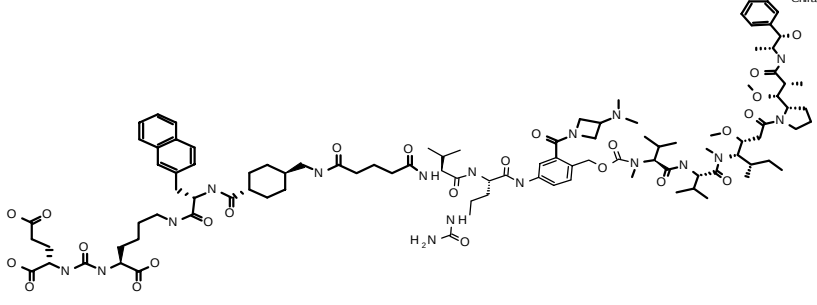
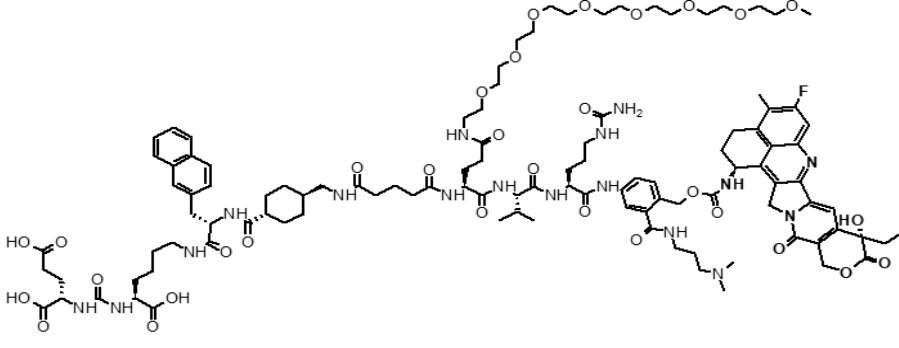
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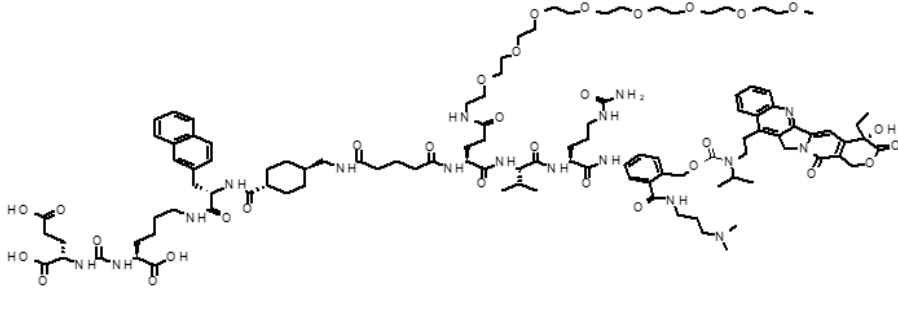
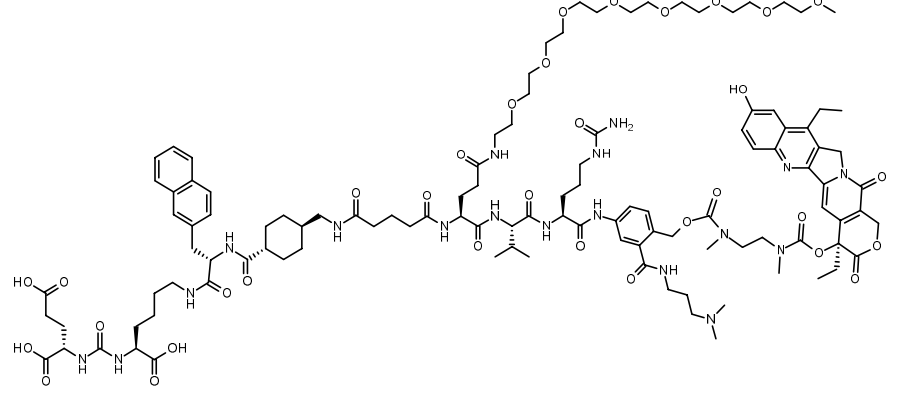
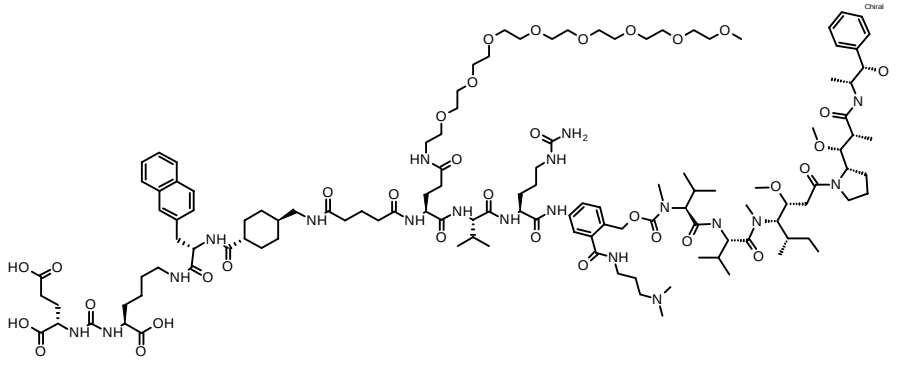
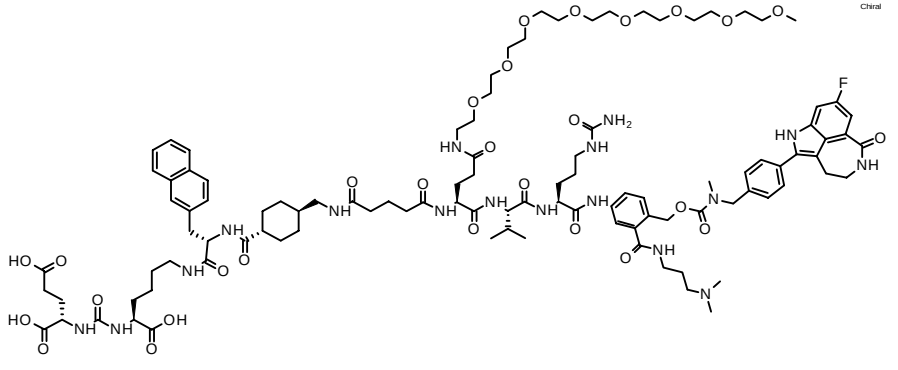
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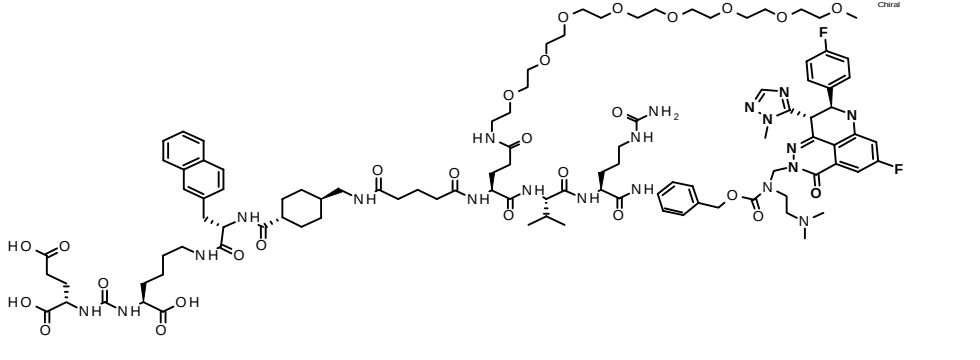
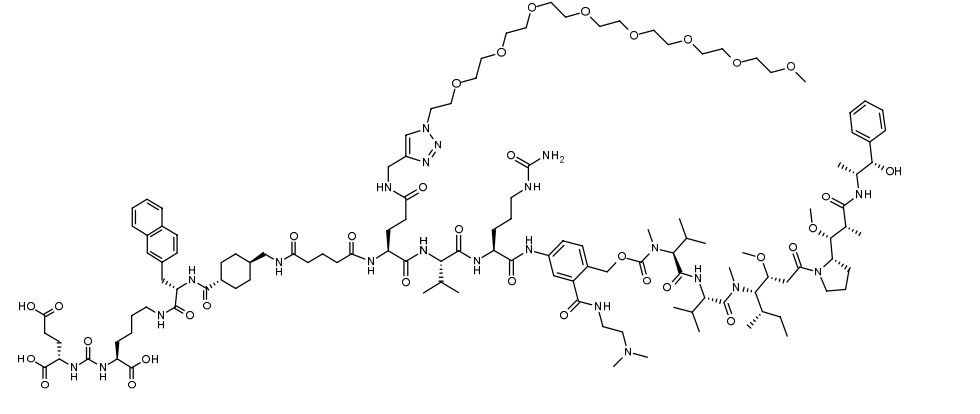
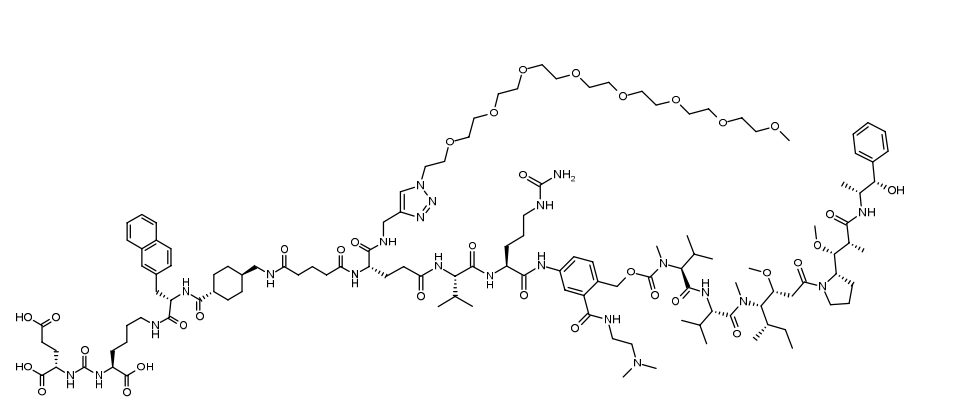
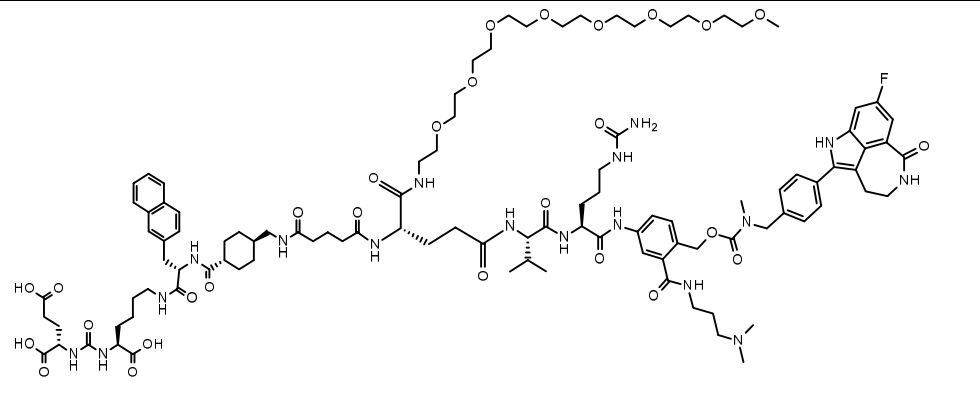
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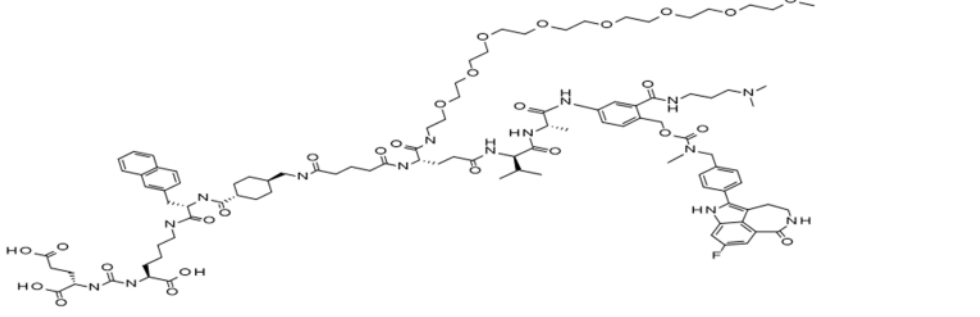
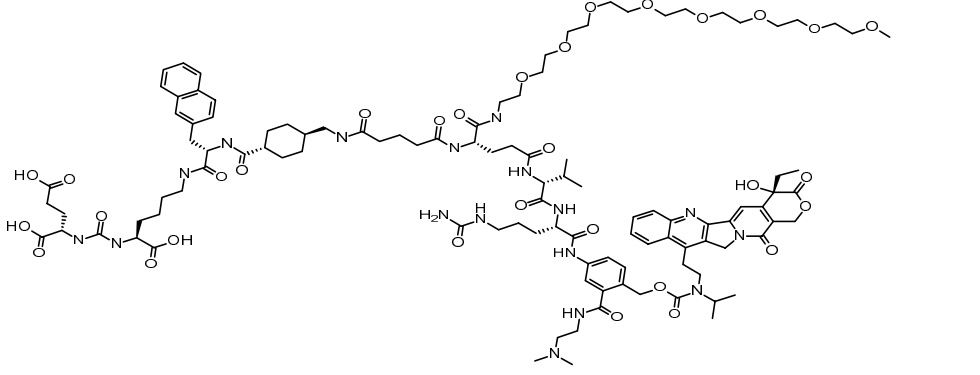
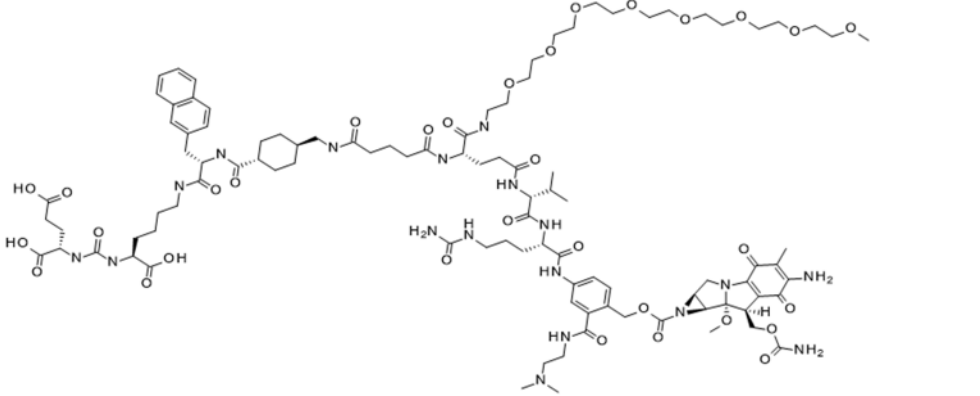
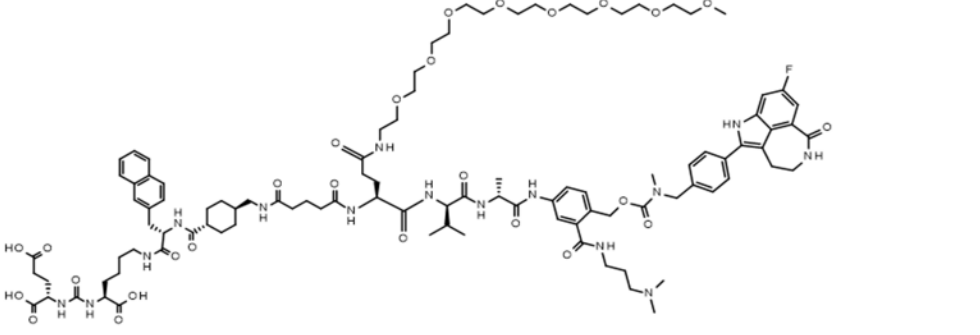
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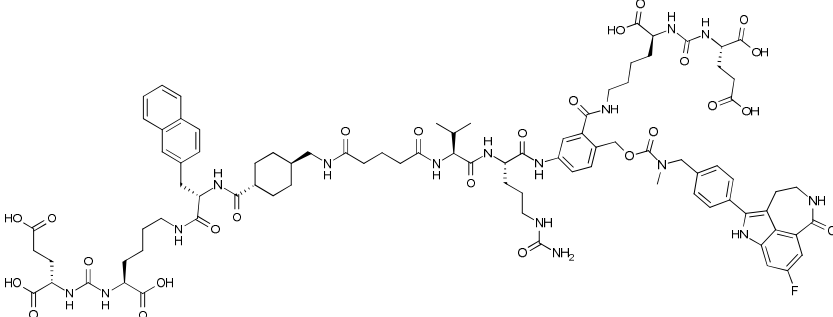
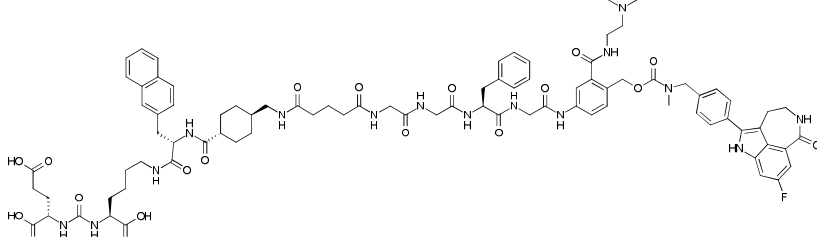
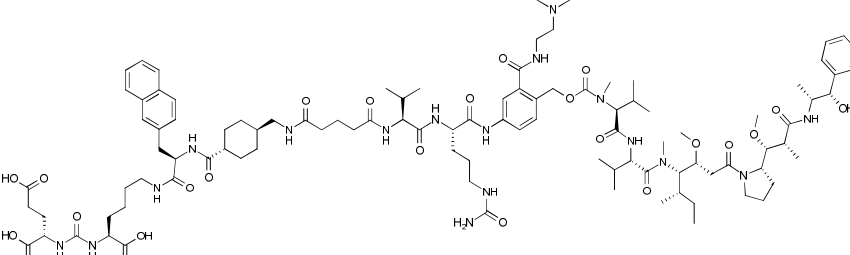
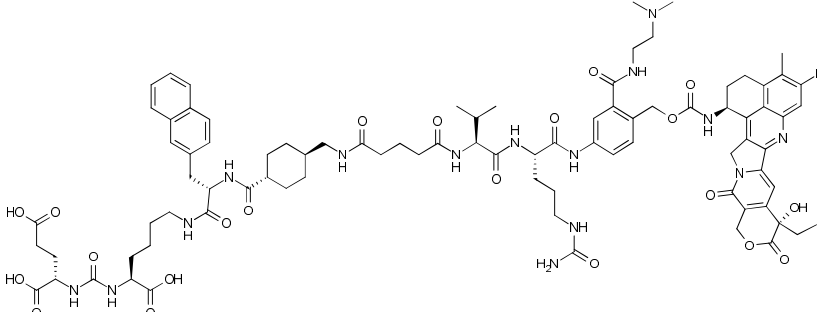
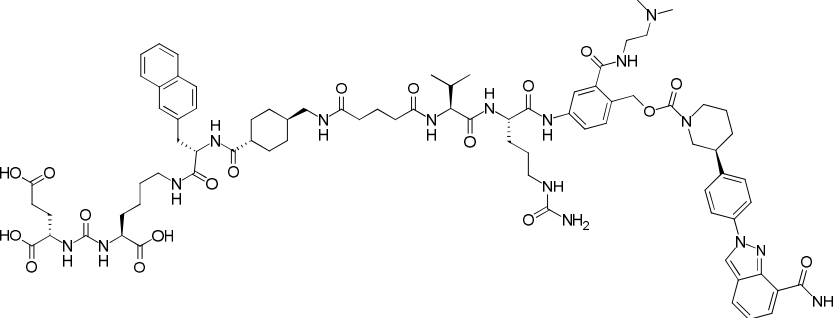
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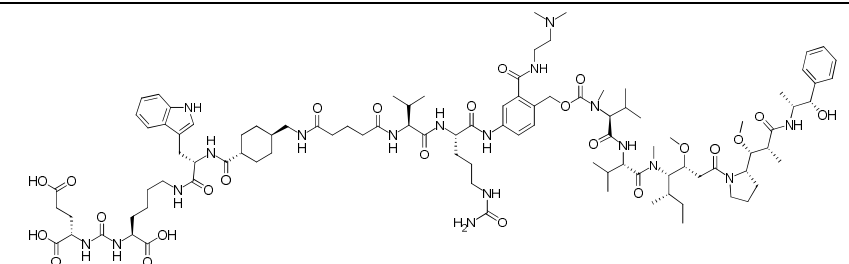
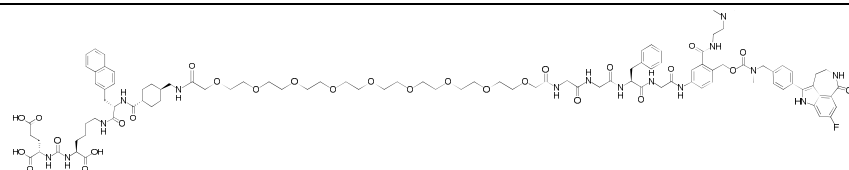
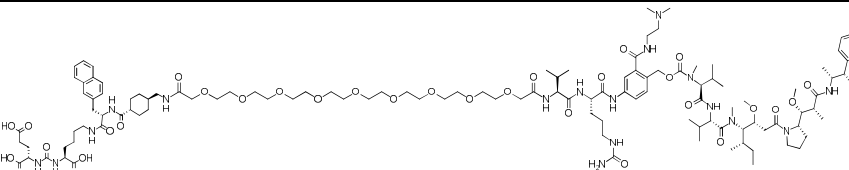
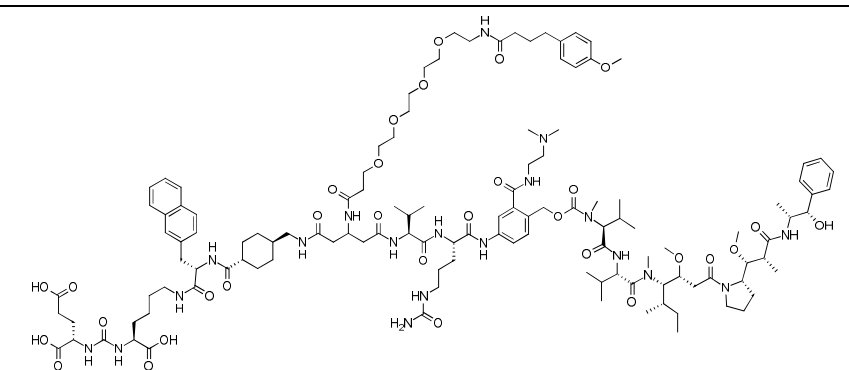
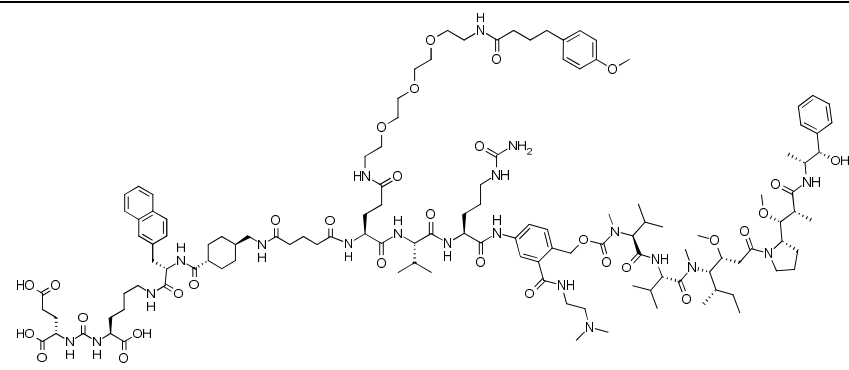
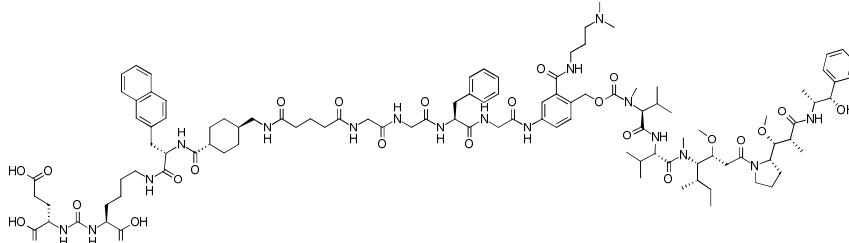
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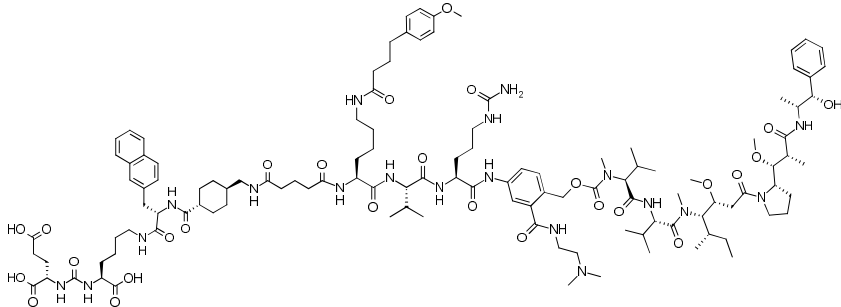
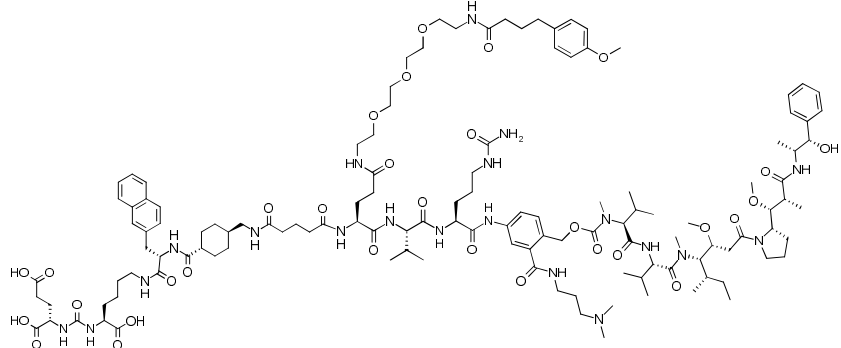
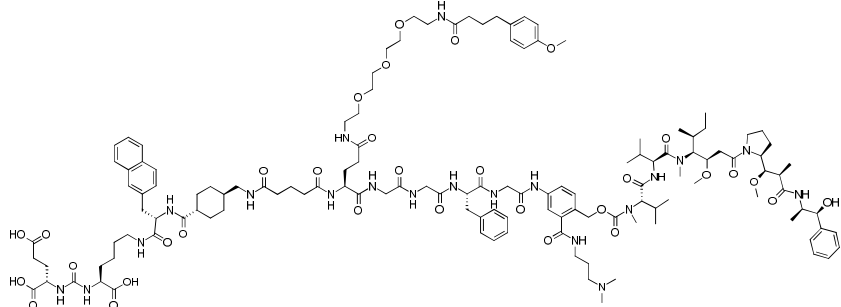
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