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CA 2466437 C 2012/10/30

(11)(21) 2 466 437

(12) BREVET CANADIEN
CANADIAN PATENT

(13) C

(86) Date de dépôt PCT/PCT Filing Date: 2002/11/08
(87) Date publication PCT/PCT Publication Date: 2003/05/15
(45) Date de délivrance/Issue Date: 2012/10/30
(85) Entrée phase nationale/National Entry: 2004/05/07
(86) N° demande PCT/PCT Application No.: CA 2002/001734
(87) N° publication PCT/PCT Publication No.: 2003/039597
(30) Priorité/Priority: 2001/11/09 (US60/338,295)

(51) Cl.Int./Int.Cl. *A61K 41/00* (2006.01),
A61K 31/40 (2006.01), *A61K 47/08* (2006.01),
A61K 47/10 (2006.01), *A61K 8/49* (2006.01),
A61N 5/06 (2006.01), *A61P 17/14* (2006.01),
A61Q 7/00 (2006.01)

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(54) Titre : COMPOSITIONS RENFERMANT UN PHOTOSENSIBILISATEUR ET UN AMPLIFICATEUR DE PENETRATION CUTANEE ET LEUR UTILISATION DANS LE TRAITEMENT PHOTODYNAMIQUE

(54) Title: COMPOSITIONS COMPRISING A PHOTOSENSITIZER AND A SKIN-PENETRATION ENHANCER AND THEIR USE IN PHOTODYNAMIC TREATMENT

(57) Abrégé/Abstract:
The present invention relates to a composition comprising a photosensitizing agent and a skin-penetration enhancer. The composition herein show improved delivery of the photosensitizer through the stratum corneum. In addition, the composition of the present invention show improved stability and a reduced incidence of skin photosensitivity.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 May 2003 (15.05.2003)

PCT

(10) International Publication Number
WO 03/039597 A1

(51) International Patent Classification[7]: A61K 41/00, 47/08, 47/10, 31/40, A61P 17/14

(21) International Application Number: PCT/CA02/01734

(22) International Filing Date:
8 November 2002 (08.11.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/338,295 9 November 2001 (09.11.2001) US

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(81) Designated States *(national)*: AE, AG, AL, AM, AT (utility model), AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, EE (utility model), EE, ES, FI (utility model), FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK (utility model), SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/039597 A1

(54) Title: COMPOSITIONS COMPRISING A PHOTOSENSITIZER AND A SKIN-PENETRATION ENHANCER AND THEIR USE IN PHOTODYNAMIC TREATMENT

(57) Abstract: The present invention relates to a composition comprising a photosensitizing agent and a skin-penetration enhancer. The composition herein show improved delivery of the photosensitizer through the stratum corneum. In addition, the composition of the present invention show improved stability and a reduced incidence of skin photosensitivity.

COMPOSITIONS COMPRISING A PHOTOSENSITIZER AND A SKIN-PENETRATION ENHANCER AND THEIR USE IN PHOTODYNAMIC TREATMENT

Technical Field

The present invention relates to a composition comprising photosensitizing agents.

Background to the Invention

Photodynamic therapy is a diverse field of medical treatment. Generally, PDT involves the delivery of a photosensitizer to the target tissue and, subsequently, irradiating the target area with light of an appropriate wavelength to activate the PS. This activation results in an agent that modifies or destroys the target tissues. The PS is usually delivered systemically although it has been proposed to deliver it locally.

Local delivery has the advantage that the PS is delivered directly to the target tissue and, consequently, high concentrations of the drug in the target tissue can be achieved. However, local delivery also has some disadvantages. Photosensitizing agents do not easily penetrate the stratum corneum. In addition, the PS agents are relatively reactive so it is difficult to formulate a stable composition.

At the time of writing, one product that is marketed for topical PDT is Levulan® Kerastick®. This product is used for the treatment of non-hyperkeratotic actinic keratosis lesions on the face or scalp. The photosensitizer in this product is a pro-drug and is converted into the active *in situ*. The product is supplied in a plastic applicator tube containing two sealed glass ampules. One ampule contains the a solution to act as the vehicle and the other the photosensitizing agent as a dry solid. The applicator tube is enclosed in a protective cardboard sleeve and cap. Immediately prior to application, the two ampules are crushed and the solution is mixed with the photosensitizer. The contents are then shaken for several minutes until the drug is dissolved. The solution containing dissolved drug must be discarded two hours after mixing due to the short stability of the product

Thus there remains a need for a stable photosensitizer composition suitable for topical application to the skin.

It has also been found that topical photosensitizer compositions can cause skin-photosensitivity reactions. In addition, it has been problematic to deliver the photosensitizer to the correct target tissue because often the stratum corneum is difficult to penetrate.

Summary of the Invention

The present invention relates to a composition comprising a photosensitizing agent and at least one skin-penetration enhancer. The compositions herein show improved delivery of the photosensitizer through the stratum corneum. In addition, the compositions of the present invention show improved stability.

The photosensitizers of the present compositions are able to penetrate the stratum corneum. Consequently, when light energy is delivered, the photosensitizer is activated at the target tissue rather than at the surface. This means that the compositions are more efficacious. In addition, it has surprisingly been found that, when using the compositions of the present invention, administration of light does not cause substantial skin photosensitivity. While not wishing to be bound by theory, it is thought that this the fact that the photosensitizer distributes to the epidermis, rather than in the dermis, means there is less skin photosensitivity.

Unless otherwise specified, all percentages herein are expressed as weight percentages.

Detailed Description

The present invention provides compositions comprising a photosensitizing agent and a skin penetration enhancer. These elements will be described in more detail below.

The compositions of the present invention are preferably substantially free of water. As used herein, the term "substantially free of water" means that the composition comprises less than about 5%, preferably less than about 3%, by weight, of free water. It is preferred that the compositions herein do not have a total water content (i.e. free water plus any water of hydration) of more than about 15%, preferably less than about 10%.

Photosensitizer

Any suitable photosensitizing agent may be used herein. Generally, these will absorb radiation in the range of from 400nm to 800nm, typically from 600nm to 750nm.

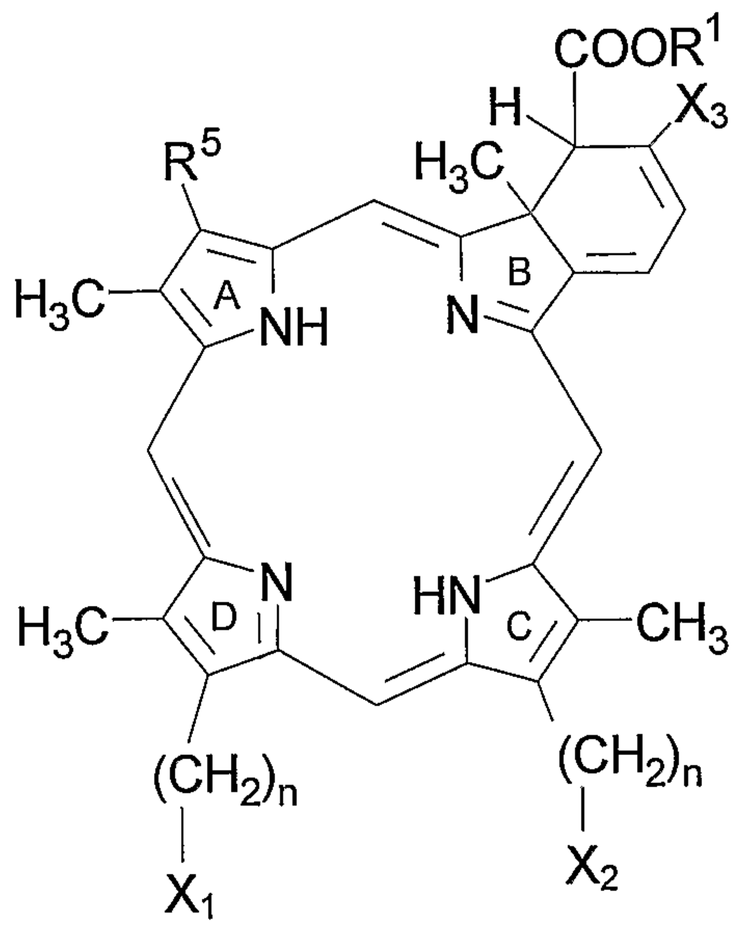
As used herein, "photosensitizer" or "photosensitizing agent" means a chemical compound which, when accumulated in selected target tissues and contacted by radiation, absorbs the light and induces changes to, or destruction of, the target. Virtually any chemical compound that ca be taken up by target cells or tissues and absorbs light may be used in this invention. Preferably, the chemical compound is nontoxic to the animal to which it is administered or is capable of being formulated in a nontoxic composition. Preferably, the chemical compound in its photodegraded form is also nontoxic. A listing of photosensitive chemicals may be found in Kreimer-Birnbaum, Sem. Hematol. 26:157-73, 1989

and in Redmond and Gamlin, Photochem. Photbiol. 70 (4): 391-475 (1999).

In preferred embodiments of the invention, the photosensitizer is selected from a particularly potent group of photosensitizers known as green porphyrins, which are described in detail in U.S. Patent No. 5,171,749 (incorporated herein by reference). The term "green porphyrins" refers to porphyrin derivatives obtained by reacting a

porphyrin nucleus with an alkyne in a Diels-Alder type reaction to obtain a mono-hydrobenzoporphyrin. Such resultant macropyrrolic compounds are called benzoporphyrin derivatives (BPDs), which is a synthetic chlorin-like porphyrin with various structural analogues, as shown in U.S. Patent 5,171,749. Typically, green porphyrins are selected from a group of tetrapyrrolic porphyrin derivatives obtained by Diels-Alder reactions of acetylene derivatives with protoporphyrin under conditions that promote reaction at only one of the two available conjugated, nonaromatic diene structures present in the protoporphyrin-IX ring systems (rings A and B). Metallated forms of a Gp, in which a metal cation replaces one or two hydrogens in the center of the ring system, may also be used in the practice of the invention. The preparation of the green porphyrin compounds useful in this invention is described in detail in U.S. Patent No. 5,095,030.

Preferably, the BPD is a benzoporphyrin derivative diester di-acid (BPD-DA), mono-acid ring A (BPD-MA), mono-acid ring B (BPD-MB), or mixtures thereof. These compounds absorb light at about 692nm wavelength and have improved tissue penetration properties. The compounds of formulas BPD-MA and BPD-MB may be homogeneous, in which only the C ring carbalkoxyethyl or only the D ring carbalkoxyethyl would be hydrolyzed, or may be mixtures of the C and D ring substituent hydrolyzates. A number of other BPD B-ring derivatives may also be used in the present methods. These derivatives have the following general formula:



wherein; R^5 is vinyl, R^1 and R^6 are methyl, and n is 2. X_1, X_2, and X_3 are listed in the tables below:

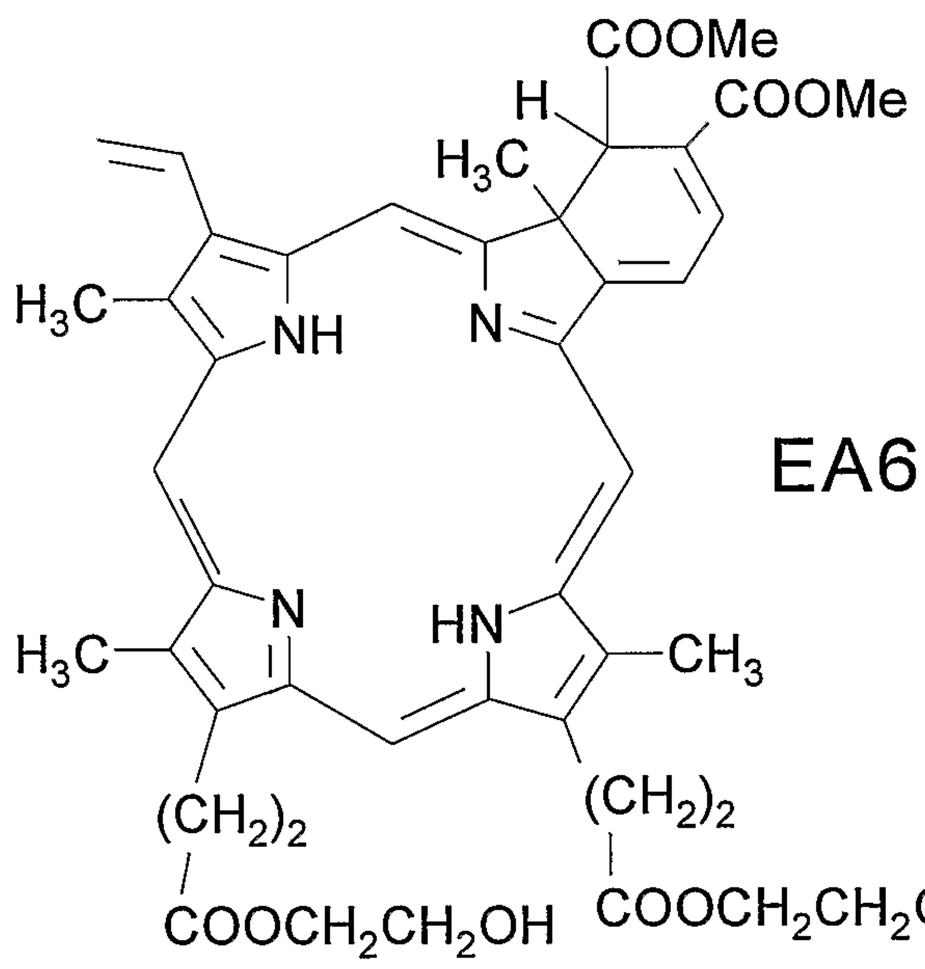
Table 1. Hydrophilic BPD B-ring analogs

Drug	X_1	X_2	X_3
QLT0061	COOH	COOH	COOH
QLT0077	$CONH(CH_2)_2N^+(CH_3)_3I^-$	$CONH(CH_2)_2N^+(CH_3)_3I^-$	$COOCH_3$
QLT0079	$CONH(CH_2)_2N^+(CH_3)_2((CH_2)_3CH_3$	$CONH(CH_2)_2N^+(CH_3)_2((CH_2)_3CH_3)$	$COOCH_3$
QLT0086	$CONHCH(COOH)CH_2COOH$	$CONHCH(COOH)CH_2COOH$	$COOCH_3$
QLT0092	$CONH(CH_2)_2NH(CH_3)_2$ CF_3COO^-	$CONH(CH_2)_2NH(CH_3)_2$ CF_3COO-	$COOCH_3$
QLT0094	$CONHCH_2COOH$	$CONHCH_2COOH$	$CONHCH_2COOH$

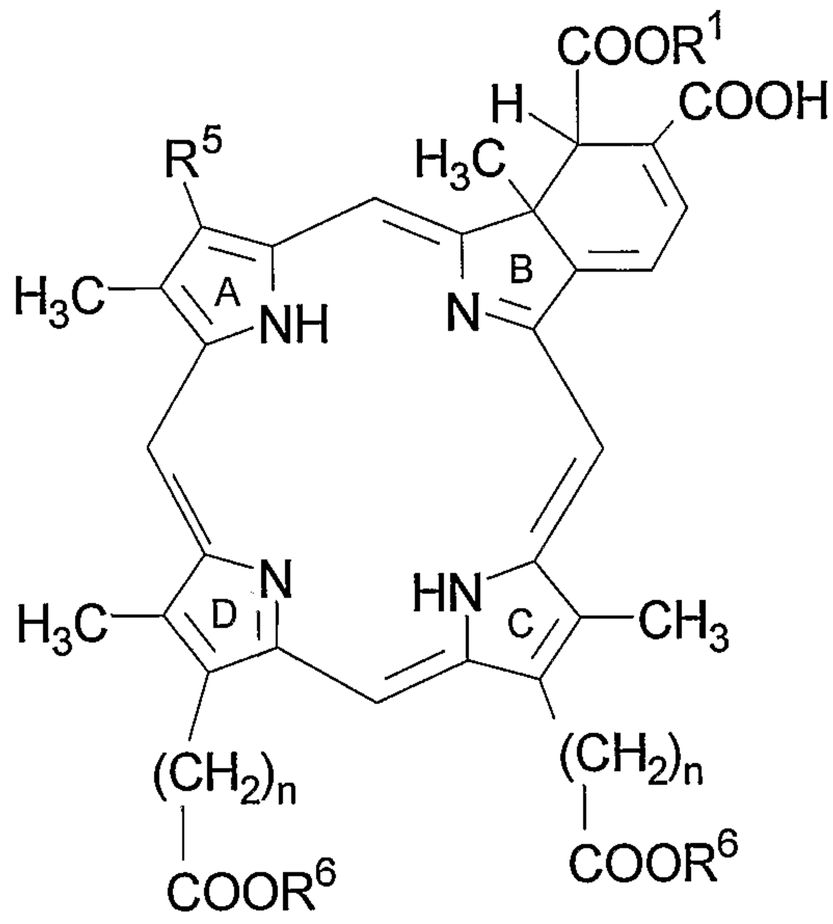
Table 2. Lipophilic BPD B-ring analogs

Drug	X1	X2	X3
QLT0060	$CO(O(CH_2)_2)0H$	$CO(O(CH_2)_2)0H$	$COOCH_3$
QLT0069	$COOCH_3$	$COOCH_3$	COOH
QLT0074	$CO(OCH_2CH_2)0H$	$CO(OCH_2CH_2)0H$	$COOCH_3$
QLT0078	$CO(O(CH_2)_2)_20H$	$CO(O(CH_2)_2)_20H$	$COOCH_3$
QLT0080	$CO(O(CH_2)_2)_3OH$	$CO(O(CH_2)_2)_3OH$	$COOCH_3$
QLT0081	$CO(O(CH_2)_2)_2OCH_3$	$CO(O(CH_2)_2)_2OCH_3$	$CO(O(CH_2)_2)_2OCH_3$
QLT0082	$CO(O(CH_2)_2)_2OH$	$CO(O(CH_2)_2)_2OH$	$CO(O(CH_2)_2)_2OH$
QLT0083	$CO(O(CH_2)_2)_3OH$	$CO(O(CH_2)_2)_3OH$	$CO(O(CH_2)_2)_3OH$
QLT0087	$CO(O(CH_2)_2)_4OH$	$CO(O(CH_2)_2)_4OH$	$COOCH_3$
QLT0088	$COOCH_3$	$COOCH_3$	$CONH(C_6H_4)(C_5H_{10}N)$
QLT0090	$CO(O(CH_2)_2)_5OH$	$CO(O(CH_2)_2)_5OH$	$COOCH_3$
QLT0093	$CO(O(CH_2)_2)_5OH$	$CO(O(CH_2)_2)_5OH$	$CO(O(CH_2)_2)_5OH$

Preferred photosensitizers are the benzoporphyrin derivative mono-acid (BPD-MA), EA6, also known as QLT 0074, (as set forth in U.S.5,929,105) and B3 (as set forth in U.S. Pat. No. 5,990,149). BPD-MA, for example, is lipophilic and a potent photosensitizer. EA6 and B3 have the following structures:



EA6



wherein; R^5 is vinyl, R^1 and R^6 are methyl, and n is 0, 1, 2, or 3. Preferably, n is 2.

Additionally, the photosensitizers used in the invention may be conjugated to various ligands to facilitate targeting. These ligands include receptor-specific ligands as well as immunoglobulins and fragments thereof. Preferred ligands include antibodies in general and monoclonal antibodies, as well as immunologically reactive fragments of both.

Dimeric forms of the green porphyrin and dimeric or multimeric forms of green porphyrin/porphyrin combinations can be used. The dimers and oligomeric compounds of the invention can be prepared using reactions analogous to those for dimerization and oligomerization of porphyrins *per se*. The green porphyrins or green porphyrin/porphyrin linkages can be made directly, or porphyrins may be coupled, followed by a Diels-Alder reaction of either or both terminal porphyrins to convert them to the corresponding green porphyrins. Of course combinations of two or more photosensitizers may be used in the practice of the invention.

In addition to the above mentioned preferred photosensitizing agents, additional examples of photosensitizers useful in the invention include, but are not limited to, green porphyrins disclosed in US Pat. Nos. 5,283,255, 4,920,143, 4,883,790, 5,095,030, and 5,171,749; and green porphyrin derivatives, discussed in US Pat.

Nos. 5,880,145 and 5,990,149. Several structures of typical green porphyrins are shown in the above cited patents, which also provide details for the production of the compounds.

The amount of photosensitizer used herein will depend on a variety of factors such as the specific type of PS and the type of activation energy source. However, it is preferred that the compositions herein comprise from about 0.0001% to about 50%, more preferably from about 0.001% to about 5%, even more preferably from about 0.01% to about 2%, still more preferably from about 0.1% to about 1%, by weight, of photosensitizer.

Skin-Penetration Enhancer

The compositions herein must comprise a skin-penetration enhancer. As used herein, the term "skin-penetration enhancer" means a substance or mixture of substances that aids in the delivery of the photosensitizing agent through the Stratum Corneum of the skin.

Any skin-penetration enhancer suitable for aiding the delivery of the photosensitizing agent can be used herein. A list of skin-penetration enhancers can be found in "Pharmaceutical Skin Penetration Enhancement" (1993) Walters, K.A., ed.; Hadgraft, J., ed - New York, N.Y. Marcel Dekker and in "Skin Penetration Enhancers cited in the Technical Literature" Osbourne, D.W. Pharmaceutical Technology, November 1997, pp 59-65.

Highly preferred for use in the compositions herein are hydrophobic skin-penetration enhancers.

Preferred skin-penetration enhancers are selected from glycol ethers, fatty acids, fatty acid esters, glycol esters, glycerides, azones, polysorbates, alcohols, dimethylsulfoxide, and mixtures thereof.

Preferred skin-penetration enhancers for use herein include, but are not limited to, diethylene glycol monoethyl ether (Transcutol®), Oleyl alcohol, Oleic acid, Azone (Laurocapram or 1-n-Dodecyl azacycloheptan-2-one), Propylene glycol mono- and

diesters of fats and fatty acids (e.g. propylene glycol monocaprylate, propylene glycol monolaurate), Triglycerides and lipids (e.g. linoleic acid), Macrogolglycerides or Polyethylene glycol glycerides and fatty esters (e.g. stearoyl macrogolglycerides, oleoyl macrogolglycerides, lauroyl macrogolglycerides, Oleyl macrogol-6-glycerides, Lauroyl macrogol-6 glycerides), Glycerides and fatty acid esters of polyethylene glycol (e.g. caprylocaproyl macrogolglycerides, capryl-caproyl macrogolglycerides, oleoyl macrogolglycerides), Polyoxyl 40 Hydrogenated Castor Oil (Cremophor™ RH 40), Polysorbate 80 (Tween™ 80), Dodecylazacycloheptanone, SEPA® such as described in US Patent 4,861,764 (e.g. 2-n-nonyl-1,3-dioxolane), and mixtures thereof.

Most preferred is diethylene glycol monoethyl ether (available from Gattefosse under the tradename Transcutol).

It is preferred that the compositions herein comprise from about 0.1% to about 99%, preferably from about 0.1% to about 90%, more preferably from about 5% to about 90%, even more preferably from about 15% to about 75%, by weight of skin penetration enhancer.

It is preferred that the ratio of photosensitizer to skin-penetration enhancer is from about 1:20 to about 1:10000 , more preferably from about 1:60 to 1:300, on the basis of percentages by weight of total composition.

It is highly preferred that the compositions of the present invention have a viscosity at 20°C of from about 50 cps to about 50000 cps, more preferably from about 500 cps to about 40000 cps, even more preferably from about 5000 cps to about 30000 cps.

Solubilizer

It is highly preferred that the compositions herein comprise a solubilizer. This is especially true when the photosensitizer is hydrophobic. Some solubilizers are also penetration enhancers and it is preferred that the compositions herein comprise a penetration enhancer that is also a solubilizer for the photosensitizer.

Preferably the solubilizer is selected from glycol ethers, polyethylene glycol, polyethylene glycol derivatives, propylene glycol, propylene glycol derivatives, fatty alcohols, aromatic alcohols, propylene glycol, glycerols, oils, surfactants, glucosides, and mixtures thereof.

More preferably the solubilizer is selected from diethylene glycol monoethyl ether (Transcutol®), polyethylene glycol of average molecular weight from 100 to 5000, triethylene glycol, tetraethylene glycol, pentaethylene glycol, hexaethylene glycol, septaethylene glycol, octaethylene glycol, propylene glycol, propylene glycol mono- and diesters of fats and fatty acids (e.g. propylene glycol monocaprylate, propylene glycol monolaurate), benzyl alcohol, glycerol, oleyl alcohol, mineral oil, lanolin/lanolin derivatives, petrolatum or other petroleum products suitable for application to the skin, propylene glycol mono- and diesters of fats and fatty acids, macrogols, macrogolglycerides or polyethylene glycol glycerides and fatty esters (e.g. stearoyl macrogolglycerides, oleoyl macrogolglycerides, lauroyl macrogolglycerides, linoleoyl macrogolglycerides), ethoxylated castor oil (e.g. Cremophor – a polyoxyl hydrogenated castor oil), C6-C30 triglycerides, natural oils, glucosides (e.g. cetearyl glucoside), surfactants, polyethylene glycol of average molecular weight from 200 to 4000, and mixtures thereof.

More preferable the solubilizer is selected from diethylene glycol monoethyl ether (Transcutol®), PEG-200, oleyl alcohol, and mixtures thereof.

It is preferred that the compositions herein comprise from about 0.1% to about 99%, more preferably from about 1% to about 75%, by weight of solubilizer.

Viscosity Modifying Agents

The compositions herein preferably comprise a viscosity modifying agent. Preferred viscosity modifiers are selected from polyethylene glycols, acrylic acid-based polymers (carbopol™ polymers or carbomers), polymers of acrylic acid crosslinked with allyl sucrose or allylpentaerythritol (carbopol homopolymers), polymers of acrylic acid modified by long chain (C10-C30) alkyl acrylates and crosslinked with allylpentaerythritol (carbopol copolymers), poloxamers also known

as pluronics (block polymers; e.g. Poloxamer 124, 188, 237, 338, 407), waxes (paraffin, glyceryl monostearate, diethylene glycol monostearate, propylene glycol monostearate, ethylene glycol monosterate, glycol stearate), hard fats (e.g. Saturated C8-C18 fatty acid glycerides), xantham gum, polyvinyl alcohol, solid alcohols, and mixtures thereof. More preferably the viscosity modifiers are selected from high molecular weight polyethylene glycols, especially PEG-3350.

Optional Ingredients

The compositions herein may comprise a variety of optional components. Any suitable ingredient may be used herein but typically these optional component will render the compositions more cosmetically acceptable or provide additional usage benefits. Some examples of preferred optional ingredients include, but are not limited to, emulsifiers, humectants, emollients, surfactants, oils, waxes, fatty alcohols, dispersants, skin-benefit agents, pH adjusters, dyes/colourants, analgesics, perfumes, preservatives, and mixtures thereof.

Examples of suitable preservatives include but are not limited to parabens, benzyl alcohol, quaternium 15, imidazolidyl urea, disodium EDTA, methylisothiazoline, alcohols, and mixtures thereof. Examples of suitable emulsifiers include but are not limited to waxes, sorbitan esters, polysorbates, ethoxylated castor oil, ethoxylated fatty alcohols, macrogolglycerides or polyethylene glycol glycerides and fatty esters (e.g. stearoyl macrogolglycerides, oleoyl macrogolglycerides, lauroyl macrogolglycerides), esters of saturated fatty acids (e.g. diethylene glycol parmitostearate), macrogols of cetostearyl ether (e.g. macrogol-6-cetostearyl ether), polymers of high molecular weight, crosslinked acrylic acid-based polymers (carbopols or carbomers) , and mixtures thereof. Examples of suitable emollients include but are not limited to propylene glycol dipelargonate, 2-octyldodecyl myristate, non-polar esters, triglycerides and esters (animal and vegetable oils), lanolin, lanolin derivatives, cholesterol, glucosides (e.g. cetearyl glucoside), pegylated lanolin, ethoxylated glycerides, and mixtures thereof. Examples of suitable surfactants include but are not limited to sorbitan esters, polysorbates, sarcosinates, taurate, ethoxylated castor oil, ethoxylated fatty alcohols, ethoxylated glycerides, caprylocaproyl macrogol-8 glycerides, polyglyceryl-6 dioleate, and

mixtures thereof. Examples of suitable oils include but are not limited to propylene glycol monocaprylate, medium chain triglycerides (MCT), 2-octyl-dodecyl myristate, cetearyl ethylhexanoate, and mixtures thereof. Examples of suitable fatty alcohols include but are not limited to cetostearyl alcohol, cetyl alcohol, stearyl alcohol, and mixtures thereof.

Also useful in the compositions herein are lipids and triglycerides (e.g. concentrates of Seed Oil Lipids, Concentrates of Marine Oil Lipids, high purity triglycerides and esters), alkyl ether sulfates, alkyl polyglycosides, alkylsulfates, amphoterics cream bases, and mixtures thereof.

A preferred embodiment of the present invention comprises green-porphyrin photosensitizer, low molecular weight PEG such as PEG200, diethylene glycol monoethyl ether (Transcutol®), high molecular weight PEG such as PEG3350 and fatty alcohol such as oleyl alcohol. While not wishing to be bound by theory it is believed that the PEG3350 acts as a viscosity modifier while the Transcutol, PEG 200, and oleyl alcohol act to deliver the photosensitizer through the stratum corneum.

Method of Use

The present invention also relates to a method of using a compositions as described hereinabove. Said method comprises:

(i) applying to the skin a composition comprising a photosensitizing agent and a carrier wherein the carrier comprises a skin-penetration enhancer,

(ii) allowing time for at least some of the photosensitizer to penetrate through the stratum corneum,

(iii) washing the skin to which the composition has been applied, and

(iv) irradiating with activation energy at a wavelength appropriate to activate the photosensitizer.

The washing step can be performed with any suitable substance.

The washing step can be performed using a composition comprising at least one of the ingredients of the carrier. Preferably, the wash composition comprises two or more, more preferably all, of the ingredients of the carrier. It is preferred that the levels of ingredient(s) in the wash composition are at the same or similar levels as in the carrier.

While not wishing to be bound by theory, it is believed that the washing step removes excess photosensitizer which might otherwise mask the target preventing the activation energy from reaching the target. The utilization of a composition similar to the carrier is believed to aid with the penetration of the photosensitizer composition through the creation of a concentration gradient.

Process

The present compositions can be made by any suitable process. Preferably, the photosensitizer is lyophilized. A preferred process for production of the present compositions comprises:

a) Preparation of lyophilized photosensitizer,
b) Manufacture of base composition comprising a skin penetration enhancer and, optionally, a solubilizer,
c) Addition of the photosensitizer to the base with stirring.

In an alternative process the photosensitizer is first dissolved in a solubilizer with heating. As mentioned above it is preferred that the solubilizer is also a skin-penetration enhancer. After cooling any remaining ingredients are added.

Method of Treatment

The compositions of the present invention may be used for promoting hair growth. The present method comprises applying a composition of the present invention to a suitable target and activating the photosensitizing agent. Typically, from about 0.1g to about 50g, preferably from about 1g to about 10g, of the composition is applied to the target. The activation energy can be from an suitable energy source.

The compositions of the present invention can be used for the treatment of androgenetic alopecia. The present method comprises applying a composition of the present invention to a suitable target and activating the photosensitizing agent. Typically, from about 0.1g to about 50g, preferably from about 1g to about 10g, of the composition is applied to the target. The activation energy can be from an suitable energy source.

The compositions of the present invention can be used for the treatment of alopecia areata. The present method comprises applying a composition of the present invention to a suitable target and activating the photosensitizing agent. Typically, from about 0.1g to about 50g, preferably from about 1g to about 10g, of the composition is applied to the target. The activation energy can be from an suitable energy source.

The compositions of the present invention can be used for the treatment of skin cancers. The present method comprises applying a composition of the present invention to a suitable target and activating the photosensitizing agent. Typically, from about 0.1g to about 50g, preferably from about 1g to about 10g, of the composition is applied to the target. The activation energy can be from an suitable energy source.

The compositions of the present invention can be used for the treatment of acne. The present method comprises applying a composition of the present invention to a suitable target and activating the photosensitizing agent. Typically, from about 0.1g to about 50g, preferably from about 1g to about 10g, of the composition is applied to the target. The activation energy can be from an suitable energy source.

The compositions of the present invention can be used for the treatment of psoriasis. The present method comprises applying a composition of the present invention to a suitable target and activating the photosensitizing agent. Typically, from about 0.1g to about 50g, preferably from about 1g to about 10g, of the composition is applied to the target. The activation energy can be from an suitable energy source.

The composition of the present invention can be used for the treatment of dermatitis.

The compositions of the present invention can be used for the treatment of atopic dermatitis. The present method comprises applying a composition of the present invention to a suitable target and activating the photosensitizing agent. Typically, from about 0.1g to about 50g, preferably from about 1g to about 10g, of the composition is applied to the target. The activation energy can be from an suitable energy source.

The compositions of the present invention can be used for the treatment of endometrial ablation. The present method comprises applying a composition of the present invention to a suitable target and activating the photosensitizing agent. Typically, from about 0.1g to about 50g, preferably from about 1g to about 10g, of the composition is applied to the target. The activation energy can be from an suitable energy source.

Examples

It will be understood that the following embodiments of the present invention are intended to be illustrative of some of the possible applications or principles. Various modifications may be made by the skilled person without departing from the true spirit and scope of the invention.

	Example 1 (wt%)	Example 2 (wt%)	Example 3 (wt%)	Comparative Example (wt%)
QLT0074	0.5	0.25	0.75	0.5
PEG-200	54	50	58	54
Transcutol®[1]	20	24	16	0
PEG-3350	15.5	10	15.5	15.5
Oleyl Alcohol	10	15.75	10	30

[1] Diethylene glycol monethyl ether available from Gattefosse Canada Inc., Baie D'Urfé, Québec, H9X 2T3, Canada

The above compositions were prepared in the following way:

a) Preparation of cryodessicated photosensitizer – the QLT0074 is dissolved in Glacial Acetic Acid. The solution is then frozen in a dry ice/isopropanol bath and the acetic acid is removed by lyophilization. The resultant material is a fine fluffy powder which goes into topical solution easily.

b) Manufacture of base – the PEG 200 is warmed to 80-90 °C with stirring. PEG 3.35K is added with stirring followed by oleyl alcohol, then where present the transcutol®. Stirring is continued until solution is clear.

c) Addition of photosensitizer - base composition is cooled to approx. 50 °C and the photosensitizer is added with stirring. Stirring is continued with cooling until homogeneous paste is achieved. The resulting formulation is checked for the absence of undissolved photosensitizer crystals by phase contrast microscopy.

It was found that Examples 1-3 gave good penetration of the QLT0074 through the stratum corneum while the comparative example did not.

Claims:

1. A composition comprising green-porphyrin photosensitizer, one or more polyethylene glycol of average molecular weight from 100-5000, diethylene glycol monoethyl ether and fatty alcohol.

2. The composition of claim 1, wherein the photosensitizer is benzoporphyrin derivative known as EA6.

3. The composition of claim 1, wherein the one or more polyethylene glycol has an average molecular weight from 200-4000.

4. The composition according to claim 1 where the photosensitizer is present at a level of from 0.0001% to 50% by weight of photosensitizer.

5. The composition according to claim 1 where the diethylene glycol monoethyl ether and fatty alcohol are present at a level of from 0.1% to 90% by weight of diethylene glycol monoethyl ether and fatty alcohol.

6. The composition according to claim 1 wherein the composition has a viscosity at 20°C of from 50 cps to 50000 cps.

7. The use of the composition according to any one of claims 1 to 6 for application to the skin for the purposes of photodynamic therapy.

8. Use of the composition according to any one of claims 1 to 6 for photodynamic treatment of androgenetic alopecia, alopecia areata, skin cancers, acne, psoriasis, atopic dermatitis, or endometrial ablation.

9. Use of the composition according to any one of claims 1 to 6 for manufacture of a medicament for photodynamic treatment of androgenetic alopecia, alopecia areata, skin cancers, acne, psoriasis, atopic dermatitis, or endometrial ablation.

10. The composition according to any one of claims 1 to 6 for use in photodynamic treatment of androgenetic alopecia, alopecia areata, skin cancers, acne, psoriasis, atopic dermatitis, or endometrial ablation.

11. Use of the composition according to any one of claims 1-6 in conjunction with irradiation with activation energy of appropriate wavelength to activate the photosensitizer for treating androgenetic alopecia, alopecia areata, skin cancers, acne, psoriasis, atopic dermatitis, or

endometrial ablation.

12. The use according to any one of claim 8, 9 and 11, or the composition of claim 10, wherein the treatment is for acne.

13. Use of the composition according to any one of claims 1-6 for the promotion of hair growth.

14. Use of the composition according to any one of claims 1-6 for the promotion of hair growth in conjunction with irradiation with activation energy of appropriate wavelength to activate the photosensitizer.

15. Use of the composition according to any one of claims 1-6 for photodynamic therapy, wherein the composition is suitable for application to skin in conjunction with irradiation with activation energy of appropriate wavelength to activate the photosensitizer, after penetration of at least some of the photosensitizer through the stratum corneum and washing of the skin.

16. A cosmetic method of photodynamic therapy comprising:

(i) applying to skin the composition according to any one of claims 1-6,

(ii) allowing time for at least some of the photosensitizer to penetrate through the stratum corneum,

(iii) washing the skin to which the composition has been applied, and

(iv) irradiating with activation energy at a wavelength appropriate to activate the photosensitizer.

17. A process of the manufacture of a composition according to claim 1, said process comprising:

(a) preparing a lyophilized green-porphyrin photosensitizer,

(b) manufacturing a base composition comprising one or more polyethylene glycol of average molecular weight from 100-5000, a diethylene glycol monoethyl ether and fatty alcohol and,

(c) adding the lyophilized photosensitizer to the base composition with stirring.

18. Use of the composition according to any one of claims 1-6 for the treatment of acne.