provide a metal-salen complex compound having a grain size capable of being guided to the target region with a magnetic field even when the metal-salen complex compound is systemically applied to a living body as a medicine. Further still, the fourth object of the present invention is to provide a method for producing these metal-salen complex compounds.

[MEANS FOR SOLVING THE PROBLEM]

[0025]

In one aspect of the present invention, there is provided a magnetic medicine comprising:

a metal-salen complex compound for application to an affected tissue of a living body,

wherein the metal-salen complex compound is to be retained in the affected tissue with an external magnetic field after the application of the metal-salen complex compound to the affected tissue,

wherein the metal-salen complex compound has a crystal grain size of 8 μm or less, and

wherein a percentage of the metal-salen complex compound having a crystal grain size of 1 μm or less, and a crystal grain size of 100 nm or more to 500 nm or less, is 70% or more.

In another aspect of the present invention, there is provided a method for producing a magnetic medicine comprising: crystallizing a metal-salen complex compound under a rapid cooling condition.

To achieve the above objects, the crystal grain size of the metal-salen complex compound according to the present ~~invention~~disclosure is confined to a crystal grain size that will not clog the capillaries of humans or animals, and the metal-salen complex compound according to the present ~~invention~~disclosure is characterized by the ability to control the dynamics with an external magnetic field. Considering that the diameter of capillaries are 8 μm to 20 μm, and the grain size of erythrocytes that pass through the capillaries is approximately 8 μm, and the grain size of leukocytes that pass through the capillaries is approximately 8 to 20 μm, the crystal grain size of the metal-salen complex compound of the present ~~invention~~disclosure is desirably 8 μm or less; preferably 1 μm or more to 8 μm or less; more preferably 1 μm or more to 5 μm or less, and even more preferably 1 μm or more to 3 μm or less. The metal-salen complex compound is auto-magnetic, and is capable of being retained in the affected site with an external magnetic field after, for example, local application to an affected site.

[0026]

When the grain size of the metal-salen complex compound is less than 1 μm, the magnetism which allows the metal-salen complex compound to be retained locally with an external magnetic field declines, and it is possible that the metal-salen complex compound may leak into capillaries outside the target affected tissue, from the target affected tissue. Thus, when the metal-salen complex compound is locally applied to the affected site, the minimum crystal grain size of the metal-salen complex compound is desirably 1 μm. The percentage of metal-salen complex compounds with a crystal grain size of 1 μm or more to 3 μm or less, is preferably 70% or more.

[0027]

For the metal-salen complex compound to reach the affected site by systemic application, and for the metal-salen complex compound to be retained in the affected site with a magnetic field, the crystal size of the metal-salen complex is of 1 μm or less so that the metal-salen complex compounds may pass through a large number of capillaries, and the percentage of the metal-salen complex compounds with a crystal grain size of 100 nm or more to 500 nm or less is preferably 70% or more.

[0028]

When the grain size of the metal-salen complex compound exceeds 1 μm, it is possible that the metal-salen complex compound may not be able to pass through the capillaries. When the grain size of the metal-salen complex compound is less than 100 nm, the ferromagnetism required for magnetic guidance cannot be obtained sufficiently. On the other hand, when the grain size exceeds 500 nm, the metal-salen complex compound may not pass through the capillaries with ease. When the percentage of particles with a grain size of 100 nm or more to 500 nm or less, is less than 70%, the proportion of the grains where the properties for passing through the capillaries is insufficient increases. The grain size is preferably 200 nm or more to 400 nm or less, the grain size is even more preferably 250 nm or more to 350 nm or less.

[0029]

The metal-salen complex compound of the present ~~invention~~disclosure generally refers to metal complexes with salen as the ligand, and also includes derivative substitutions and derivatives of metal complexes. The structural formula of the metal-salen complex compound is as indicated below in Formula (I). Each of "a" to "h" may represent hydrogen, or at least one of "a" to "h" may be substituted with functional groups/substituents other than hydrogen.

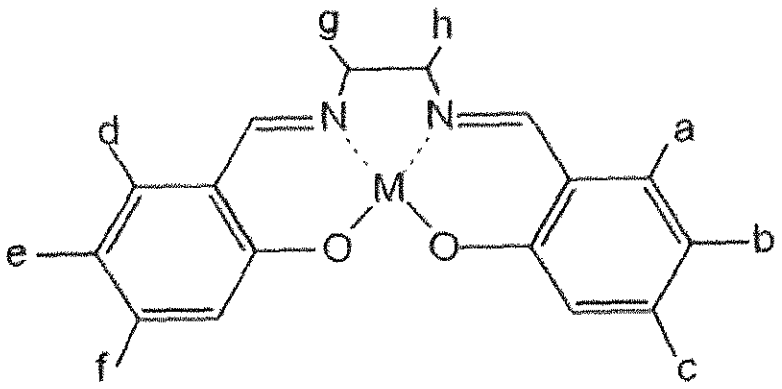
[0030]

Derivatives of the metal-salen complex compound of the present ~~invention~~disclosure includes metal-salen complex compounds or their derivative substitutions bound to functional molecules such as medicinal molecules, enzymes, and antibodies, as in, for example, WO 2010/058280. The disclosure

made in the publication is incorporated in the specification of the present application by reference in its entirety. The derivative of the metal-salen complex compound in complex with a medicinal molecule is useful as a carrier for guiding or localizing the medicinal molecules at the target affected tissue.

[0031]

(I)



N,N'-Bis(salicylidene)ethylenediamine metal

In Formula (I), "M" represents Fe, Cr, Mn, Co, Ni, Mo, Ru, Rh, Pd, W, Re, Os, Ir, Pt, Nd, Sm, Eu, or Gd.

[0032]

One example~~Preferred embodiments~~ of locally applying the metal-salen complex compound of the present ~~invention~~disclosure to the affected tissue of a human body or an animal involves an arterial injection into an artery in the vicinity of the affected tissue, or an injection into the affected tissue itself. Publicly known ~~embodiments~~examples such as ointments, lotions, or adhesive skin patches may be adopted as other ~~embodiments~~examples of local application. ~~Embodiments~~Examples of systemically applying the metal-salen complex compound involve an intravenous injection and/or an infusion injection. Typical prescription examples of injections and infusions of the metal-salen complex compound involve physiological saline as a solvent, and suspensions or opalizers may be used. The metal-salen complex compound of the present ~~invention~~disclosure is preferably used as an anti-tumor agent, as disclosed in the above prior art. Other uses include

use as a carrier for drug delivery of the medicinal molecule by binding the metal-salen complex compound to another medicinal molecule as mentioned above, and furthermore, use as an MRI diagnostic agent.

[0033]

When applying the metal-salen complex compound of the present ~~invention~~disclosure to an individual (a human or an animal), by providing a magnetic field (500 mT to 1 T (1,000 mT)) to a target region where the affected organ or the affected tissue is present, the metal-salen complex compound may be guided to or retained at the target affected region at least while magnetism is provided.

[EFFECTS OF THE INVENTION]

[0034]

As described above, according to the present invention, a metal-salen complex compound which is controlled to have an appropriate crystal grain size may be provided. Furthermore, according to the present invention, a metal-salen complex compound that can be locally applied to a target region such as an affected tissue may be provided. Further still, the present invention can provide a metal-salen complex compound having a grain size capable of being guided to the target region with a magnetic field even when the metal-salen complex compound is systemically applied to a living body as a medicine. Furthermore, the present invention can provide a method for producing these metal-salen complex compounds.

[BRIEF DESCRIPTION OF THE DRAWINGS]

[0035]

[FIG. 1]

FIG. 1 is a photograph taken with a transmission electron microscope, of iron-salen complex compounds in which the crystal grain size is coarse (the long side exceeding 1 μm), according to an example (Example I) of the present invention.

[FIG. 2]

[CLAIMS]

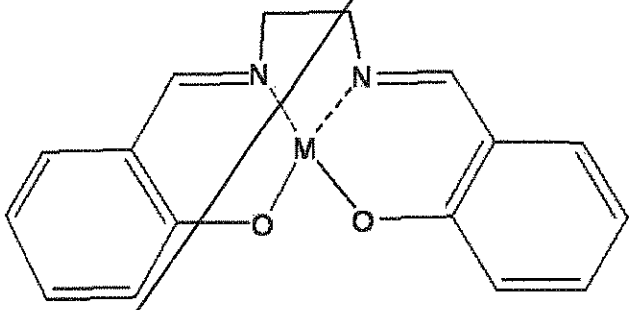
[Claim 1] A metal-salen complex compound having a crystal grain size of 8 μm or less.

[Claim 2] The metal-salen complex compound according to claim 1, wherein the crystal grain size is 1 μm or more.

[Claim 3] The metal-salen complex compound according to claim 1, wherein a percentage of 1 μm or less in the crystal grain size, and 100 nm or more to 500 nm or less in crystal grain size, is 70% or more.

[Claim 4] The metal-salen complex compound according to one of claims 1 to 3, containing a compound of Structural Formula (I) below.

(I)



N,N'-Bis(salicylidene)ethylenediamine metal

M is Fe, Cr, Mn, Co, Ni, Mo, Ru, Rh, Pd, W, Re, Os, Ir, Pt, Nd, Sm, Eu, or Gd.

[Claim 5] A magnetic medicine containing a metal-salen complex compound according to one of claims 1 to 3, to be provided to an affected tissue of a living body with an external magnetic field after application to the living body.

[Claim 6] The magnetic medicine containing a metal-salen complex compound according to claim 2, to be locally applied to an affected tissue of a living body, and to be retained in the affected tissue with an external magnetic field.

[Claim 7] The magnetic medicine containing a metal-salen complex compound according to claim 3, to be guided to an affected tissue of the living body with an external magnetic field after systemic application to a living body.

[Claim 8] The magnetic medicine according to one of claims 5 to 7, having an antitumor effect.

[Claim 9] A method for producing a metal-salen complex compound comprising:

crystallizing a metal-salen complex compound under a rapid cooling condition.

[Claim 10] The method for producing the metal-salen complex compound according to claim 9, further comprising:

allowing salen to react with a metal compound, and then obtaining a crystal particle of the metal-salen complex by rapidly cooling a heated reactant.

The invention claimed is:

1. A magnetic medicine comprising:
a metal-salen complex compound for application to an affected tissue of a living body,

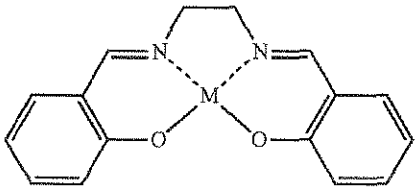
wherein the metal-salen complex compound is to be retained in the affected tissue with an external magnetic field after the application of the metal-salen complex compound to the affected tissue,

wherein the metal-salen complex compound has a crystal grain size of 8 μm or less, and

wherein a percentage of the metal-salen complex compound having a crystal grain size of 1 μm or less, and a crystal grain size of 100 nm or more to 500 nm or less, is 70% or more.

2. The magnetic medicine according to claim 1, wherein the crystal grain size is at least 1 μm.

3. The magnetic medicine according to claim 1, wherein the metal-salen complex compound comprises a compound of Structural Formula (I) below:



(I)

N,N'-Bis(salicylidene)ethylenediamine metal

M is Fe, Cr, Mn, Co, Ni, Mo, Ru, Rh, Pd, W, Re, Os, Ir, Pt, Nd, Sm, Eu, or Gd.

4. The magnetic medicine according to claim 1, wherein the metal-salen complex compound is to be locally applied to the affected tissue of the living body.

5. The magnetic medicine according to claim 1, wherein the metal-salen complex compound is to be guided to the affected tissue of the living body with an external magnetic field after the application of the metal-salen complex compound to the affected tissue, the application to the affected tissue being a systemic application.

6. The magnetic medicine according to claim 1, wherein the metal-salen complex compound is an antitumor agent.

7. A method for producing a magnetic medicine comprising: crystallizing a metal-salen complex compound under a rapid cooling condition.

8. The method for producing the magnetic medicine according to claim 7, further comprising: allowing salen to react with a metal compound, and then obtaining a crystal particle of the metal-salen complex compound by rapidly cooling a heated reactant.