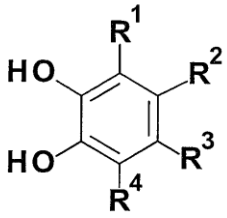
Claims

Claim 1

A nanoparticle comprising: at least one zwitterionic ligand represented by a formula (I); and a metal particle containing iron oxide, the at least one zwitterionic ligand being coordinately bound to the metal particle:



(I)

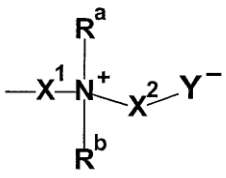
~~where~~

~~one of R^1 and R^2 is a group represented by a formula (a) or a formula (b), and the other of R^1 and R^2 is H, lower alkyl, O lower alkyl, or halogen,~~

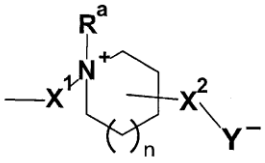
wherein:

in the at least one zwitterionic ligand,

R^1 is a group represented by a formula (a) or a formula (b), and R^2 is H or halogen,



(a)、



(b)

X^1 is a bond or methylene, or X^1 is optionally ethylene when R^1 is a group represented by the formula (a),

X^2 is C_{1-5} alkylene, or X^2 is optionally a bond when R^1

is a group represented by the formula (b),

R^a and R^b are methyl,

Y^- is SO_3^- or CO_2^-,

R^3 and R^4 are the same as or different from each other and represent H, C_{1-3} alkyl, or halogen,

n is 1,

and,

i) when R^1 is a group represented by the formula (a) and X^1 is methylene, R^2 optionally forms ethylene together with R^a or R^b.

~~X^1 is a bond or methylene, or X^1 is optionally ethylene when R^1 is a group represented by the formula (a),~~

~~X^2 is C_{1-5} alkylene that is optionally substituted with OH or is C_{1-2} alkylene O C_{1-3} alkylene , or X^2 is optionally a bond when R^1 is a group represented by the formula (b),~~

~~R^a and R^b are the same as or different from each other and represent C_{1-3} alkyl or C_{1-3} alkylene O C_{1-2} alkyl, or R^a and R^b form a 5- or 6-membered nitrogen-containing saturated heterocycle together with a quaternary nitrogen atom to which R^a and R^b are bound,~~

~~Y^- is SO_3^-, HPO_3^-, or CO_2^-,~~

~~R^3 and R^4 are the same as or different from each other and represent H, C_{1-3} alkyl, -O-C_{1-3} alkyl, or halogen,~~

~~n is an integer of 0 to 2,~~

~~and,~~

~~i) when R^1 is a group represented by the formula (a) and X^1 is methylene, R^2 optionally forms ethylene together with R^a or R^b,~~

~~ii) when R^1 is a group represented by the formula (a) and X^1 is ethylene, R^2 optionally forms methylene together with R^a or R^b, and~~

~~iii) when R^2 is a group represented by the formula (a) and X^1 is methylene, R^3 optionally forms ethylene together with R^a or R^b,~~

~~provided that, when R^2 is a group represented by the formula (a), R^a and R^b are methyl, X^1 is a bond, X^2 is C_{1-4} alkylene, and R^1, R^3 and R^4 are H, Y^- is HPO_3^- or CO_2^-.~~

~~Claim 2~~

~~The nanoparticle as set forth in claim 1, wherein:~~

~~in the at least one zwitterionic ligand,~~

~~one of R^1 and R^2 is a group represented by the formula (a) or the formula (b), and the other of R^1 and R^2 is H, lower alkyl, or halogen,~~

~~X^1 is a bond or methylene, or X^1 is optionally ethylene when R^1 is a group represented by the formula (a),~~

~~X^2 is C_{1-5} alkylene that is optionally substituted with OH or is -C_{1-2} alkylene-O-C_{1-3} alkylene-, or X^2 is optionally a bond when R^1 is a group represented by the formula (b),~~

~~R^a and R^b are the same as or different from each other~~

and represent C_{1-3} alkyl or -C_{1-3} alkylene-O-C_{1-2} alkyl, or R^a and R^b form a pyrrolidine ring together with a quaternary nitrogen atom to which R^a and R^b are bound,

Y^- is SO_3^-, HPO_3^-, or CO_2^-,

R^3 and R^4 are the same as or different from each other and represent H, C_{1-3} alkyl, or halogen,

n is 1,

and,

i) when R^1 is a group represented by the formula (a) and X^1 is methylene, R^2 optionally forms ethylene together with R^a or R^b.

Claim 3

The nanoparticle as set forth in claim 2, wherein:

in the at least one zwitterionic ligand,

R^1 is a group represented by the formula (a) or the formula (b), and R^2 is H or halogen,

X^1 is a bond or methylene, or X^1 is optionally ethylene when R^1 is a group represented by the formula (a),

X^2 is C_{1-5} alkylene, or X^2 is optionally a bond when R^1 is a group represented by the formula (b),

R^a and R^b are methyl, and

Y^- is SO_3^- or CO_2^-.

Claim 4

~~The nanoparticle as set forth in claim 1, wherein:~~

~~in the at least one zwitterionic ligand,~~

~~one of R^1 and R^2 is a group represented by the formula (a), and the other of R^1 and R^2 is H, lower alkyl, -O-lower alkyl, or halogen.~~

~~Claim 5~~

~~The nanoparticle as set forth in claim 4, wherein:~~

~~in the at least one zwitterionic ligand,~~

~~1) R^1 is a group represented by the formula (a), and R^2 is H, lower alkyl, O lower alkyl, or halogen, or~~

~~2) R^1 is H, R^2 is a group represented by the formula (a), R^3 is C_{1-3} alkyl or halogen, and R^4 is H.~~

Claim ~~6~~2

The nanoparticle as set forth in claim ~~5~~1, wherein:

in the at least one zwitterionic ligand, R^1 is a group represented by the formula (a), and R^2 is H~~, lower alkyl, -O-lower alkyl,~~ or halogen.

Claim ~~7~~3

The nanoparticle as set forth in claim ~~6~~2, wherein:

in the at least one zwitterionic ligand,

R^2 is H or halogen,

X^1 is a bond, methylene, or ethylene,

X^2 is C_{2-4} alkylene,

R^a and R^b are methyl,

R^3 and R^4 are the same as or different from each other and represent H, C_{1-3} alkyl, or halogen,

and, when X^1 is methylene, R^2 optionally forms ethylene together with R^a or R^b.

Claim ~~8~~4

The nanoparticle as set forth in claim ~~7~~3, wherein:

in the at least one zwitterionic ligand,

R^2 is H or F,

X^2 is ethylene or propylene, and

R^3 and R^4 are H.

Claim ~~9~~5

The nanoparticle as set forth in claim ~~8~~4, wherein:

in the at least one zwitterionic ligand,

R^2 is H, and

X^1 is a bond or ethylene.

~~Claim 10~~

~~The nanoparticle as set forth in any one of claims 4 through 9, wherein:~~

~~in the at least one zwitterionic ligand,~~

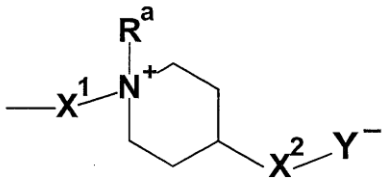
~~Y^- is SO_3^- or CO_2^-.~~

Claim ~~116~~

The nanoparticle as set forth in claim ~~31~~, wherein:

in the at least one zwitterionic ligand,

R^1 is a group represented by the following formula (b-1),



(b-1)

R^2 is H or halogen,

X^1 is a bond or methylene,

X^2 is C_{1-5} alkylene or a bond,

R^a is methyl, and

Y^- is SO_3^- or CO_2^-.

Claim ~~127~~

The nanoparticle as set forth in any one of claims 1 through ~~116~~, wherein the metal particle contains only iron oxide.

Claim ~~138~~

The nanoparticle as set forth in any one of claims 1 through ~~127~~, wherein: the at least one zwitterionic ligand is coordinately bound to an outer surface of the metal particle

containing iron oxide; and the metal particle is coated with the at least one zwitterionic ligand.

Claim ~~14~~9

The nanoparticle as set forth in any one of claims 1 through ~~12~~7, wherein said nanoparticle is a composite comprising the at least one zwitterionic ligand and the metal particle containing iron oxide, the at least one zwitterionic ligand being coordinately bound to the metal particle.

Claim ~~15~~10

The nanoparticle as set forth in any one of claims 1 through ~~12~~7, wherein said nanoparticle is a cluster comprising two or more zwitterionic ligand compounds and two or more metal particles, each of the two or more metal particles containing iron oxide, and at least one zwitterionic ligand compound being coordinately bound to each of the two or more metal particles.

Claim ~~16~~11

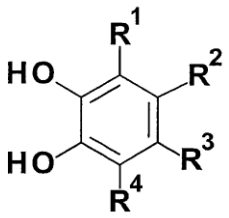
A contrast agent for magnetic resonance imaging comprising a nanoparticle recited in any one of claims 1 through ~~15~~10.

Claim ~~17~~12

The contrast agent as set forth in claim ~~16~~11, wherein said contrast agent is a positive contrast agent.

Claim ~~18~~13

Use of a zwitterionic ligand compound represented by the following formula (I) for producing a nanoparticle recited in claim 1:



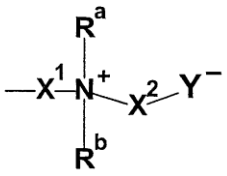
(I)

~~where~~

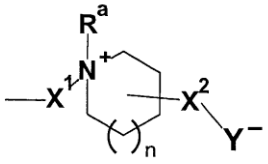
~~one of R^1 and R^2 is a group represented by a formula (a) or a formula (b) below, and the other of R^1 and R^2 is H, lower alkyl, -O- lower alkyl, or halogen,~~

in the at least one zwitterionic ligand,

R^1 is a group represented by a formula (a) or a formula (b), and R^2 is H or halogen,



(a)、



(b)

X^1 is a bond or methylene, or X^1 is optionally ethylene when R^1 is a group represented by the formula (a),

X^2 is C_{1-5} alkylene, or X^2 is optionally a bond when R^1

is a group represented by the formula (b),

R^a and R^b are methyl,

Y^- is SO_3^- or CO_2^-,

R^3 and R^4 are the same as or different from each other and represent H, C_{1-3} alkyl, or halogen,

n is 1,

and,

i) when R^1 is a group represented by the formula (a) and X^1 is methylene, R^2 optionally forms ethylene together with R^a or R^b.

~~X^1 is a bond or methylene, or X^1 is optionally ethylene when R^1 is a group represented by the formula (a),~~

~~X^2 is C_{1-5} alkylene that is optionally substituted with OH or is C_{1-2} alkylene O C_{1-3} alkylene , or X^2 is optionally a bond when R^1 is a group represented by the formula (b),~~

~~R^a and R^b are the same as or different from each other and represent C_{1-3} alkyl or C_{1-3} alkylene O C_{1-2} alkyl, or R^a and R^b form a 5- or 6-membered nitrogen-containing saturated heterocycle together with a quaternary nitrogen atom to which R^a and R^b are bound,~~

~~Y^- is SO_3^-, HPO_3^-, or CO_2^-,~~

~~R^3 and R^4 are the same as or different from each other and represent H, C_{1-3} alkyl, -O-C_{1-3} alkyl, or halogen,~~

~~n is an integer of 0 to 2,~~

~~and,~~

~~i) when R^1 is a group represented by the formula (a) and X^1 is methylene, R^2 optionally forms ethylene together with R^a or R^b,~~

~~ii) when R^1 is a group represented by the formula (a) and X^1 is ethylene, R^2 optionally forms methylene together with R^a or R^b, and~~

~~iii) when R^2 is a group represented by the formula (a) and X^1 is methylene, R^3 optionally forms ethylene together with R^a or R^b,~~

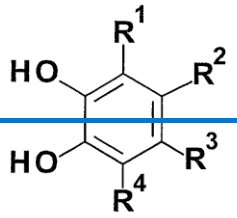
~~provided that, when R^2 is a group represented by the formula (a), R^a and R^b are methyl, X^1 is a bond, X^2 is C_{1-4} alkylene, and R^1, R^3 and R^4 are H, Y^- is HPO_3^- or CO_2^-.~~

~~Claim 19~~

~~The use as set forth in claim 18, wherein, in the zwitterionic ligand compound, one of R^1 and R^2 is a group represented by the formula (a), and the other of R^1 and R^2 is H, lower alkyl, -O-lower alkyl, or halogen.~~

~~Claim 20~~

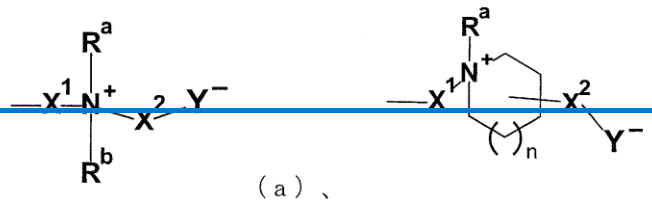
~~A compound represented by the following formula (I) or a salt thereof:~~



(I)

where

one of R^1 and R^2 is a group represented by a formula (a) or a formula (b) below, and the other of R^1 and R^2 is H, lower alkyl, -O- lower alkyl, or halogen,



(a) 、 (b)

X^1 is a bond or methylene, or X^1 is optionally ethylene when R^1 is a group represented by the formula (a),

X^2 is C_{1-5} alkylene that is optionally substituted with OH or is C_{1-2} alkylene O C_{1-3} alkylene , or X^2 is optionally a bond when R^1 is a group represented by the formula (b),

R^a and R^b are the same as or different from each other and represent C_{1-3} alkyl or C_{1-3} alkylene O C_{1-2} alkyl, or R^a and R^b form a 5 or 6 membered nitrogen containing saturated heterocycle together with a quaternary nitrogen atom to which R^a and R^b are bound,

Y^- is SO_3^-, HPO_3^-, or CO_2^-,

R^3 and R^4 are the same as or different from each other and represent H, C_{1-3} alkyl, -O-C_{1-3} alkyl, or halogen,

n is an integer of 0 to 2,

and,

i) when R^1 is a group represented by the formula (a) and X^1 is methylene, R^2 optionally forms ethylene together with R^a or R^b,

ii) when R^1 is a group represented by the formula (a) and X^1 is ethylene, R^2 optionally forms methylene together with R^a or R^b, and

iii) when R^2 is a group represented by the formula (a) and X^1 is methylene, R^3 optionally forms ethylene together with R^a or R^b,

provided that, when R^2 is a group represented by the formula (a), R^a and R^b are methyl, X^1 is a bond, X^2 is C_{1-4} alkylene, and R^1, R^3 and R^4 are H, Y^- is HPO_3^- or CO_2^-.

Claim 21

The compound as set forth in claim 20 or a salt thereof, wherein:

one of R^1 and R^2 is a group represented by the formula (a) or the formula (b), and the other of R^1 and R^2 is H, lower alkyl, or halogen,

X^1 is a bond or methylene, or X^1 is optionally ethylene when R^1 is a group represented by the formula (a),

X^2 is C_{1-5} alkylene that is optionally substituted with OH or is $-C_{1-2}$ alkylene-O-C_{1-3} alkylene-, or X^2 is optionally

~~a bond when R^1 is a group represented by the formula (b),~~

~~R^a and R^b are the same as or different from each other and represent C_{1-3} alkyl or C_{1-3} alkylene O C_{1-2} alkyl, or R^a and R^b form a pyrrolidine ring together with a quaternary nitrogen atom to which R^a and R^b are bound,~~

~~Y^- is SO_3^-, HPO_3^-, or CO_2^-,~~

~~R^3 and R^4 are the same as or different from each other and represent H, C_{1-3} alkyl, or halogen,~~

~~n is 1,~~

~~and, i) when R^1 is a group represented by the formula (a) and X^1 is methylene, R^2 optionally forms ethylene together with R^a or R^b.~~

Claim ~~22~~14

The compound as set forth in claim ~~21~~ 13 or a salt thereof, wherein:

R^1 is a group represented by the formula (a) or the formula (b), and R^2 is H or halogen,

X^1 is a bond or methylene, or X^1 is optionally ethylene when R^1 is a group represented by the formula (a),

X^2 is C_{1-5} alkylene, or X^2 is optionally a bond when R^1 is a group represented by the formula (b),

R^a and R^b are methyl, and

Y^- is SO_3^- or CO_2^-.

~~Claim 23~~

~~The compound as set forth in claim 20 or a salt thereof, wherein: one of R^1 and R^2 is a group represented by the formula (a), and the other of R^1 and R^2 is H, lower alkyl, -O-lower alkyl, or halogen.~~

Claim ~~24~~15

The compound as set forth in claim ~~20~~ 14 or a salt thereof, which is selected from the group consisting of:

4-{[(2,3-dihydroxyphenyl)methyl](dimethyl)azaniumyl}butane-1-sulfonate,

3-{[(6-fluoro-2,3-dihydroxyphenyl)methyl](dimethyl)azaniumyl}propane-1-sulfonate,

~~Hydrogen (3-{[(2,3-dihydroxyphenyl)methyl](dimethyl)azaniumyl}propyl)phosphonate,~~

5-{[(2,3-dihydroxyphenyl)methyl](dimethyl)azaniumyl}pentanoate,

{1-[(2,3-dihydroxyphenyl)methyl]-1-methylpiperidin-1-ium-4-yl}acetate,

1-[(2,3-dihydroxyphenyl)methyl]-1-methylpiperidin-1-ium-4-carboxylate,

4-{[2-(2,3-

dihydroxyphenyl)ethyl](dimethyl)azaniumyl}butanoate,

2-{[2-(2,3-dihydroxyphenyl)ethyl](dimethyl)azaniumyl}ethane-1-sulfonate, and

3-[(2,3-dihydroxyphenyl)(dimethyl)azaniumyl]propane-1-sulfonate.

Claim ~~25~~16

The compound as set forth in claim ~~24~~15 or a salt thereof, which is selected from the group consisting of:

{1-[(2,3-dihydroxyphenyl)methyl]-1-methylpiperidin-1-ium-4-yl}acetate, and

2-{[2-(2,3-dihydroxyphenyl)ethyl](dimethyl)azaniumyl}ethane-1-sulfonate.

Claim ~~26~~17

The compound as set forth in claim ~~24~~ 15 or a salt thereof, which is selected from the group consisting of:

4-{[(2,3-dihydroxyphenyl)methyl](dimethyl)azaniumyl}butane-1-sulfonate, and

3-{[(6-fluoro-2,3-dihydroxyphenyl)methyl](dimethyl)azaniumyl}propane-1-sulfonate.