[CLAIMS]

[Claim 1]

A radiopharmaceutical comprising a conjugate as an active ingredient in a form of a buffer,

wherein the conjugate is a conjugate of an anti-HER2 antibody site-specifically modified with a peptide and a chelating agent, wherein

the chelating agent is chelated with a metal radionuclide, the peptide and the chelating agent are linked by a linker (L),

the linker (L) does not contain a thiourea bond, and

wherein the buffer includes a histidine buffer or a succinate buffer. [Claim 2]

The radiopharmaceutical according to claim 1, wherein the chelating agent is DOTAGA (α-(2-Carboxyethyl)-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid).

[Claim 3]

The radiopharmaceutical according to claim 1, wherein the peptide is an amino acid sequence consisting of not less than 13 and not more than 17 amino acid residues and is represented by the following formula:

(Xa)-Xaa1-(Xb)-Xaa2-(Xc)-Xaa3-(Xd)···(i)

in the formula (i), Xa, Xb, Xc and Xd are continuous X in the number of a, continuous X in the number of b, continuous X in the number of c, and continuous X in the number of d, respectively,

X is an amino acid residue having neither a thiol group nor a haloacetyl group in the side chain,

a, b, c and d are each independently an integer of not less than one and not more than 5, and satisfy $a+b+c+d \leq 14$,

Xaa1 and Xaa3 are each independently an amino acid residue derived from an amino acid having a thiol group in the side chain, or an amino acid residue derived from an amino acid having a haloacetyl group in the side chain, provided that one of Xaa1 and Xaa3 is an amino acid residue derived from an amino

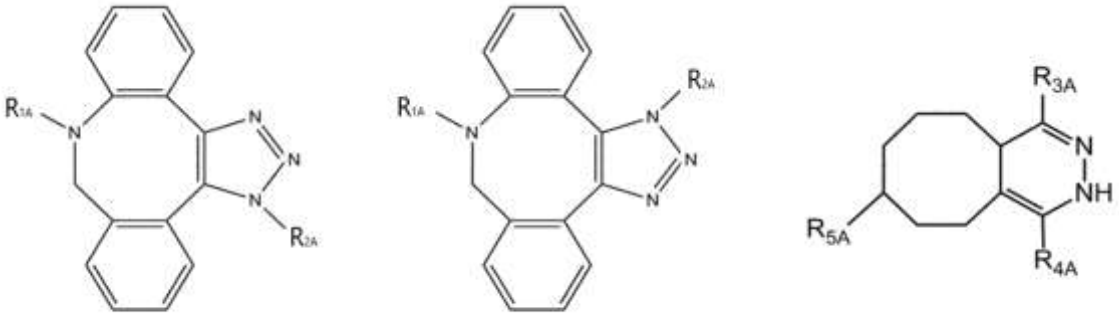
acid having a thiol group in the side chain,
Xaa1 and Xaa3 are connected to form a ring structure, and
Xaa2 is a lysine residue, an arginine residue, a cysteine residue, an aspartic acid residue, a glutamic acid residue, 2-aminosuberic acid, or diamino propionic acid, and modified with a crosslinking agent.

[Claim 4]

The radiopharmaceutical according to any one of claims 1 to 3, wherein the metal radionuclide is Ac-225, Y-90, Lu-177, or Zr-89.

[Claim 5]

The radiopharmaceutical according to any one of claims 1 to 4, wherein the linker (L) comprises the formula (10a), the formula (10b), or the formula (10c):



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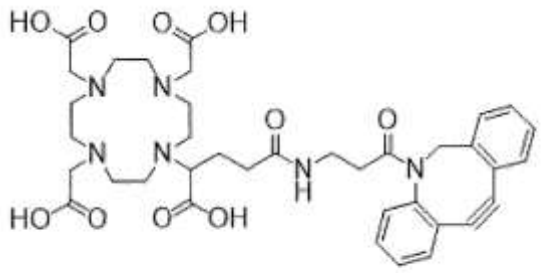
in the formula (10a) and the formula (10b), R_{1A} is a binding site with a chelating agent, and R_{2A} is a binding site with the peptide. In the formula (10c), one of R_{3A} and R_{4A} is a hydrogen atom, a methyl group, a phenyl group or a pyridyl group, and the other is a binding site with the chelating agent, and R_{5A} is a binding site with the peptide.

[Claim 6]

The radiopharmaceutical according to claim 5, comprising a polyethylene glycol group between the linkage site with the peptide and the peptide.

[Claim 7]

The radiopharmaceutical according to any one of claims 1 to 6, which is conjugated by a click reaction of an anti-HER2 antibody site-specifically modified with the peptide having an azide group introduced into the N-terminal, and a radioactive metal complex of DOTAGA-DBCO represented by the following formula:



DOTAGA-DBCO .

[Claim 8]

The radiopharmaceutical according to any one of claims 1 to 7, wherein the anti-HER2 antibody is trastuzumab or pertuzumab.

[Claim 9]

A conjugate of an anti-HER2 antibody site-specifically modified with a peptide and a chelating agent, wherein

the chelating agent is chelated with a metal radionuclide,

the peptide and the chelating agent are linked by a linker (L),

the linker (L) does not contain a thiourea bond, and

the anti-HER2 antibody is pertuzumab.

[Claim 10]

A radiopharmaceutical comprising the conjugate according to claim 9 as an active ingredient.

[Claim 11]

Use of the radiopharmaceutical according to any one of claims 1 to 8 and 10 in the manufacture of a medicament for radionuclide therapy for cancer.

[Claim 12]

The radiopharmaceutical according to any one of claims 1 to 8 and 10 for use in cancer diagnosis.

[Claim 13]

The radiopharmaceutical according to claim 12 for use in combined cancer diagnosis and radionuclide therapy for cancer, wherein the radionuclide therapy usesthe radiopharmaceutical according to any one of claims 1 to 8.

[Claim 14]

A radiopharmaceutical containing a conjugate of a chelating agent chelated with a metal radionuclide and an anti-HER2 antibody as an active ingredient and satisfying the following condition (1) or (2), wherein

the linkage between the anti-HER2 antibody and the chelating agent does not contain a thiourea bond:

(1) the metal radionuclide is ^{177}Lu or ^{90}Y, and the conjugate has a radiochemical purity of not less than 90% when stored at room temperature for 7 days

(2) the metal radionuclide is ^{225}Ac, and the conjugate has a radiochemical purity of not less than 90% when stored at room temperature for 14 days.

[Claim 15]

A radiopharmaceutical comprising a conjugate of a chelating agent chelated with a metal radionuclide and an anti-HER2 antibody as an active ingredient, wherein

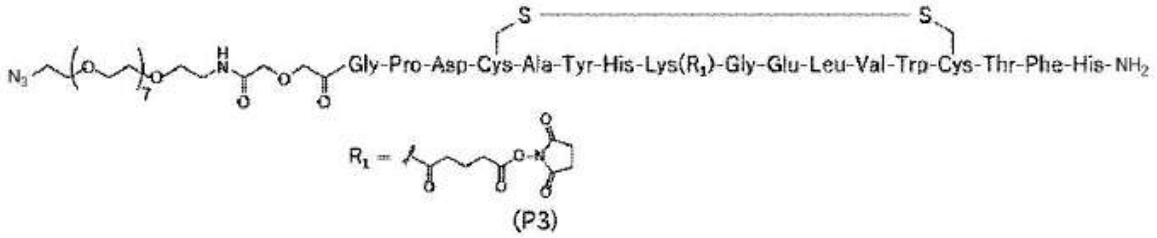
the linkage between the anti-HER2 antibody and the chelating agent does not comprise a thiourea bond, and

the conjugate has a radiochemical purity of not less than 90% at the time of expiry of a period that is a multiple of not less than 1 and not more than 5 of the half-life, based on the half-life of the metal radionuclide.

[Claim 16]

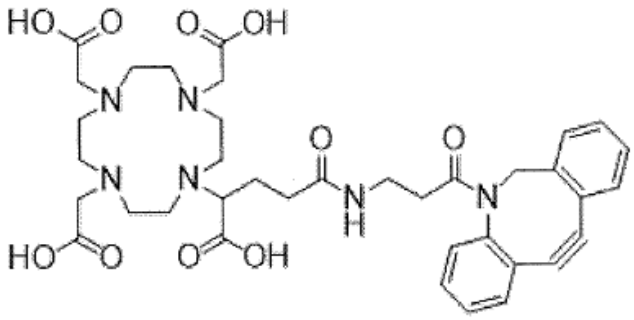
The radiopharmaceutical according to any one of claims 1 to 8 and 10,

wherein a succinimidyl group in the structure represented by the following formula (P3):



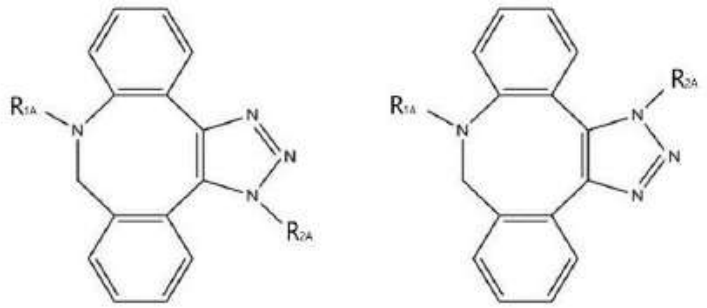
(P3)

reacts with a Lys248 residue or a Lys246 residue (according to Eu numbering) in a human anti-HER2 antibody, thereby site-specifically modifying the anti-HER2 antibody with the peptide; and an azide group in the structure represented by formula (P3) is reacted by click reaction with a dibenzocyclooctyne group of DOTAGA-DBCO represented by the following formula:



DOTAGA-DBCO

thereby forming a triazole skeleton-containing structure represented by the following formula (10a) or (10b):



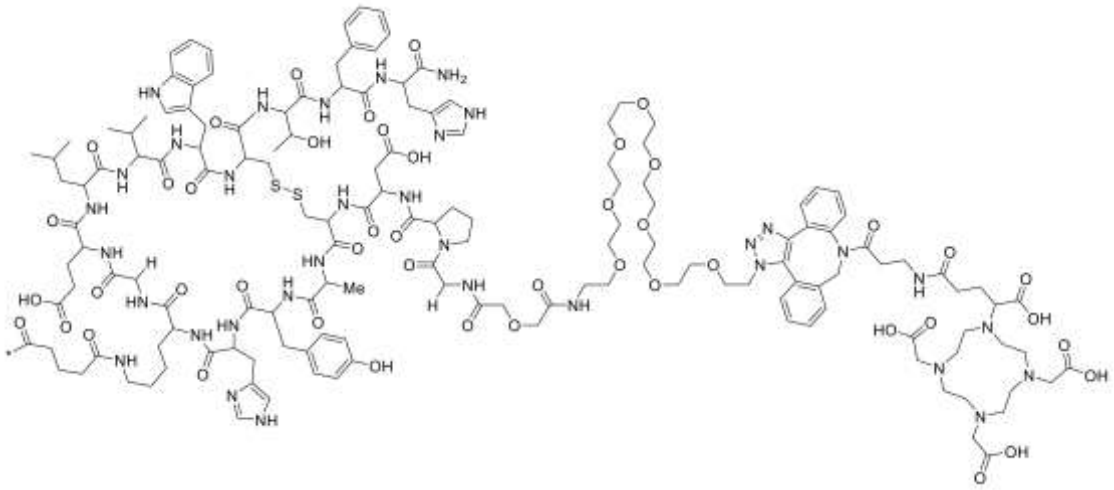
(10a) (10b)

(wherein, in formulas (10a) and (10b), R_{1A} represents a linkage site to a chelating agent, and R_{2A} represents a linkage site to the peptide).

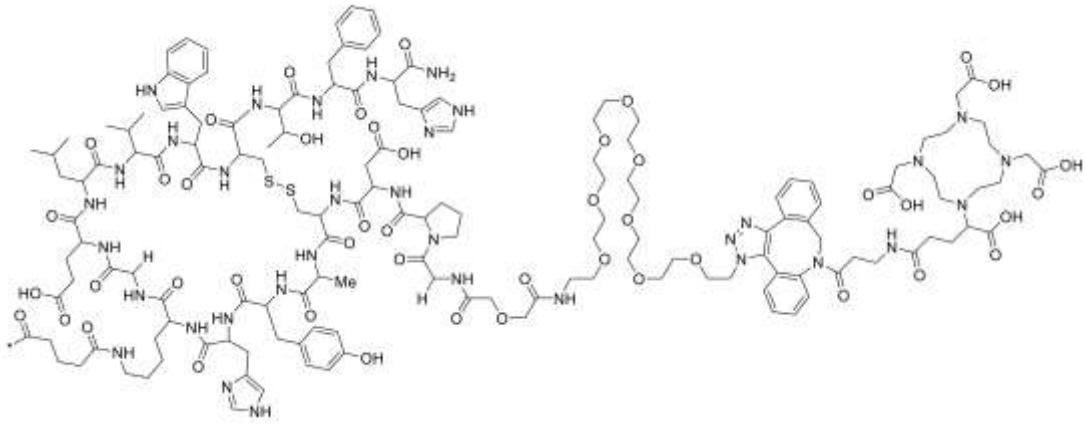
[Claim 17]

The radiopharmaceutical according to claim 16, wherein

the structure in which the peptide and the chelating agent are linked via a linker (L) is represented by the following structure, and is bound, at the position indicated by *, to a Lys248 residue or a Lys246 residue (according to Eu numbering) in a human anti-HER2 antibody:



or



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