Summary of Disclosure

[0006]

In achieving: improvement in specific accumulation at a target tissue and site; and reduction in accumulation at a non-target tissue and site, it is important to control pharmacokinetics, such as retention in blood. As a method to effectively control pharmacokinetics, chemical structures are desired to be further optimized. In general, a compound with a small molecular weight has poor retention in blood, which may result in: insufficient accumulation at a target tissue; and unintended accumulation at a normal tissue. In addition, the compounds disclosed in Patent Literature 1 and 2 undesirably show much unspecific accumulation at the kidney, still having had room for improvement in this respect.

[0007]

Therefore, the present disclosure relates to a compound and a radiolabeled compound capable of achieving both of: improvement in accumulation at a target tissue; and reduction in accumulation at a non-target tissue, particularly reduction in accumulation at the kidney.

[0008]

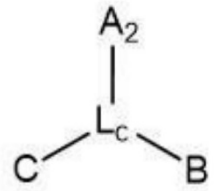
The present disclosure provides a compound including a structure having: a chelating part capable of coordinating with a radioactive metal ion; a first atomic group containing an albumin-binding part; and a second atomic group containing a PSMA molecule-binding part,

wherein the first atomic group and the second atomic group are bonded with each other through the chelating part.

[0009]

The present disclosure provides a compound represented by the following general formula (2):

[0010]



(2)

wherein, in the formula (2), A_2 represents a chelating part capable of coordinating with a radioactive metal ion;

B represents an atomic group containing an albumin-binding part;

C represents an atomic group containing a PSMA molecule-binding part;

A_2 represents Neunpa, Octapa, or a derivative thereof;

L_c represents a linker structure; and

when A_2 represents Octapa, L_c contains a polyethylene glycol structure.

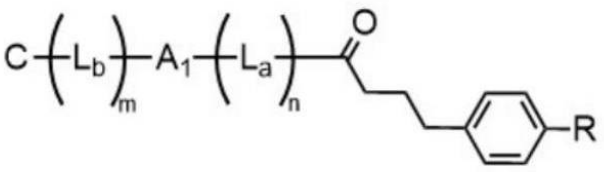
[0011]

The present disclosure provides a radiolabeled compound comprising a radioactive metal ion and the compound which is coordinated with a radioactive metal ion.

[0012]

The present disclosure provides a method for manufacturing a radiolabeled compound, the method including: coordinating the compound to a radioactive metal ion to obtain a radiolabeled compound.

[0012a] In one aspect, the present disclosure provides a compound represented by the following general formula (1S):



(1S)

wherein, in the formula (1S), A_1 represents a chelating part capable of coordinating with a radioactive metal ion;

C represents an atomic group containing a PSMA molecule-binding part;

L_a represents a linker structure, with the provision that L_a does not contain a polyethylene glycol group;

L_b represents a linker structure that is identical to or different from L_a and comprises a structure derived from an amino acid having a structure containing an alicycle of 5 to 10 carbon atoms;

"m" represents 1;

"n" is 1; and

R represents a hydrogen atom, a halogen atom, or an alkyl group having 1 or more and 5 or less carbon atoms.

[0012b] In another aspect, the present disclosure provides a radiolabeled compound comprising: a radioactive metal ion and the compound as defined herein which is coordinated with the radioactive metal ion.

[0012c] In yet another aspect, the present disclosure provides a radioactive pharmaceutical composition comprising the radiolabeled compound as defined herein, as an active ingredient.

[0012d] In yet another aspect, the present disclosure provides a method for manufacturing a radiolabeled compound, the method comprising: coordinating the compound as defined herein to a radioactive metal ion to obtain a radiolabeled compound.

Brief Description of Drawings

[0013]

[Fig.1] Fig. 1 is graphs showing the results of the cell-binding assay in Example 1-1 ([^{111}In]In-PSMA-DA1) and Comparative Example 1-1 ([^{111}In]In-PSMA-DB).

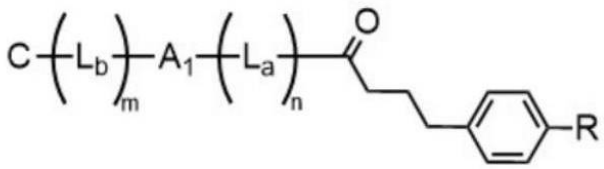
[Fig. 2] Fig. 2 is a graph showing the results of the albumin-binding experiments in [^{111}In]In-PSMA-DA1 and [^{111}In]In-PSMA-DB.

[Fig. 3] Fig. 3 is graphs showing the results of the internal radioactivity distribution experiments in [^{111}In]In-PSMA-DA1 and [^{111}In]In-PSMA-DB.

[Fig. 4] Fig. 4 is SPECT/CT images in [^{111}In]In-PSMA-DA1 and [^{111}In]In-PSMA-DB.

CLAIMS

1. A compound represented by the following general formula (1S):



(1S)

wherein, in the formula (1S), A_1 represents a chelating part capable of coordinating with a radioactive metal ion;

C represents an atomic group containing a PSMA molecule-binding part;

L_a represents a linker structure, with the provision that L_a does not contain a polyethylene glycol group;

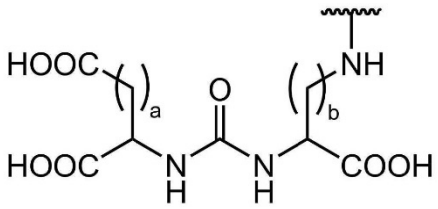
L_b represents a linker structure that is identical to or different from L_a and comprises a structure derived from an amino acid having a structure containing an alicycle of 5 to 10 carbon atoms;

"m" represents 1;

"n" is 1; and

R represents a hydrogen atom, a halogen atom, or an alkyl group having 1 or more and 5 or less carbon atoms.

2. The compound according to claim 1, wherein, in the formula (1S), C represents the following formula (C1):



(C1)

wherein, in the formula (C1), the wavy line part represents a part bonding to A_1 or L_b in the formula (1S); and

"a" and "b" each independently represent an integer of 1 or more and 7 or less.

3. The compound according to claim 1 or 2, wherein, in the formula (1S), A_1 has a cyclic

structure, the cyclic structure has two or more nitrogen atoms, and each of the nitrogen atoms is connected with one another through two or more adjacent carbon atoms; or A_1 has an open chain structure, the open chain structure has two or more nitrogen atoms, and each of the nitrogen atoms is connected with one another through two or more adjacent carbon atoms,

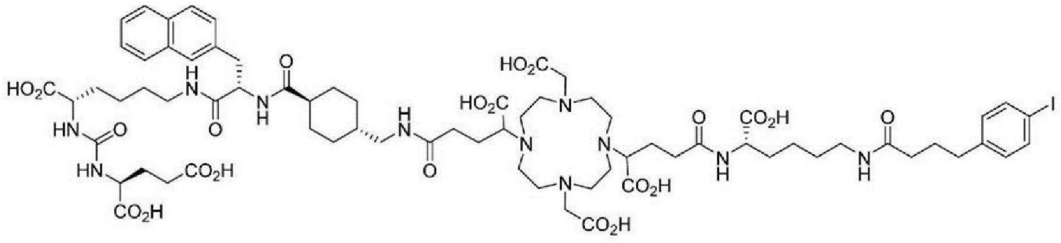
A_1 has a nitrogen-bonding atomic group directly bonded with a nitrogen atom constituting the cyclic structure or the open chain structure,

the nitrogen-bonding atomic group contain one or more groups selected from the group consisting of a carboxy group, a phosphate group, an amide group, a benzene ring, and a pyridine ring, and

when L_a is bonded to the nitrogen-bonding atomic group, C is bonded to a nitrogen-bonding atomic group other than the atomic group to which L_a is bonded.

4. The compound according to any one of claims 1 to 3, wherein, in the formula (1S), A_1 is DOTA, HOPO, Octapa, Macropa, or a derivative thereof.

5. The compound according to any one of claims 1 to 4, wherein the compound is represented by the following formula:



6. A radiolabeled compound comprising: a radioactive metal ion and the compound according to any one of claims 1 to 5 which is coordinated with the radioactive metal ion.

7. The radiolabeled compound according to claim 6, wherein the radioactive metal is ^{68}Ga, ^{64}Cu, ^{67}Cu, ^{89}Zr, ^{90}Y, ^{99m}Tc, ^{111}In, ^{177}Lu, ^{186}Re, ^{188}Re, or ^{225}Ac.

8. A radioactive pharmaceutical composition comprising the radiolabeled compound according to claim 6 or 7, as an active ingredient.

9. A method for manufacturing a radiolabeled compound, the method comprising:

coordinating the compound according to any one of claims 1 to 5 to a radioactive metal ion to obtain a radiolabeled compound.