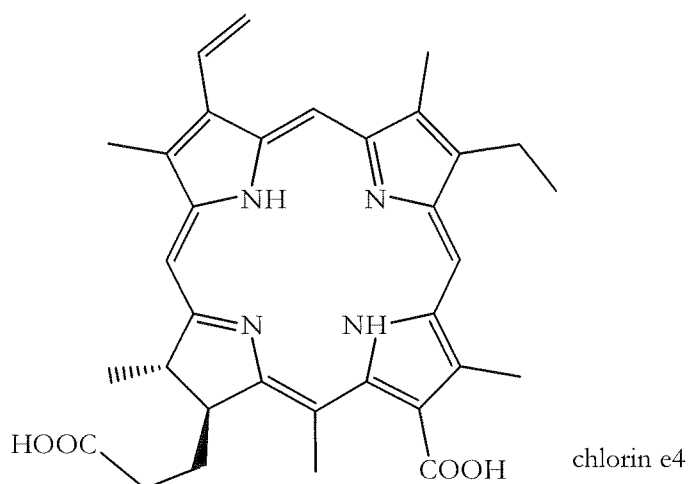
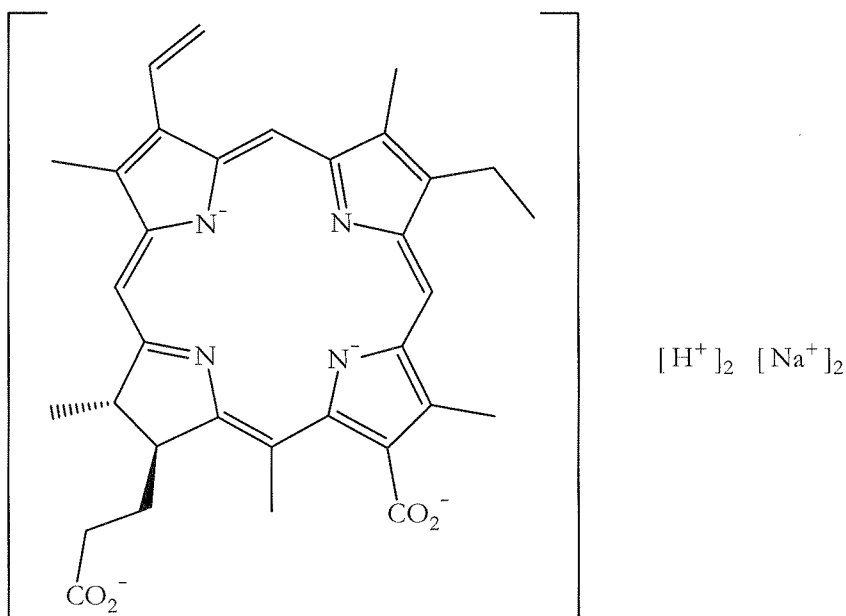


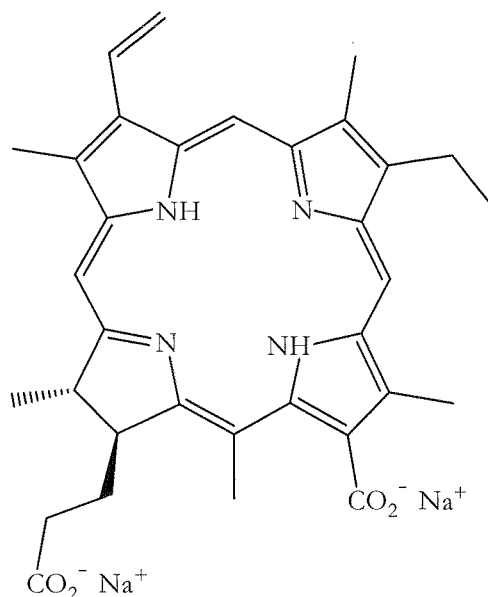


However, there is an ongoing need for better photosensitizers. There is a need for compounds that have a high singlet oxygen quantum yield and for compounds that have a strong photosensitizing ability, preferably in organic and aqueous media. There is also a need for compounds that have a high fluorescence quantum yield.

Summary of the invention

A first aspect of the present invention provides chlorin e4 sodium. Preferably the chlorin e4 sodium comprises chlorin e4 and sodium in a ratio of 1:2. Preferably the chlorin e4 sodium has the structure:





Chlorin e4 sodium has two chiral centres. The chlorin e4 sodium of the present invention described herein is preferably substantially enantiomerically pure, which means that the chlorin e4 sodium comprises less than 10% of other stereoisomers, preferably less than 5%, preferably less than 3%, preferably less than 2%, preferably less than 1%.

A second aspect of the present invention example provides a process of preparing chlorin e4 sodium, comprising the step of reacting chlorin e4 with a sodium compound. Preferably the chlorin e4 sodium obtained comprises chlorin e4 and sodium in a ratio of 1:2. Preferably the chlorin e4 sodium obtained has the structure:

hydride. Preferably the sodium compound is sodium hydroxide or sodium carbonate. More preferably the sodium compound is sodium hydroxide.

5 Optionally chlorin e4 is reacted with the sodium compound in the presence of a base. Preferably the base is an amine base, preferably an aromatic amine base such as thiamine pyrophosphate or DMAP. If used, the base is preferably thiamine pyrophosphate.

10 Preferably chlorin e4, the sodium compound and the optional base are used in a molar ratio of 0.15-1 : 45-60 : 0-12.

15 Preferably chlorin e4 is reacted with the sodium compound in the presence of a solvent. Preferably the solvent is selected from an alcohol (such as methanol, ethanol, n-propanol or isopropanol), water, DMF, chloroform, DMSO, toluene or a mixture thereof. Preferably the solvent is selected from methanol, ethanol, water or a mixture thereof. Preferably the solvent is selected from methanol, water or a mixture thereof. Preferably the solvent is a mixture of methanol and water.

20 Preferably the reaction is carried out at a temperature of 60°C or less. Preferably the reaction is carried out at a temperature in the range of 25-60°C.

Preferably the reaction is carried out over 1 to 12 hours, preferably over 3 to 8 hours.

25 The chlorin e4 sodium obtained may be purified by filtering, for example through a 45µm Millipore filter. Alternatively or additionally, the chlorin e4 sodium obtained may be purified by chromatography, for example by flash chromatography on a silica gel column. The chlorin e4 sodium may be isolated by lyophilisation.

30 A third ~~aspect of the present invention~~example provides chlorin e4 sodium preparable by a process according to the second ~~aspect of the present invention~~example. The third ~~aspect of the present invention~~example also provides chlorin e4 sodium when prepared by a process according to the second ~~aspect of the present invention~~example.

A fourth ~~aspect of the present invention~~example provides a pharmaceutical composition comprising chlorin e4 sodium according to the first or third ~~aspect of the present invention~~example and a pharmaceutically acceptable carrier or diluent.

5

Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present invention~~example is suitable for use in medicine.

10

Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present invention~~example and the pharmaceutical composition according to the fourth ~~aspect of the present invention~~example are suitable for use in photodynamic therapy or cytoluminescent therapy.

15

20

25

Preferably the chlorin e4 sodium according to first or third ~~aspect of the present invention~~example and the pharmaceutical composition according to the fourth ~~aspect of the present invention~~example are suitable for the treatment of atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus, Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones.

30

Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present invention~~example and the pharmaceutical composition according to the fourth ~~aspect of the~~

~~present inventionexample~~ are suitable for the treatment of a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation.

5 Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present inventionexample~~ and the pharmaceutical composition according to the fourth ~~aspect of the present inventionexample~~ are suitable for the treatment of a benign or malignant tumour.

10 Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present inventionexample~~ and the pharmaceutical composition according to the fourth ~~aspect of the present inventionexample~~ are suitable for the treatment of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas. Preferably they are suitable for the treatment of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; 20 retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones. Preferably they are 25 suitable for the treatment of lymphoma; Hodgkin's lymphoma; oral or mouth cancer; or cancer of the prostate, cervix, vaginal or other female adnexa, breast, naso-pharynx, lung, esophagus, kidney, liver, brain, lymphatic system, bones, skin or pancreas. Preferably they are suitable for the treatment of lymphoma; oral or mouth cancer; or cancer of the prostate, cervix, vaginal or other female adnexa, 30 breast, naso-pharynx, lung, esophagus, bones or skin.

Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present inventionexample~~ and the pharmaceutical composition according to the fourth ~~aspect of the present inventionexample~~ are suitable for use in photodynamic diagnosis.

Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present inventionexample~~ and the pharmaceutical composition according to the fourth ~~aspect of the present inventionexample~~ are suitable for the detection of atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; 5 rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus, Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or 10 malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, 15 stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones.

Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present inventionexample~~ and the pharmaceutical composition according to the fourth 20 ~~aspect of the present inventionexample~~ are suitable for the detection of an area that is affected by benign or malignant cellular hyperproliferation or by neovascularisation.

Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present inventionexample~~ and the pharmaceutical composition according to the fourth 25 ~~aspect of the present inventionexample~~ are suitable for the detection of a benign or malignant tumour.

Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present inventionexample~~ and the pharmaceutical composition according to the fourth 30 ~~aspect of the present inventionexample~~ are suitable for the detection of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other

female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas. Preferably they are suitable for the detection of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones. Preferably they are suitable for the detection of lymphoma; Hodgkin's lymphoma; oral or mouth cancer; or cancer of the prostate, cervix, vaginal or other female adnexa, breast, naso-pharynx, lung, esophagus, kidney, liver, brain, lymphatic system, bones, skin or pancreas. Preferably they are suitable for the detection of lymphoma; oral or mouth cancer; or cancer of the prostate, cervix, vaginal or other female adnexa, breast, naso-pharynx, lung, esophagus, bones or skin.

Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present inventionexample~~ and the pharmaceutical composition according to the fourth ~~aspect of the present inventionexample~~ are suitable for the fluorescent or phosphorescent detection of the diseases listed above, preferably for the fluorescent or phosphorescent detection and quantification of the said diseases.

Preferably the chlorin e4 sodium according to the first or third ~~aspect of the present inventionexample~~ and the pharmaceutical composition according to the fourth ~~aspect of the present inventionexample~~ are adapted for administration simultaneous with or prior to administration of irradiation or sound, preferably for administration prior to administration of irradiation.

If the chlorin e4 sodium according to the first or third ~~aspect of the present inventionexample~~ or the pharmaceutical composition according to the fourth ~~aspect of the present inventionexample~~ are for use in photodynamic therapy or cytoluminescent therapy, then they are preferably adapted for administration 5 to 100 hours before the

irradiation, preferably 6 to 72 hours before the irradiation, preferably 24 to 48 hours before the irradiation.

5 | If the chlorin e4 sodium according to the first or third ~~aspect of the present invention~~example or the pharmaceutical composition according to the fourth ~~aspect of the present invention~~example are for use in photodynamic diagnosis, then they are preferably adapted for administration 3 to 60 hours before the irradiation, preferably 8 to 40 hours before the irradiation.

10 | Preferably the irradiation used in the photodynamic therapy, cytoluminescent therapy or photodynamic diagnosis is electromagnetic radiation with a wavelength in the range of from 500nm to 1000nm, preferably from 600nm to 790nm. The electromagnetic radiation may be administered for about 5-60 minutes, preferably for about 15-20 minutes, at about 0.1-5W, preferably at about 1W. In one
15 | ~~embodiment of the present invention~~example, two sources of electromagnetic radiation are used (for example a laser light and an LED light), one source with a wavelength in the range of from 600nm to 690nm, preferably about 660nm, the other source with a wavelength in the range of from 700nm to 790nm, preferably about 760nm. In another ~~embodiment of the present invention~~example, two
20 | sources of electromagnetic radiation are used (for example a laser light and an LED light), both sources adapted to provide irradiation with a wavelength in the range of from 600nm to 690nm, preferably about 660nm, and irradiation with a wavelength in the range of from 700nm to 790nm, preferably about 760nm. In another ~~embodiment of the present invention~~example, the irradiation may be provided by a
25 | prostate, anal, vaginal, mouth and nasal device for insertion into a body cavity. In another ~~embodiment of the present invention~~example, the irradiation may be provided by interstitial light activation, for example, using a fine needle to insert an optical fibre laser into the lung, liver, lymph nodes or breast. In another ~~embodiment of the present invention~~example, the irradiation may be provided by
30 | endoscopic light activation, for example, for delivering light to the lung, stomach, colon, bladder or neck.

| The pharmaceutical composition according to the fourth ~~aspect of the present invention~~example may be in a form suitable for oral, parental (including intravenous,

subcutaneous, intramuscular, intradermal, intratracheal, intraperitoneal, intraarticular, intraabdominal, intracranial and epidural), transdermal, airway (aerosol), rectal, vaginal or topical (including buccal, mucosal and sublingual) administration. The pharmaceutical composition may also be in a form suitable for administration by enema or for administration by injection into a tumour. Preferably the pharmaceutical composition is in a form suitable for oral, parental or airway administration, preferably in a form suitable for oral or parental administration, preferably in a form suitable for oral administration.

10 | In one preferred ~~embodiment~~example, the pharmaceutical composition is in a form suitable for oral administration. Preferably the pharmaceutical composition is provided in the form of a tablet, capsule, hard or soft gelatine capsule, caplet, troche or lozenge, as a powder or granules, or as an aqueous solution, suspension or dispersion. More preferably the pharmaceutical composition is provided in the form of an aqueous solution, suspension or dispersion for oral administration, or alternatively in the form of a freeze-dried powder which can be mixed with water before administration to provide an aqueous solution, suspension or dispersion for oral administration. Preferably the pharmaceutical composition is in a form suitable for providing 0.01 to 10 mg/kg/day of the chlorin e4 sodium, preferably 0.1 to 5 mg/kg/day, preferably about 3 mg/kg/day.

25 | In another preferred ~~embodiment~~example, the pharmaceutical composition is in a form suitable for parental administration. Preferably the pharmaceutical composition is in a form suitable for intravenous administration. Preferably the pharmaceutical composition is provided in the form of an aqueous solution for parental administration, or alternatively in the form of a freeze-dried powder which can be mixed with water before administration to provide an aqueous solution for parental administration. Preferably the pharmaceutical composition is an aqueous solution or suspension having a pH of from 6 to 8.5.

30

| In another preferred ~~embodiment~~example, the pharmaceutical composition is in a form suitable for airway administration. Preferably the pharmaceutical composition is provided in the form of an aqueous solution, suspension or dispersion for airway

administration, or alternatively in the form of a freeze-dried powder which can be mixed with water before administration to provide an aqueous solution, suspension or dispersion for airway administration. Preferably the pharmaceutical composition is in a form suitable for providing 0.01 to 10 mg/kg/day of the chlorin e4 sodium, preferably 0.1 to 5 mg/kg/day, preferably about 3 mg/kg/day.

A fifth ~~aspect of the present invention~~example provides use of chlorin e4 sodium according to the first or third ~~aspect of the present invention~~example in the manufacture of a medicament for the treatment of atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus, Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones.

The fifth ~~aspect of the present invention~~example also provides use of chlorin e4 sodium according to the first or third ~~aspect of the present invention~~example in the manufacture of a phototherapeutic agent for use in photodynamic therapy or cytoluminescent therapy. Preferably the phototherapeutic agent is suitable for the treatment of atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus, Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or

malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones.

Preferably the medicament or the phototherapeutic agent of the fifth ~~aspect of the present invention~~ example is suitable for the treatment of a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation.

Preferably the medicament or the phototherapeutic agent of the fifth ~~aspect of the present invention~~ example is suitable for the treatment of a benign or malignant tumour.

Preferably the medicament or the phototherapeutic agent of the fifth ~~aspect of the present invention~~ example is suitable for the treatment of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas. Preferably it is suitable for the treatment of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones. Preferably it is suitable for the treatment of lymphoma; Hodgkin's lymphoma; oral or mouth cancer; or cancer of the prostate, cervix, vaginal or other female adnexa, breast, naso-pharynx, lung, esophagus, kidney, liver, brain, lymphatic system, bones, skin or pancreas. Preferably it is suitable for the

treatment of lymphoma; oral or mouth cancer; or cancer of the prostate, cervix, vaginal or other female adnexa, breast, naso-pharynx, lung, esophagus, bones or skin.

5 | The fifth ~~aspect of the present invention~~example also provides use of chlorin e4 sodium according to the first or third ~~aspect of the present invention~~example in the manufacture of a photodiagnostic agent for use in photodynamic diagnosis.

10 | Preferably the photodiagnostic agent of the fifth ~~aspect of the present invention~~example is suitable for the detection of atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus, Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid
15 | artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus,
20 | vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones.

25 | Preferably the photodiagnostic agent of the fifth ~~aspect of the present invention~~example is suitable for the detection of an area that is affected by benign or malignant cellular hyperproliferation or by neovascularisation.

30 | Preferably the photodiagnostic agent of the fifth ~~aspect of the present invention~~example is suitable for the detection of a benign or malignant tumour.

Preferably the photodiagnostic agent of the fifth ~~aspect of the present invention~~example is suitable for the detection of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma;

Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas. Preferably it is suitable for the detection of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones. Preferably it is suitable for the detection of lymphoma; Hodgkin's lymphoma; oral or mouth cancer; or cancer of the prostate, cervix, vaginal or other female adnexa, breast, naso-pharynx, lung, esophagus, kidney, liver, brain, lymphatic system, bones, skin or pancreas. Preferably it is suitable for the detection of lymphoma; oral or mouth cancer; or cancer of the prostate, cervix, vaginal or other female adnexa, breast, naso-pharynx, lung, esophagus, bones or skin.

Preferably the photodiagnostic agent of the fifth ~~aspect of the present invention~~example is suitable for the fluorescent or phosphorescent detection of the said diseases, preferably the fluorescent or phosphorescent detection and quantification of the said diseases.

Preferably the medicament, the phototherapeutic agent or the photodiagnostic agent is adapted for administration simultaneous with or prior to administration of irradiation or sound, preferably for administration prior to administration of irradiation.

If the medicament or the phototherapeutic agent is for use in photodynamic therapy or cytoluminescent therapy, then it is preferably adapted for administration 5 to 100 hours before the irradiation, preferably 6 to 72 hours before the irradiation, preferably 24 to 48 hours before the irradiation.

If the photodiagnostic agent is for use in photodynamic diagnosis, then it is preferably adapted for administration 3 to 60 hours before the irradiation, preferably 8 to 40 hours before the irradiation.

5 Preferably the irradiation used in the photodynamic therapy, cytoluminescent therapy or photodynamic diagnosis is electromagnetic radiation with a wavelength in the range of from 500nm to 1000nm, preferably from 600nm to 790nm. The electromagnetic radiation may be administered for about 5-60 minutes, preferably for about 15-20 minutes, at about 0.1-5W, preferably at about 1W. In one
10 ~~embodiment of the present invention example~~, two sources of electromagnetic radiation are used (for example a laser light and an LED light), one source with a wavelength in the range of from 600nm to 690nm, preferably about 660nm, the other source with a wavelength in the range of from 700nm to 790nm, preferably
15 about 760nm. In another ~~embodiment of the present invention example~~, two sources of electromagnetic radiation are used (for example a laser light and an LED light), both sources adapted to provide irradiation with a wavelength in the range of from 600nm to 690nm, preferably about 660nm, and irradiation with a wavelength in the range of from 700nm to 790nm, preferably about 760nm. In another
20 ~~embodiment of the present invention example~~, the irradiation may be provided by a prostate, anal, vaginal, mouth and nasal device for insertion into a body cavity. In another ~~embodiment of the present invention example~~, the irradiation may be provided by interstitial light activation, for example, using a fine needle to insert an optical fibre laser into the lung, liver, lymph nodes or breast. In another
25 ~~embodiment of the present invention example~~, the irradiation may be provided by endoscopic light activation, for example, for delivering light to the lung, stomach, colon, bladder or neck.

30 A sixth ~~aspect of the present invention example~~ provides a method of treating atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus, Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or

malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast,
5 naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones; the method comprising administering a therapeutically effective amount of chlorin e4 sodium according to the first or third aspect of the present invention to a human or animal in need
10 thereof.

The sixth ~~aspect of the present invention~~example also provides a method of photodynamic therapy or cytoluminescent therapy of a human or animal disease, the method comprising administering a therapeutically effective amount of chlorin e4
15 sodium according to the first or third ~~aspect of the present invention~~example to a human or animal in need thereof. Preferably the human or animal disease is atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus, Asian (chicken) flu virus,
20 herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell
25 tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones.

30

Preferably the method of the sixth ~~aspect of the present invention~~example is a method of treating benign or malignant cellular hyperproliferation or areas of neovascularisation.

Preferably the method of the sixth ~~aspect of the present invention~~example is a method of treating a benign or malignant tumour.

5 | Preferably the method of the sixth ~~aspect of the present invention~~example is a method of treating early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile
10 | duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas. Preferably the method is a method of treating early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; Hodgkin's lymphoma; or cancer of the blood, prostate, cervix, uterus, vaginal or other female
15 | adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system or bones. Preferably the method is a method of treating lymphoma; Hodgkin's lymphoma; oral or mouth cancer; or cancer of the prostate, cervix, vaginal or other female
20 | adnexa, breast, naso-pharynx, lung, esophagus, kidney, liver, brain, lymphatic system, bones, skin or pancreas. Preferably the method is a method of treating lymphoma; oral or mouth cancer; or cancer of the prostate, cervix, vaginal or other female adnexa, breast, naso-pharynx, lung, esophagus, bones or skin.

25 | The sixth ~~aspect of the present invention~~example also provides a method of photodynamic diagnosis of a human or animal disease, the method comprising administering a diagnostically effective amount of chlorin e4 sodium according to the first or third ~~aspect of the present invention~~example to a human or animal.
30 | Preferably the human or animal disease is atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus, Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular

preferably for the fluorescent or phosphorescent detection and quantification of the said diseases.

5 In any of the methods of the sixth ~~aspect of the present invention~~example, the human or animal is preferably further subjected to irradiation or sound simultaneous with or after the administration of the chlorin e4 sodium. Preferably the human or animal is subjected to irradiation after the administration of the chlorin e4 sodium.

10 If the method is a method of photodynamic therapy or cytoluminescent therapy, then the human or animal is preferably subjected to irradiation 5 to 100 hours after administration of the chlorin e4 sodium, preferably 6 to 72 hours after administration, preferably 24 to 48 hours after administration.

15 If the method is a method of photodynamic diagnosis, then the human or animal is preferably subjected to irradiation 3 to 60 hours after administration of the chlorin e4 sodium, preferably 8 to 40 hours after administration.

Preferably the irradiation is electromagnetic radiation with a wavelength in the range
20 of from 500nm to 1000nm, preferably from 600nm to 790nm. The electromagnetic radiation may be administered for about 5-60 minutes, preferably for about 15-20 minutes, at about 0.1-5W, preferably at about 1W. In one ~~embodiment of the present invention~~example, two sources of electromagnetic radiation are used (for example a laser light and an LED light), one source with a wavelength in the range
25 of from 600nm to 690nm, preferably about 660nm, the other source with a wavelength in the range of from 700nm to 790nm, preferably about 760nm. In another ~~embodiment of the present invention~~example, two sources of electromagnetic radiation are used (for example a laser light and an LED light), both sources adapted to provide irradiation with a wavelength in the range of from 600nm to 690nm, preferably about
30 660nm, and irradiation with a wavelength in the range of from 700nm to 790nm, preferably about 760nm. In another ~~embodiment of the present invention~~example, the irradiation may be provided by a prostate, anal, vaginal, mouth and nasal device for insertion into a body cavity. In another ~~embodiment of the present invention~~example, the irradiation may be provided by interstitial light activation, for example, using a

fine needle to insert an optical fibre laser into the lung, liver, lymph nodes or breast. In another ~~embodiment of the present invention~~ example, the irradiation may be provided by endoscopic light activation, for example, for delivering light to the lung, stomach, colon, bladder or neck.

5

Preferably the human or animal is a human.

Brief description of the drawings

10 Figure 1 shows a modified Jablonski diagram for a typical photosensitizer, outlining the principle photophysical processes of interest.

Figure 2 depicts schematically the metalation and demetalation of a porphyrin ring.

15 Figure 3 depicts schematically the reaction of 1,3-diphenylisobenzofuran (DPIBF) with two singlet oxygens ($^1\text{O}_2$).

Figure 4 shows the absorption spectrum of a chlorin e4 sodium solution (about 10 μM) in ethanol.

20

Figure 5 shows the absorption spectrum of a chlorin e4 sodium solution (about 10 μM) in water.

Figure 6 shows the absorption spectrum of a chlorin e4 sodium solution (about 10 μM) in water with 0.2 M detergent sodium dodecyl sulphate (SDS).

25

Figure 7 shows the fluorescence spectrum of a chlorin e4 sodium solution (about 10 μM) in ethanol. Excitation wavelength was 403 nm; the absorbance at this wavelength was 0.10; cuvette size 1 cm.

30

Figure 8 shows the fluorescence spectrum of a chlorin e4 sodium solution (about 10 μM) in water. Excitation wavelength was 403 nm; the absorbance at this wavelength was 0.13; cuvette size 1 cm.

duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas; the method comprising administering a therapeutically effective amount of chlorin e4 sodium of any one of claims 1-4 or 14-24 to a human or animal in need thereof.

5

46. A method of photodynamic therapy or cytoluminescent therapy of a human or animal disease, the method comprising administering a therapeutically effective amount of chlorin e4 sodium of any one of claims 1-4 or 14-24 to a human or animal in need thereof.

10

47. The method of claim 46, wherein the human or animal disease is atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus, Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas.

25

48. The method of any one of claims 45 to 47, wherein the human or animal disease is characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation.

30

49. The method of any one of claims 45 to 48, wherein the human or animal disease is a benign or malignant tumour.

50. The method of any one of claims 45 to 49, wherein the human or animal disease is early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas.
51. A method of photodynamic diagnosis of a human or animal disease, the method comprising administering a diagnostically effective amount of chlorin e4 sodium of any one of claims 1-4 or 14-24 to a human or animal.
52. The method of any one of claims 45 to 51, wherein the human or animal is subjected to irradiation after the administration of the chlorin e4 sodium.
53. The method of claim 52, wherein the irradiation is electromagnetic radiation with a wavelength in the range of from 500nm to 1000nm.

41. The use of any one of claims 36 to 40, wherein the medicament or the phototherapeutic agent is for the treatment of early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile duct, intestine, colon, colorectum, rectum, bladder, ureter, kidney, liver, gall bladder, spleen, brain, lymphatic system, bones, skin or pancreas.

42. Use of chlorin e4 sodium of any one of claims 1-4 or 14-24 in the manufacture of a photodiagnostic agent for use in photodynamic diagnosis.

43. The use of any one of claims 36 to 42, wherein the medicament, the phototherapeutic agent or the photodiagnostic agent is adapted for administration prior to administration of irradiation.

44. The use of claim 43, wherein the irradiation is electromagnetic radiation with a wavelength in the range of from 500nm to 1000nm.

45. ~~A method of treating atherosclerosis; multiple sclerosis; diabetes; diabetic retinopathy; arthritis; rheumatoid arthritis; a fungal, viral, chlamydial, bacterial, nanobacterial or parasitic infectious disease; HIV; Aids; infection with sars virus, Asian (chicken) flu virus, herpes simplex or herpes zoster; hepatitis; viral hepatitis; a cardiovascular disease; coronary artery stenosis; carotid artery stenosis; intermittent claudication; a dermatological condition; acne; psoriasis; a disease characterised by benign or malignant cellular hyperproliferation or by areas of neovascularisation; a benign or malignant tumour; early cancer; cervical dysplasia; soft tissue sarcoma; a germ cell tumour; retinoblastoma; age-related macular degeneration; lymphoma; Hodgkin's lymphoma; head and neck cancer; oral or mouth cancer; or cancer of the blood, prostate, cervix, uterus, vaginal or other female adnexa, breast, naso-pharynx, trachea, larynx, bronchi, bronchioles, lung, hollow organs, esophagus, stomach, bile~~