

CLAIMS

1. A bile acid or a pharmaceutically acceptable salt thereof, for use in a method of treatment of the human or animal body, which method comprises administering a therapeutic compound to the human or animal body, wherein:
 - a) said bile acid is chenodeoxycholic acid or deoxycholic acid, and
 - b) said method the bile acid or salt is used to enable or enhance intracellular uptake of the therapeutic compound.
2. A bile acid or salt according to claim 1, for use in a method as defined in claim 1, wherein said bile salt is employed in conjunction with EDTA.
3. A bile acid or salt according to claim 1 or 2, for use in a method as defined in claim 1 or 2, wherein said therapeutic compound is a macromolecule.
4. A bile acid or salt according to claim 1 or 2, for use in a method as defined in claim 1 or 2, wherein said therapeutic compound is a protein.
5. A bile acid or salt according to any one of claims 1 to 4, for use in a method as defined in any one of claims 1 to 4, wherein said bile acid or pharmaceutically acceptable salt thereof is a chenodeoxycholate salt, preferably sodium chenodeoxycholate.
6. A bile acid or salt according to any one of the preceding claims, for use in a method as defined in any one of the preceding claims, wherein in said method, the concentration of the bile acid or salt which is achieved at the surface of the cells into which intracellular uptake is to be enabled or enhanced, is from 2 mg/ml to 40 mg/ml.
7. A bile acid or salt according to any one of claims 2 to 6, for use in a method as defined in any one of claims 2.6, wherein in said method, the concentration of the EDTA which is achieved at the surface of the cells into which intracellular uptake is to be enabled or enhanced, is from 0.1 mg/ml to 10 mg/ml.
8. A bile acid or salt according to any one of claims 2 to 6, for use in a method as defined in any one of claims 2.6, wherein in said method, the concentration of the EDTA which is achieved at the surface of the cells into which intracellular uptake is to be enabled or enhanced, is from 0.2 mg/ml to 10 mg/ml.

9. A bile acid or salt according to any one of the preceding claims, for use in a method as defined in any one of the preceding claims, wherein in said method bile acid or salt receptor-mediated internalisation via clathrin-coated pits is used to enable or enhance intracellular uptake of the therapeutic compound.
10. A bile acid or salt according to any one of the preceding claims, for use in a method as defined in any one of the preceding claims, wherein in said use of the bile acid or salt, said bile acid or salt is in micellar form.
11. A bile acid or salt according to any one of the preceding claims, for use in a method as defined in any one of the preceding claims, wherein in said method the bile acid or salt thereof is used in combination with one or more additional agents.
12. A bile acid or salt according to claim 11, for use in a method as defined in claim 11, wherein in said use of the bile acid or salt, said bile acid or salt is in micellar form, and said one or more additional agents comprise one or more agents which:
 - a) stabilise said micellar form of the bile acid or salt thereof; and/or
 - b) enable or enhance the formation of said micellar form.
13. A bile acid or salt according to claim 11 or 12, for use in a method as defined in claim 11 or 12, wherein said one or more agents include propyl gallate.
14. A bile acid or salt according to claim 11, 12 or 13, for use in a method as defined in claim 11, 12 or 13, wherein said one or more additional agents comprise one or more agents selected from:
 - a) a fusogenic lipid, which is preferably selected from cationic liposomes, neutral helper lipids such as DOPE, and anionic lipids such as phosphatidic acid;
 - b) a cell penetrating peptide, which is preferably a cell penetrating peptide having 2 to 12 amino acids, such as octaarginine, nonaarginine and octalysine;
 - c) a lysosomotropic agent, which is preferably chloroquine;
 - d) a membrane-disruptive peptide which is preferably INF7, H5WYG, 43E or Histidine 10;
 - e) a membrane-disruptive polymer, which is preferably polyethyleneimine;
 - f) a photochemical internalisation agent, which is preferably fluorescein isothiocyanate or a compound comprising it; and/or

- g) an agent that alters intracellular vesicle transport, which is preferably Brefeldin A.
15. A bile acid or salt according to any one of the preceding claims, for use in a method as defined in any one of the preceding claims, wherein the therapeutic compound is a nucleic acid polymer and the method of treatment is a method of gene therapy.
 16. A bile acid or salt according to any one of the preceding claims, for use in a method as defined in any one of the preceding claims, wherein said therapeutic compound comprises a hydrophobic moiety.
 17. A bile acid or salt according to any one of the preceding claims, for use in a method as defined in any one of the preceding claims, wherein in said method, the bile acid or salt thereof is used in the form of micelles conjugated non-covalently to the therapeutic compound, to enable or enhance intracellular uptake of the therapeutic compound.
 18. A bile acid or salt according to any one of the preceding claims, for use in a method as defined in any one of the preceding claims, wherein in said method, the bile acid or salt thereof is used to enable or enhance intracellular uptake of one or more therapeutic compounds located in the vicinity of the cell.
 19. A bile acid or salt according to any one of the preceding claims, for use in a method as defined in any one of the preceding claims, wherein said method comprises administering a composition comprising the bile acid or salt thereof and the therapeutic compound, and, if one or more additional agents are being used in combination with the bile acid or salt thereof in said method, preferably also one or more of said one or more additional agents.
 20. A bile acid or salt according to claim 19, for use in a method as defined in claim 16, wherein the weight ratio of the bile acid or salt : the therapeutic compound in said composition is from 20:1 to 5:1.
 21. A bile acid or salt according to claim 19 or 20, for use in a method as defined in claim 19 or 20, wherein said composition is in the form of a solution, suspension or dispersion.

22. A bile acid or salt according to claim 19 or 20, for use in a method as defined in claim 19 or 20, wherein said composition is in the form of a powder, said powder being comprised in a capsule or pellet.
23. A bile acid or salt according to claim 19 or 20, for use in a method as defined in claim 19 or 20, wherein said composition is in the form of a paste, ointment or gel.
24. A bile acid or salt according to claim 21, for use in a method as defined in claim 21 wherein said composition is a composition for intravenous administration, and the bile acid or salt and therapeutic compound in the composition are encapsulated by a coating which restricts dissolution of the bile acid or salt and therapeutic compound, wherein the coating (a) ceases to restrict dissolution of the bile acid or salt and therapeutic compound at a pH of less than 7.4, and/or (b) contains one or more moieties capable of binding to a target cell population within the body.
25. A therapeutic compound as defined in any one of claims 1 to 24, for use in a method as defined in any one of claims 1 to 24.
26. Use of a bile acid or salt as defined in any one of claims 1 to 24, in the manufacture of a medicament for use in a method as defined in any one of claims 1 to 24.
27. Use of therapeutic compound as defined in any one of claims 1 to 24, in the manufacture of a medicament for use in a method as defined in any one of claims 1 to 24.
28. A method of treatment of the human or animal body, which method is as defined in any one of claims 1 to 24.
29. A pharmaceutical composition comprising:
 - a) a bile acid or a pharmaceutically acceptable salt thereof, wherein said bile acid is chenodeoxycholic acid or deoxycholic acid;
 - b) a therapeutic compound; and
 - c) one or more further compounds selected from fusogenic lipids, cell penetrating peptides, lysosomotropic agents, membrane-disruptive peptides, membrane-disruptive polymers, photochemical internalisation agents, and agents that alter intracellular vesicle transport.

30. A pharmaceutical composition according to claim 29, wherein said bile salt is employed in conjunction with EDTA.
31. A pharmaceutical composition comprising:
 - a) a bile acid or a pharmaceutically acceptable salt thereof, wherein said bile acid is chenodeoxycholic acid or deoxycholic acid; and
 - b) a therapeutic compound;
 - c) wherein the bile acid or salt and therapeutic compound are encapsulated by a coating which (a) restricts dissolution of the bile acid or salt and therapeutic compound under aqueous conditions at a pH of 7.4 but ceases to restrict dissolution of the bile acid or salt and therapeutic compound at a pH which is lower than 7.4, and/or (b) contains one or more moieties capable of binding to a target cell population within the body.
32. A pharmaceutical composition according to claim 31, wherein said bile salt is employed in conjunction with EDTA.
33. A composition according to claim 32, wherein the composition further comprises one or more additional agents as defined in any one of claims 11 to 13.
34. A composition according to any one of claims 29 to 33, wherein said bile acid or pharmaceutically acceptable salt thereof is a chenodeoxycholate salt, preferably sodium chenodeoxycholate.
35. A composition according to any one of claims 29 to 34, wherein said therapeutic compound is a macromolecule.
36. A composition according to any one of claims 29 to 35, wherein said therapeutic compound is a protein.
37. A composition according to any one of claims 29 to 36, wherein the ratio of the bile acid or salt to the therapeutic compound is from 20:1 to 5:1.
38. A composition according to any one of claims 29 to 37, wherein the concentration of the EDTA which is achieved at the surface of the cells into which intracellular uptake is to be enabled or enhanced, is from 0.1 mg/ml to 10 mg/ml.

39. A composition according to any one of claims 29 to 38, wherein the concentration of the EDTA which is achieved at the surface of the cells into which intracellular uptake is to be enabled or enhanced, is from 0.2 mg/ml to 10 mg/ml.