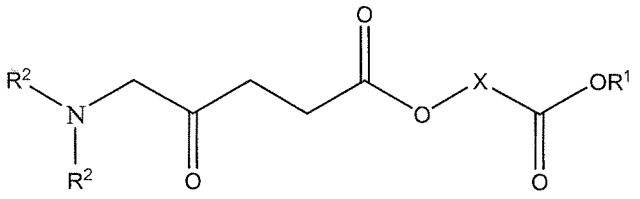
an ester thereof are in clinical use for PDT and photodynamic diagnosis (PDD). One of them is Metvix®, a dermal product in the form of a cream comprising 5-ALA methyl ester (developed by Photocure ASA, Norway, and now sold by Galderma, Switzerland), for the photodynamic treatment of actinic keratosis and basal cell carcinoma. Another one is Levulan Kerastick® (DUSA Pharmaceuticals, Canada), a product for the photodynamic treatment of actinic keratosis which contains 5-ALA. Hexvix® (developed by Photocure ASA) is an aqueous solution which comprises 5-ALA hexyl ester for instillation into the bladder for diagnosis of bladder cancer.

However, a need still exists for alternative photosensitisers or precursors thereof. The present invention addresses this need by providing precursors of photosensitisers according to general formula I below.

Summary

In one aspect, there is provided a compound of general formula I, or a pharmaceutically acceptable salt thereof:



(I)

wherein

R^1 represents a hydrogen atom or a methyl, ethyl, n-propyl or isopropyl group ~~an optionally substituted alkyl or cycloalkyl group~~;

R^2~~, each of which may be the same or different,~~ represents a hydrogen atom ~~or an optionally substituted alkyl group; and~~

X is a ~~linking group.~~straight-chained or branched alkylene group, a cycloalkylene, arylene, or aralkylene group, each of which may optionally be substituted by one or more non-hydrophilic substituents selected from halo, nitro and aryl, wherein the aryl is optionally substituted by one or more halo, alkyl, haloalkyl, alkoxy or nitro groups; and

wherein the $-CO_2R^1$ group of the $-X-CO_2R^1$ portion is hydrophilic.

In another aspect, there is provided a composition comprising a compound of formula I, or a pharmaceutically acceptable salt thereof as disclosed herein, together with at least one pharmaceutically acceptable or cosmetically acceptable carrier or excipient.

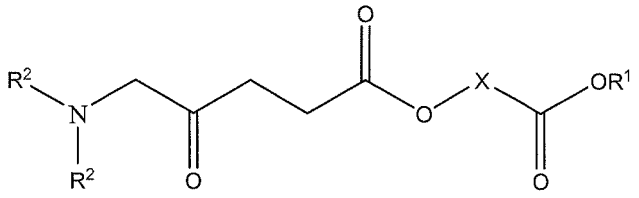
In a further aspect, there is provided a compound ~~or a composition~~ as disclosed herein for use in a method of photodynamic treatment or diagnosis~~, preferably for the treatment or diagnosis of a disorder or abnormality of an external or internal surface of the body which is responsive to photodynamic treatment or diagnosis.~~.

In a further aspect, there is provided use of a compound as disclosed above in the manufacture of a medicament for the treatment or diagnosis of cancer (e.g. bladder cancer, colon cancer or stomach cancer); an infection associated with cancer, such as a viral infection (e.g. human papilloma virus, hepatitis B or Epstein Barr virus); a viral, bacterial or fungal infection (e.g. *Helicobacter pylori* infection or acne); or a non-cancerous condition such as inflammation (e.g. inflammatory acne, colitis or infective dermatitis).

In a further aspect, there is provided a composition as disclosed herein for use in a method of photodynamic treatment or diagnosis.

Description

Thus, viewed from a first aspect, the invention provides a compound of general formula I, or a pharmaceutically acceptable salt thereof:



(I)

wherein

R^1 represents a hydrogen atom or an optionally substituted alkyl or cycloalkyl group;

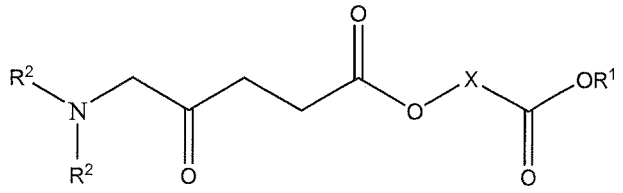
R^2, each of which may be the same or different, represents a hydrogen atom or an optionally substituted alkyl group; and

X is a linking group.

In the compounds of formula I, it is preferred that the $-X-CO_2R^1$ portion is hydrophilic in nature. The term "hydrophilic" means that the $-X-CO_2R^1$ portion of the molecule has a tendency to interact with or be dissolved by water or other polar solvents and/or substances. The hydrophilic nature of this portion of the molecule may arise from the nature of group X and/or from the nature of the $-CO_2R^1$ group.

Claims:

1. A compound of general formula I, or a pharmaceutically acceptable salt thereof:



(I)

wherein

R^1 represents a hydrogen atom or ~~an optionally substituted alkyl or cycloalkyl group~~a methyl, ethyl, n-propyl or isopropyl group;

R^2, ~~each of which may be the same or different,~~ represents a hydrogen atom ~~or an optionally substituted alkyl group~~; and

X is a ~~linking group.~~ straight-chained or branched alkylene group, a cycloalkylene, arylene, or aralkylene group, each of which may optionally be substituted by one or more non-hydrophilic substituents selected from halo, nitro and aryl, wherein the aryl is optionally substituted by one or more halo, alkyl, haloalkyl, alkoxy or nitro groups; and

wherein the $-CO_2R^1$ group of the $-X-CO_2R^1$ portion is hydrophilic.

2. A compound as claimed in claim 1, ~~wherein the $-X-CO_2R^1$ portion is hydrophilic.~~ wherein X is a straight-chained alkylene group which consists of 1 to 16 carbon atoms.

3. A compound as claimed in claim ~~1 or claim~~ 2, wherein ~~the $-CO_2R^1$ group of the $-X-CO_2R^1$ portion is hydrophilic.~~ X is a straight-chained alkylene group which consists of 1 to 6 carbon atoms.

4. A compound as claimed in claim ~~3~~2, wherein ~~R^1 is hydrogen or a short, straight-chained or branched alkylene group, preferably methyl, ethyl, n-propyl or isopropyl.~~ X is a straight-chained alkylene group which consists of 1 to 4 carbon atoms.

~~5. A compound as claimed in claim 3 or claim 4, wherein group X is a straight-chained or branched alkylene group, a cycloalkylene, arylene, or aralkylene group, each of which may optionally be substituted by one or more non-hydrophilic substituents, preferably non-hydrophilic substituents selected from halo, nitro and~~

~~aryl, wherein the aryl is optionally substituted by one or more halo, alkyl, haloalkyl, alkoxy or nitro groups.~~

56. A compound as claimed in claim 15, wherein group X is an optionally substituted, straight-chained C_{1-4} alkylene group, an optionally substituted branched C_{2-6} alkylene group, an optionally substituted C_{5-6} cycloalkylene group, an optionally substituted C_{6-12} arylene group, or an optionally substituted C_{7-15} aralkylene group.

67. A compound as claimed in claim 56, wherein group X is an unsubstituted straight-chained C_{1-4} alkylene group, an unsubstituted branched C_{2-6} alkylene group, or a straight-chained C_{1-2} alkylene group substituted by one or more halo or aryl groups.

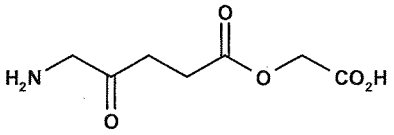
~~8. A compound as claimed in claim 1 or claim 2, wherein the X group of the X-CO_2R^1 portion is hydrophilic.~~

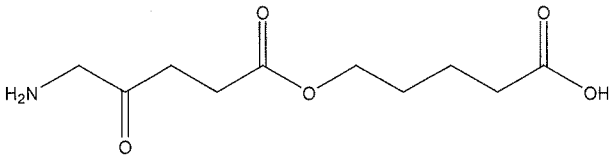
~~9. A compound as claimed in claim 8, wherein the X group is an alkylene group which is either interrupted by one or more heteroatoms, preferably by one or more oxygen atoms or which carries one or more hydrophilic substituents, preferably hydroxyl, thiol, carboxyl, carbamoyl, ester or amine groups.~~

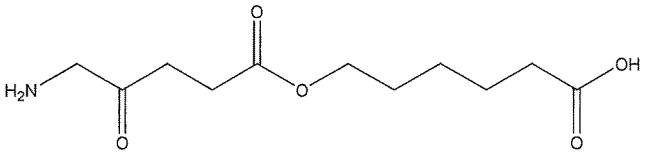
~~10. A compound as claimed in claim 9, wherein R^1 is an unsubstituted, straight-chained or branched alkyl group containing 4 to 10 carbon atoms or an unsubstituted cycloalkyl group containing 3 to 6 carbon atoms or a C_{1-2} alkyl group substituted by an optionally substituted aryl group.~~

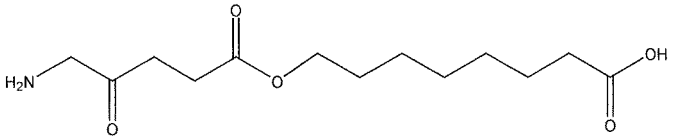
~~11. A compound as claimed in any preceding claim, wherein each R^2 represents hydrogen.~~

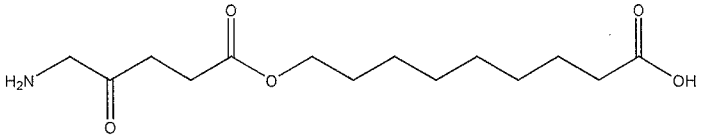
712. A compound as claimed in claim 1 which is a compound selected from any of the following, or a pharmaceutically acceptable salt thereof:

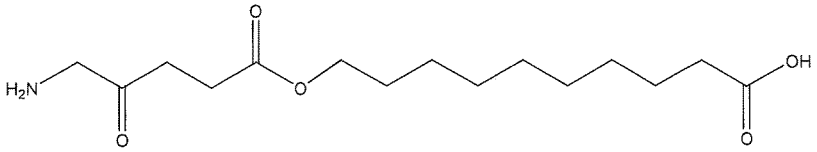


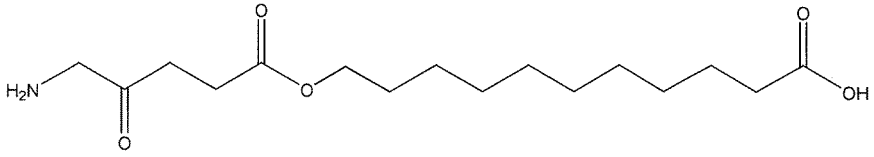


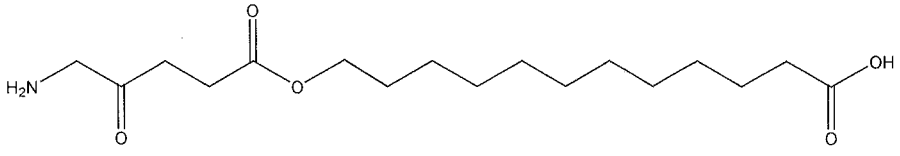




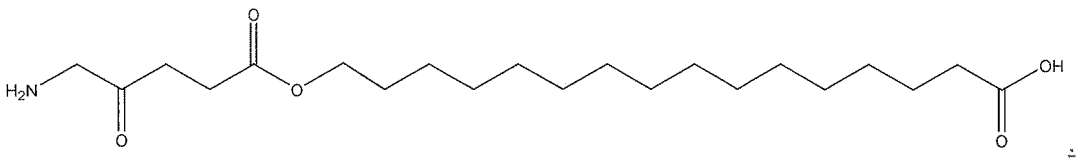








; and



8~~13~~. A composition comprising a compound of formula I, or a pharmaceutically acceptable salt thereof as claimed in any one of claims 1 to 7~~12~~, together with at least one pharmaceutically acceptable or cosmetically acceptable carrier or excipient.

9. A composition as claimed in claim 8, wherein the compound of formula I is one wherein X is a straight-chained alkylene group which consists 1 to 16 carbon atoms.

10. A composition as claimed in claim 8, wherein the compound of formula I is one wherein X is a straight-chained alkylene group which consists 1 to 6 carbon atoms.

11. A composition as claimed in claim 8, wherein the compound of formula I is one wherein X is a straight-chained alkylene group which consists 1 to 4 carbon atoms.

12. A compound as claimed in any one of claims 1 to 7 for use in a method of photodynamic treatment or diagnosis.

13. A compound for use as claimed in claim 12, wherein said method is for the treatment or diagnosis of a disorder or abnormality of an external or internal surface of the body which is responsive to photodynamic treatment or diagnosis.

14. A compound for use as claimed in claim 12, wherein said method is for the treatment or diagnosis of cancer (e.g. bladder cancer, colon cancer or stomach cancer); an infection associated with cancer, such as a viral infection (e.g. human papilloma virus, hepatitis B or Epstein Barr virus); a viral, bacterial or fungal infection (e.g. *Helicobacter pylori* infection or acne); or a non-cancerous condition such as inflammation (e.g. inflammatory acne, colitis or infective dermatitis).

15. Use of a compound of any one of claims 1 to 7 in the manufacture of a medicament for the treatment or diagnosis of cancer (e.g. bladder cancer, colon cancer or stomach cancer); an infection associated with cancer, such as a viral infection (e.g. human papilloma virus, hepatitis B or Epstein Barr virus); a viral, bacterial or fungal infection (e.g. *Helicobacter pylori* infection or acne); or a non-cancerous condition such as inflammation (e.g. inflammatory acne, colitis or infective dermatitis).

1614. ~~A compound as claimed in any one of claims 1 to 12 or a~~ A composition as claimed in any one of claims 8 to 11~~claim 13~~ for use in a method of photodynamic treatment or diagnosis~~, preferably for the treatment or diagnosis of a disorder or abnormality of an external or internal surface of the body which is responsive to photodynamic treatment or diagnosis~~.

17. A composition for use as claimed in claim 16, wherein said method is for the treatment or diagnosis of a disorder or abnormality of an external or internal surface of the body which is responsive to photodynamic treatment or diagnosis.

1815. A composition~~und~~ for use as claimed in claim 1614, wherein said method is for the treatment or diagnosis of cancer (e.g. bladder cancer, colon cancer or stomach cancer); an infection associated with cancer, such as a viral infection (e.g. human papilloma virus, hepatitis B or Epstein Barr virus); a viral, bacterial or fungal infection (e.g. *Helicobacter pylori* infection or acne); or a non-cancerous condition such as inflammation (e.g. inflammatory acne, colitis or infective dermatitis).