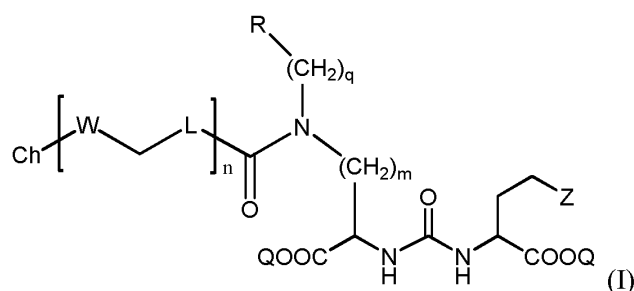


CLAIMS

1. A method for labeling a PSMA binding ligand with a radioactive isotope, preferably ^{68}Ga , ^{67}Ga or ^{64}Cu , said method comprising the steps of:
- i. providing a first vial comprising said PSMA binding ligand, and optionally a bulking agent, in dried form,
 - ii. adding a solution of said radioactive isotope into said first vial, thereby obtaining a solution of said PSMA binding ligand with said radioactive isotope,
 - iii. mixing the solution obtained in ii. with at least a buffering agent and incubating it for a sufficient period of time for obtaining said PSMA binding ligand labeled with said radioactive isotope, and,
 - iv. optionally, adjusting the pH of the solution.
2. The method of Claim 1, wherein said PSMA binding ligand is a compound of formula (I):



wherein:

Z is tetrazole or COOQ, preferably Z is COOQ;

Q is independently H or a protecting group, preferably Q is H;

m is an integer selected from the group consisting of 1, 2, 3, 4, and 5, preferably m is 4;

q is an integer selected from the group consisting of 1, 2, 3, 4, 5, and 6, preferably q is 1;

R is selected from the group consisting of C₆-C₁₀ aryl and heteroaryl containing 5 to 10 ring atoms, said aryl and heteroaryl being substituted 1 or more times with X;

X is -V-Y;

V is a bond or a C₁-C₆ alkylene, preferably V is a bond;

Y is a halogen;

L is a linker selected from the group consisting of C₁-C₆ alkylene, C₃-C₆ cycloalkylene and C₆-C₁₀ arylene, said alkylene, cycloalkylene and arylene being optionally substituted with one or more substituents selected from: -OR', =O, =NR', =N-OR', -NR'R'', -SR', -halogen, -SiR'R''R''', -OC(O)R', -C(O)R', -CO₂R', -C(O)NR'R'', -OC(O)NR'R'', -NR''C(O)R', -NR'-C(O)NR''R''', -NR''C(O)OR', -NR'-C(NR''R''')=NR''', -S(O)R', -S(O)₂R', -S(O)₂NR'R'', -NRSO₂R', -CN and -NO₂ in a number ranging from zero to 2m', where m' is the total number of carbon atoms in such groups. R', R'', R''' and R'''' each may independently refer to hydrogen, alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl;

W is selected from the group consisting of -NR²-(C=O), -NR²-(C=S), -(C=O)-NR²-, and -(C=S)-NR²-, preferably, W is -(C=O)-NR²-;

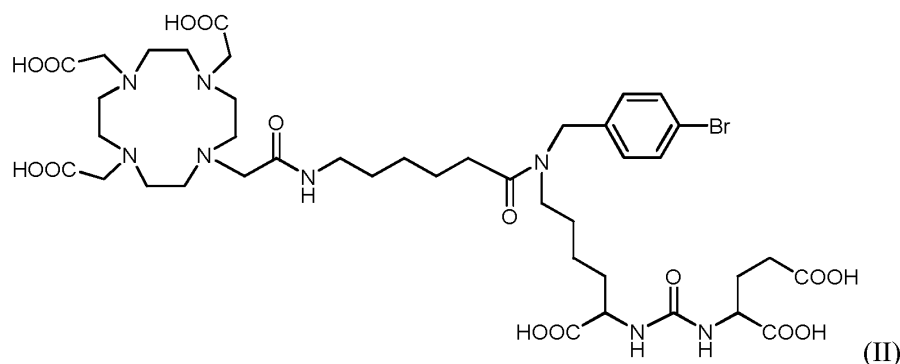
each occurrence of L and W can be the same or different;

R² is H or C₁-C₄ alkyl, preferably R² is H;

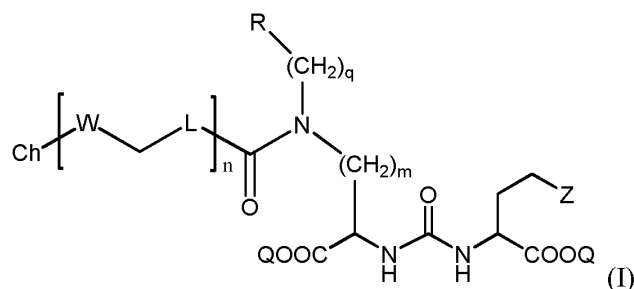
n is an integer selected from the group consisting of 1, 2 and 3;

Ch is a chelating agent, typically DOTA.

3. The method of Claim 2, wherein said PSMA binding ligand is a compound of formula (II):



4. The method of any one of Claims 1-3, wherein said buffering agent comprises formic acid and sodium hydroxide as buffering agents.
5. A solution comprising a PSMA binding ligand labeled with a radioactive isotope, obtainable or obtained by the method of any one of Claims 1-4, for use as an injectable solution for in vivo detection of tumors, typically PSMA-expressing tumors, by imaging in a subject in need thereof.
6. A solution comprising a PSMA binding ligand of formula (II) labeled with ^{68}Ga , ^{67}Ga or ^{64}Cu obtainable or obtained by the method of Claim 3, for use as an injectable solution for in vivo detection of tumors, typically PSMA-expressing tumors, by imaging in a subject in need thereof.
7. A powder for a solution for injection, comprising the following components in dried forms:
- i. a PSMA binding ligand of formula (I):



wherein:

Z is tetrazole or COOQ, preferably Z is COOQ;

Q is independently H or a protecting group, preferably Q is H;

m is an integer selected from the group consisting of 1, 2, 3, 4, and 5, preferably m is 4;

q is an integer selected from the group consisting of 1, 2, 3, 4, 5, and 6, preferably q is 1;

R is selected from the group consisting of C₆-C₁₀ aryl and heteroaryl containing 5 to 10 ring atoms, said aryl and heteroaryl being substituted 1 or more times with X; X is -V-Y;

V is a bond or a C₁-C₆ alkylene, preferably V is a bond;

Y is a halogen;

L is a linker selected from the group consisting of C₁-C₆ alkylene, C₃-C₆ cycloalkylene and C₆-C₁₀ arylene, said alkylene, cycloalkylene and arylene being optionally substituted with one or more substituents selected from: -OR', =O, =NR', =N-OR', -NR'R'', -SR', -halogen, -SiR'R''R''', -OC(O)R', -C(O)R', -CO₂R', -C(O)NR'R'', -OC(O)NR'R'', -NR''C(O)R', -NR'-C(O)NR''R''', -NR''C(O)OR', -NR'-C(NR''R''')=NR''', -S(O)R', -S(O)₂R', -S(O)₂NR'R'', -NRSO₂R', -CN and -NO₂ in a number ranging from zero to 2m', where m' is the total number of carbon atoms in such groups. R', R'', R''' and R'''' each may independently refer to hydrogen, alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl;

W is selected from the group consisting of -NR²-(C=O), -NR²-(C=S), -(C=O)-NR²-, and -(C=S)-NR²-, preferably, W is -(C=O)-NR²-;

each occurrence of L and W can be the same or different;

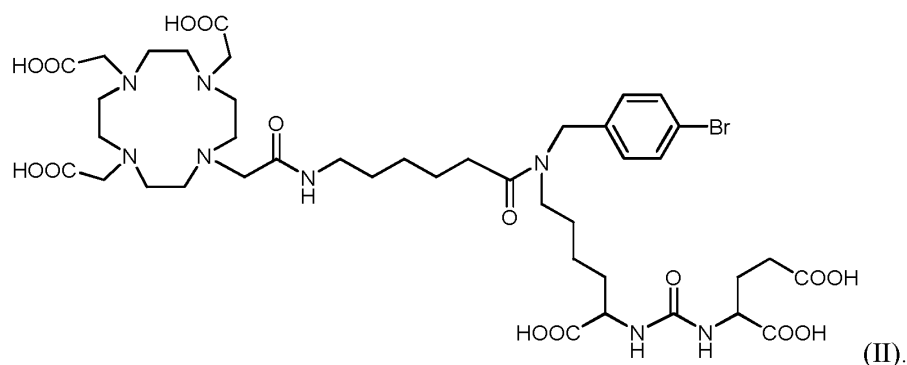
R² is H or C₁-C₄ alkyl, preferably R² is H;

n is an integer selected from the group consisting of 1, 2 and 3;

Ch is a chelating agent, typically DOTA; and

ii. a bulking agent, preferably mannitol.

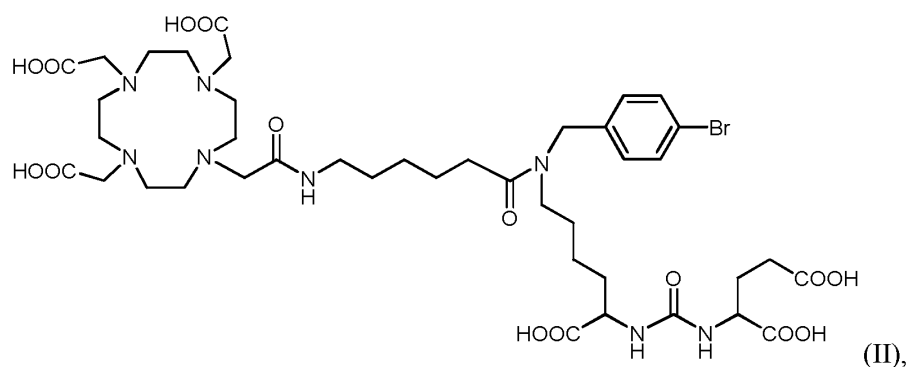
8. The powder for a solution for injection of Claim 7, wherein said PSMA binding ligand is of formula (II):



9. The powder for a solution for injection of any of Claims 7-8, comprising the following components:

- i. a PSMA binding ligand of formula (II) in an amount between 10 and 100 μg , preferably between 15 and 60 μg , even more preferably about 30 μg

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and

- ii. mannitol in an amount between 5 and 50 mg, preferably between 10 and 30 mg, even more preferably about 20 mg.

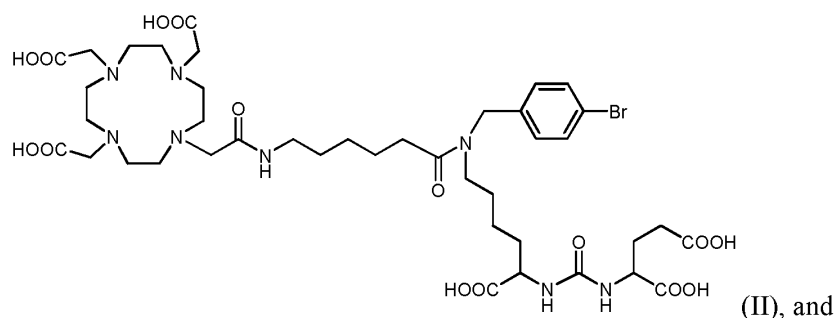
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10. The powder for a solution for injection of any of Claims 7-9, wherein said powder does not contain an antioxidant, for example the powder does not contain gentisic acid.

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11. A kit for carrying out the method of Claim 3, comprising

- i. a first vial with the following components, preferably in dried forms:
- i. a PSMA binding ligand of formula (II):



- ii. optionally a bulking agent, preferably mannitol, and

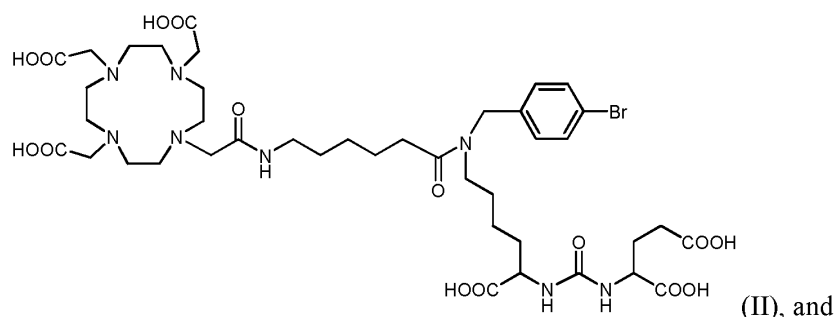
- ii. a second vial comprising at least a buffering agent, preferably in dried form, and,
- iii. optionally, an accessory cartridge for eluting a radioactive isotope generated by a radioactive isotope generator or a cyclotron.

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12. The kit of Claim 11, wherein the first vial comprises the following components:

- i. a PSMA binding ligand of formula (II) in an amount between 10 and 100 μg , preferably between 15 and 60 μg , even more preferably about 30 μg ;

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- ii. mannitol in an amount between 5 and 50 mg, preferably between 10 and 30 mg, even more preferably about 20 mg.

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13. The kit of any one of Claims 11-12, wherein the second vial comprises buffering agents for maintaining a pH between 2.5 and 4.0, preferably between 2.8 and 4.0, more preferably between 3.0 and 4.0, and even more preferably between 3.2 and 3.8.

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14. The kit of any one of Claims 11-13, wherein the kit does not contain an antioxidant, preferably the kit does not contain gentisic acid, and said second vial comprises buffering agents for maintaining a pH between 2.5 and 4.0, preferably between 2.8 and 4.0, more preferably between 3.0 and 4.0, and even more preferably between 3.2 and 3.8.

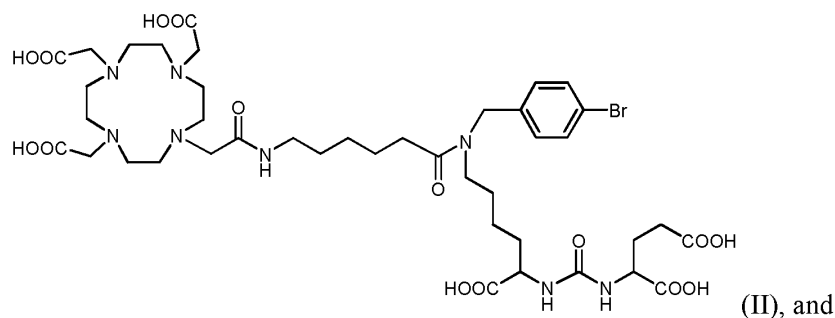
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15. The kit of any one of Claims 11-14, wherein the second vial comprises formic acid and sodium hydroxide as buffering agents.

16. A kit for carrying out the method of Claim 3, comprising

i. a single vial with the following components, preferably in dried forms:

i. a PSMA binding ligand of formula (II):



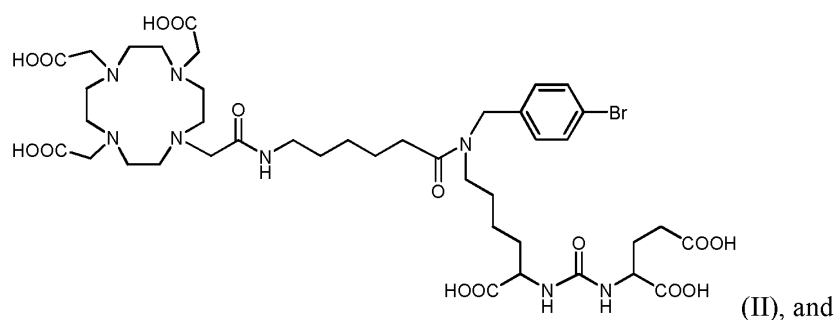
ii. optionally a bulking agent, preferably mannitol, and

iii. at least a buffering agent, preferably in dried form, and,

ii. optionally, an accessory cartridge for eluting a radioactive isotope generated by a radioactive isotope generator or a cyclotron.

17. The kit of Claim 16, wherein said single vial comprises the following components:

i. a PSMA binding ligand of formula (II) in an amount between 10 and 100 μg , preferably between 15 and 60 μg , even more preferably about 30 μg ;



ii. mannitol in an amount between 5 and 50 mg, preferably between 10 and 30 mg, even more preferably about 20 mg.

18. The kit of any one of Claims 16-17, wherein the single vial comprises buffering agents for maintaining a pH between 2.5 and 4.0, preferably between 2.8 and 4.0,

more preferably between 3.0 and 4.0, and even more preferably between 3.2 and 3.8.

- 5 19. The kit of any one of Claims 16-18, wherein the kit does not contain an antioxidant, preferably the kit does not contain gentisic acid, and said second vial comprises buffering agents for maintaining a pH between 2.5 and 4.0, preferably between 2.8 and 4.0, more preferably between 3.0 and 4.0, and even more preferably between 3.2 and 3.8.
- 10 20. The kit of any one of Claims 16-19, wherein said single vial comprises formic acid and sodium hydroxide as buffering agents.