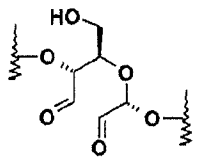
CLAIMS

1. An oxidized avidin in which at least one mannose residue per avidin molecule is replaced by a residue of the following formula



2. An oxidized avidin according to claim 1 containing about 8 to 15 aldehydes moieties.

3. An oxidized avidin according to any of claims 1-2 having a thermal stability equal or greater than 78°C.

4. A complex consisting of an oxidized avidin according to any of claims 1 to 3 and a biotinylated therapeutic agent.

5. A complex according to claim 4, wherein the biotinylated therapeutic agent is an anticancer agent.

6. Use of a complex according to claims 4 or 5 as a medicament.

7. Use of an oxidized avidin according to any of claims 1 to 3, wherein the oxidized avidin is administered in the first step of the treatment, followed by administration of a biotinylated therapeutic agent.

8. Use according to claims 6 or 7 in brachytherapy to treat a patient affected by a cancer disease.

9. Use according to claim 8, wherein the cancer disease is a cancer of the breasts, pancreas, lung, pleura, peritoneum, face and neck, bladder, brain, prostate, ovaries or eyes.

10. Use according to claim 8 wherein the anticancer agent is selected from the group consisting of radioisotopes, chemotherapeutic agents, cytokines, toxins and anticancer cells.

11. Use according to claims 6 or 7 wherein the therapeutic agent is represented by biotinylated stem cells or somatic cells for the treatment of cancer, degenerative or genetic diseases.

12. Use of oxidized avidins according to claims 4 or 7 for applications in tissue regeneration useful for the treatment of autoimmune/degenerative/genetic diseases including, diabetes, multiple sclerosis, rheumatoid arthritis, Alzheimer, spinal injury, Duchenne muscular dystrophy, myocardial infarct and stroke.

13. Use according to claim 10 in which said radioisotope is selected from the group consisting of Fe-52, Mn-52m, Co-55, Cu-64, Ga-67, Ga-68, Tc-99m, In-111, I-123, I-125, I-131, P-32, Sc-47, Cu-67, Y-90, Pd-109, Ag-111, I-131, Pm-149, Re-186, Re-188, At-211, Pb-212, Bi-212 and Lu-177.

14. A pharmaceutical composition comprising an oxidized avidin or a complex according to any of claims 1 to 5 together with a pharmaceutically acceptable excipient.

15. A kit comprising a pharmaceutical composition according to claim 14 containing an oxidized avidin according to any of claims 1-3 in a container and a biotinylated therapeutic agent in a second container.

16. A kit according to claim 15 for a two-step adjuvant intra-and perioperative locoregional and/or systemic therapy, wherein the two containers have the form of a syringe.

17. A process of oxidation of avidin wherein the oxidation comprises the following steps:

a) incubating wild type avidin pre-mixed with a molar excess of (HABA), with an oxidizing agent such as 10-20 mM sodium periodate in 50-100 mM acetate buffer at pH below 6.0 for 1-5 hours at 4°C or at room temperature;

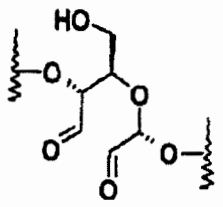
b) blocking of the reaction and purification by removal of the oxidizing agent and HABA by chromatography, ultrafiltration, dialysis or other purification methods known to the expert in the field; and

c) lyophylizing or formulating at an acidic pH.

18. A method of treatment of a patient affected by a cancer disease characterized in that the tissue or organ to be treated is first avidinated with an oxidized avidin according to any of claims 1-3 and subsequently administered a biotinylated anticancer agent or is directly administered a complex according to claim 4.

CLAIMS

1. An oxidized avidin in which at least one mannose residue per avidin molecule is replaced by a residue of the following formula



wherein said oxidized avidin contains about 8 to 15 aldehydes moieties and has a thermal stability equal or greater than 78°C.

2. A complex consisting of an oxidized avidin according to claim 1 and a biotinylated therapeutic agent.
3. A complex according to claim 2, wherein the biotinylated therapeutic agent is an anticancer agent.
4. Use of a complex according to claim 2 in the manufacture of a medicament for treating a disease selected from the group consisting of cancer, autoimmune, degenerative or genetic disease.
5. Use of an oxidized avidin according to claim 1 in the manufacture of a medicament for treating a disease selected from the group consisting of cancer, degenerative or genetic disease, and wherein the medicament further comprises a biotinylated therapeutic agent.
6. Use according to claim 5, wherein the medicament is formulated for separate, sequential or combined administration with a biotinylated therapeutic agent.

7. Use according to claims 4 or 5, wherein the cancer disease is a cancer of the breasts, pancreas, lung, pleura, peritoneum, face and neck, bladder, brain, prostate, ovaries or eyes.
8. A complex according to claim 3 wherein the anticancer agent is selected from the group consisting of radioisotopes, chemotherapeutic agents, cytokines, toxins and anticancer cells.
9. Use according to claim 5 wherein the therapeutic agent is represented by biotinylated stem cells or somatic cells for the treatment of cancer, degenerative or genetic diseases.
10. Use according to claims 4 or 5 for applications in tissue regeneration useful for the treatment of said autoimmune/degenerative/genetic diseases.
11. Use according to claim 10 wherein the autoimmune/degenerative/genetic disease is selected from diabetes, multiple sclerosis, rheumatoid arthritis, Alzheimer, spinal injury, Duchenne muscular dystrophy, myocardial infarct and stroke.
12. A complex according to claim 8 in which said radioisotope is selected from the group consisting of Fe-52, Mn-52m, Co-55, Cu-64, Ga-67, Ga-68, Tc-99m, In-111, I-123, I-125, I-131, P-32, Sc-47, Cu-67, Y-90, Pd-109, Ag-111, I-131, Pm-149, Re-186, Re-188, At-211, Pb-212, Bi-212 and Lu-177.
13. A pharmaceutical composition comprising an oxidized avidin or a complex according to any of claims 1 to 3 together with a pharmaceutically acceptable excipient.
14. A kit comprising a pharmaceutical composition according to claim 13 containing an oxidized avidin according to claim 1 in a first container and a biotinylated therapeutic agent in a second container.

15. A kit according to claim 14 for a two-step adjuvant intra-and perioperative locoregional and/or systemic therapy, wherein the two containers have the form of a syringe.

16. A process of oxidation of avidin wherein the oxidation comprises the following steps:

    a) incubating wild type avidin pre-mixed with a molar excess of (HABA), with an oxidizing agent in 50-100 mM acetate buffer at pH below 6.0 for 1-5 hours at 4°C or at room temperature;

    b) blocking of the reaction and purification by removal of the oxidizing agent and HABA; and

    c) lyophylizing or formulating at an acidic pH.

17. A process according to claim 16 wherein the oxidizing agent is 10-20 mM sodium periodate.

18. A process according to claim 16 or 17, wherein purification is by chromatography, ultrafiltration or dialysis.