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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
18 September 2014 (18.09.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/138930 A1

(51) International Patent Classification:
A61K 41/00 (2006.01) *A61N 5/06* (2006.01)
A61K 8/02 (2006.01) *A61P 17/00* (2006.01)
A61K 9/00 (2006.01) *A61P 17/02* (2006.01)
A61L 15/42 (2006.01) *A61Q 19/08* (2006.01)

(21) International Application Number:
PCT/CA2014/000261

(22) International Filing Date:
14 March 2014 (14.03.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/786,197 14 March 2013 (14.03.2013) US
61/873,747 4 September 2013 (04.09.2013) US
14/204,741 11 March 2014 (11.03.2014) US

(71) Applicant: **KLOX TECHNOLOGIES INC.** [CA/CA]; 275 Boulevard Armand-Frappier, Laval, Quebec H7V 4A7 (CA).

(72) Inventors: **LOUPIS, Nikolaos**; Kifissias 228 Avenue, 14562 Kifissia, Athens (GR). **PIERGALLINI, Remigio**; Via Bologna 11, 63038 Grottammare (IT). **DESROSIERS, Éric**; 1132 St-Viateur, Montréal, Québec H2V 1Y7 (CA).

(74) Agent: **SMART & BIGGAR**; 1000 de la Gauchetière Street West, Suite 3300, Montréal, Québec H3B 4W5 (CA).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

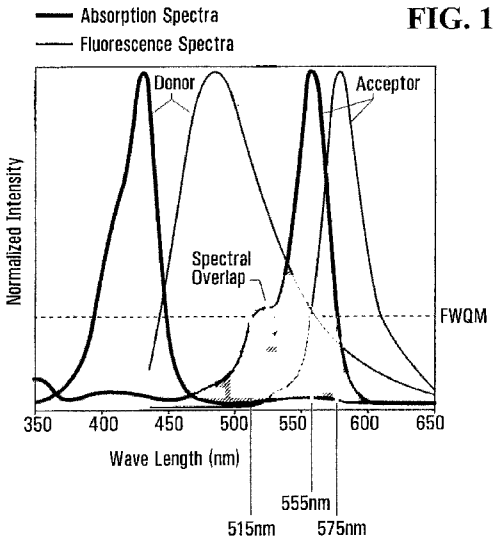
Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(54) Title: BIOPHOTONIC MATERIALS AND USES THEREOF

FIG. 1



(57) Abstract: The present disclosure provides topical biophotonic materials and methods useful in phototherapy. In particular, the topical biophotonic materials of the present disclosure include a cohesive matrix, and at least one chromophore which can absorb and emit light from within the topical biophotonic material, wherein the topical biophotonic material is elastic. The topical bio-photonic materials and the methods of the present disclosure are useful for promoting wound healing and skin rejuvenation, as well as treating acne and various other skin disorders.

WO 2014/138930 A1

BIOPHOTONIC MATERIALS AND USES THEREOF

FIELD OF THE INVENTION

The present disclosure generally relates to biophotonic materials for phototherapy.

BACKGROUND OF THE DISCLOSURE

Phototherapy has recently been recognized as having wide range of applications in both the medical and cosmetic fields including use in surgery, therapy and diagnostics. For example, phototherapy has been used to treat cancers and tumors with lessened invasiveness, to disinfect target sites as an antimicrobial treatment, to promote wound healing, and for facial skin rejuvenation.

Photodynamic therapy is a type of phototherapy involving the application of a photosensitive agent to target tissue then exposing the target tissue to a light source after a determined period of time during which the photosensitizer is absorbed by the target tissue. Such regimens, however, are often associated with undesired side-effects, including systemic or localized toxicity to the patient or damage to non-targeted tissue. Moreover, such existing regimens often demonstrate low therapeutic efficacy due to, for example, the poor selectivity of the photosensitive agents into the target tissues.

Therefore, it is an object of the present disclosure to provide new and improved compositions and methods useful in phototherapy.

SUMMARY OF THE DISCLOSURE

The present disclosure provides topical biophotonic materials and methods useful in phototherapy.

In particular, the biophotonic materials of the present disclosure include a cohesive matrix, and at least one chromophore, wherein the at least one chromophore can absorb and emit light from within the biophotonic material. In certain embodiments of any of the foregoing or following, the biophotonic material is an elastic material.

From another aspect, there is provided a topical biophotonic material comprising: a cohesive matrix, and at least one chromophore which can absorb and emit light from within the biophotonic material, wherein the topical biophotonic material is a peelable film.

From another aspect, there is provided a topical biophotonic material comprising: a cohesive matrix, and at least one chromophore which can absorb and emit light from within the biophotonic material, wherein the topical biophotonic material is elastic.

From yet another aspect, there is provided a topical biophotonic material comprising: a cohesive matrix, and at least one chromophore which can absorb and emit light from within the biophotonic material, wherein the topical biophotonic material is rigid.

From another aspect, there is provided a topical biophotonic material comprising: a cohesive matrix, and at least one chromophore which can absorb and emit light from within the biophotonic material, wherein a tear and/or a tensile strength of the topical biophotonic material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied.

From a yet further aspect, there is provided a topical biophotonic material comprising: a cohesive matrix, and at least one chromophore which can absorb and emit light from within the biophotonic material, wherein the topical biophotonic material has a well-defined shape under steady state conditions.

From another aspect, there is provided a topical biophotonic material comprising: a cohesive matrix, and at least one chromophore which can absorb and emit light from within the biophotonic material, wherein the topical biophotonic material is a mask or a dressing. In certain embodiments, the mask and/or the dressing has a pre-formed configuration. In certain embodiments, the mask and/or the dressing is elastic. In certain embodiments, the mask and/or the dressing is rigid.

From another aspect, there is provided a biophotonic material comprising: a cohesive matrix, and at least one chromophore which can absorb and emit light from within the biophotonic material, wherein the biophotonic material has a pre-formed configuration

which is a shape and/or a size corresponding with a shape and/or a size of a light source or lamp to which the biophotonic material can be attached.

In certain embodiments of the above aspects, the biophotonic material is a peelable film. In some embodiments, the biophotonic material is rigid.

In certain embodiments of any of the foregoing or following, the biophotonic material has a tear and/or a tensile strength greater than an adhesive strength of the biophotonic material to a surface to which it is applied. The adhesive strength may comprise a force required to overcome static friction.

In certain embodiments of any of the foregoing or following, the biophotonic material is at least substantially translucent. The biophotonic material may be transparent. In some embodiments, the biophotonic material has a translucency of at least about 40%, about 50%, about 60%, about 70%, or about 80% in a visible range. Preferably, the light transmission through the material is measured in the absence of the at least one chromophore.

In certain embodiments of any of the foregoing or following, the biophotonic material has a thickness of about 0.1 mm to about 50 mm, about 0.5 mm to about 20 mm, or about 1 mm to about 10 mm.

In certain embodiments of any of the foregoing or following, the biophotonic material has a pre-formed configuration. In some embodiments, the pre-formed configuration is a shape and/or a size corresponding with a shape and/or a size of a body part to which the biophotonic material can be applied. In some embodiments, the body part to which the material is applied is a head, scalp, forehead, nose, cheeks, ears, lip, face, neck, shoulder, arm pit, arm, elbow, hand, finger, abdomen, chest, stomach, back, sacrum, buttocks, genitals, legs, knee, feet, nails, hair, toes, or bony prominences, or combinations thereof.

In certain embodiments of any of the foregoing or following, the biophotonic material is a mask. In some embodiments, the mask is a face mask having at least one opening for the eyes, nose or mouth. In certain embodiments, the mask is disposable. The mask may

also be reusable. The chromophore may at least substantially photobleach after a single use or single light illumination.

In certain embodiments of any of the foregoing or following, the biophotonic material has a pre-formed configuration and the pre-formed configuration is a shape and/or a size corresponding with a shape and/or a size of a light source or lamp to which the biophotonic material can be attached.

In certain embodiments of any of the foregoing or following, the biophotonic material can be removed without leaving substantially any residue on a surface to which the biophotonic material is applied.

In certain embodiments of any of the foregoing or following, the at least one chromophore included in the biophotonic material is a fluorophore. In certain embodiments, the chromophore can absorb and/or emit light within the visible range. The chromophore may be water soluble. In certain embodiments, the chromophore can emit light from around 500 nm to about 700 nm. In some embodiments, the chromophore or the fluorophore is a xanthene dye. The xanthene dye may be selected from Eosin Y, Erythrosine B, Fluorescein, Rose Bengal and Phloxin B In some embodiments, the chromophore is included in the cohesive matrix. In certain embodiments of any of the foregoing or following, the cohesive matrix is in particulate form.

In certain embodiments of any of the foregoing or following, the cohesive matrix of the biophotonic material comprises at least one polymer. In some embodiments, the polymer is selected from a cross-linked polyacrylic polymer, a hyaluronate, a hydrated polymer, a hydrophilic polymer and a liposoluble polymer. In some embodiments, the cohesive matrix comprises sodium hyaluronate. In some embodiments, sodium hyaluronate is present in an amount of about 2% to about 8%.

In certain embodiments, the cohesive matrix is a liposoluble polymer, such as silicone. The chromophore(s) may be water soluble and be within an aqueous phase within the liposoluble polymer. In this case, the biophotonic material comprises an aqueous phase containing the chromophore within the liposoluble polymer phase. The aqueous phase

may comprise about 2 wt% to about 40 wt% of the liposoluble polymer phase. The aqueous phase may be a liquid or a gel. The biophotonic material may further comprise a stabilizing agent such as CMC or gelatin.

In certain embodiments, the cohesive matrix comprises gelatin or chitosan. In certain embodiments, the biophotonic material further comprises an oxygen-rich compound which may be selected from hydrogen peroxide, carbamide peroxide and benzoyl peroxide.

In some embodiments, the chromophore is included in a carrier medium which can form a cohesive matrix. In some embodiments, the chromophore can absorb and emit light within the cohesive matrix when illuminated with light. In some embodiments, the carrier medium is at least one polymer or a polymer pre-cursor which can form the cohesive matrix by polymerizing, cross-linking or drying.

From another aspect, there is provided a topical biophotonic material comprising a water soluble chromophore within an aqueous cohesive matrix, and wherein the aqueous cohesive matrix is dispersed within a liposoluble polymer. In certain embodiments, the liposoluble polymer is silicone. The aqueous phase may be a liquid or a gel. In certain embodiments, the aqueous cohesive matrix may be gelatin, water or carboxymethylcellulose. The chromophore may comprise a fluorophore, such as a xanthene dye selected from eosin y, fluorescein, erythrosine, Phloxine b and rose bengal. The aqueous phase may comprise about 2 wt% to about 40 wt% of the liposoluble polymer phase. In certain embodiments, the topical biophotonic material may be used to treat wounds, or to treat or prevent scarring.

The biophotonic material of any aspects and embodiments of the disclosure may be used as a mask, dressing or filter. The biophotonic material of any aspects or embodiments of the disclosure may also be used for cosmetic or medical treatment of tissue. In some embodiments, the cosmetic treatment is skin rejuvenation and conditioning, and the medical treatment is wound healing, periodontal treatment or acne treatment or treatment of other skin conditions including acne, eczema, psoriasis or dermatitis. In some aspects, the topical biophotonic material is used for modulating inflammation, or for promoting angiogenesis.

The present disclosure also provides containers comprising the biophotonic material or precursor material according to various embodiments of the disclosure. In some embodiments, the container comprises a sealed chamber for holding a biophotonic material, and an outlet in communication with the chamber for discharging the biophotonic material from the container, wherein the biophotonic material comprises at least one chromophore in a carrier medium which can form a cohesive matrix after being discharged from the sealed chamber. In some embodiments, the container is a spray can. The container may be opaque.

The present disclosure also provides kits for preparing or providing the biophotonic material or precursor according to various embodiments of the disclosure. In some embodiments, the kit comprises a first container comprising a first chromophore; and a second component comprising a thickening agent, wherein the thickening agent can form a cohesive matrix when mixed with the first component. In some embodiments, the second container may comprise an oxygen-rich compound.

The present disclosure also provides methods for biophotonic treatment comprising applying the topical biophotonic material of the disclosure to a target tissue and illuminating the material with light.

From one aspect, there is provided a method for biophotonic treatment of a skin disorder wherein the method comprises placing a biophotonic material on or over a target skin tissue, wherein the biophotonic material is elastic and comprises at least one chromophore and a cohesive matrix; and illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said biophotonic material emits fluorescence at a wavelength and intensity that promotes healing of said skin disorder. The skin disorder may be selected from acne, eczema, psoriasis or dermatitis.

From another aspect, there is provided a method for biophotonic treatment of a skin disorder comprising: placing a topical biophotonic material on or over a target skin tissue, wherein the biophotonic material comprises at least one chromophore and a cohesive matrix, and wherein a tear and/or tensile strength of the topical biophotonic material is greater than an adhesive strength of the topical biophotonic material to a

surface to which it is applied; and illuminating said topical biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said biophotonic material emits fluorescence at a wavelength and intensity that promotes healing of said skin disorder.

From another aspect, there is provided a method for biophotonic treatment of acne comprising: placing a topical biophotonic material on or over a target skin tissue, wherein the topical biophotonic material is elastic and comprises at least one chromophore and a cohesive matrix; and illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that treats the acne.

From another aspect, there is provided a method for biophotonic treatment of acne comprising: placing a topical biophotonic material on or over a target skin tissue, wherein the topical biophotonic material comprises at least one chromophore and a cohesive matrix, and wherein a tear and/or tensile strength of the topical biophotonic material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied; and illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that treats the acne.

From another aspect, there is provided a method for promoting wound healing comprising: placing a topical biophotonic material over or within a wound, wherein the topical biophotonic material is elastic and comprises at least one chromophore and a cohesive matrix; and illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes wound healing.

A method for promoting wound healing comprising: placing a topical biophotonic material over or within a wound, wherein the topical biophotonic material comprises at least one chromophore and a cohesive matrix; and wherein a tear and/or tensile strength

of the topical biophotonic material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied; and illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes wound healing.

From another aspect, there is provided a method for promoting skin rejuvenation comprising: placing a topical biophotonic material on or over a target skin tissue, wherein the topical biophotonic material is elastic and comprises at least one chromophore and a cohesive matrix; and illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes skin rejuvenation.

From another aspect, there is provided a method for promoting skin rejuvenation comprising: placing a topical biophotonic material on or over a target skin tissue, wherein the topical biophotonic material comprises at least one chromophore and a cohesive matrix; and wherein a tear and/or tensile strength of the topical biophotonic material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied; and illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes skin rejuvenation.

In certain embodiments, the biophotonic material is removed after illumination. In certain embodiments, the biophotonic material is peelable and is peeled off after illumination. In certain other embodiments, the biophotonic material is not peelable but can be removed in one or more pieces. The biophotonic material may be a mask or a dressing such a face mask or a wound dressing.

From another aspect, there is provided a method for promoting skin rejuvenation comprising: placing a topical biophotonic material which is a mask on or over a target skin tissue, wherein the topical biophotonic material comprises at least one chromophore and a cohesive matrix; and illuminating said biophotonic material with light having a

wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes skin rejuvenation.

In certain embodiments, the mask is a face mask having at least one opening for the eyes, nose or mouth. The mask may be disposable or reusable.

From another aspect, there is provided a method for promoting wound healing comprising: placing a topical biophotonic material which is a dressing over or within a wound, wherein the topical biophotonic material comprises at least one chromophore and a cohesive matrix; and illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes wound healing.

From another aspect, there is provided a method for preventing or treating scarring comprising: placing a topical biophotonic material which is a membrane over or within a wound, wherein the topical biophotonic material comprises at least one chromophore and a cohesive matrix; and illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes wound healing.

In certain embodiments, the biophotonic material is left in place after illumination for re-illumination. In certain embodiments, the chromophore at least partially photobleaches after illumination. In certain embodiments, the biophotonic material is illuminated until the chromophore is at least partially photobleached.

In certain embodiments, the topical biophotonic material is illuminated with visible light. In certain embodiments of any of the foregoing or following, the at least one chromophore included in the biophotonic material is a fluorophore. In certain embodiments, the chromophore can absorb and/or emit light within the visible range. The chromophore may be water soluble. In certain embodiments, the chromophore can emit light from around 500 nm to about 700 nm. In some embodiments, the

chromophore or the fluorophore is a xanthene dye. The xanthene dye may be selected from Eosin Y, Erythrosine B, Fluorescein, Rose Bengal and Phloxin B In some embodiments, the chromophore is included in the cohesive matrix.

In certain embodiments of any of the foregoing or following, the biophotonic material is at least substantially translucent. The biophotonic material may be transparent. In some embodiments, the biophotonic material has a translucency of at least about 40%, about 50%, about 60%, about 70%, or about 80% in a visible range. Preferably, the light transmission through the material is measured in the absence of the at least one chromophore. In certain embodiments of any of the foregoing or following, the biophotonic material has a thickness of about 0.1 mm to about 50 mm, about 0.5 mm to about 20 mm, or about 1 mm to about 10 mm.

BRIEF DESCRIPTION OF THE DRAWINGS

Further aspects and advantages of the present invention will become better understood with reference to the description in association with the following in which:

Figure 1 illustrates the absorption and emission spectra of donor and acceptor chromophores. The spectral overlap between the absorption spectrum of the acceptor chromophore and the emission spectrum of the donor chromophore is also shown.

Figure 2 is a schematic of a Jablonski diagram that illustrates the coupled transitions involved between a donor emission and acceptor absorbance.

Figure 3 is an emission fluorescence spectrum from an activated biophotonic material according to an embodiment of the present disclosure (Example 1).

Figure 4 is an emission fluorescence spectrum from a photoactivated biophotonic material irradiating fibroblasts and keratinocytes for evaluating protein regulation and gene expression (Example 2).

Figures 5a and 5b are emission fluorescence spectra for Eosin Y and Fluorescein, respectively, and the activating light passing through the composition, at different concentrations of the chromophores (Example 4).

Figures 6a and 6b are absorbance and emission spectra, respectively, of Eosin and Fluorescein in a gel (Example 5).

Figures 7a and 7b are absorbance and emission spectra, respectively, of Eosin, Fluorescein and Rose Bengal in a gel (Example 6).

Figures 8a and 8b are stress-strain curves of cohesive biophotonic materials according to embodiments of the present disclosure (Example 10).

DETAILED DESCRIPTION

(1) Overview

The present disclosure provides biophotonic materials and uses thereof. Biophotonic therapy using these materials would not involve substantial direct contact of a photosensitive agent (or chromophore) with the therapeutic target, which includes, but is not limited to, skin, mucous membranes, wounds, hair and nails. Therefore, undesired side effects caused by such direct contact may be reduced, minimized, or prevented. Furthermore, in certain embodiments, phototherapy using the biophotonic materials of the present disclosure will for instance rejuvenate the skin by, e.g., promoting collagen synthesis, promote wound healing, treat skin conditions such as acne, and treat periodontitis.

(2) Definitions

Before continuing to describe the present disclosure in further detail, it is to be understood that this disclosure is not limited to specific compositions or process steps, as such may vary. It must be noted that, as used in this specification and the appended claims, the singular form "a", "an" and "the" include plural referents unless the context clearly dictates otherwise.

As used herein, the term "about" in the context of a given value or range refers to a value or range that is within 20%, preferably within 10%, and more preferably within 5% of the given value or range.

It is convenient to point out here that "and/or" where used herein is to be taken as specific disclosure of each of the two specified features or components with or without the other. For example "A and/or B" is to be taken as specific disclosure of each of (i) A, (ii) B and (iii) A and B, just as if each is set out individually herein.

"Biophotonic" means the generation, manipulation, detection and application of photons in a biologically relevant context. In other words, biophotonic compositions and materials exert their physiological effects primarily due to the generation and manipulation of photons.

"Biophotonic material" is a material which may be activated by light to produce photons for biologically relevant applications. Biophotonic materials, as referred to herein, may be cohesive gels, semi-solids or solids. The biophotonic material can be in the form of, including, but not limited to, a film or the like, for uses such as a mask, a dressing or a light attachment. The biophotonic material can be a composite and include fibres, particulates, ribs, supporting structures, networks, non-biophotonic layers or biophotonic layers with the same or different compositions.

"Cohesive matrix" refers to a medium which is, or which can form, a self-supporting material e.g. a material with a defined shape under steady state conditions. This may be due to internal attractive forces. The property of cohesion in a material can allow the material to be handled without tearing.

"Topical application" or "topical uses" means application to body surfaces, such as the skin, mucous membranes, vagina, oral cavity, internal surgical wound sites, and the like.

Terms "chromophore" and "photoactivator" are used herein interchangeably. A chromophore means a chemical compound, when contacted by light irradiation, is capable of absorbing the light. The chromophore readily undergoes photoexcitation and can transfer its energy to other molecules or emit it as light (fluorescence).

"Photobleaching" or "photobleaches" means the photochemical destruction of a chromophore. A chromophore may fully or partially photobleach.

The term "actinic light" is intended to mean light energy emitted from a specific light source (e.g. lamp, LED, or laser) and capable of being absorbed by matter (e.g. the chromophore or photoactivator). In a preferred embodiment, the actinic light is visible light.

A "peel-off" or "peelable" film, membrane or matrix is one that can be mechanically removed, such as by hand, after application. It can be removed as a single piece, or as a small number of large pieces.

"Skin rejuvenation" means a process of reducing, diminishing, retarding or reversing one or more signs of skin aging or generally improving the condition of skin. For instance, increasing luminosity of the skin, reducing pore size, reducing fine lines or wrinkles, improving thin and transparent skin, improving firmness, improving sagging skin (such as that produced by bone loss), improving dry skin (which might itch), reducing or reversing freckles, age spots, spider veins, rough and leathery skin, fine wrinkles that disappear when stretched, reducing loose skin, or improving a blotchy complexion. According to the present disclosure, one or more of the above conditions may be improved or one or more signs of aging may be reduced, diminished, retarded or even reversed by certain embodiments of the compositions, methods and uses of the present disclosure.

"Wound" means an injury to any tissue, including for example, acute, subacute, delayed or difficult to heal wounds, and chronic wounds. Examples of wounds may include both open and closed wounds. Wounds include, for example, amputations, burns, incisions, excisions, lesions, lacerations, abrasions, puncture or penetrating wounds, surgical wounds, amputations, contusions, hematomas, crushing injuries, ulcers (such as for example pressure, diabetic, venous or arterial), wounds caused by periodontitis (inflammation of the periodontium).

Features and advantages of the subject matter hereof will become more apparent in light of the following detailed description of selected embodiments, as illustrated in the accompanying figures. As will be realized, the subject matter disclosed and claimed is capable of modifications in various respects, all without departing from the scope of the claims. Accordingly, the drawings and the description are to be regarded as illustrative

in nature, and not as restrictive and the full scope of the subject matter is set forth in the claims.

(3) Biophotonic Materials

The present disclosure provides, in a broad sense, topical biophotonic materials which are cohesive and methods of using the biophotonic materials. Biophotonic materials can be, in a broad sense, activated by light (e.g., photons) of specific wavelength. A biophotonic material according to various embodiments of the present disclosure contains a cohesive matrix and at least one chromophore in or on the cohesive matrix which is activated by light and accelerates the dispersion of light energy, which leads to light carrying on a therapeutic effect on its own, and/or to the photochemical activation of other agents contained in the composition (e.g., acceleration in the breakdown process of peroxide (an oxidant) when such compound is present in the composition or in contact with the composition, leading to the formation of oxygen radicals, such as singlet oxygen).

When a chromophore absorbs a photon of a certain wavelength, it becomes excited. This is an unstable condition and the molecule tries to return to the ground state, giving away the excess energy. For some chromophores, it is favorable to emit the excess energy as light when returning to the ground state. This process is called fluorescence. The peak wavelength of the emitted fluorescence is shifted towards longer wavelengths compared to the absorption wavelengths due to loss of energy in the conversion process. This is called the Stokes' shift. In the proper environment (e.g., in a biophotonic material) much of this energy is transferred to the other components of the biophotonic material or to the treatment site directly.

Without being bound to theory, it is thought that fluorescent light emitted by photoactivated chromophores may have therapeutic properties due to its femto-, pico-, or nano-second emission properties which may be recognized by biological cells and tissues, leading to favourable biomodulation. Furthermore, the emitted fluorescent light has a longer wavelength and hence a deeper penetration into the tissue than the activating light. Irradiating tissue with such a broad range of wavelength, including in some embodiments the activating light which passes through the composition, may have different and complementary effects on the cells and tissues. In other words,

chromophores are used in the biophotonic materials of the present disclosure for therapeutic effect on tissues. This is a distinct application of these photoactive agents and differs from the use of chromophores as simple stains or as catalysts for photo-polymerization.

The biophotonic materials of the present disclosure may have topical uses such as a mask or a wound dressing, or as an attachment to a light source, as a waveguide or as a light filter. The cohesive nature of these biophotonic materials may provide ease of removal from the site of treatment and hence a faster and less messy treatment. In addition the biophotonic materials can limit the contact between the chromopore and the tissue. These materials may be described based on the components making up the composition. Additionally or alternatively, the compositions of the present disclosure have functional and structural properties and these properties may also be used to define and describe the compositions. Individual components of the biophotonic materials of the present disclosure, including chromophores, thickening agents and other optional ingredients, are detailed below.

The present disclosure also provides a precursor composition to the material described herein, which will become cohesive on drying, heating, light exposure, application to tissue or mixing. The precursor composition comprises at least one chromophore in a carrier medium, or at least one chromophore and a cohesive matrix.

(a) Chromophores

Suitable chromophores can be fluorescent compounds (or stains) (also known as "fluorochromes" or "fluorophores"). Other dye groups or dyes (biological and histological dyes, food colorings, carotenoids, naturally occurring fluorescent and other dyes) can also be used. Suitable photoactivators can be those that are Generally Regarded As Safe (GRAS). Advantageously, photoactivators which are not well tolerated by the skin or other tissues can be included in the biophotonic material of the present disclosure, as in certain embodiments, the photoactivators are encapsulated within the cohesive matrix and may not contact the tissues

In certain embodiments, the biophotonic material of the present disclosure comprises a first chromophore which undergoes partial or complete photobleaching upon application

of light. In some embodiments, the first chromophore absorbs at a wavelength in the range of the visible spectrum, such as at a wavelength of about 380-800 nm, 380-700, 400-800, or 380-600 nm. In other embodiments, the first chromophore absorbs at a wavelength of about 200-800 nm, 200-700 nm, 200-600 nm or 200-500 nm. In one embodiment, the first chromophore absorbs at a wavelength of about 200-600 nm. In some embodiments, the first chromophore absorbs light at a wavelength of about 200-300 nm, 250-350 nm, 300-400 nm, 350-450 nm, 400-500 nm, 450-650 nm, 600-700 nm, 650-750 nm or 700-800 nm.

It will be appreciated to those skilled in the art that optical properties of a particular chromophore may vary depending on the chromophore's surrounding medium. Therefore, as used herein, a particular chromophore's absorption and/or emission wavelength (or spectrum) corresponds to the wavelengths (or spectrum) measured in a biophotonic material of the present disclosure.

The biophotonic material disclosed herein may include at least one additional chromophore. Combining chromophores may increase photo-absorption by the combined dye molecules and enhance absorption and photo-biomodulation selectivity. This creates multiple possibilities of generating new photosensitive, and/or selective chromophores mixtures. Thus, in certain embodiments, biophotonic materials of the disclosure include more than one chromophore. When such multi-chromophore materials are illuminated with light, energy transfer can occur between the chromophores. This process, known as resonance energy transfer, is a widely prevalent photophysical process through which an excited 'donor' chromophore (also referred to herein as first chromophore) transfers its excitation energy to an 'acceptor' chromophore (also referred to herein as second chromophore). The efficiency and directedness of resonance energy transfer depends on the spectral features of donor and acceptor chromophores. In particular, the flow of energy between chromophores is dependent on a spectral overlap reflecting the relative positioning and shapes of the absorption and emission spectra. More specifically, for energy transfer to occur, the emission spectrum of the donor chromophore must overlap with the absorption spectrum of the acceptor chromophore (**Figure 1**).

Energy transfer manifests itself through decrease or quenching of the donor emission and a reduction of excited state lifetime accompanied also by an increase in acceptor emission intensity. **Figure 2** is a Jablonski diagram that illustrates the coupled transitions involved between a donor emission and acceptor absorbance.

To enhance the energy transfer efficiency, the donor chromophore should have good abilities to absorb photons and emit photons. Furthermore, the more overlap there is between the donor chromophore's emission spectra and the acceptor chromophore's absorption spectra, the better a donor chromophore can transfer energy to the acceptor chromophore.

In certain embodiments, the biophotonic material of the present disclosure further comprises a second chromophore. In some embodiments, the first chromophore has an emission spectrum that overlaps at least about 80%, 50%, 40%, 30%, 20% or 10% with an absorption spectrum of the second chromophore. In one embodiment, the first chromophore has an emission spectrum that overlaps at least about 20% with an absorption spectrum of the second chromophore. In some embodiments, the first chromophore has an emission spectrum that overlaps at least 1-10%, 5-15%, 10-20%, 15-25%, 20-30%, 25-35%, 30-40%, 35-45%, 50-60%, 55-65% or 60-70% with an absorption spectrum of the second chromophore.

% spectral overlap, as used herein, means the % overlap of a donor chromophore's emission wavelength range with an acceptor chromophore's absorption wavelength rage, measured at spectral full width quarter maximum (FWQM). For example, **Figure 1** shows the normalized absorption and emission spectra of donor and acceptor chromophores. The spectral FWQM of the acceptor chromophore's absorption spectrum is from about 60 nm (515 nm to about 575 nm). The overlap of the donor chromophore's spectrum with the absorption spectrum of the acceptor chromophore is about 40 nm (from 515 nm to about 555 nm). Thus, the % overlap can be calculated as 40nm / 60nm x 100 = 66.6%.

In some embodiments, the second chromophore absorbs at a wavelength in the range of the visible spectrum. In certain embodiments, the second chromophore has an absorption

wavelength that is relatively longer than that of the first chromophore within the range of about 50-250, 25-150 or 10-100 nm.

The first chromophore can be present in an amount of about 0.001-40% per weight of the biophotonic material. When present, the second chromophore can be present in an amount of about 0.001-40% per weight of the biophotonic material. In certain embodiments, the first chromophore is present in an amount of about 0.001-3%, 0.001-0.01%, 0.005-0.1%, 0.1-0.5%, 0.5-2%, 1-5%, 2.5-7.5%, 5-10%, 7.5-12.5%, 10-15%, 12.5-17.5%, 15-20%, 17.5-22.5%, 20-25%, 22.5-27.5%, 25-30%, 27.5-32.5%, 30-35%, 32.5-37.5%, or 35-40% per weight of the biophotonic material. In certain embodiments, the second chromophore is present in an amount of about 0.001-3%, 0.001-0.01%, 0.005-0.1%, 0.1-0.5%, 0.5-2%, 1-5%, 2.5-7.5%, 5-10%, 7.5-12.5%, 10-15%, 12.5-17.5%, 15-20%, 17.5-22.5%, 20-25%, 22.5-27.5%, 25-30%, 27.5-32.5%, 30-35%, 32.5-37.5%, or 35-40% per weight of the biophotonic material. In certain embodiments, the total weight per weight of chromophore or combination of chromophores may be in the amount of about 0.005-1%, 0.05-2%, 1-5%, 2.5-7.5%, 5-10%, 7.5-12.5%, 10-15%, 12.5-17.5%, 15-20%, 17.5-22.5%, 20-25%, 22.5-27.5%, 25-30%, 27.5-32.5%, 30-35%, 32.5-37.5%, or 35-40.001% per weight of the biophotonic material.

The concentration of the chromophore to be used can be selected based on the desired intensity and duration of the biophotonic activity from the biophotonic material, and on the desired medical or cosmetic effect. For example, some dyes such as xanthene dyes reach a 'saturation concentration' after which further increases in concentration do not provide substantially higher emitted fluorescence. Further increasing the chromophore concentration above the saturation concentration can reduce the amount of activating light passing through the matrix. Therefore, if more fluorescence is required for a certain application than activating light, a high 'saturation' concentration of chromophore can be used. However, if a balance is required between the emitted fluorescence and the activating light, a concentration close to or lower than the saturation concentration can be chosen.

Suitable chromophores that may be used in the biophotonic materials of the present disclosure include, but are not limited to the following:

Chlorophyll dyes

Exemplary chlorophyll dyes include but are not limited to chlorophyll a; chlorophyll b; chlorophyllin, oil soluble chlorophyll; bacteriochlorophyll a; bacteriochlorophyll b; bacteriochlorophyll c; bacteriochlorophyll d; protochlorophyll; protochlorophyll a; amphiphilic chlorophyll derivative 1; and amphiphilic chlorophyll derivative 2.

Xanthene derivatives

Exemplary xanthene dyes include but are not limited to Eosin B (4',5'-dibromo,2',7'-dinitr- o-fluorescein, dianion); eosin Y; eosin Y (2',4',5',7'-tetrabromo-fluoresc- ein, dianion); eosin (2',4',5',7'-tetrabromo-fluorescein, dianion); eosin (2',4',5',7'-tetrabromo-fluorescein, dianion) methyl ester; eosin (2',4',5',7'-tetrabromo-fluorescein, monoanion) p-isopropylbenzyl ester; eosin derivative (2',7'-dibromo-fluorescein, dianion); eosin derivative (4',5'-dibromo-fluorescein, dianion); eosin derivative (2',7'-dichloro-fluorescein, dianion); eosin derivative (4',5'-dichloro-fluorescein, dianion); eosin derivative (2',7'-diiodo-fluorescein, dianion); eosin derivative (4',5'-diiodo-fluorescein, dianion); eosin derivative (tribromo-fluorescein, dianion); eosin derivative (2',4',5',7'-tetrachlor- o-fluorescein, dianion); eosin; eosin dicetylpyridinium chloride ion pair; erythrosin B (2',4',5',7'-tetraiodo-fluorescein, dianion); erythrosin; erythrosin dianion; erythiosin B; fluorescein; fluorescein dianion; phloxin B (2',4',5',7'-tetrabromo-3,4,5,6-tetrachloro-fluorescein, dianion); phloxin B (tetrachloro-tetrabromo-fluorescein); phloxine B; rose bengal (3,4,5,6-tetrachloro-2',4',5',7'-tetraiodofluorescein, dianion); pyronin G, pyronin J, pyronin Y; Rhodamine dyes such as rhodamines include 4,5-dibromo-rhodamine methyl ester; 4,5-dibromo-rhodamine n-butyl ester; rhodamine 101 methyl ester; rhodamine 123; rhodamine 6G; rhodamine 6G hexyl ester; tetrabromo-rhodamine 123; and tetramethyl-rhodamine ethyl ester.

Methylene blue dyes

Exemplary methylene blue derivatives include but are not limited to 1-methyl methylene blue; 1,9-dimethyl methylene blue; methylene blue; methylene blue (16 μM); methylene blue (14 μM); methylene violet; bromomethylene violet; 4-iodomethylene violet; 1,9-dimethyl-3-dimethyl-amino-7-diethyl-a- mino-phenothiazine; and 1,9-dimethyl-3-diethylamino-7-dibutyl-amino-phenot- hiazine.

Azo dyes

Exemplary azo (or diazo-) dyes include but are not limited to methyl violet, neutral red, para red (pigment red 1), amaranth (Azorubine S), Carmoisine (azorubine, food red 3, acid red 14), allura red AC (FD&C 40), tartrazine (FD&C Yellow 5), orange G (acid orange 10), Ponceau 4R (food red 7), methyl red (acid red 2), and murexide-ammonium purpurate.

In some aspects of the disclosure, the one or more chromophores of the biophotonic materials disclosed herein can be independently selected from any of Acid black 1, Acid blue 22, Acid blue 93, Acid fuchsin, Acid green, Acid green 1, Acid green 5, Acid magenta, Acid orange 10, Acid red 26, Acid red 29, Acid red 44, Acid red 51, Acid red 66, Acid red 87, Acid red 91, Acid red 92, Acid red 94, Acid red 101, Acid red 103, Acid roseine, Acid rubin, Acid violet 19, Acid yellow 1, Acid yellow 9, Acid yellow 23, Acid yellow 24, Acid yellow 36, Acid yellow 73, Acid yellow S, Acridine orange, Acriflavine, Alcian blue, Alcian yellow, Alcohol soluble eosin, Alizarin, Alizarin blue 2RC, Alizarin carmine, Alizarin cyanin BBS, Alizarol cyanin R, Alizarin red S, Alizarin purpurin, Aluminon, Amido black 10B, Amidoschwarz, Aniline blue WS, Anthracene blue SWR, Auramine O, Azocannine B, Azocarmine G, Azoic diazo 5, Azoic diazo 48, Azure A, Azure B, Azure C, Basic blue 8, Basic blue 9, Basic blue 12, Basic blue 15, Basic blue 17, Basic blue 20, Basic blue 26, Basic brown 1, Basic fuchsin, Basic green 4, Basic orange 14, Basic red 2, Basic red 5, Basic red 9, Basic violet 2, Basic violet 3, Basic violet 4, Basic violet 10, Basic violet 14, Basic yellow 1, Basic yellow 2, Biebrich scarlet, Bismarck brown Y, Brilliant crystal scarlet 6R, Calcium red, Carmine, Carminic acid, Celestine blue B, China blue, Cochineal, Coelestine blue, Chrome violet CG, Chromotrope 2R, Chromoxane cyanin R, Congo corinth, Congo red, Cotton blue, Cotton red, Croceine scarlet, Crocin, Crystal ponceau 6R, Crystal violet, Dahlia, Diamond green B, Direct blue 14, Direct blue 58, Direct red, Direct red 10, Direct red 28, Direct red 80, Direct yellow 7, Eosin B, Eosin Bluish, Eosin, Eosin Y, Eosin yellowish, Eosinol, Erie garnet B, Eriochrome cyanin R, Erythrosin B, Ethyl eosin, Ethyl green, Ethyl violet, Evans blue, Fast blue B, Fast green FCF, Fast red B, Fast yellow, Fluorescein, Food green 3, Gallein, Gallamine blue, Gallocyanin, Gentian violet, Haematein, Haematine, Haematoxylin, Helio fast rubin BBL, Helvetia blue, Hematein, Hematine, Hematoxylin, Hoffman's violet, Imperial red, Indocyanin Green, Ingrain blue, Ingrain blue 1, Ingrain yellow 1, INT, Kermes, Kermesic acid, Kernechtrot, Lac, Laccaic acid, Lauth's violet, Light green, Lissamine green SF, Luxol fast blue, Magenta 0, Magenta I, Magenta II,

Magenta III, Malachite green, Manchester brown, Martius yellow, Merbromin, Mercurochrome, Metanil yellow, Methylene azure A, Methylene azure B, Methylene azure C, Methylene blue, Methyl blue, Methyl green, Methyl violet, Methyl violet 2B, Methyl violet 10B, Mordant blue 3, Mordant blue 10, Mordant blue 14, Mordant blue 23, Mordant blue 32, Mordant blue 45, Mordant red 3, Mordant red 11, Mordant violet 25, Mordant violet 39 Naphthol blue black, Naphthol green B, Naphthol yellow S, Natural black 1, Natural green 3(chlorophyllin), Natural red, Natural red 3, Natural red 4, Natural red 8, Natural red 16, Natural red 25, Natural red 28, Natural yellow 6, NBT, Neutral red, New fuchsin, Niagara blue 3B, Night blue, Nile blue, Nile blue A, Nile blue oxazone, Nile blue sulphate, Nile red, Nitro BT, Nitro blue tetrazolium, Nuclear fast red, Oil red O, Orange G, Orcein, Pararosanilin, Phloxine B, Picric acid, Ponceau 2R, Ponceau 6R, Ponceau B, Ponceau de Xylidine, Ponceau S, Primula, Purpurin, Pyronin B, phycobilins, Phycocyanins, Phycoerythrins. Phycoerythrincyanin (PEC), Phthalocyanines, Pyronin G, Pyronin Y, Quinine, Rhodamine B, Rosanilin, Rose bengal, Saffron, Safranin O, Scarlet R, Scarlet red, Scharlach R, Shellac, Sirius red F3B, Solochrome cyanin R, Soluble blue, Solvent black 3, Solvent blue 38, Solvent red 23, Solvent red 24, Solvent red 27, Solvent red 45, Solvent yellow 94, Spirit soluble eosin, Sudan III, Sudan IV, Sudan black B, Sulfur yellow S, Swiss blue, Tartrazine, Thioflavine S, Thioflavine T, Thionin, Toluidine blue, Toluyline red, Tropaeolin G, Trypaflavine, Trypan blue, Uranin, Victoria blue 4R, Victoria blue B, Victoria green B, Vitamin B, Water blue I, Water soluble eosin, Xylidine ponceau, or Yellowish eosin.

In certain embodiments, the biophotonic material of the present disclosure includes any of the chromophores listed above, or a combination thereof, so as to provide a synergistic biophotonic effect at the application site.

Without being bound to any particular theory, a synergistic effect of the chromophore combinations means that the biophotonic effect is greater than the sum of their individual effects. Advantageously, this may translate to increased reactivity of the biophotonic material, faster or improved treatment time. Also, the treatment conditions need not be altered to achieve the same or better treatment results, such as time of exposure to light, power of light source used, and wavelength of light used. In other words, use of synergistic combinations of chromophores may allow the same or better

treatment without necessitating a longer time of exposure to a light source, a higher power light source or a light source with different wavelengths.

In some embodiments, the material includes Eosin Y as a first chromophore and any one or more of Rose Bengal, Fluorescein, Erythrosine, Phloxine B, chlorophyllin as a second chromophore. It is believed that these combinations have a synergistic effect as they can transfer energy to one another when activated due in part to overlaps or close proximity of their absorption and emission spectra. This transferred energy is then emitted as fluorescence or leads to production of reactive oxygen species. This absorbed and re-emitted light is thought to be transmitted throughout the composition, and also to be transmitted into the site of treatment.

In further embodiments, the material includes the following synergistic combinations: Eosin Y and Fluorescein; Fluorescein and Rose Bengal; Erythrosine in combination with Eosin Y, Rose Bengal or Fluorescein; Phloxine B in combination with one or more of Eosin Y, Rose Bengal, Fluorescein and Erythrosine. Other synergistic chromophore combinations are also possible.

By means of synergistic effects of the chromophore combinations in the material, chromophores which cannot normally be activated by an activating light (such as a blue light from an LED), can be activated through energy transfer from chromophores which are activated by the activating light. In this way, the different properties of photoactivated chromophores can be harnessed and tailored according to the cosmetic or the medical therapy required.

For example, Rose Bengal can generate a high yield of singlet oxygen when activated in the presence of molecular oxygen, however it has a low quantum yield in terms of emitted fluorescent light. Rose Bengal has a peak absorption around 540 nm and so can be activated by green light. Eosin Y has a high quantum yield and can be activated by blue light. By combining Rose Bengal with Eosin Y, one obtains a composition which can emit therapeutic fluorescent light and generate singlet oxygen when activated by blue light. In this case, the blue light photoactivates Eosin Y which transfers some of its energy to Rose Bengal as well as emitting some energy as fluorescence.

In some embodiments, the chromophore or chromophores are selected such that their emitted fluorescent light, on photoactivation, is within one or more of the green, yellow, orange, red and infrared portions of the electromagnetic spectrum, for example having a peak wavelength within the range of about 490 nm to about 800 nm. In certain embodiments, the emitted fluorescent light has a power density of between 0.005 to about 10 mW/cm^2, about 0.5 to about 5 mW/cm^2.

(b) Cohesive matrix

The biophotonic materials of the present disclosure comprise a cohesive matrix made from one or more thickening agents, or a carrier medium. In other words, the biophotonic material of the present disclosure comprise one or more thickening agents, or a carrier medium which can form a cohesive matrix. These agents are present in an amount and ratio sufficient to provide a desired viscosity, flexibility, rigidity, tensile strength, tear strength, elasticity, and adhesiveness. The desired properties may be one of achieving a peelable film, or a rigid or flexible matrix. The thickening agents are selected so that the chromophore can remain photoactive in the cohesive matrix. The thickening agents are also selected according to the optical transparency of the cohesive matrix which they will form. The cohesive matrix should be able to transmit sufficient light to activate the at least one chromophore and, in embodiments where fluorescence is emitted by the activated chromophore, the cohesive matrix should also be able to transmit the emitted fluorescent light to tissues. It will be recognized by persons skilled in the art that the thickening agent is an appropriate medium for the chromophore selected. For example, the inventors have noted that some xanthene dyes do not fluoresce in non-hydrated media, so hydrated polymers or polar solvents may be used. The thickening agents should also be selected according to the intended use. For example, if the biophotonic material is to be applied onto tissue, the cohesive matrix is preferably a biocompatible material, or the cohesive matrix has an outside layer of a biocompatible material which will interface the tissue.

Thickening agents

In some embodiments, the content of a thickening agent used to make the cohesive matrix is from about 0.001 % to about 40 % (w/w %) of the total weight. In certain embodiments, the total content of the thickening agent is about 0.001-0.01%, about 0.005-0.05%, about 0.01-0.1, about 0.05-0.5% about 0.1-1%, about 0.5-5%, about 1-5%, about 2.5-7.5%, about 5-10%, about 7.5-12.5%, about 10-15%, about 12.5-17.5%, or

about 15-20%, or about 15-25%, or about 20-30%, or about 25-35%, or about 30-40%. It will be recognized by one of skill in the art that the viscosity, flexibility, rigidity, tensile strength, tear strength, elasticity, and adhesiveness can be adjusted by varying the content of the thickening material. Methods of determining viscosity, flexibility, rigidity, tensile strength, tear strength, elasticity, and adhesiveness are known in the art.

Thickening agents that can be used to prepare the biophotonic materials of the present disclosure include polymers, copolymers, and monomers of: vinylpyrrolidones, methacrylamides, acrylamides N-vinylimidazoles, carboxy vinyls, vinyl esters, vinyl ethers, silicones, polyethyleneoxides, polyethyleneglycols, vinylalcohols, sodium acrylates, acrylates, maleic acids, NN-dimethylacrylamides, diacetone acrylamides, acrylamides, acryloyl morpholine, pluronic, collagens, polyacrylamides, polyacrylates, polyvinyl alcohols, polyvinylenes, polyvinyl silicates, polyacrylates substituted with a sugar (e.g., sucrose, glucose, glucosamines, galactose, trehalose, mannose, or lactose), acylamidopropane sulfonic acids, tetramethoxyorthosilicates, methyltrimethoxyorthosilicates, tetraalkoxyorthosilicates, trialkoxyorthosilicates, glycols, propylene glycol, glycerine, polysaccharides, alginates, dextrans, cyclodextrin, celluloses, modified celluloses, oxidized celluloses, chitosans, chitins, guars, carrageenans, hyaluronic acids, inulin, starches, modified starches, agarose, methylcelluloses, plant gums, hylaronans, hydrogels, gelatins, glycosaminoglycans, carboxymethyl celluloses, hydroxyethyl celluloses, hydroxy propyl methyl celluloses, pectins, low-methoxy pectins, cross-linked dextrans, starch-acrylonitrile graft copolymers, starch sodium polyacrylate, hydroxyethyl methacrylates, hydroxyl ethyl acrylates, polyvinylene, polyethylvinylethers, polymethyl methacrylates, polystyrenes, polyurethanes, polyalkanoates, polylactic acids, polylactates, poly(3-hydroxybutyrate), sulfonated hydrogels, AMPS (2-acrylamido-2-methyl-1-propanesulfonic acid), SEM (sulfoethylmethacrylate), SPM (sulfopropyl methacrylate), SPA (sulfopropyl acrylate), N,N-dimethyl-N-methacryloxyethyl-N-(3-sulfopropyl)ammonium betaine, methacryllic acid amidopropyl-dimethyl ammonium sulfobetaine, SPI {itaconic acid-bis(1-propyl sulfonizacid-3) ester di-potassium salt}, itaconic acids, AMBC (3-acrylamido-3-methylbutanoic acid), beta-carboxyethyl acrylate (acrylic acid dimers), and maleic anhydride-methylvinyl ether polymers, derivatives thereof, salts thereof, acids thereof, combinations thereof, and the like.

Thickening agents also include poly (ethylene oxide) polymers (such as POLYOX from Dow Chemical), linear PVP and cross-linked PVP, PEG/PPG copolymers (such as BASF Pluracare L1220), ethylene oxide (EO)--propylene oxide (PO) block copolymers (such as polymers sold under the trade mark Pluronic available from BASF Corporation), ester gum, shellac, pressure sensitive silicone adhesives (such as BioPSA from Dow-Corning), or mixtures thereof. In some embodiments, a copolymer comprises (PVM/MA). In an embodiment, a copolymer comprises poly (methylvinylether/maleic anhydride). In some embodiments, a copolymer comprises poly (methylvinylether/maleic acid). In some embodiments, a copolymer comprises poly (methylvinylether/maleic acid) half esters. In some embodiments, a copolymer comprises poly (methylvinylether/maleic acid) mixed salts.

Thickening agents can also include carbomers which are a synthetic high molecular weight polymer of acrylic acid that is crosslinked with either allylsucrose or allylethers of pentaerythritol having a molecular weight of about 3×10^6. The gelation mechanism depends on neutralization of the carboxylic acid moiety to form a soluble salt. The polymer is hydrophilic and produces sparkling clear gels when neutralized. Carbomers are available as fine white powders which disperse in water to form acidic colloidal suspensions (a 1% dispersion has approx. pH 3) of low viscosity. Neutralization of these suspensions using a base, for example sodium, potassium or ammonium hydroxides, low molecular weight amines and alkanolamines, results in the formation of clear translucent gels.

In one embodiment of the disclosure, the carbomer is Carbopol®. Such polymers are commercially available from B.F. Goodrich or Lubrizol under the designation Carbopol® 71G NF, 420, 430, 475, 488, 493, 910, 934, 934P, 940, 971PNF, 974P NF, 980 NF, 981 NF and the like. Carbopols are versatile controlled-release polymers, as described by Brock (Pharmacotherapy, 14:430-7 (1994)) and Durrani (Pharmaceutical Res. (Supp.) 8:S-135 (1991)), and belong to a family of carbomers which are synthetic, high molecular weight, non-linear polymers of acrylic acid, cross-linked with polyalkenyl polyether. In some embodiments, the carbomer is Carbopol® 974P NF, 980 NF, 5984 EP, ETD 2020NF, Ultrez 10 NF, 934 NF, 934P NF or 940 NF. In certain embodiments, the carbomer is Carbopol® 980 NF, ETD 2020 NF, Ultrez 10 NF, Ultrez 21 or 1382 Polymer, 1342 NF, 940 NF.

In certain embodiments of the disclosure, the thickening agent or the carrier medium may comprise gelatin. For example, the cohesive matrix may comprise at least about 5%, about 5 to about 25 weight%, or about 10 to about 20 weight% gelatin within the cohesive biophotonic material. Alternatively, a lower weight percentage of gelatin may be used together with chemical cross-linkers or any other cross-linking means.

In certain embodiments of the disclosure, the thickening agent or the carrier medium may comprise sodium hyaluronate, which may be present in an amount of about 2% to about 14%.

The biophotonic material of the present disclosure may be water soluble. Alternatively, the biophotonic material of the present disclosure may optionally include a water-insoluble or liposoluble substrate. By "water insoluble", it is meant that the substrate does not dissolve in or readily break apart upon immersion in water. In some embodiments, the water-insoluble substrate is the implement or vehicle for delivering the treatment composition to the skin or target tissue. A wide variety of materials can be used as the water-insoluble substrate. The following non-limiting characteristics may be desirable: (i) sufficient wet strength for use, (ii) sufficient softness, (iii) sufficient thickness, (iv) appropriate size, (v) air permeability, and (vi) hydrophilicity.

Non-limiting examples of suitable water-insoluble substrates which meet the above criteria include nonwoven substrates, woven substrates, hydroentangled substrates, air entangled substrates, natural sponges, synthetic sponges, polymeric netted meshes, and the like. Preferred embodiments employ nonwoven substrates since they are economical and readily available in a variety of materials. By "nonwoven", it is meant that the layer is comprised of fibers which are not woven into a fabric but rather are formed into a sheet, mat, or pad layer.

In one embodiment of the disclosure, the thickening agent or the cohesive agent may comprise a silicone membrane. In this embodiment, the chromophore or chromophores can be included directly within the silicone membrane or if they are water soluble within inclusions in the membrane as an aqueous phase. For example, the aqueous phase may be present as a micro-emulsion within the silicone. The aqueous phase may be a liquid or

a semi-solid. The aqueous phase may further comprise a stabilizing agent to stabilize the emulsion such as gelatin or CMC. The aqueous phase may comprise up to 40wt% of the silicone polymer phase.

Antimicrobials

Antimicrobials kill microbes or inhibit their growth or accumulation, and are optionally included in the biophotonic materials of the present disclosure. Exemplary antimicrobials (or antimicrobial agent) are recited in U.S. Patent Application Publications 20040009227 and 20110081530. Suitable antimicrobials for use in the methods and compositions of the present disclosure include, but not limited to, hydrogen peroxide, urea hydrogen peroxide, benzoyl peroxide, phenolic and chlorinated phenolic and chlorinated phenolic compounds, resorcinol and its derivatives, bisphenolic compounds, benzoic esters (parabens), halogenated carbonilides, polymeric antimicrobial agents, thazolines, trichloromethylthioimides, natural antimicrobial agents (also referred to as "natural essential oils"), metal salts, and broad-spectrum antibiotics.

Hydrogen peroxide (H_2O_2) is a powerful oxidizing agent, and breaks down into water and oxygen and does not form any persistent, toxic residual compound. A suitable range of concentration over which hydrogen peroxide can be used in the biophotonic material is from about 0.1% to about 3%, about 0.1 to 1.5%, about 0.1% to about 1%, about 1%, less than about 1%.

Urea hydrogen peroxide (also known as urea peroxide, carbamide peroxide or percarbamide) is soluble in water and contains approximately 35% hydrogen peroxide. A suitable range of concentration over which urea peroxide can be used in the biophotonic material of the present disclosure is less than about 0.25 %, or less than about 0.3%, from 0.001 to 0.25%, or from about 0.3% to about 5%. Urea peroxide breaks down to urea and hydrogen peroxide in a slow-release fashion that can be accelerated with heat or photochemical reactions.

Benzoyl peroxide consists of two benzoyl groups (benzoic acid with the H of the carboxylic acid removed) joined by a peroxide group. It is found in treatments for acne, in concentrations varying from 2.5% to 10%. The released peroxide groups are effective

at killing bacteria. Benzoyl peroxide also promotes skin turnover and clearing of pores, which further contributes to decreasing bacterial counts and reduce acne. Benzoyl peroxide breaks down to benzoic acid and oxygen upon contact with skin, neither of which is toxic. A suitable range of concentration over which benzoyl peroxide can be used in the matrix biophotonic is from about 2.5% to about 5%.

According to certain embodiments, the biophotonic material of the present disclosure may optionally comprise one or more additional components, such as oxygen-rich compounds as a source of oxygen radicals. Peroxide compounds are oxidants that contain the peroxy group (R-O-O-R), which is a chainlike structure containing two oxygen atoms, each of which is bonded to the other and a radical or some element. When a biophotonic material of the present disclosure comprising an oxidant is illuminated with light, the chromophores are excited to a higher energy state. When the chromophores' electrons return to a lower energy state, they emit photons with a lower energy level, thus causing the emission of light of a longer wavelength (Stokes' shift). In the proper environment, some of this energy is transferred to oxygen or the reactive hydrogen peroxide and causes the formation of oxygen radicals, such as singlet oxygen. The singlet oxygen and other reactive oxygen species generated by the activation of the biophotonic material are thought to operate in a hormetic fashion. That is, a health beneficial effect that is brought about by the low exposure to a normally toxic stimuli (e.g. reactive oxygen), by stimulating and modulating stress response pathways in cells of the targeted tissues. Endogenous response to exogenous generated free radicals (reactive oxygen species) is modulated in increased defense capacity against the exogenous free radicals and induces acceleration of healing and regenerative processes. Furthermore, activation of the oxidant may also produce an antibacterial effect. The extreme sensitivity of bacteria to exposure to free radicals makes the biophotonic material of the present disclosure potentially a bactericidal composition.

Specific phenolic and chlorinated phenolic antimicrobial agents that can be used in the disclosure include, but are not limited to: phenol; 2-methyl phenol; 3-methyl phenol; 4-methyl phenol; 4-ethyl phenol; 2,4-dimethyl phenol; 2,5-dimethyl phenol; 3,4-dimethyl phenol; 2,6-dimethyl phenol; 4-n-propyl phenol; 4-n-butyl phenol; 4-n-amyl phenol; 4-

tert-amyl phenol; 4-n-hexyl phenol; 4-n-heptyl phenol; mono- and poly-alkyl and aromatic halophenols; p-chlorophenyl; methyl p-chlorophenol; ethyl p-chlorophenol; n-propyl p-chlorophenol; n-butyl p-chlorophenol; n-amyl p-chlorophenol; sec-amyl p-chlorophenol; n-hexyl p-chlorophenol; cyclohexyl p-chlorophenol; n-heptyl p-chlorophenol; n-octyl; p-chlorophenol; o-chlorophenol; methyl o-chlorophenol; ethyl o-chlorophenol; n-propyl o-chlorophenol; n-butyl o-chlorophenol; n-amyl o-chlorophenol; tert-amyl o-chlorophenol; n-hexyl o-chlorophenol; n-heptyl o-chlorophenol; o-benzyl p-chlorophenol; o-benxyl-m-methyl p-chlorophenol; o-benzyl-m,m-dimethyl p-chlorophenol; o-phenylethyl p-chlorophenol; o-phenylethyl-m-methyl p-chlorophenol; 3-methyl p-chlorophenol 3,5-dimethyl p-chlorophenol, 6-ethyl-3-methyl p-chlorophenol, 6-n-propyl-3-methyl p-chlorophenol; 6-iso-propyl-3-methyl p-chlorophenol; 2-ethyl-3,5-dimethyl p-chlorophenol; 6-sec-butyl-3-methyl p-chlorophenol; 2-iso-propyl-3,5-dimethyl p-chlorophenol; 6-diethylmethyl-3-methyl p-chlorophenol; 6-iso-propyl-2-ethyl-3-methyl p-chlorophenol; 2-sec-amyl-3,5-dimethyl p-chlorophenol; 2-diethylmethyl-3,5-dimethyl p-chlorophenol; 6-sec-octyl-3-methyl p-chlorophenol; p-chloro-m-cresol p-bromophenol; methyl p-bromophenol; ethyl p-bromophenol; n-propyl p-bromophenol; n-butyl p-bromophenol; n-amyl p-bromophenol; sec-amyl p-bromophenol; n-hexyl p-bromophenol; cyclohexyl p-bromophenol; o-bromophenol; tert-amyl o-bromophenol; n-hexyl o-bromophenol; n-propyl-m,m-dimethyl o-bromophenol; 2-phenyl phenol; 4-chloro-2-methyl phenol; 4-chloro-3-methyl phenol; 4-chloro-3,5-dimethyl phenol; 2,4-dichloro-3,5-dimethylphenol; 3,4,5,6-tetabromo-2-methylphenol- ; 5-methyl-2-pentylphenol; 4-isopropyl-3-methylphenol; para-chloro-metaxylenol (PCMX); chlorothymol; phenoxyethanol; phenoxyisopropanol; and 5-chloro-2-hydroxydiphenylmethane.

Resorcinol and its derivatives can also be used as antimicrobial agents. Specific resorcinol derivatives include, but are not limited to: methyl resorcinol; ethyl resorcinol; n-propyl resorcinol; n-butyl resorcinol; n-amyl resorcinol; n-hexyl resorcinol; n-heptyl resorcinol; n-octyl resorcinol; n-nonyl resorcinol; phenyl resorcinol; benzyl resorcinol; phenylethyl resorcinol; phenylpropyl resorcinol; p-chlorobenzyl resorcinol; 5-chloro-2,4-dihydroxydiphenyl methane; 4'-chloro-2,4-dihydroxydiphenyl methane; 5-bromo-2,4-dihydroxydiphenyl methane; and 4'-bromo-2,4-dihydroxydiphenyl methane.

Specific bisphenolic antimicrobial agents that can be used in the disclosure include, but are not limited to: 2,2'-methylene bis-(4-chlorophenol); 2,4,4'trichloro-2'-hydroxy-diphenyl ether, which is sold by Ciba Geigy, Florham Park, N.J. under the tradename Triclosan®; 2,2'-methylene bis-(3,4,6-trichlorophenol); 2,2'-methylene bis-(4-chloro-6-bromophenol); bis-(2-hydroxy-3,5-dichlorop- henyl) sulphide; and bis-(2-hydroxy-5-chlorobenzyl)sulphide.

Specific benzoie esters (parabens) that can be used in the disclosure include, but are not limited to: methylparaben; propylparaben; butylparaben; ethylparaben; isopropylparaben; isobutylparaben; benzylparaben; sodium methylparaben; and sodium propylparaben.

Specific halogenated carbanilides that can be used in the disclosure include, but are not limited to: 3,4,4'-trichlorocarbanilides, such as 3-(4-chlorophenyl)-1-(3,4-dichlorphenyl)urea sold under the tradename Triclocarban® by Ciba-Geigy, Florham Park, N.J.; 3-trifluoromethyl-4,4'-dichlorocarbanilide; and 3,3',4-trichlorocarbanilide.

Specific polymeric antimicrobial agents that can be used in the disclosure include, but are not limited to: polyhexamethylene biguanide hydrochloride; and poly(iminoimidocarbonyl iminoimidocarbonyl iminohexamethylene hydrochloride), which is sold under the tradename Vantocil® IB.

Specific thazolines that can be used in the disclosure include, but are not limited to that sold under the tradename Micro-Check®; and 2-n-octyl-4-isothiazolin-3-one, which is sold under the tradename Vinyzene® IT-3000 DIDP.

Specific trichloromethylthioimides that can be used in the disclosure include, but are not limited to: N-(trichloromethylthio)phthalimide, which is sold under the tradename Fungitrol®; and N-trichloromethylthio-4-cyclohexene-1,2-dicarboximide, which is sold under the tradename Vancide®.

Specific natural antimicrobial agents that can be used in the disclosure include, but are not limited to, oils of: anise; lemon; orange; rosemary; wintergreen; thyme; lavender; cloves; hops; tea tree; citronella; wheat; barley; lemongrass; cedar leaf; cedarwood; cinnamon; fleagrass; geranium; sandalwood; violet; cranberry; eucalyptus; vervain; peppermint; gum benzoin; basil; fennel; fir; balsam; menthol; ocmea origanuin; hydastis; carradensis; Berberidaceac daceae; Ratanhiae longa; and Curcuma longa. Also included in this class of natural antimicrobial agents are the key chemical components of the plant oils which have been found to provide antimicrobial benefit. These chemicals include, but are not limited to: anethol; catechole; camphene; thymol; eugenol; eucalyptol; ferulic acid; farnesol; hinokitiol; tropolone; limonene; menthol; methyl salicylate; carvacol; terpineol; verbenone; berberine; ratanhiae extract; caryophellene oxide; citronellic acid; curcumin; nerolidol; and geraniol.

Specific metal salts that can be used in the disclosure include, but are not limited to, salts of metals in groups 3a-5a, 3b-7b, and 8 of the periodic table. Specific examples of metal salts include, but are not limited to, salts of: aluminum; zirconium; zinc; silver; gold; copper; lanthanum; tin; mercury; bismuth; selenium; strontium; scandium; yttrium; cerium; praseodymiun; neodymium; promethum; samarium; europium; gadolinium; terbium; dysprosium; holmium; erbium; thalium; ytterbium; lutetium; and mixtures thereof. An example of the metal-ion based antimicrobial agent is sold under the tradename HealthShield®, and is manufactured by HealthShield Technology, Wakefield, Mass.

Specific broad-spectrum antimicrobial agents that can be used in the disclosure include, but are not limited to, those that are recited in other categories of antimicrobial agents herein.

Additional antimicrobial agents that can be used in the methods of the disclosure include, but are not limited to: pyrithiones, and in particular pyrithione-including zinc complexes such as that sold under the tradename Octopirox®; dimethyidimethylol hydantoin, which is sold under the tradename Glydant®; methylchloroisothiazolinone/methylisothiazolinone, which is sold under the tradename Kathon CG®; sodium sulfite; sodium bisulfite; imidazolidinyl urea, which is sold under the tradename Germall 115®; diazolidinyl urea, which is sold under the tradename Germall 11®; benzyl alcohol v2-bromo-2-nitropropane-1,3-diol, which is sold under the tradename Bronopol®; formalin or formaldehyde; iodopropenyl butylcarbamate, which is sold under the tradename Polyphase P100®; chloroacetamide; methanamine; methyldibromonitrile glutaronitrile (1,2-dibromo-2,4-dicyanobutane), which is sold under the tradename Tektamer®; glutaraldehyde; 5-bromo-5-nitro-1,3-dioxane, which is sold under the tradename Bronidox®; phenethyl alcohol; o-phenylphenol/sodium o-phenylphenol sodium hydroxymethylglycinate, which is sold under the tradename Suttocide A®; polymethoxy bicyclic oxazolidine; which is sold under the tradename Nuosept C®; dimethoxane; thimersal; dichlorobenzyl alcohol; captan; chlorphenenesin; dichlorophene; chlorbutanol; glyceryl laurate; halogenated diphenyl ethers; 2,4,4'-trichloro-2'-hydroxy-diphenyl ether, which is sold under the tradename Triclosan® and is available from Ciba-Geigy, Florham Park, N.J.; and 2,2'-dihydroxy-5,5'-dibromo-diphenyl ether.

Additional antimicrobial agents that can be used in the methods of the disclosure include those disclosed by U.S. Pat. Nos. 3,141,321; 4,402,959; 4,430,381; 4,533,435; 4,625,026; 4,736,467; 4,855,139; 5,069,907; 5,091,102; 5,639,464; 5,853,883; 5,854,147; 5,894,042; and 5,919,554, and U.S. Pat. Appl. Publ. Nos. 20040009227 and 20110081530.

(4) Optical properties of the Biophotonic Materials

In certain embodiments, biophotonic materials of the present disclosure are substantially transparent or translucent. The % transmittance of the biophotonic material can be measured in the range of wavelengths from 250 nm to 800 nm using, for example, a Perkin-Elmer Lambda 9500 series UV-visible spectrophotometer. In some embodiments, transmittance within the visible range is measured and averaged. In some other embodiments, transmittance of the biophotonic material is measured with the chromophore omitted. As transmittance is dependent upon thickness, the thickness of each sample can be measured with calipers prior to loading in the spectrophotometer. Transmittance values can be normalized according to

$$F_{T-corr}(\lambda, t_2) = [e^{-\sigma_t(\lambda)t_1}]^{\frac{t_2}{t_1}} = [F_{T-corr}(\lambda, t_1)]^{\frac{t_2}{t_1}},$$

where t_1=actual specimen thickness, t_2=thickness to which transmittance measurements can be normalized. In the art, transmittance measurements are usually normalized to 1 cm.

In certain embodiments, the biophotonic materials are substantially opaque. In these embodiments, the biophotonic materials may include light transmitting structures such as fibres, particles, networks, which are made of materials which can transmit light. The light transmitting structures can be waveguides such as optical fibres.

In some embodiments, the biophotonic material has a transmittance that is more than about 20%, 30%, 40%, 50%, 60%, 70%, or 75% within the visible range. In some embodiments, the transmittance exceeds 40%, 41%, 42%, 43%, 44%, or 45% within the visible range.

(5) Forms of the Biophotonic Materials

The biophotonic materials of the present disclosure may be in the form of a cohesive film or matrix containing at least one chromophore. The cohesive film or matrix may be a cohesive gel, or a paste, a putty, a semi-solid, or a solid.

The biophotonic materials of the present disclosure may be deformable. They may be elastic or non-elastic (i.e. flexible or rigid). The biophotonic materials, for example, may be in a peel-off form ('peelable') to provide ease and speed of use. In certain embodiments, the tear strength and/or tensile strength of the peel-off form is greater than its adhesion strength. This may help handleability of the material. It will be recognized by one of skill in the art that the properties of the peel-off biophotonic material such as cohesiveness, flexibility, elasticity, tensile strength, and tearing strength, can be determined and/or adjusted by methods known in the art such as by selecting suitable thickening agents and adapting their relative ratios.

The biophotonic material may be in a pre-formed shape. In certain embodiments, the pre-formed shape is in the form of, including, but not limited to, a film, a face mask, a patch, a dressing, or bandage. In certain embodiments, the pre-formed shapes can be customized for the individual user by trimming to size. In certain embodiments, perforations are provided around the perimeter of the pre-formed shape to facilitate trimming. In certain embodiments, the pre-shaping can be performed manually or by mechanical means such as 3-D printing. In the case of the 3-D printing the size of the area to be treated can be imaged, such as a wound or a face, then a 3-D printer configured to build or form a cohesive biophotonic material to match the size and shape of the imaged treatment area.

A biophotonic material of the disclosure can be configured with a shape and/or size for application to a desired portion of a subject's body. For example, the biophotonic material can be shaped and sized to correspond with a desired portion of the body to receive the biophotonic treatment. Such a desired portion of skin can be selected from, but not limited to, the group consisting of a skin, head, forehead, scalp, nose, cheeks, lips, ears, face, neck, shoulder, arm pit, arm, elbow, hand, finger, abdomen, chest, stomach, back, buttocks, sacrum, genitals, legs, knee, feet, toes, nails, hair, any boney prominences, and combinations thereof, and the like. Thus, the biophotonic material of the disclosure can be shaped and sized to be applied to any portion of skin on a subject's body. For example, the biophotonic material can be sock, hat, glove or mitten shaped. In embodiments where the biophotonic material is elastic or rigid, it can be peeled-off without leaving any residue on the tissue.

In certain embodiments, the biophotonic material is in the form of an elastic and peelable face mask, which may be pre-formed. In other embodiments, the biophotonic material is in the form of a non-elastic (rigid) face mask, which may also be pre-formed. The mask can have openings for one or more of the eyes, nose and mouth. In a further embodiment, the openings are protected with a covering, or the exposed skin such as on the nose, lips or eyes are protected using for example cocoa butter. In certain embodiments, the pre-formed face mask is provided in the form of multiple parts, e.g., an upper face part and a lower face part. In certain embodiments, the uneven proximity of the face to a light source is compensated for, e.g., by adjusting the thickness of the mask, or by adjusting the amount of chromophore in the different areas of the mask, or by blocking the skin in closest proximity to the light. In certain embodiments, the pre-formed shapes come in a one-size fits all form.

In certain aspects, the mask (or patch) is not pre-formed and is applied e.g., by spreading a composition making up the mask (or patch), on the skin or target tissue, or alternatively by spraying, smearing, dabbing or rolling the composition on target tissue. It can then be converted to a peel-off form after application, by means such as, but not limited to, drying, illumination with light, change in temperature or pH upon application to the skin or tissue. The mask (or patch) can then be peeled off without leaving any flakes on the skin or tissue, preferably without wiping or washing.

In certain aspects, the biophotonic material may have shape memory properties. For example, the biophotonic material can include a shape memory material, such as a shape memory polymer whose original shape is reverted to on activation by light. The original shape can be a flat or concave configuration which allows the film/matrix to be readily peeled off the tissue. The shape memory material may be included as a layer attached to the biophotonic material, or integrated with the biophotonic material.

In certain aspects, the biophotonic material forms part of a composite and can include fibres, particulates, non-biophotonic layers or biophotonic layers with the same or different compositions.

In certain embodiments, the biophotonic material may comprise a plurality of waveguides extending at least partially through the biophotonic material or contained at

least partially within the biophotonic material. The waveguides can be attached to a light source to thereby illuminate the biophotonic material from within. The biophotonic material may further include the light source attached to the waveguides. The waveguides can be optical fibres which can transmit light, not only from their ends, but also from their body. For example, made of polycarbonate or polymethylmethacrylate or any other suitable material.

In a different embodiment, the biophotonic material comprises a layer of a woven or non-woven fabric dressing or a mask. Waveguides or a light source may be included within the dressing or mask fabric. For example, the dressing or mask fabric can be in the form of an envelope which receives the biophotonic material, and which comprises at least one light emitting surface.

In certain aspects, the biophotonic material is formed as a filter. For example, the biophotonic material can be made to have a shape and a size which can be connected to, or spaced from, a light emitting surface of a lamp. In one embodiment, the lamp can be a hand-held lamp such as a torch or a dentist's curing lamp. The lamp with the biophotonic filter can then be used to treat tissue sites of patient in a contacting or non-contacting manner. In this embodiment, the filter has a body having a first end which is sized and shaped to be connectable to a light emitting surface, and a second end shaped to treat tissues.

In certain aspects, the biophotonic material is formed as a waveguide. In certain embodiments, at least one chromophore is included in an elongate solid matrix having good light propagation properties and appropriate mechanical properties. The waveguide may be flexible. The waveguide can be shaped as an optical fibre. Such an optical fibre can be connected to a light source, and the at least one chromophore in the cohesive matrix activated by the light source to deliver therapeutic fluorescent light to hard to reach places, such as internal cavities and periodontal pockets. Polymethylmethacrylate is an example of an appropriate cohesive matrix for use as a biophotonic waveguide. Such a waveguide may additionally include a coating to prevent light dissipation from along its length.

In other aspects, the biophotonic material comprising at least one chromophore and a cohesive matrix is in the form of particulates. Material processing techniques known in the art can be used to form particulates of any shape or size. These particulates can be contained in semi-solid or liquid preparations. For example, such biophotonic particulates can be used in skin preparations such as creams, emulsions to provide therapeutic effect to the skin. In this case, a biocompatible solid matrix is used and can be used to encapsulate all types of chromophores, even those not well tolerated by the skin.

The biophotonic materials of the present disclosure may have a thickness of from about 0.1 mm to about 50 mm, about 0.5 mm to about 20 mm, or about 1 mm to about 10 mm. It will be appreciated that the thickness of the biophotonic materials will vary based on the intended use. In some embodiments, the biophotonic material has a thickness of from about 0.1-1 mm. In some embodiments, the biophotonic material has a thickness of about 0.5-1.5 mm, about 1-2 mm, about 1.5-2.5 mm, about 2-3 mm, about 2.5-3.5 mm, about 3-4 mm, about 3.5-4.5 mm, about 4-5 mm, about 4.5-5.5 mm, about 5-6 mm, about 5.5-6.5 mm, about 6-7 mm, about 6.5-7.5 mm, about 7-8 mm, about 7.5-8.5 mm, about 8-9 mm, about 8.5-9.5, about 9-10 mm, about 10-11mm, about 11-12 mm, about 12-13 mm, about 13-14 mm, about 14-15 mm, about 15-16 mm, about 16-17 mm, about 17-18 mm, about 18-19 mm, about 19-20 mm, about 20-22mm, about 22-24mm, about 24-26mm, about 26-28mm, about 28-30mm, about 30-35mm, about 35-40mm, about 40-45mm, about 45-50mm.

The tensile strength of the biophotonic materials will vary based on the intended use. The tensile strength can be determined by performing a tensile test and recording the force and displacement. These are then converted to stress (using cross sectional area) and strain; the highest point of the stress-strain curve is the "ultimate tensile strength." In some embodiments, tensile strength can be characterized using a 500N capacity tabletop mechanical testing system (#5942R4910, Instron®) with a 5N maximum static load cell (#102608, Instron). Pneumatic side action grips can be used to secure the samples (#2712-019, Instron). In some embodiments, a constant extension rate (for example, of about 2 mm/min) until failure can be applied and the tensile strength is calculated from the stress vs. strain data plots. In some embodiments, the tensile strength can be measured using methods as described in or equivalent to those described in American

Society for Testing and Materials tensile testing methods such as ASTM D638, ASTM D882 and ASTM D412.

In some embodiments, the biophotonic material has a tensile strength of from about 1-50 kPa, 1 to about 1000 kPa, 1 to about 500 kPa, 50 kPa to about 600 kPa. In some embodiments, the tensile strength is from about 75 kPa to about 500 kPa, from about 100 kPa to about 200 kPa, 100-300 kPa, 400 kPa, from about 150 kPa to about 350 kPa, or from about 200 kPa to about 300 kPa.

In some embodiments, the tensile strength is at least about 50 kPa, at least about 75 kPa, at least about 100 kPa, at least about 150 kPa, at least about 200 kPa, at least about 250 kPa, at least about 300 kPa, at least about 350 kPa, at least about 400 kPa, at least about 450 kPa, at least about 500 kPa, at least about 550 kPa or at least about 600 kPa.

In some embodiments, the tensile strength of the biophotonic material is up to about 8 MPa.

The tear strength of the biophotonic material will vary depending on the intended use. The tear strength property of the biophotonic material can be tested using a 500N capacity tabletop mechanical testing system (#5942R4910, Instron) with a 5N maximum static load cell (#102608, Instron). Pneumatic side action grips can be used to secure the samples (#2712-019, Instron). Samples can be tested with a constant extension rate (for example, of about 2 mm/min) until failure. In accordance with the invention, tear strength is calculated as the force at failure divided by the average thickness (N/mm).

In some embodiments, the biophotonic material has a tear strength of from about 0.1 N/mm to about 1 N/mm. In some embodiments, the tear strength is from about 0.20 N/mm to about 0.40 N/mm, from about 0.25 N/mm to about 0.35 N/mm, from about 0.25 N/mm to about 0.45 N/mm, from about 0.35 N/mm to about 0.535 N/mm, from about 0.45 N/mm to about 0.65 N/mm, from about 0.55 N/mm to about 0.75 N/mm, from about 0.65 N/mm to about 0.85 N/mm, from about 0.75 N/mm to about 0.95 N/mm.

In some embodiments, the tear strength is at least about 0.10 N/mm, at least about 0.15 N/mm, at least about 0.20 N/mm, at least about 0.25 N/mm, at least about 0.30 N/mm, at least about 0.35 N/mm, at least about 0.40 N/mm, at least about 0.45 N/mm, at least about 0.55 N/mm or at least about 1 N/mm.

The adhesion strength of the biophotonic material will vary depending on the intended use. Adhesion strength can be determined in accordance with ASTM D-3330-78, PSTC-101 and is a measure of the force required to remove a biophotonic material from a test panel at a specific angle and rate of removal. In some embodiments, a predetermined size of a biophotonic material is applied to a horizontal surface of a clean glass test plate. A hard rubber roller is used to firmly apply the piece and remove all discontinuities and entrapped air. The free end of the piece of biophotonic material is then doubled back nearly touching itself so that the angle of removal of the piece from the glass plate will be 180 degrees. The free end of the piece of biophotonic material is attached to the adhesion tester scale (e.g. an Instron tensile tester or Harvey tensile tester). The test plate is then clamped in the jaws of the tensile testing machine capable of moving the plate away from the scale at a predetermined constant rate. The scale reading in kg is recorded as the biophotonic material is peeled from the glass surface.

In some embodiments, the adhesion strength can be measured by taking into account the static friction of the biophotonic material. For some embodiments of the cohesive biophotonic materials of the present disclosure, the adhesive properties are linked to their levels of static friction, or stiction. In these cases, the adhesion strength can be measured by placing the sample on a test surface and pulling one end of the sample at an angle of approximately 0° (substantially parallel to the surface) whilst applying a known downward force (e.g. a weight) on the sample and measuring the weight at which the sample slips from the surface. The normal force F_n, is the force exerted by each surface on the other in a perpendicular (normal) direction to the surface and is calculated by multiplying the combined weight of the sample and the weight by the gravity constant (g) ($9.8 m/s^2$). The biophotonic material with the weight on top is then pulled away from a balance until the biophotonic material slips from the surface and the weight is recorded on the scale. The weight recorded on the scale is equivalent to the force required to overcome the friction. The force of friction (F_f) is then calculated by multiplying the weight recorded on the scale by g. Since $F_f \leq \mu F_n$ (Coulomb's friction law), the friction

coefficient μ can be obtained by dividing F_f / F_n. The stress required to shear a material from a surface (adhesion strength) can then be calculated from the friction coefficient, μ, by multiplying the weight of the material by the friction coefficient.

In some embodiments, the biophotonic material has an adhesion strength that is less than its tensile strength. In some embodiments, the biophotonic material has an adhesion strength that is less than its tear strength.

In some embodiments, the biophotonic material has an adhesion strength of from about 0.01 N/mm to about 0.60 N/mm. In some embodiments, the adhesion strength is from about 0.20 N/mm to about 0.40 N/mm, or from about 0.25 N/mm to about 0.35 N/mm. In some embodiments, the adhesion strength is less than about 0.10 N/mm, less than about 0.15 N/mm, less than about 0.20 N/mm, less than about 0.25 N/mm, less than about 0.30 N/mm, less than about 0.35 N/mm, less than about 0.40 N/mm, less than about 0.45 N/mm, less than about 0.55 N/mm or less than about 0.60 N/mm.

(6) Methods of Use

The biophotonic materials of the present disclosure may have cosmetic and/or medical benefits. They can be used to promote skin rejuvenation and skin conditioning, promote the treatment of a skin disorder such as acne, eczema or psoriasis, promote tissue repair, and promote wound healing including periodontitis pockets. They can be used to treat acute inflammation. Acute inflammation can present itself as pain, heat, redness, swelling and loss of function. It includes those seen in allergic reactions such as insect bites e.g.; mosquito, bees, wasps, poison ivy, or post-ablative treatment.

Accordingly, in certain embodiments, the present disclosure provides a method for treating acute inflammation.

In certain embodiments, the present disclosure provides a method for providing skin rejuvenation or for improving skin condition, treating a skin disorder, preventing or treating scarring, and/or accelerating wound healing and/or tissue repair, the method comprising: applying a biophotonic material of the present disclosure to the area of the

skin or tissue in need of treatment, and illuminating the biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the chromophore(s) present in the biophotonic material.

In the methods of the present disclosure, any source of actinic light can be used. Any type of halogen, LED or plasma arc lamp, or laser may be suitable. The primary characteristic of suitable sources of actinic light will be that they emit light in a wavelength (or wavelengths) appropriate for activating the one or more photoactivators present in the composition. In one embodiment, an argon laser is used. In another embodiment, a potassium-titanyl phosphate (KTP) laser (e.g. a GreenLight™ laser) is used. In yet another embodiment, a LED lamp such as a photocuring device is the source of the actinic light. In yet another embodiment, the source of the actinic light is a source of light having a wavelength between about 200 to 800 nm. In another embodiment, the source of the actinic light is a source of visible light having a wavelength between about 400 and 600 nm. In another embodiment, the source of the actinic light is a source of visible light having a wavelength between about 400 and 700 nm. In yet another embodiment, the source of the actinic light is blue light. In yet another embodiment, the source of the actinic light is red light. In yet another embodiment, the source of the actinic light is green light. Furthermore, the source of actinic light should have a suitable power density. Suitable power density for non-collimated light sources (LED, halogen or plasma lamps) are in the range from about 0.1 mW/cm^2 to about 200 mW/cm^2. Suitable power density for laser light sources are in the range from about 0.5 mW/cm^2 to about 0.8 mW/cm^2.

In some embodiments of the methods of the present disclosure, the light has an energy at the subject's skin surface of between about 0.1 mW/cm^2 and about 500 mW/cm^2, or 0.1-300 mW/cm^2, or 0.1-200 mW/cm^2, wherein the energy applied depends at least on the condition being treated, the wavelength of the light, the distance of the skin from the light source and the thickness of the biophotonic material. In certain embodiments, the light at the subject's skin is between about 1-40 mW/cm^2, or 20-60 mW/cm^2, or 40-80 mW/cm^2, or 60-100 mW/cm^2, or 80-120 mW/cm^2, or 100-140 mW/cm^2, or 30-180 mW/cm^2, or 120-160 mW/cm^2, or 140-180 mW/cm^2, or 160-200 mW/cm^2, or 110-240 mW/cm^2, or 110-150 mW/cm^2, or 190-240 mW/cm^2.

The activation of the chromophore(s) within the biophotonic material may take place almost immediately on illumination (femto- or pico seconds). A prolonged exposure period may be beneficial to exploit the synergistic effects of the absorbed, reflected and reemitted light of the biophotonic material of the present disclosure and its interaction with the tissue being treated. In one embodiment, the time of exposure to actinic light of the tissue or skin or biophotonic material is a period between 1 minute and 5 minutes. In another embodiment, the time of exposure to actinic light of the tissue or skin or biophotonic material is a period between 1 minute and 5 minutes. In some other embodiments, the biophotonic material is illuminated for a period between 1 minute and 3 minutes. In certain embodiments, light is applied for a period of 1-30 seconds, 15-45 seconds, 30-60 seconds, 0.75-1.5 minutes, 1-2 minutes, 1.5-2.5 minutes, 2-3 minutes, 2.5-3.5 minutes, 3-4 minutes, 3.5-4.5 minutes, 4-5 minutes, 5-10 minutes, 10-15 minutes, 15-20 minutes, or 20-30 minutes. The treatment time may range up to about 90 minutes, about 80 minutes, about 70 minutes, about 60 minutes, about 50 minutes, about 40 minutes or about 30 minutes. It will be appreciated that the treatment time can be adjusted in order to maintain a dosage by adjusting the rate of fluence delivered to a treatment area. For example, the delivered fluence may be about 4 to about 60 J/cm^2, about 10 to about 60 J/cm^2, about 10 to about 50 J/cm^2, about 10 to about 40 J/cm^2, about 10 to about 30 J/cm^2, about 20 to about 40 J/cm^2, about 15 J/cm^2 to 25 J/cm^2, or about 10 to about 20 J/cm^2.

In certain embodiments, the biophotonic material may be re-illuminated at certain intervals. In yet another embodiment, the source of actinic light is in continuous motion over the treated area for the appropriate time of exposure. In yet another embodiment, the biophotonic composition may be illuminated until the biophotonic composition is at least partially photobleached or fully photobleached.

In certain embodiments, the chromophore(s) in the cohesive matrix can be photoexcited by ambient light including from the sun and overhead lighting. In certain embodiments, the chromophore(s) can be photoactivated by light in the visible range of the electromagnetic spectrum. The light can be emitted by any light source such as sunlight, light bulb, an LED device, electronic display screens such as on a television, computer, telephone, mobile device, flashlights on mobile devices. In the methods of the present disclosure, any source of light can be used. For example, a combination of ambient light

and direct sunlight or direct artificial light may be used. Ambient light can include overhead lighting such as LED bulbs, fluorescent bulbs etc, and indirect sunlight.

In the methods of the present disclosure, the biophotonic material may be removed from the skin following application of light. In some embodiments the biophotonic material is peeled off from the skin following application of light. In some embodiments, the biophotonic material is removed as a single piece from the skin following application of light. In other embodiments, the biophotonic material is left on the tissue for an extended period of time and re-activated with direct or ambient light at appropriate times to treat the condition.

In certain embodiments of the method of the present disclosure, the biophotonic material can be applied to the tissue, such as on the face, once, twice, three times, four times, five times or six times a week, daily, or at any other frequency. The total treatment time can be one week, two weeks, three weeks, four weeks, five weeks, six weeks, seven weeks, eight weeks, nine weeks, ten weeks, eleven weeks, twelve weeks, or any other length of time deemed appropriate. In certain embodiments, the total tissue area to be treated may be split into separate areas (cheeks, forehead), and each area treated separately. For example, the composition may be applied topically to a first portion, and that portion illuminated with light, and the biophotonic composition then removed. Then the composition is applied to a second portion, illuminated and removed. Finally, the composition is applied to a third portion, illuminated and removed.

In certain embodiments, the biophotonic material can be used following wound closure to optimize scar revision. In this case, the biophotonic material may be applied at regular intervals such as once a week, or at an interval deemed appropriate by the physician.

In certain embodiments, the biophotonic material can be used following acne treatment to maintain the condition of the treated skin. In this case, the biophotonic material may be applied at regular intervals such as once a week, or at an interval deemed appropriate by the physician.

In certain embodiments, the biophotonic material can be used following ablative skin rejuvenation treatment to maintain the condition of the treated skin. In this case, the

biophotonic material may be applied at regular intervals such as once a week, or at an interval deemed appropriate by the physician.

In the methods of the present disclosure, additional components may optionally be included in the biophotonic materials or used in combination with the biophotonic materials. Such additional components include, but are not limited to, healing factors, antimicrobials, oxygen-rich agents, wrinkle fillers such as botox, hyaluronic acid and polylactic acid, fungal, anti-bacterial, anti-viral agents and/or agents that promote collagen synthesis. These additional components may be applied to the skin in a topical fashion, prior to, at the same time of, and/or after topical application of the biophotonic materials of the present disclosure. Suitable healing factors comprise compounds that promote or enhance the healing or regenerative process of the tissues on the application site. During the photoactivation of a biophotonic material of the present disclosure, there may be an increase of the absorption of molecules of such additional components at the treatment site by the skin or the mucosa. In certain embodiments, an augmentation in the blood flow at the site of treatment can observed for a period of time. An increase in the lymphatic drainage and a possible change in the osmotic equilibrium due to the dynamic interaction of the free radical cascades can be enhanced or even fortified with the inclusion of healing factors. Healing factors may also modulate the biophotonic output from the biophotonic composition such as photobleaching time and profile, or modulate leaching of certain ingredients within the composition. Suitable healing factors include, but are not limited to glucosamines, allantoins, saffron, agents that promote collagen synthesis, anti-fungal, anti-bacterial, anti-viral agents and wound healing factors such as growth factors.

(i) Skin Rejuvenation

The biophotonic material of the present disclosure may be useful in promoting skin rejuvenation or improving skin condition and appearance. The dermis is the second layer of skin, containing the structural elements of the skin, the connective tissue. There are various types of connective tissue with different functions. Elastin fibers give the skin its elasticity, and collagen gives the skin its strength.

The junction between the dermis and the epidermis is an important structure. The dermal-epidermal junction interlocks forming finger-like epidermal ridges. The cells of the epidermis receive their nutrients from the blood vessels in the dermis. The epidermal ridges increase the surface area of the epidermis that is exposed to these blood vessels and the needed nutrients.

The aging of skin comes with significant physiological changes to the skin. The generation of new skin cells slows down, and the epidermal ridges of the dermal-epidermal junction flatten out. While the number of elastin fibers increases, their structure and coherence decreases. Also the amount of collagen and the thickness of the dermis decrease with the ageing of the skin.

Collagen is a major component of the skin's extracellular matrix, providing a structural framework. During the aging process, the decrease of collagen synthesis and insolubilization of collagen fibers contribute to a thinning of the dermis and loss of the skin's biomechanical properties.

The physiological changes to the skin result in noticeable aging symptoms often referred to as chronological-, intrinsic- and photo-ageing. The skin becomes drier, roughness and scaling increase, the appearance becomes duller, and most obviously fine lines and wrinkles appear. Other symptoms or signs of skin aging include, but are not limited to, thinning and transparent skin, loss of underlying fat (leading to hollowed cheeks and eye sockets as well as noticeable loss of firmness on the hands and neck), bone loss (such that bones shrink away from the skin due to bone loss, which causes sagging skin), dry skin (which might itch), inability to sweat sufficiently to cool the skin, unwanted facial hair, freckles, age spots, spider veins, rough and leathery skin, fine wrinkles that disappear when stretched, loose skin, a blotchy complexion.

The dermal-epidermal junction is a basement membrane that separates the keratinocytes in the epidermis from the extracellular matrix, which lies below in the dermis. This membrane consists of two layers: the basal lamina in contact with the keratinocytes, and the underlying reticular lamina in contact with the extracellular matrix. The basal lamina is rich in collagen type IV and laminin, molecules that play a role in providing a structural network and bioadhesive properties for cell attachment.

Laminin is a glycoprotein that only exists in basement membranes. It is composed of three polypeptide chains (alpha, beta and gamma) arranged in the shape of an asymmetric cross and held together by disulfide bonds. The three chains exist as different subtypes which result in twelve different isoforms for laminin, including Laminin-1 and Laminin-5.

The dermis is anchored to hemidesmosomes, specific junction points located on the keratinocytes, which consist of α-integrins and other proteins, at the basal membrane keratinocytes by type VII collagen fibrils. Laminins, and particularly Laminin-5, constitute the real anchor point between hemidesmosomal transmembrane proteins in basal keratinocytes and type VII collagen.

Laminin-5 synthesis and type VII collagen expression have been proven to decrease in aged skin. This causes a loss of contact between dermis and epidermis, and results in the skin losing elasticity and becoming saggy.

Recently another type of wrinkles, generally referred to as expression wrinkles, got general recognition. These wrinkles require loss of resilience, particularly in the dermis, because of which the skin is no longer able to resume its original state when facial muscles which produce facial expressions exert stress on the skin, resulting in expression wrinkles.

The biophotonic material of the present disclosure and methods of the present disclosure promote skin rejuvenation. In certain embodiments, the biophotonic material and methods of the present disclosure promote skin condition such as skin luminosity, reduction of pore size, reducing blotchiness, making even skin tone, reducing dryness, and tightening of the skin. In certain embodiments, the biophotonic material and methods of the present disclosure promote collagen synthesis. In certain other embodiments, the biophotonic material and methods of the present disclosure may reduce, diminish, retard or even reverse one or more signs of skin aging including, but not limited to, appearance of fine lines or wrinkles, thin and transparent skin, loss of underlying fat (leading to hollowed cheeks and eye sockets as well as noticeable loss of firmness on the hands and neck), bone loss (such that bones shrink away from the skin

due to bone loss, which causes sagging skin), dry skin (which might itch), inability to sweat sufficiently to cool the skin, unwanted facial hair, freckles, age spots, spider veins, rough and leathery skin, fine wrinkles that disappear when stretched, loose skin, or a blotchy complexion. In certain embodiments, the biophotonic material and methods of the present disclosure may induce a reduction in pore size, enhance sculpturing of skin subsections, and/or enhance skin translucence.

In certain embodiments, the biophotonic material may be used in conjunction with collagen promoting agents. Agents that promote collagen synthesis (i.e., pro-collagen synthesis agents) include amino acids, peptides, proteins, lipids, small chemical molecules, natural products and extracts from natural products.

For instance, it was discovered that intake of vitamin C, iron, and collagen can effectively increase the amount of collagen in skin or bone. See, e.g., U.S. Patent Application Publication 20090069217. Examples of the vitamin C include an ascorbic acid derivative such as L-ascorbic acid or sodium L-ascorbate, an ascorbic acid preparation obtained by coating ascorbic acid with an emulsifier or the like, and a mixture containing two or more of those vitamin Cs at an arbitrary rate. In addition, natural products containing vitamin C such as acerola and lemon may also be used. Examples of the iron preparation include: an inorganic iron such as ferrous sulfate, sodium ferrous citrate, or ferric pyrophosphate; an organic iron such as heme iron, ferritin iron, or lactoferrin iron; and a mixture containing two or more of those irons at an arbitrary rate. In addition, natural products containing iron such as spinach or liver may also be used. Moreover, examples of the collagen include: an extract obtained by treating bone, skin, or the like of a mammal such as bovine or swine with an acid or alkaline; a peptide obtained by hydrolyzing the extract with a protease such as pepsin, trypsin, or chymotrypsin; and a mixture containing two or more of those collagens at an arbitrary rate. Collagens extracted from plant sources may also be used.

Additional pro-collagen synthesis agents are described, for example, in U.S. Patent Patents 7598291, 7722904, 6203805 , 5529769, etc, and U.S. Patent Application Publications 20060247313, 20080108681, 20110130459, 20090325885, 20110086060, etc.

(ii) Skin disorders

The biophotonic materials and methods of the present disclosure may be used to treat skin disorders that include, but are not limited to, erythema, telangiectasia, actinic telangiectasia, psoriasis, skin cancer, pemphigus, sunburn, dermatitis, eczema, rashes, impetigo, lichen simplex chronicus, rhinophyma, perioral dermatitis, pseudofolliculitis barbae, drug eruptions, erythema multiforme, erythema nodosum, granuloma annulare, actinic keratosis, purpura, alopecia areata, aphthous stomatitis, drug eruptions, dry skin, chapping, xerosis, ichthyosis vulgaris, fungal infections, herpes simplex, intertrigo, keloids, keratoses, milia, moluscum contagiosum, pityriasis rosea, pruritus, urticaria, and vascular tumors and malformations. Dermatitis includes contact dermatitis, atopic dermatitis, seborrheic dermatitis, nummular dermatitis, generalized exfoliative dermatitis, and statis dermatitis. Skin cancers include melanoma, basal cell carcinoma, and squamous cell carcinoma.

(iii) Acne and Acne Scars

The biophotonic materials and methods of the present disclosure may be used to treat acne. As used herein, "acne" means a disorder of the skin caused by inflammation of skin glands or hair follicles. The biophotonic materials and methods of the disclosure can be used to treat acne at early pre-emergent stages or later stages where lesions from acne are visible. Mild, moderate and severe acne can be treated with embodiments of the biophotonic compositions and methods. Early pre-emergent stages of acne usually begin with an excessive secretion of sebum or dermal oil from the sebaceous glands located in the pilosebaceous apparatus. Sebum reaches the skin surface through the duct of the hair follicle. The presence of excessive amounts of sebum in the duct and on the skin tends to obstruct or stagnate the normal flow of sebum from the follicular duct, thus producing a thickening and solidification of the sebum to create a solid plug known as a comedone. In the normal sequence of developing acne, hyperkeratinazation of the follicular opening is stimulated, thus completing blocking of the duct. The usual results are papules, pustules, or cysts, often contaminated with bacteria, which cause secondary infections. Acne is characterized particularly by the presence of comedones, inflammatory papules, or cysts. The appearance of acne may range from slight skin irritation to pitting and even the development of disfiguring scars. Accordingly, the biophotonic materials and

methods of the present disclosure can be used to treat one or more of skin irritation, pitting, development of scars, comedones, inflammatory papules, cysts, hyperkeratinazation, and thickening and hardening of sebum associated with acne.

Some types of acne include, for example, acne vulgaris, cystic acne, acne atrophica, bromide acne, chlorine acne, acne conglobata, acne cosmetica, acne detergicans, epidemic acne, acne estivalis, acne fulminans, halogen acne, acne indurata, iodide acne, acne keloid, acne mechanica, acne papulosa, pomade acne, premenstral acne, acne pustulosa, acne scorbutica, acne scrofulosorum, acne urticata, acne varioliformis, acne venenata, propionic acne, acne excoriee, gram negative acne, steroid acne, and nodulocystic acne.

Some skin disorders present various symptoms including redness, flushing, burning, scaling, pimples, papules, pustules, comedones, macules, nodules, vesicles, blisters, telangiectasia, spider veins, sores, surface irritations or pain, itching, inflammation, red, purple, or blue patches or discolorations, moles, and/or tumors.

The biophotonic materials and methods of the present disclosure may be used to treat various types of acne. Some types of acne include, for example, acne vulgaris, cystic acne, acne atrophica, bromide acne, chlorine acne, acne conglobata, acne cosmetica, acne detergicans, epidemic acne, acne estivalis, acne fulminans, halogen acne, acne indurata, iodide acne, acne keloid, acne mechanica, acne papulosa, pomade acne, premenstral acne, acne pustulosa, acne scorbutica, acne scrofulosorum, acne urticata, acne varioliformis, acne venenata, propionic acne, acne excoriee, gram negative acne, steroid acne, and nodulocystic acne.

In certain embodiments, the biophotonic material of the present disclosure is used in conjunction with systemic or topical antibiotic treatment. For example, antibiotics used to treat acne include tetracycline, erythromycin, minocycline, doxycycline, which may also be used with the compositions and methods of the present disclosure. The use of the biophotonic material can reduce the time needed for the antibiotic treatment or reduce the dosage.

(iv) Wound Healing

The biophotonic materials and methods of the present disclosure may be used to treat wounds, promote wound healing, promote tissue repair and/or prevent or reduce cosmesis including improvement of motor function (e.g. movement of joints). Wounds that may be treated by the biophotonic materials and methods of the present disclosure include, for example, injuries to the skin and subcutaneous tissue initiated in different ways (e.g., pressure ulcers from extended bed rest, wounds induced by trauma or surgery, burns, ulcers linked to diabetes or venous insufficiency, wounds induced by conditions such as periodontitis) and with varying characteristics. In certain embodiments, the present disclosure provides biophotonic materials and methods for treating and/or promoting the healing of, for example, burns, incisions, excisions, lesions, lacerations, abrasions, puncture or penetrating wounds, surgical wounds, contusions, hematomas, crushing injuries, amputations, sores and ulcers.

Biophotonic materials and methods of the present disclosure may be used to treat and/or promote the healing of chronic cutaneous ulcers or wounds, which are wounds that have failed to proceed through an orderly and timely series of events to produce a durable structural, functional, and cosmetic closure. The vast majority of chronic wounds can be classified into three categories based on their etiology: pressure ulcers, neuropathic (diabetic foot) ulcers and vascular (venous or arterial) ulcers.

For example, the present disclosure provides biophotonic materials and methods for treating and/or promoting healing of a diabetic ulcer. Diabetic patients are prone to foot and other ulcerations due to both neurologic and vascular complications. Peripheral neuropathy can cause altered or complete loss of sensation in the foot and/or leg. Diabetic patients with advanced neuropathy lose all ability for sharp-dull discrimination. Any cuts or trauma to the foot may go completely unnoticed for days or weeks in a patient with neuropathy. A patient with advanced neuropathy loses the ability to sense a sustained pressure insult, as a result, tissue ischemia and necrosis may occur leading to for example, plantar ulcerations. Microvascular disease is one of the significant complications for diabetics which may also lead to ulcerations. In certain embodiments, biophotonic materials and methods of treating a chronic wound are provided here in, where the chronic wound is characterized by diabetic foot ulcers and/or ulcerations due to neurologic and/or vascular complications of diabetes.

In other examples, the present disclosure provides biophotonic materials and methods for treating and/or promoting healing of a pressure ulcer. Pressure ulcers include bed sores, decubitus ulcers and ischial tuberosity ulcers and can cause considerable pain and discomfort to a patient. A pressure ulcer can occur as a result of a prolonged pressure applied to the skin. Thus, pressure can be exerted on the skin of a patient due to the weight or mass of an individual. A pressure ulcer can develop when blood supply to an area of the skin is obstructed or cut off for more than two or three hours. The affected skin area can turn red, become painful and necrotic. If untreated, the skin can break open and become infected. A pressure ulcer is therefore a skin ulcer that occurs in an area of the skin that is under pressure from e.g. lying in bed, sitting in a wheelchair, and/or wearing a cast for a prolonged period of time. Pressure ulcers can occur when a person is bedridden, unconscious, unable to sense pain, or immobile. Pressure ulcers often occur in boney prominences of the body such as the buttocks area (on the sacrum or iliac crest), or on the heels of foot.

Additional types of wounds that can be treated by the biophotonic materials and methods of the present disclosure include those disclosed by U.S. Pat. Appl. Publ. No. 20090220450, which is incorporated herein by reference.

There are three distinct phases in the wound healing process. First, in the inflammatory phase, which typically occurs from the moment a wound occurs until the first two to five days, platelets aggregate to deposit granules, promoting the deposit of fibrin and stimulating the release of growth factors. Leukocytes migrate to the wound site and begin to digest and transport debris away from the wound. During this inflammatory phase, monocytes are also converted to macrophages, which release growth factors for stimulating angiogenesis and the production of fibroblasts.

Second, in the proliferative phase, which typically occurs from two days to three weeks, granulation tissue forms, and epithelialization and contraction begin. Fibroblasts, which are key cell types in this phase, proliferate and synthesize collagen to fill the wound and provide a strong matrix on which epithelial cells grow. As fibroblasts produce collagen, vascularization extends from nearby vessels, resulting in granulation tissue. Granulation tissue typically grows from the base of the wound. Epithelialization involves the migration of epithelial cells from the wound surfaces to seal the wound. Epithelial cells

are driven by the need to contact cells of like type and are guided by a network of fibrin strands that function as a grid over which these cells migrate. Contractile cells called myofibroblasts appear in wounds, and aid in wound closure. These cells exhibit collagen synthesis and contractility, and are common in granulating wounds.

Third, in the remodeling phase, the final phase of wound healing which can take place from three weeks up to several years, collagen in the scar undergoes repeated degradation and re-synthesis. During this phase, the tensile strength of the newly formed skin increases.

However, as the rate of wound healing increases, there is often an associated increase in scar formation. Scarring is a consequence of the healing process in most adult animal and human tissues. Scar tissue is not identical to the tissue which it replaces, as it is usually of inferior functional quality. The types of scars include, but are not limited to, atrophic, hypertrophic and keloidal scars, as well as scar contractures. Atrophic scars are flat and depressed below the surrounding skin as a valley or hole. Hypertrophic scars are elevated scars that remain within the boundaries of the original lesion, and often contain excessive collagen arranged in an abnormal pattern. Keloidal scars are elevated scars that spread beyond the margins of the original wound and invade the surrounding normal skin in a way that is site specific, and often contain whorls of collagen arranged in an abnormal fashion.

In contrast, normal skin consists of collagen fibers arranged in a basket-weave pattern, which contributes to both the strength and elasticity of the dermis. Thus, to achieve a smoother wound healing process, an approach is needed that not only stimulates collagen production, but also does so in a way that reduces scar formation.

The biophotonic materials and methods of the present disclosure promote the wound healing by promoting the formation of substantially uniform epithelialization; promoting collagen synthesis; promoting controlled contraction; and/or by reducing the formation of scar tissue. In certain embodiments, the biophotonic materials and methods of the present disclosure may promote wound healing by promoting the formation of substantially uniform epithelialization. In some embodiments, the biophotonic materials and methods of the present disclosure promote collagen synthesis. In some other

embodiments, the biophotonic materials and methods of the present disclosure promote controlled contraction. In certain embodiments, the biophotonic materials and methods of the present disclosure promote wound healing, for example, by reducing the formation of scar tissue.

In the methods of the present disclosure, the biophotonic materials of the present disclosure may also be used in combination with negative pressure assisted would closure devices and systems.

In certain embodiments, the biophotonic material is kept in place for up to one, two or 3 weeks, and illuminated with light which may include ambient light at various intervals. In this case, the composition may be covered up in between exposure to light with an opaque material or left exposed to light.

(6) Kits

The present disclosure also provides kits for preparing a biophotonic material and/or providing any of the components required for forming biophotonic materials of the present disclosure.

In some embodiments, the kit includes containers comprising the components or compositions that can be used to make the biophotonic materials of the present disclosure. In some embodiments, the kit includes a biophotonic material of the present disclosure. The different components making up the biophotonic materials of the present disclosure may be provided in separate containers. For example, if the biophotonic material is to include an oxygen-rich agent, the oxygen-rich agent is preferably provided in a container separate from the chromophore. Examples of such containers are dual chamber syringes, dual chamber containers with removable partitions, sachets with pouches, and multiple-compartment blister packs. Another example is one of the components being provided in a syringe which can be injected into a container of another component.

In other embodiments, the kit comprises a systemic drug for augmenting the treatment of the biophotonic material of the present disclosure. For example, the kit may include a

systemic or topical antibiotic, hormone treatment (e.g. for acne treatment or wound healing), or a negative pressure device.

In certain embodiments, the kit comprises a first component comprising a first chromophore; and a second component comprising at least one thickening agent, wherein the thickening agent can form a cohesive matrix when mixed with the first component, when the mixture is applied to skin, or when illuminated with light.

In other embodiments, the kit comprises a means for applying the components of the biophotonic materials.

In certain aspects, there is provided a container comprising a chamber for holding a biophotonic material, and an outlet in communication with the chamber for discharging the biophotonic material from the container, wherein the biophotonic material comprises at least one chromophore in a carrier medium which can form a biophotonic material after being discharged from the sealed chamber, for example on contact with skin or on illumination with a light. The container can be a pressurized or non-pressurized spray can.

In certain embodiments, the kit comprises a first component comprising the biophotonic material or a non-cohesive form of the biophotonic material ('precursor'), and the second component comprises a dressing or a mask. The dressing or mask may be a porous or semi-porous structure for receiving the biophotonic material. The dressing or mask may also comprise woven or non-woven fibrous materials. The biophotonic material or its precursor can be incorporated, such as by injection, into the dressing before the biophotonic material takes on a cohesive form within the dressing or mask.

In certain embodiments of the kit, the kit may further comprise a light source such as a portable light with a wavelength appropriate to activate the chromophore the biophotonic material. The portable light may be battery operated or re-chargeable.

Written instructions on how to use the biophotonic materials in accordance with the present disclosure may be included in the kit, or may be included on or associated with the containers comprising the compositions or components making up the biophotonic

materials of the present disclosure. The instructions can include information on how to form the cohesive matrix from the thickening agent(s) or matrix precursors provided with the kit.

Identification of equivalent biophotonic materials, methods and kits are well within the skill of the ordinary practitioner and would require no more than routine experimentation, in light of the teachings of the present disclosure.

Variations and modifications will occur to those of skill in the art after reviewing this disclosure. The disclosed features may be implemented, in any combination and subcombinations (including multiple dependent combinations and subcombinations), with one or more other features described herein. The various features described or illustrated above, including any components thereof, may be combined or integrated in other systems. Moreover, certain features may be omitted or not implemented. Examples of changes, substitutions, and alterations are ascertainable by one skilled in the art and could be made without departing from the scope of the information disclosed herein. All references cited herein are incorporated by reference in their entirety and made part of this application.

Practice of the disclosure will be still more fully understood from the following examples, which are presented herein for illustration only and should not be construed as limiting the disclosure in any way.

EXAMPLES

Example 1- Preparation of an exemplary cohesive biophotonic material

A cohesive biophotonic material was prepared according to an embodiment of the present disclosure and as summarized in Table 1.

Table 1. Composition of a cohesive biophotonic material according to an embodiment of the present disclosure.

Ingredients	% in composition (wt/wt)
Water	60-95
Glycerine	5-15

Propylene Glycol	2-6
Sodium hyaluronate	2-8
Urea peroxide	1-5
Glucosamine sulfate	0.5-4
Carbopol	0.1-2
First Chromophore	0.001-0.01
Second chromophore	0.001-0.01

Phase A was prepared by mixing water, eosin Y, rose bengal and glucosamine sulphate. Phase B (water, glycerine, propylene glycol, urea peroxide, carbopol) was then added to Phase A, and mixed until a light viscous liquid was obtained. Phase C (sodium hyaluronate) was then added to the mixture, and mixed until a homogenous thick cohesive gel was obtained. This cohesive homogenous gel was spread onto a flat surface, covered with an aluminum sheet and allowed to dry for 24 hours. After 24 hours, the resulting membrane was , easy to manipulate, and could be applied to the skin and peeled off with little or no residue remaining. A 5-20% weight loss of the total weight of the material was found to occur after drying for 24 hours. The membrane could be stored between two layers of saran wrap, paraffin etc. On illumination with light (peak wavelength between 400-470nm and a power density of about 30-150 mW/cm^2) for 5 minutes at a distance of 5 cm from the light source, the film emitted fluorescent light which was captured by a photospectrometer (SP-100 spectroradiometer (SP-100, ORB Optronix) to measure the power density spectra versus wavelength and is illustrated in **Figure 3**. The emitted fluorescent light was in the green, yellow and orange portions of the electromagnetic spectrum. An at least partial photobleaching of the chromophores was observed after 5 minutes of illumination.

Example 2 – Angiogenic potential of a biophotonic composition

The angiogenic potential of a biophotonic composition was evaluated using a human skin model containing fibroblasts and keratinocytes. The composition was a transparent gel comprising fluorescent chromophores, eosin Y and erythrosine. Briefly, the biophotonic composition was placed on top of the human skin model such that they were separated by a nylon mesh of 20 micron pore size. The composition was then irradiated with blue light ('activating light') for 5 minutes at a distance of 10 cm from the light

source. The activating light consisted of light emitted from an LED lamp having an average peak wavelength of about 400-470 nm and a power density of about 30-150 mW/cm^2. At a 10cm distance from the LEDs, the activating light had a power at the peak wavelength of about 2-3 $mW/cm^2/nm$ (about 2.5 $mW/cm^2/nm$), an average power of about 55-65 mW/cm^2, and a fluence in 5 minutes of irradiation of about 15-25 J/cm^2 (about 16-20 J/cm^2). Upon illumination with the activating light, the biophotonic composition emitted fluorescent light, as measured using a SP-100 spectroradiometer (SP-100, ORB Optronix) and illustrated in **Figure 4**. As the composition allowed the activating light to pass therethrough, the skin model was illuminated substantially simultaneously by both the activating light and the fluorescent light.

Since the biophotonic composition was in limited contact with the cells, the fibroblasts and keratinocytes were exposed mainly to the activating light and the fluorescent light emitted from the biophotonic composition. Conditioned media from the treated human 3D skin model were then applied to human aortic endothelial cells and diseased microvascular endothelial cells from diabetic patients previously plated in Matrigel™. The formation of tubes by endothelial cells was observed and monitored by microscopy after 24 hours. The conditioned medium from 3D skin models treated with light illumination induced endothelial tube formation in vitro, suggesting an indirect effect of the light treatment (blue light and fluorescence) on angiogenesis via the production of factors by fibroblasts and keratinocytes. Plain medium and conditioned medium of untreated skin samples were used as a control, and did not induce endothelial tube formation.

Example 3- Protein secretion and gene expression profiles of a biophotonic composition

Wounded and unwounded 3D human skin models (EpiDermFT™, MatTek Corporation) were used to assess the potential of a composition to trigger distinct protein secretion and gene expression profiles. The biophotonic composition comprised fluorescent chromophores eosin Y and erythrosine. The composition was placed on top of wounded and unwounded 3D human skin models cultured under different conditions (with growth factors, 50% growth factors and no growth factors). The skin models and the composition were separated by a nylon mesh of 20 micron pore size. Each skin model-composition combination was then irradiated with blue light ('activating light') for 2 minutes by light having a profile similar to that described in Example 2. The

fluorescence emission is shown in **Figure 4**. The controls consisted of 3D skin models not illuminated with light.

Gene expression and protein secretion profiles were measured 24 hours post-light exposure. Cytokine secretion was analyzed by antibody arrays (RayBio Human Cytokine antibody array), gene expression was analyzed by PCR array (PAHS-013A, SABioscience) and cytotoxicity was determined by GAPDH and LDH release. Results (Tables 2 and 3) showed that the light treatment is capable of increasing the level of protein secreted and gene expression involved in the early inflammatory phase of wound healing in wounded skin inserts and in non-starvation conditions. Interestingly, the effect of the light treatment on unwounded skin models has a much lower impact at the cellular level than on wounded skin insert, which suggests an effect at the cellular effect level of the light treatment. It seems to modulate the mediators involved in inflammation. Cytotoxicity was not observed in the light treatments.

Table 2 – List of proteins with statistically significant difference secretion ratio between treated and untreated control at day 3. Two arrows mean that the ratio was over 2 folds.

	Medium 1X	**Medium 0.5X**	**Medium 0X**
Increase		**ENA78 p=0.04** ↑↑ **Il-1R4/ST2 p=0.02** ↑↑ **MMP3 p=0.01** ↑↑ **MCP-2 p=0.04** ↑↑	Angiogenin p=0.03 ↑ CXCL16 p=0.04 ↑
Decrease	BMP6 p=0.01 ↓ TNFα p=0.005 ↓	BMP6 p=0.02 ↓	

Table 3 – List of genes with statistically significant difference expression ratio between treated and untreated control during the first 24 hours. Two arrows mean that the ratio was over 2 folds.

	Medium 1X	**Medium 0.5X**	**Medium 0X**
Increase	CTGF p=0.02 ↑ ITGB3 p=0.03 ↑ MMP1 p=0.03 ↑ MMP3 p=0.01 ↑ THBS1 P=0.02 ↑	CTGF P=0.04 ↑ ITGB3 p=0.05 ↑ **MMP1 p=0.02** ↑↑ **MMP10 p=0.003** ↑↑ **MMP3 p=0.007** ↑↑ **MMP8 p=0.02** ↑↑ THBS1 p=0.03 ↑	**MMP3 p=0.007** ↑↑ LAMA1 p=0.03 ↑ ITGA2 p=0.03 ↑

Decrease	HAS1 p=0.009 ↓↓ NCAM1 p=0.05 ↓↓ VCAM1 p=0.03 ↓↓ COL7A1 p=0.04 ↓ CTNNA1 p=0.03 ↓	**NCAM1 p=0.02** ↓↓ VCAN p=0.02 ↓ LAMC1 p=0.002 ↓ COL6A1 p=0.007 ↓ MMP7 p=0.003 ↓	

Example 4 - Selecting concentration of chromophore in composition

The fluorescence spectra of biophotonic materials with different concentrations of chromophores were investigated using a spectrophotometer and an activating blue light. Exemplary fluorescence spectra of Eosin Y and Fluorescein are presented in **Figures 5a** and **5b**, respectively. It was found that emitted fluorescence from the chromophores increase rapidly with increasing concentration but slows down to a plateau with further concentration increase. Activating light passing through the composition decreases with increasing chromophore composition as more light is absorbed by the chromophores. Therefore, the concentration of chromophores in biophotonic materials of the present disclosure can be selected according to a required ratio and level of activating light and fluorescence treating the tissue based on this example. The thickness of the biophotonic material can also be modulated to control the light treating the tissues, as well as the optical properties of the composition such as transparency.

Example 5 – Synergistic combination of Eosin Y and Fluorescein

The photodynamic properties of (i) Fluorescein sodium salt at about 0.09 mg/mL, (ii) Eosin Y at about 0.305 mg/mL, and (iii) a mixture of Fluorescein sodium salt at about 0.09 mg/mL and Eosin Y at about 0.305 mg/mL in a gel (comprising about 12% carbamide peroxide), were evaluated. A flexstation 384 II spectrometer was used with the following parameters: mode fluorescence, excitation 460 nm, emission spectra 465-750 nm. The absorption and emission spectra are shown in **Figures 6a** and **6b**, respectively, which indicate an energy transfer between the chromophores in the combination. It is to be reasonably inferred that this energy transfer can also occur in biophotonic materials of the present disclosure.

Example 6 – Synergistic combination of Eosin Y, Fluorescein and Rose Bengal

The photodynamic properties of (i) Rose Bengal at about 0.085 mg/mL, (ii) Fluorescein sodium salt at about 0.44 mg/mL final concentration, (ii) Eosin Y at about 0.305 mg/mL,

and (iii) a mixture of (i), (ii) and (iii) in a gel (comprising about 12% carbamide peroxide) (Set A), were evaluated. A flexstation 384 II spectrometer was used with the following parameters: mode fluorescence, excitation 460 nm, emission spectra 465-750 nm. The absorbance and emission spectra are shown in **Figures 7a** and **7b**, respectively, which indicate an energy transfer between the chromophores in the chromophore combination. It is to be reasonably inferred that this energy transfer can also occur in biophotonic materials of the present disclosure.

Energy transfer was also seen between: Eosin Y and Rose Bengal; Phloxine B and Eosin Y; Phloxine B, Eosin Y and Fluorescein, amongst other combinations. It is to be reasonably inferred that energy transfer can also occur in biophotonic materials of the present disclosure.

Example 7 – Collagen formation potential of a biophotonic composition

A biophotonic composition comprising 0.01% eosin Y and 0.01% fluorescein in a carrier matrix (1.8% carbopol gel) was evaluated for its potential to induce collagen formation. Dermal human fibroblasts were plated in glass-bottomed dishes with wells (MatTek®). There were approximately 4000 cells per well. After 48 hours, the glass-bottomed dishes were inverted and the cells were treated through the glass bottom with (i) no light (control), (ii) sunlight exposure for about 13 minutes at noon (control), (iii) the composition applied to the glass well bottom on the other side of the cells (no light exposure), (iv) the composition applied to the glass well bottom on the other side of the cells and exposed to sunlight for about 13 minutes at noon, and (v) the composition applied to the glass well bottom on the other side of the cells and illuminated with blue light. In the case of (iii), (iv) and v), there was no direct contact between the cells and the composition. In the case of (iv), the cells were exposed to emitted light from and through the Eosin Y and Fluorescein composition when exposed to sunlight. A partial photobleaching was observed in (iv) and total photobleaching in (v). After the treatment, the cells were washed and incubated in regular medium for 48 hours. A collagen assay was then performed on the supernatant using the Picro-Sirius red method. This involved adding Sirius red dye solution in picric acid to the supernatant, incubating with gentle agitation for 30 minutes followed by centrifugation to form a pellet. The pellet was washed first with 0.1N HCl and then 0.5 N NaOH to remove free dye. After centrifugation, the suspension was read at 540 nm for collagen type I. The results are shown in Table 4.

Table 4 – A qualitative comparison of collagen type I concentration in a dermal human fibroblast supernatant exposed to (i) no light (control), (ii) sunlight exposure for about 13 minutes at noon (control), (iii) any light emitted from the Eosin Y and Fluorescein composition through a glass separation (no activating light exposure), (iv) any light emitted from and through the Eosin Y and Fluorescein composition through a glass separation when illuminated with sunlight exposure for about 13 minutes at noon, and (v) light emitted from and through the composition through a glass separation when illuminated with blue light. ++ indicates collagen levels about twice as high as +, and +++ indicates collagen levels about three times as high as +.

	No light (control)	Sunlight alone (alone)	Eosin Y and Fluorescein – no light	Eosin Y and Fluorescein – sunlight	Eosin Y and Fluorescein – blue light
Collagen formation	+	+	++	+++	+++

There was a statistical difference between the collagen levels induced by the Eosin Y and Fluorescein composition exposed to sunlight compared to the no light and sunlight alone controls. There was also a statistical difference between the collagen levels induced by composition exposed to blue light compared to the no light and sunlight alone controls. Collagen generation is indicative of a potential for tissue repair including stabilization of granulation tissue and decreasing of wound size. It is also linked to reduction of fine lines, a decrease in pore size, improvement of texture and improvement of tensile strength of intact skin.

It is to be reasonably expected that the same or similar biophotonic effects can be obtained with a cohesive biophotonic material of the present disclosure providing substantially similar or equivalent light emission properties as the compositions described in Examples 2, 3 and 7.

Example 8 – Preparation of an exemplary cohesive biophotonic material based on silicone

Cohesive biophotonic membranes were made, according to embodiments of the present disclosure, comprising a silicone membrane having incorporated therein chromophores, specifically water soluble chromophores Eosin Y and Fluorescein. The biophotonic

membranes were based on a colloidal system comprising an aqueous phase of solubilized chromophores within a solid silicone phase (micro-emulsion). The cohesive biophotonic membrane was made by mixing a base (B) comprising (i) dimethyl siloxane, dimethylvinyl terminated, (ii) dimethylvinylated and trimethylated silica, and (iii) tetra (trimethoxysiloxy) silane in ethyl benzene and with a curing agent (C) comprising (i) dimethyl, methylhydrogen siloxane, (ii) dimethyl siloxane, dimethylvinyl terminated, (iii) dimethylvinylated and trimethylated silica, and (iv) tetramethyl tetravinyl cyclotetra siloxane in ethyl benzene (both in liquid form from a Sylgard® 184 silicone elastomer kit, Dow Corning Corp, Ltd). When mixed at a ratio of 10 (B): 1 (C), the mixture cures to an elastic material. The material obtained was a flexible and transparent/translucent elastomer. A stabilizing agent was also used to stabilize the emulsion and avoid phase separation. In one example, carboxymethyl cellulose (CMC) was used as the stabilizing agent (about 2%). In another example, gelatin was used as the stabilizing agent.

In one embodiment, 9.4 g of the base was mixed with 0.94 g of the curing agent, and to this was added 2 mL of 2% CMC solution (18 wt%) containing 0.327 mg (0.011 wt% within the aqueous phase) of eosin Y and 0.327 mg (0.011 wt% within the aqueous phase) of fluorescein. The whole mixture was emulsified vigorously for about 15 minutes and cast on a petri dish for curing at 35°C for about 16 hours forming a translucent/transparent membrane comprising a silicone matrix with embedded droplets of the chromophore in CMC phase. In another embodiment, 2mL of gelatin solution (5%) was used as the stabilizing agent instead of CMC. This also formed a translucent/transparent membrane comprising a silicone matrix with embedded droplets of the chromophores in the gelatin phase. In both cases, a 2 mm thick membrane was achieved, although it will be understood that the thickness of the membrane can be controlled by the volume of cast solution. In both cases, the membranes could be applied and removed from tissue (human skin) in one piece.

It will be appreciated that other stabilizing agents which can be used which include but are not limited to methyl cellulose or hydroxyethylcellulose. Other concentrations of gelatin can be used such as from about 1 to about 20 wt%. The total weight percent of the aqueous phase can range from about 2 weight% to about 40 weight %.

When the biophotonic membranes were illuminated with blue light, the chromophores absorbed and emitted light. An at least partial photobleaching of the chromophores was observed with time of illumination. When the water soluble fluorescent chromophores were incorporated directly into the silicone (i.e. as a single phase), they did not absorb or emit light. It is believed by the inventors that their inclusion in the silicone membrane as an aqueous phase provided the appropriate medium to allow biophotonic activity. Instead of a liquid phase, the water soluble chromophores could also be directly surrounded by any other medium which allows the absorption and emission of light, such as a gel or water, or adsorbed on fine solid particles such as, but not limited to, silica and hydroxyapatite particles.

The above example can also be demonstrated using any other liposoluble polymers or matrices, instead of silicone.

Example 9 – Preparation of an exemplary cohesive biophotonic material based on gelatin

A cohesive biophotonic material was made, according to another embodiment of the present disclosure, comprising a cohesive gelatin matrix incorporating therein chromophores. In a typical preparation, 10 g of gelatin was dispersed in 50 mL of de-ionized water then heated to around 65°C in a hot water bath under continuous stirring until complete dissolution of gelatin. While the temperature was decreased to around 40°C, 0.5 mL of eosin Y solution (10.9 mg/mL) was added to the gelatin solution, and the resulting gelatin solution (20% w/v) including eosin Y was cast on a petridish and cooled down to room temperature to form a hydrogel membrane of gelatin containing eosin Y. A transparent elastic membrane of 2 mm was obtained. The membrane could be applied and removed from tissue in one piece. When the gelatin membrane was illuminated with blue light, the chromophore absorbed and emitted light. An at least partial photobleaching of the chromophore within the cohesive membrane was observed after illumination. A similarly peelable membrane was also obtained with a gelatin matrices having more than 5 wt%. Peelable biophotonic membranes having < about 5 weight % gelatin could be obtained by adding chemical cross-linkers such as glutaraldehyde or glyoxal. Similar results were also obtained using chitosan as the cohesive matrix instead of gelatin.

Example 10 - Measurement of Tensile Strength

The tensile strength of certain embodiments of the silicone and gelatin-based cohesive biophotonic materials formed according to Examples 8 and 9 were measured according to the following method. Rectangular test samples of 50 mm x 10 mm having a 2 mm thickness were prepared based on the silicone and gelatin membranes of Examples 8 and 9 as well the membranes without chromophore(s). Sample length, width and thickness were verified at 3 points per dimension using a Vernier caliper and were used to calculate the cross-section area of the samples.

Each end of the sample was tightly fixed between a clamp with a 15mm rubber grip linked to a 1/16'' steel cable. This sample/clamp assembly was installed vertically in a rigid scaffold made of steel tubes. The top cable was hung from a manual ratcheting device for winching the top cable away from the bottom cable, and the bottom cable was attached to a weight. The weight was loaded on a precision balance which was installed vertically under the manual ratcheting device. The sample between the clamps was then stretched at a steady slow rate using the winch. The force required to deform the sample was measured by the decrease of weight measured on the balance relative to a baseline length. The baseline was measured by relaxing the sample so that the weight measured by the balance was maximal. The top cable was then pulled away from the bottom cable via the ratcheting mechanism until a weight decrease was observed on the scale. This point was considered baseline and the reading on the balance was recorded and the length of the sample (distance between the clamps) was measured with a Vernier caliper. This length was defined as the initial length of the sample. The ratchet was then activated stepwise to stretch the sample with the balance reading and sample length being recorded at every step until rupture of the sample. Absence of grip slippage was verified by checking the stabilization of the measured weight and using visual indicators on the samples.

Typical stress-strain curves for the silicone-based and the gelatin-based membranes are shown in **Figures 8a** and **8b**, respectively. The silicone membranes with and without chromophores, and with different thickening agents, had substantially similar tensile properties. The gelatin membranes with and without chromophores also had substantially similar tensile properties. The gelatin-based membranes had a tensile strength of about 0.01 MPa (±10%) (100 kPa) and an Elastic Modulus (slope of the

stress/strain curve) of about 0.01 MPa (±10%) (100 kPa). The silicone-based membranes were stiffer than the gelatin-based membranes and had an average Elastic Modulus of about 1.11 MPa (±10%) (1110 kPa). This was well within the range reported in literature of about 1.2-1.8 MPa) The measured tensile strength was 0.405MPa (826g) due to grip slippage but is expected to be up to about 8 MPa based on literature reports on cured silicone.

This methodology was based on a similar principle of operation as American Society for Testing and Materials tensile testing methods such as ASTM D638, ASTM D882 and ASTM D412. However, instead of a pneumatic force, in the present example, gravity was used for sample extension.

Example 11 - Measurement of Adhesion Strength

The adhesion strength of certain embodiments of the biophotonic materials formed according to Examples 8 and 9 were measured according to the following method. Samples were prepared as described in Example 10. One end of each sample was fixed to a clamp with a 15mm rubber grip linked to one end of a 1/16'' steel cable. The other end of the cable, via a low-friction pulley, was attached to a weight placed on a balance. The sample was laid flat on the skin of an inside forearm of a volunteer. A known weight, of surface area matching the sample, was then placed on the sample in order to apply a homogenous and known downwards force on the sample contacting the skin. The normal force F_n (force exerted by each surface on the other in a perpendicular direction to the surface) was calculated by multiplying the combined weight of the sample and the weight on the sample by the gravity constant, g (9.8m/s^2). The forearm, with the sample loaded with the weight, was then pulled away from the cable until the sample slipped from the skin surface. The weight recorded on the balance at this time was calculated by multiplying g to obtain the force of friction (F_f) (force required to overcome the friction between the sample and the skin). The friction coefficient of the sample can then be calculated using $F_f \leq \mu F_n$ (Coulomb's friction law).

On average, the silicone-based membranes had a friction coefficient of about 1.43, and the gelatin-based membranes had a friction coefficient of about 1.04. These values can be converted to the weight required to shear off a sample from the test surface by

multiplying the friction coefficient by the sample weight. So, for the silicone-based membranes, a weight of 1.50 g is required to shear-off the membranes from skin. From **Figure 8a**, this is equivalent to an elongation of about 0.1% and is well below its tensile strength. For the gelatin-based membranes, a weight of about 1.04 g was required to shear-off the membranes from skin. From **Figure 8b**, this is equivalent to an elongation of about 1.5% and is well below its tensile strength (equivalent to 24.12 g). Therefore, all the silicone-based membranes and gelatin-based membranes of Examples 8 and 9 were peelable.

Example 12 – Demonstration of peelable nature of cohesive biophotonic materials of the present disclosure

The biophotonic materials described in Examples 1, 8 and 9 were evaluated for peelability by applying them to the skin of volunteers and peeling off by hand. All membranes could be peeled off, reapplied and peeled off again without damage to the membranes and without leaving residues on the volunteer skins.

Example 13 – Cell studies

Certain embodiments of the cohesive biophotonic materials of Example 8 were evaluated for their ability to modulate inflammation, specifically cytokines IL6 and IL8. HaCaT cells were used as an accepted in vitro module for assessing modulation of these inflammatory cytokines. A non-toxic concentration of IFNγ was used to modulate the secretion of IL6 and IL8 by the HaCaT cells.

Silicone membranes containing an aqueous phase of eosin y and fluorescein and including either CMC or gelatin in the aqueous phase were evaluated. The anti-inflammatory effect of Dexamethasone was used as a positive control at a concentration of 5 μM. The materials were illuminated with blue light for 90 seconds at a distance of 5 cm at a fluence of about 11.5 J/cm^2. Cytokine quantification was performed by cytokine ELISA on the culture supernatant 24 hours after treatment. The quantity of cytokine secreted was normalized to cell viability. No toxic effect was observed for all the test samples as measured by cell viability using a spectrophotometric evaluation of viable cell number 24 hours after treatment. All of the membranes tested, produced a downward modulation of IL6 and IL8 on IFNγ stimulated HaCaT cells.

It should be appreciated that the invention is not limited to the particular embodiments described and illustrated herein but includes all modifications and variations falling within the scope of the invention as defined in the appended claims.

5

What is claimed is:

1. A topical biophotonic material comprising:

a cohesive matrix, and

at least one chromophore which can absorb and emit light from within the biophotonic material, wherein the topical biophotonic material is elastic.

2. A topical biophotonic material comprising:

a cohesive matrix, and

at least one chromophore which can absorb and emit light from within the biophotonic material, wherein a tear and/or a tensile strength of the topical biophotonic material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied.

3. The topical biophotonic material of claim 1 or claim 2, wherein the topical biophotonic material isa peelable film.

4. The topical biophotonic material of claims 1 or claim 3, wherein the tear and/or tensile strength of the biophotonic material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied.

5. The topical biophotonic material of claim 2, wherein the biophotonic material is rigid.

6. The topical biophotonic material of any of claims 1 to 5, wherein the topical biophotonic material is at least substantially translucent.

7. The topical biophotonic material of any of claims 1 to 6, wherein the topical biophotonic material has a translucency of at least about 40%, about 50%, about 60%, about 70%, or about 80% in a visible range.

8. The topical biophotonic material of any of claims 1 to 7, wherein the topical biophotonic material has a thickness of about 0.1 mm to about 50 mm, about 0.5 mm to about 20 mm, or about 1 mm to about 10 mm.

9. The topical biophotonic material of any of claims 1 to 8, wherein the topical biophotonic material has a pre-formed configuration.

10. The topical biophotonic material of claim 9, wherein the pre-formed configuration is a shape and/or a size corresponding with a shape and/or a size of a body part to which the topical biophotonic material can be applied.

11. The topical biophotonic material of claim 10, wherein the body part is selected from a head, scalp, forehead, nose, cheeks, ears, lip, face, neck, shoulder, arm pit, arm, elbow, hand, finger, abdomen, chest, stomach, back, sacrum, buttocks, genitals, legs, knee, feet, nails, hair, toes, boney prominences, and combinations thereof.

12. The topical biophotonic material of any of claims 9 to 11, wherein the topical biophotonic material is a mask.

13. The topical biophotonic material of claim 12, wherein the mask is disposable.

14. The topical biophotonic material of claim 12 or claim 13, wherein the mask is a face mask having at least one opening for the eyes, nose or mouth.

15. The topical biophotonic material of any of claims 9 to 11, wherein the pre-formed configuration is a shape and/or a size corresponding with a shape and/or a size of a light source or lamp to which the topical biophotonic material can be attached.

16. The topical biophotonic material of any of claims 1 to 15, wherein the topical biophotonic material can be removed without leaving substantially any residue on a surface to which the topical biophotonic material is applied.

17. The topical biophotonic material of any of claims 1 to 16, wherein the chromophore can absorb and/or emit light within the visible range.

18. The topical biophotonic material of any of claims 1 to 17, wherein the chromophore can emit light from around 500 nm to about 700 nm.

19. The topical biophotonic material of any of claims 1 to 18, wherein the chromophore can at least partially photobleach when illuminated with light.

20. The topical biophotonic material of any of claims 1 to 19, wherein the chromophore is a xanthene dye.

21. The topical biophotonic material of claim 20, wherein the xanthene dye is selected from Eosin Y, Erythrosine B, Fluorescein, Rose Bengal and Phloxin B.

22. The topical biophotonic material of any of claims 1 to 21, wherein the at least one chromophore is within the cohesive matrix.

23. The topical biophotonic material of any of claims 1 to 22, wherein the cohesive matrix is in particulate form.

24. The topical biophotonic material of any of claims 1 to 23, wherein the cohesive matrix comprises at least one polymer.

25. The topical biophotonic material of claim 24, wherein the polymer is selected from a cross-linked polyacrylic polymer, a hyaluronate, a hydrated polymer, a liposoluble polymer and a hydrophilic polymer.

26. The topical biophotonic material of claim 24 or 25, wherein the cohesive matrix comprises sodium hyaluronate.

27. The topical biophotonic material of claim 26, wherein sodium hyaluronate is present in an amount of about 2 wt% to about 8 wt%.

28. The topical biophotonic material of any of claims 24 to 27, wherein the cohesive matrix is a liposoluble polymer.

29. The topical biophotonic material of claim 28, wherein the chromophore is water soluble and is within an aqueous phase within the liposoluble polymer.

30. The topical biophotonic material of claim 29, wherein the aqueous phase is a liquid or a gel.

31. The topical biophotonic material of any of claims 28 to 30, wherein the liposoluble polymer is silicone.

32. The topical biophotonic material of any of claims 28 to 31, further comprising a stabilizing agent for stabilizing the aqueous phase.

33. The topical biophotonic material of any of claims 1 to 32, further comprising an oxygen-rich compound.

34. The topical biophotonic material of claim 33, wherein the oxygen-rich compound is selected from hydrogen peroxide, carbamide peroxide and benzoyl peroxide.

35. A topical biophotonic material comprising:

a cohesive matrix, and

at least one chromophore which can absorb and emit light from within the biophotonic material, wherein the topical biophotonic material is a mask or a dressing.

36. The topical biophotonic material of claim 35, wherein a tear and/or a tensile strength of the topical biophotonic material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied.

37. The topical biophotonic material of claim 35 or claim 36, wherein the topical biophotonic material is elastic.

38. The topical biophotonic material of claim 37, wherein the topical biophotonic material is a peelable film.

39. The topical biophotonic material of claim 35 or claim 36, wherein the topical biophotonic material is rigid.

40. The topical biophotonic material of any of claims 35 to 39, wherein the topical biophotonic material is at least substantially translucent.

41. The topical biophotonic material of any of claims 35 to 40, wherein the topical biophotonic material has a translucency of at least about 40%, about 50%, about 60%, about 70%, or about 80% in a visible range.

42 The topical biophotonic material of any of claims 35 to 41, wherein the topical biophotonic material has a thickness of about 0.1 mm to about 50 mm, about 0.5 mm to about 20 mm, or about 1 mm to about 10 mm.

43. The topical biophotonic material of any of claims 35 to 42, wherein the topical biophotonic material has a pre-formed configuration.

44. The topical biophotonic material of claim 43, wherein the pre-formed configuration is a shape and/or a size corresponding with a shape and/or a size of a body part to which the topical biophotonic material can be applied.

45. The topical biophotonic material of claim 44, wherein the body part is selected from a head, scalp, forehead, nose, cheeks, ears, lip, face, neck, shoulder, arm pit, arm, elbow, hand, finger, abdomen, chest, stomach, back, sacrum, buttocks, genitals, legs, knee, feet, nails, hair, toes, boney prominences, and combinations thereof.

46. The topical biophotonic material of any of claims 35 to 43, wherein the mask is a face mask having at least one opening for the eyes, nose or mouth.

47. The topical biophotonic material of any of claims 35 to 45, wherein the dressing is a wound dressing.

48. The topical biophotonic material of any of claims 35 to 47, wherein the biophotonic material is reusable or disposable.

49. The topical biophotonic material of any of claims 35 to 48, wherein the topical biophotonic material can be removed without leaving substantially any residue on a surface to which the topical biophotonic material is applied.

50. The topical biophotonic material of any of claims 35 to 49, wherein the chromophore can absorb and/or emit light within the visible range.

51. The topical biophotonic material of any of claims 35 to 50, wherein the chromophore can emit light from around 500 nm to about 700 nm.

52. The topical biophotonic material of any of claims 35 to 51, wherein the chromophore can at least partially photobleach when illuminated with light.

53. The topical biophotonic material of any of claims 35 to 52, wherein the chromophore is a xanthene dye.

54. The topical biophotonic material of claim 53, wherein the xanthene dye is selected from Eosin Y, Erythrosine B, Fluorescein, Rose Bengal and Phloxin B.

55. The topical biophotonic material of any of claims 35 to 54, wherein the at least one chromophore is within the cohesive matrix.

56. The topical biophotonic material of any of claims 35 to 55, wherein the cohesive matrix is in particulate form.

57. The topical biophotonic material of any of claims 35 to 56, wherein the cohesive matrix comprises at least one polymer.

58. The topical biophotonic material of any of claims 35 to 57, further comprising an oxygen-rich compound.

59. The topical biophotonic material of claim 58, wherein the oxygen-rich compound is selected from hydrogen peroxide, carbamide peroxide and benzoyl peroxide.

60. Use of the topical biophotonic material of any of claims 1 to 34, or claims 35 to 59, as a mask, a dressing or a filter.

61. Use of the topical biophotonic material of any of claims 1 to 34, or claims 35 to 59, for cosmetic or medical treatment of tissue.

62. The use of claim 61, wherein the cosmetic treatment includes skin rejuvenation and conditioning, and medical treatment includes wound healing, periodontitis treatment, and treatment of skin conditions.

63. The use of claim 62, wherein the skin conditions comprise acne, eczema, psoriasis or dermatitis.

64. Use of the topical biophotonic material of any of claims 1 to 34, or claims 35 to 59, for modulating inflammation.

65. Use of the topical biophotonic material of any of claims 1 to 34, or claims 35 to 59, for promoting angiogenesis.

66. A method for biophotonic treatment of a skin disorder comprising:

placing a topical biophotonic material over a target skin tissue, wherein the topical biophotonic material is elastic and comprises at least one chromophore and a cohesive matrix; and

illuminating said topical biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore;

wherein said biophotonic material emits fluorescence at a wavelength and intensity that promotes healing of said skin disorder.

67. A method for biophotonic treatment of a skin disorder comprising:

placing a topical biophotonic material over a target skin tissue, wherein the biophotonic material comprises at least one chromophore and a cohesive matrix, and wherein a tear and/or tensile strength of the topical biophotonic

material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied; and

illuminating said topical biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore;

wherein said biophotonic material emits fluorescence at a wavelength and intensity that promotes healing of said skin disorder.

68. The method of claim 66 or claim 67, wherein the skin disorder is selected from acne, eczema, psoriasis or dermatitis.

69. A method for biophotonic treatment of acne comprising:

placing a topical biophotonic material over a target skin tissue, wherein the topical biophotonic material is elastic and comprises at least one chromophore and a cohesive matrix; and

illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore;

wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that treats the acne.

70. A method for biophotonic treatment of acne comprising:

placing a topical biophotonic material over a target skin tissue, wherein the topical biophotonic material comprises at least one chromophore and a cohesive matrix, and wherein a tear and/or tensile strength of the topical biophotonic material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied; and

illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore;

wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that treats the acne.

71. A method for promoting wound healing comprising:

placing a topical biophotonic material over or within a wound, wherein the topical biophotonic material is elastic and comprises at least one chromophore and a cohesive matrix; and

illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore;

wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes wound healing.

72. A method for promoting wound healing comprising:

placing a topical biophotonic material over or within a wound, wherein the topical biophotonic material comprises at least one chromophore and a cohesive matrix; and wherein a tear and/or tensile strength of the topical biophotonic material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied; and

illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore;

wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes wound healing.

73. A method for promoting skin rejuvenation comprising:

placing a topical biophotonic material over a target skin tissue, wherein the topical biophotonic material is elastic and comprises at least one chromophore and a cohesive matrix; and

illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore;

wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes skin rejuvenation.

74. A method for promoting skin rejuvenation comprising:

placing a topical biophotonic material over a target skin tissue, wherein the topical biophotonic material comprises at least one chromophore and a cohesive matrix; and wherein a tear and/or tensile strength of the topical biophotonic material is greater than an adhesive strength of the topical biophotonic material to a surface to which it is applied; and

illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore;

wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes skin rejuvenation.

75. The method of any of claims 66 to 74, wherein the biophotonic material is a mask or a dressing.

76. A method for promoting skin rejuvenation comprising:

placing a topical biophotonic material on a target skin tissue, wherein the topical biophotonic material is a mask and comprises at least one chromophore and a cohesive matrix; and

illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes skin rejuvenation.

77. The method of claim 76, wherein the mask is a face mask having at least one opening for the eyes, nose or mouth.

78. A method for promoting wound healing comprising:

placing a topical biophotonic material over or within a wound, wherein the topical biophotonic material is a dressing comprising at least one chromophore and a cohesive matrix; and

illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes wound healing.

79. A method for preventing or treating scars comprising:

placing a topical biophotonic material over a scar or a wound, wherein the topical biophotonic material is a membrane comprising at least one chromophore and a cohesive matrix; and

illuminating said biophotonic material with light having a wavelength that overlaps with an absorption spectrum of the at least one chromophore; wherein said topical biophotonic material emits fluorescence at a wavelength and intensity that promotes wound healing.

80. The method of any of claims 66 to 79, wherein the biophotonic material is removed after illumination.

81. The method of any of claims 66 to 80, wherein the biophotonic material is peelable and is peeled off.

82. The method of any of claims 66 to 79, wherein the biophotonic material is left in place after illumination for re-illumination.

83. The method of any of claims 66 to 82, wherein the chromophore at least partially photobleaches after illumination.

84. The method of any of claims 66 to 83 wherein the biophotonic material is illuminated until the chromophore is at least partially photobleached.

85. The method of any of claims 66 to 84, wherein the chromophore can absorb and/or emit light in the visible range.

86. The method of any of claims 66 to 85, wherein the chromophore is a xanthene dye.

87. The method of any of claims 66 to 86, wherein the xanthene dye is selected from Eosin Y, Erythrosine B, Fluorescein, Rose Bengal and Phloxin B.

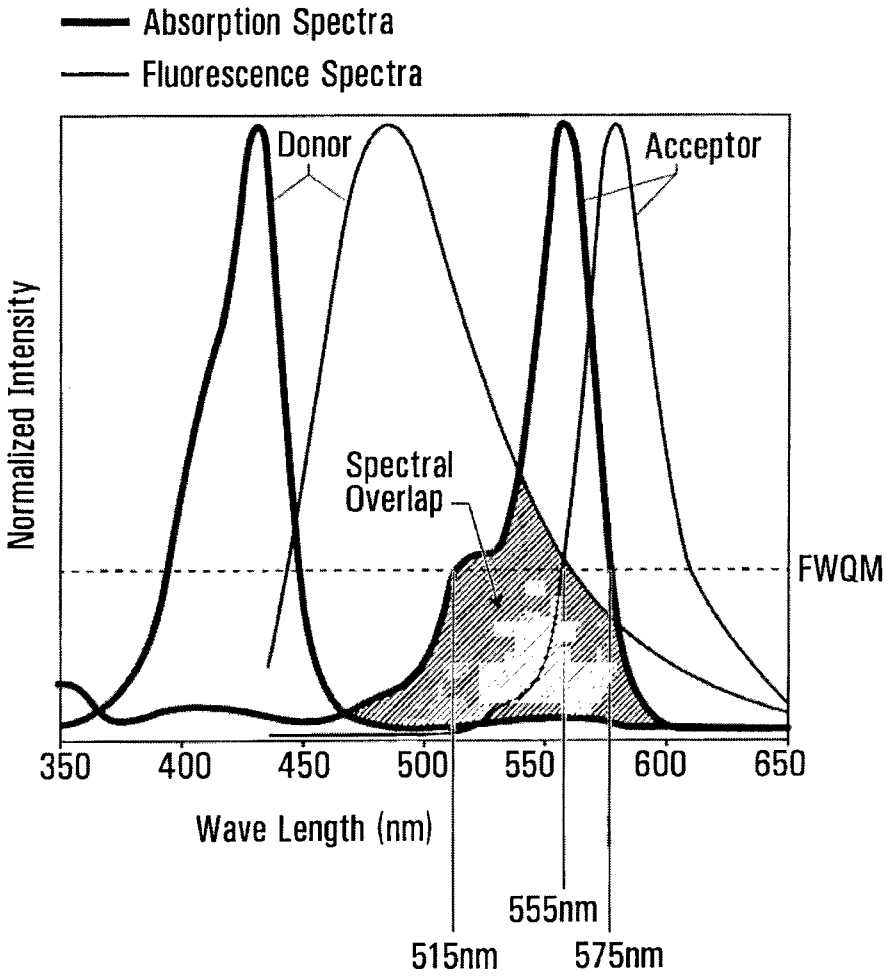

Absorption Spectra
Fluorescence Spectra
Donor
Acceptor
Normalized Intensity
Spectral Overlap
FWQM
350
400
450
500
550
600
650
Wave Length (nm)
555nm
515nm
575nm

FIG. 1

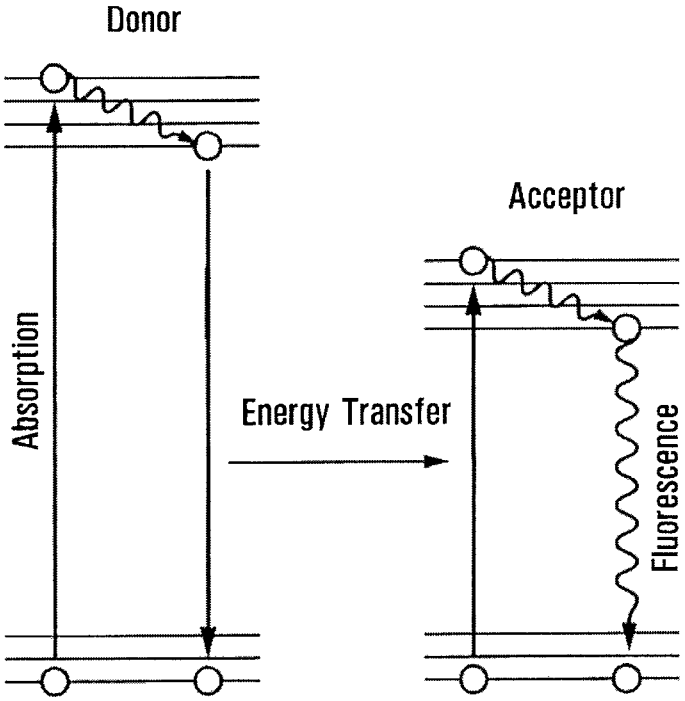


FIG. 2

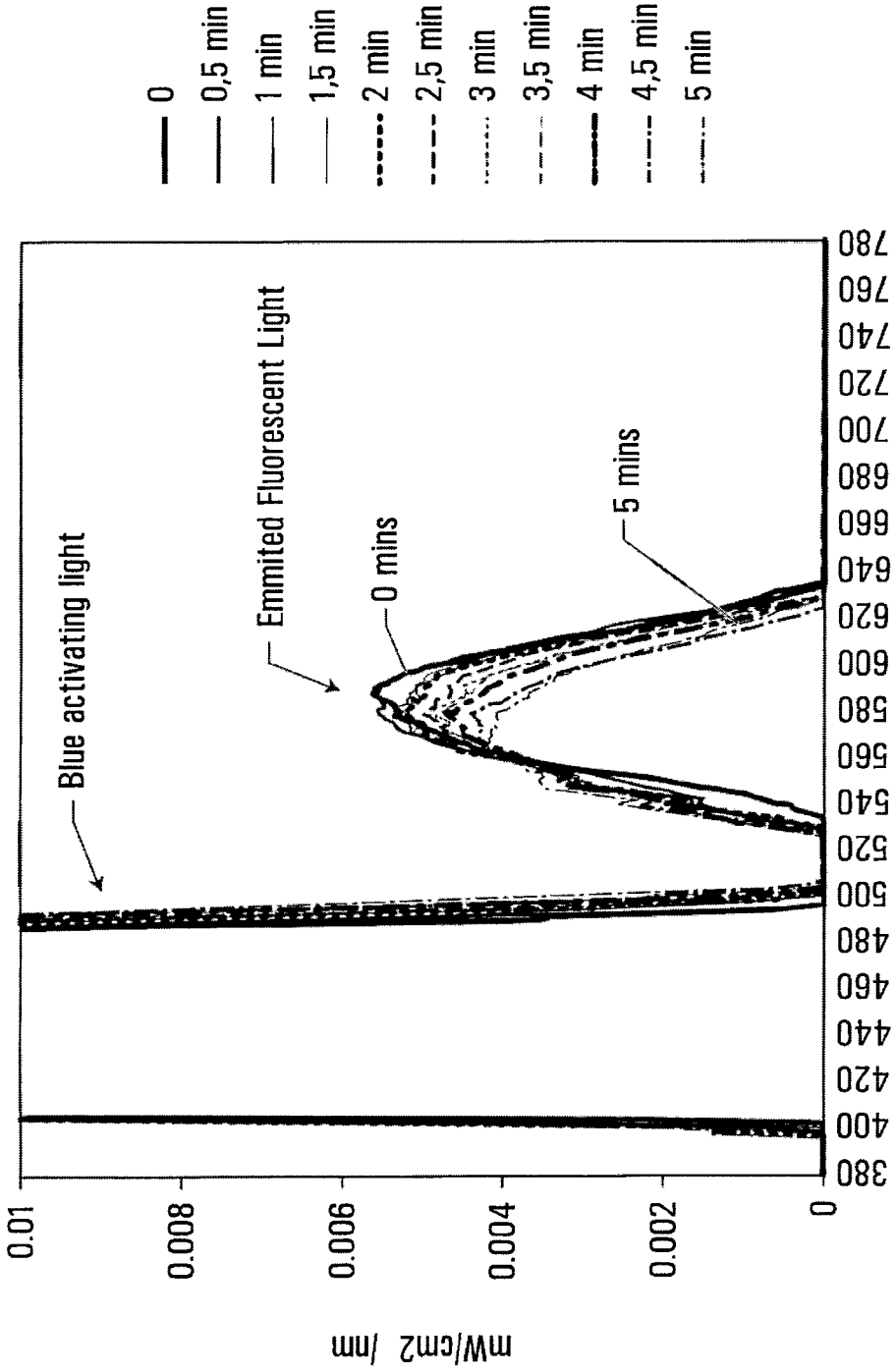

0
0,5 min
1 min
1,5 min
2 min
2,5 min
3 min
3,5 min
4 min
4,5 min
5 min
Blue activating light
Emmited Fluorescent Light
0 mins
5 mins
mW/cm2 /nm
0.01
0.008
0.006
0.004
0.002
0
380
400
420
440
460
480
500
520
540
560
580
600
620
640
660
680
700
720
740
760
780
Wavelength nm

FIG. 3

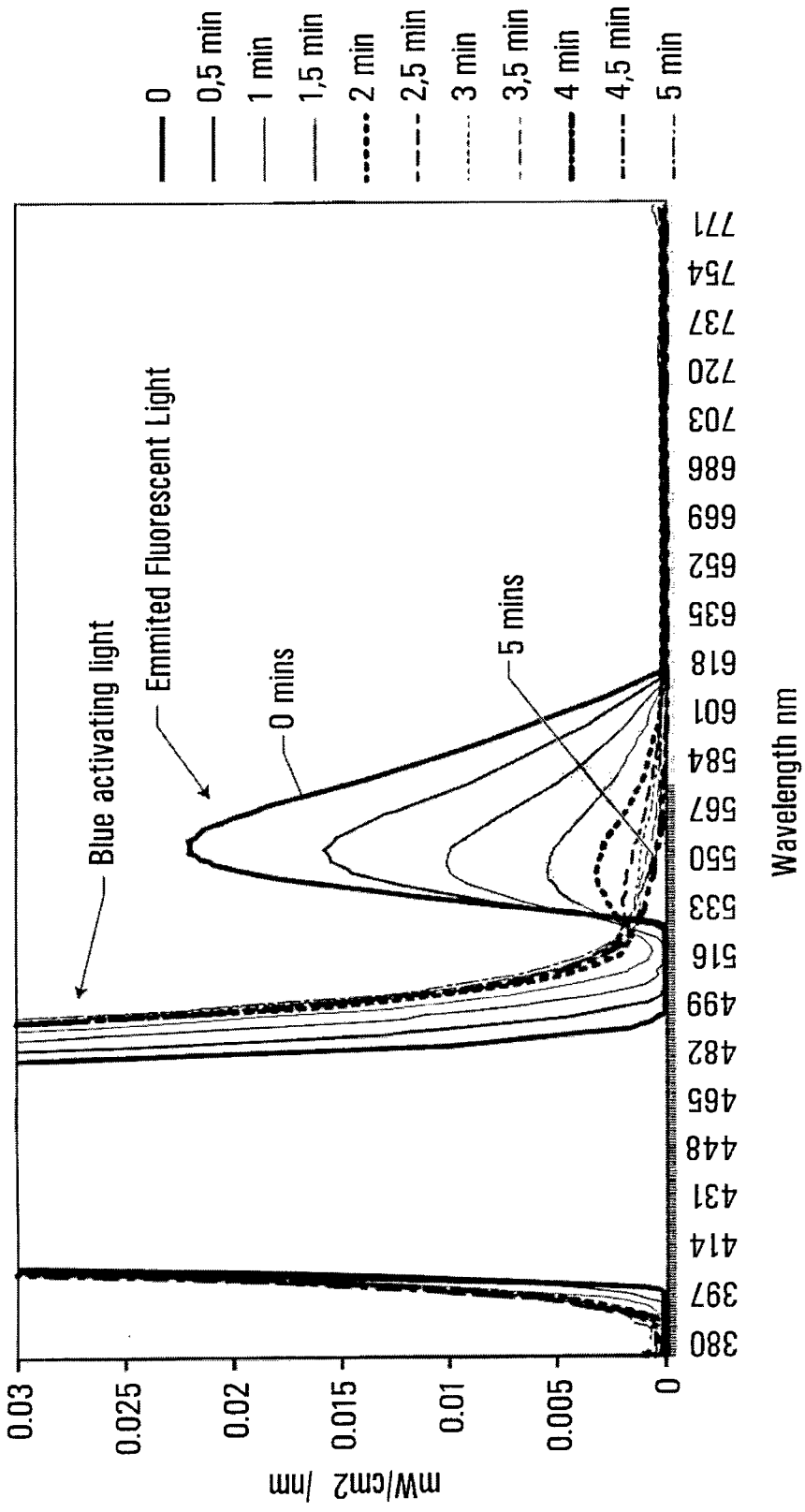

0
0,5 min
1 min
1,5 min
2 min
2,5 min
3 min
3,5 min
4 min
4,5 min
5 min
Blue activating light
Emmited Fluorescent Light
0 mins
5 mins
mW/cm2 /nm
0.03
0.025
0.02
0.015
0.01
0.005
0
380
397
414
431
448
465
482
499
516
533
550
567
584
601
618
635
652
669
686
703
720
737
754
771
Wavelength nm

FIG. 4

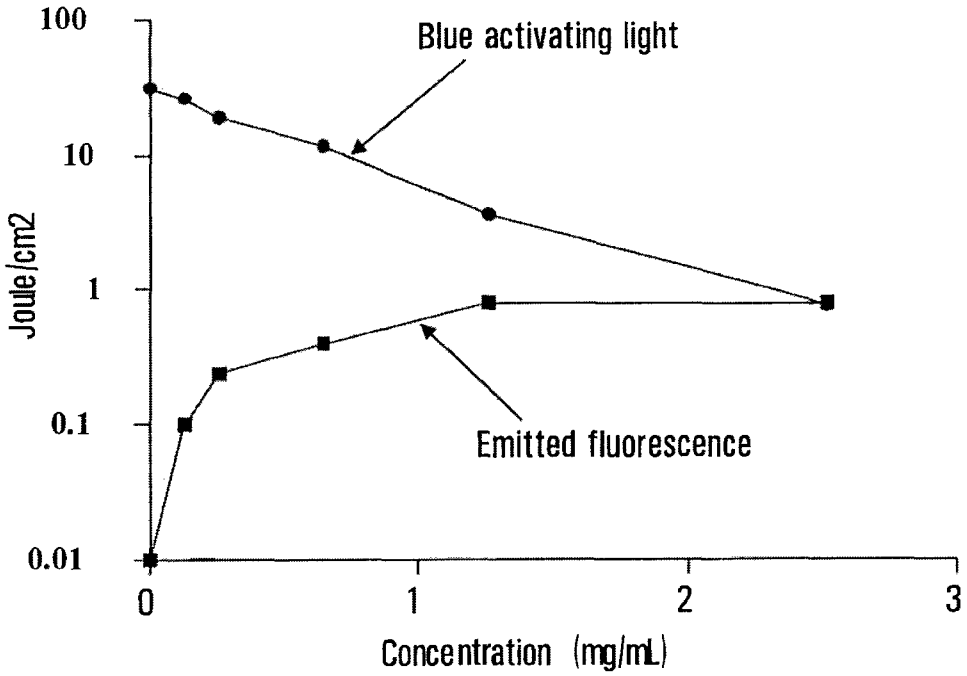

100
10
1
0.1
0.01
Joule/cm2
Blue activating light
Emitted fluorescence
0
1
2
3
Concentration (mg/mL)

FIG. 5A

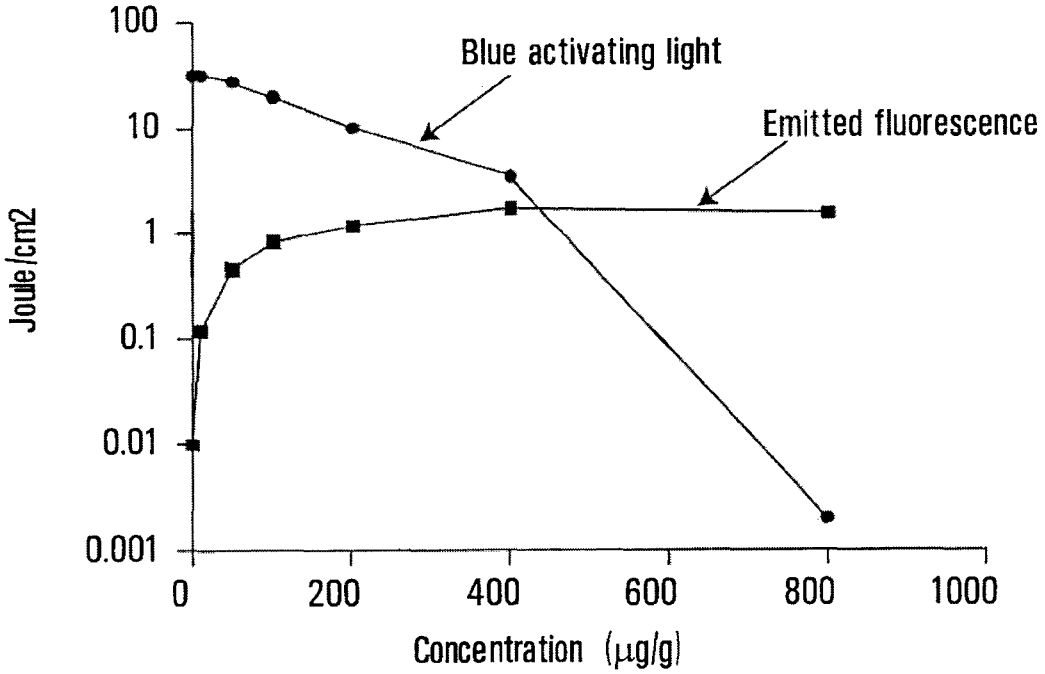

100
10
1
0.1
0.01
0.001
Joule/cm2
Blue activating light
Emitted fluorescence
0
200
400
600
800
1000
Concentration (µg/g)

FIG. 5B

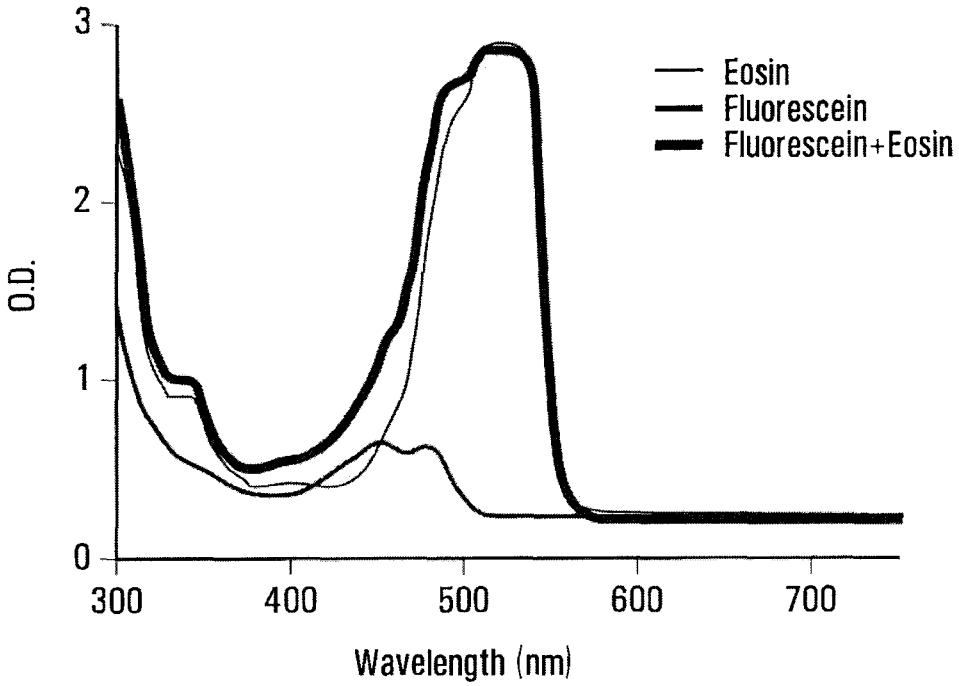

3
2
1
0
O.D.
300
400
500
600
700
Wavelength (nm)
Eosin
Fluorescein
Fluorescein+Eosin

FIG. 6A

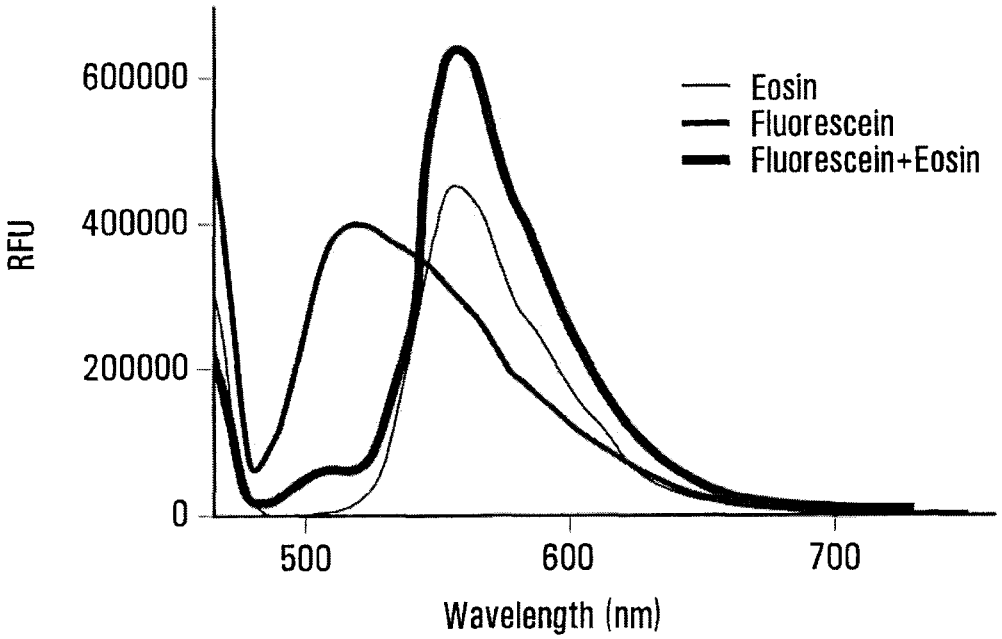

600000
400000
200000
0
RFU
500
600
700
Wavelength (nm)
Eosin
Fluorescein
Fluorescein+Eosin

FIG. 6B

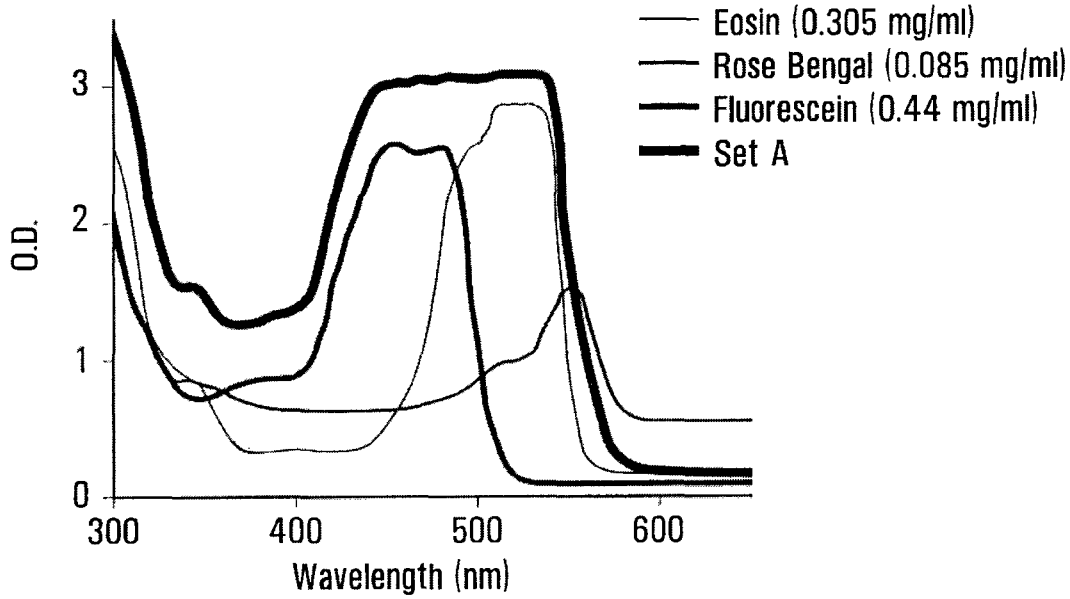

Eosin (0.305 mg/ml)
Rose Bengal (0.085 mg/ml)
Fluorescein (0.44 mg/ml)
Set A
O.D.
3
2
1
0
300
400
500
600
Wavelength (nm)

FIG. 7A

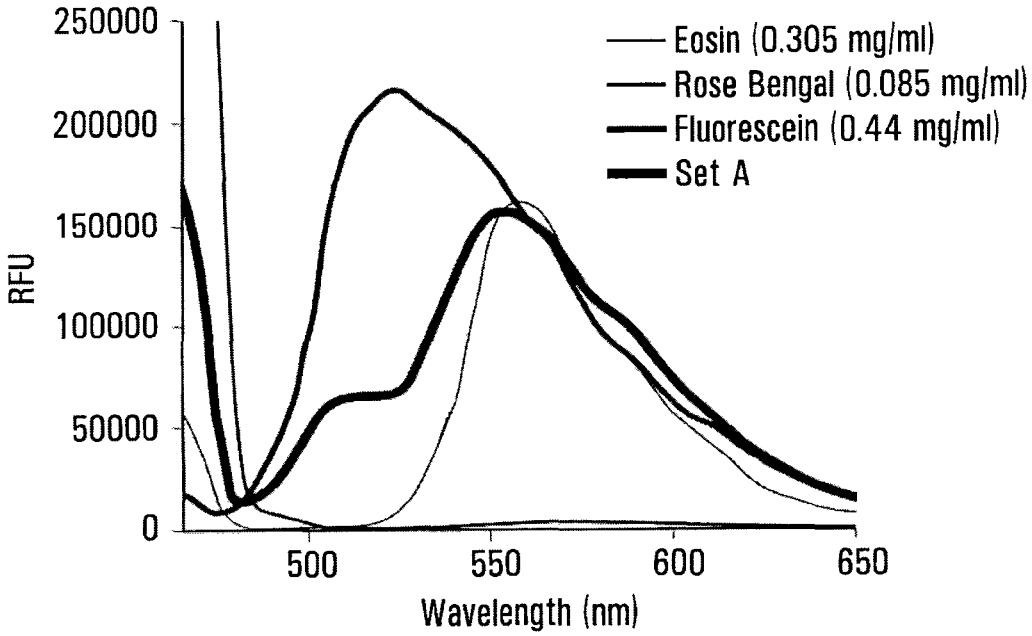

Eosin (0.305 mg/ml)
Rose Bengal (0.085 mg/ml)
Fluorescein (0.44 mg/ml)
Set A
RFU
250000
200000
150000
100000
50000
0
500
550
600
650
Wavelength (nm)

FIG. 7B

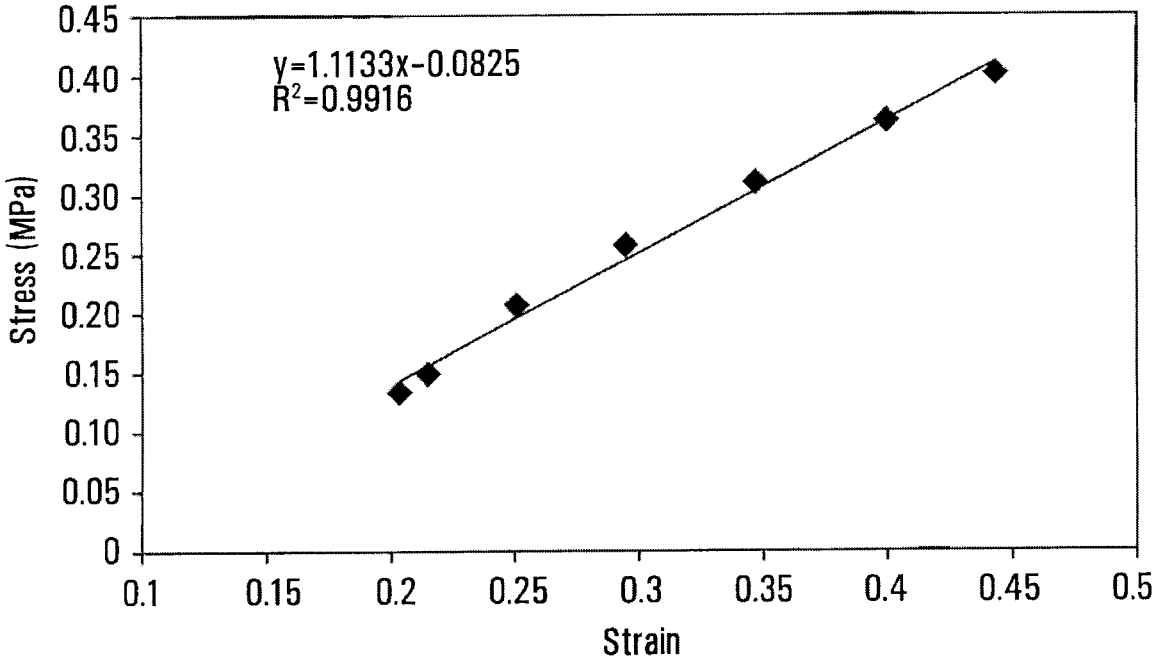

y=1.1133x-0.0825
R²=0.9916
Stress (MPa)
Strain
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
0.5

FIG. 8A

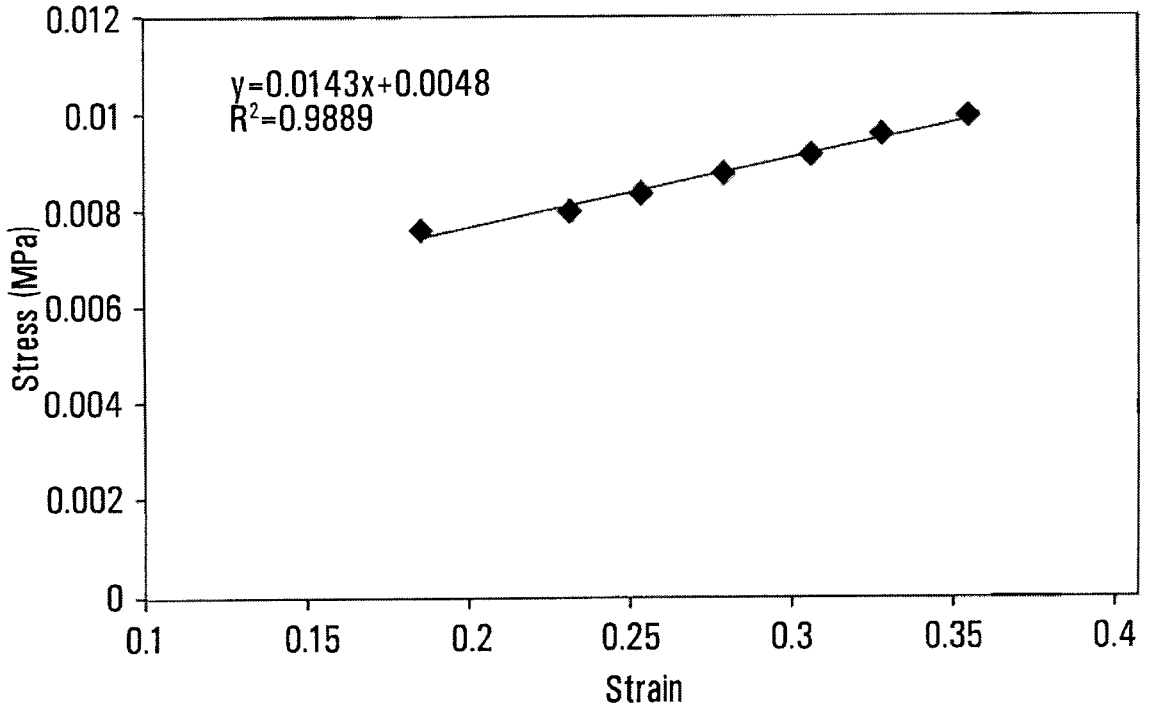

y=0.0143x+0.0048
R²=0.9889
Stress (MPa)
Strain
0.012
0.01
0.008
0.006
0.004
0.002
0
0.1
0.15
0.2
0.25
0.3
0.35
0.4

FIG. 8B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2014/000261

A. CLASSIFICATION OF SUBJECT MATTER
IPC: ***A61K 41/00*** (2006.01), ***A61K 8/02*** (2006.01), ***A61K 9/00*** (2006.01), ***A61L 15/42*** (2006.01), ***A61N 5/06*** (2006.01), ***A61P 17/00*** (2006.01), ***A61P 17/02*** (2006.01), ***A61Q 19/08*** (2006.01)

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) ***A61K 41/00*** (2006.01), ***A61K 8/02*** (2006.01), ***A61K 9/00*** (2006.01), ***A61L 15/42*** (2006.01), ***A61N 5/06*** (2006.01), ***A61P 17/00*** (2006.01), ***A61P 17/02*** (2006.01), ***A61Q 19/08*** (2006.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)

Canadian Patent Database, Epoque, Scopus
Keywords: chromophore, matrix, biophotonic, wound, dressing, photodynamic therapy, mask, film, membrane, light

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 2013/155620 A1 (Loupis et al.) 24 October 2013 (24-10-2013) Pages 3-11, 34 and 58-59 Claims	1-28 and 33-87
X,P	WO 2014/040176 A1 (Loupis et al.) 20 March 2014 (20-03-2014) Pages 1-7 Claims Examples	1-7, 9-18, 20-28, 33-41, 43-51, 53-82 and 85-87
A	CA 2 457 590 A1 (McDaniel) 06 March 2003 (06-03-2003) Whole document	1-87

☑ Further documents are listed in the continuation of Box C.

☑ See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	
"E" earlier application or patent but published on or after the international filing date	
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	
	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
	"&" document member of the same patent family

Date of the actual completion of the international search 19 June 2014 (19-06-2014)	Date of mailing of the international search report 23 July 2014 (23-07-2014)
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Authorized officer Pierre Tessier (819) 934-0073

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CA 2 809 405 A1 (Bandyopadhyay), 26 January 2012 (26-01-2012) Whole document	1-87
A	CA 2 360 202 C (Anderson), 13 July 2000 (13-07-2000) Whole Document	1-87
A	US 2008/0058689 A1 (Holloway et al.), 06 March 2008 (06-03-2008) Whole Document	1-87

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2014/000261

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☑ Claim Nos.: 66-87
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 66-87 are directed to a method of treatment of the human or animal body by surgery or therapy, and are not required to be searched, nor is a written opinion required by this Authority. Regardless, this Authority has established a written opinion based on the alleged effect or purpose/use of the product defined in claims 66-87.

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant=s protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

No protest accompanied the payment of additional search fees.

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
WO2013155620A1	24 October 2013 (24-10-2013)	WO2013155620A1	24 October 2013 (24-10-2013)
		WO2014040176A1	20 March 2014 (20-03-2014)
		GB201307157D0	29 May 2013 (29-05-2013)
		GB2499921A	04 September 2013 (04-09-2013)
		US2013281913A1	24 October 2013 (24-10-2013)
WO2014040176A1	20 March 2014 (20-03-2014)	WO2014040176A1	20 March 2014 (20-03-2014)
		WO2013155620A1	24 October 2013 (24-10-2013)
		GB201307157D0	29 May 2013 (29-05-2013)
		GB2499921A	04 September 2013 (04-09-2013)
		US2013281913A1	24 October 2013 (24-10-2013)
CA2457590A1	06 March 2003 (06-03-2003)	CA2457590A1	06 March 2003 (06-03-2003)
		AU1746600A	19 June 2000 (19-06-2000)
		AU2002320215B2	21 February 2008 (21-02-2008)
		AU2002326716B2	23 August 2007 (23-08-2007)
		AU2002357695B2	17 April 2008 (17-04-2008)
		AU2003220671A1	27 October 2003 (27-10-2003)
		AU2003220671B2	01 May 2008 (01-05-2008)
		AU2007212519A1	16 August 2007 (16-08-2007)
		AU2007212519B2	06 October 2011 (06-10-2011)
		AU2007212519C1	01 March 2012 (01-03-2012)
		BR0210739A	23 May 2006 (23-05-2006)
		BR0212142A	24 August 2004 (24-08-2004)
		BR0213996A	31 August 2004 (31-08-2004)
		CA2452408A1	09 January 2003 (09-01-2003)
		CA2452408C	24 May 2011 (24-05-2011)
		CA2465906A1	15 May 2003 (15-05-2003)
		CA2465906C	07 February 2012 (07-02-2012)
		CA2482934A1	23 October 2003 (23-10-2003)
		CA2640203A1	16 August 2007 (16-08-2007)
		CA2644219A1	13 September 2007 (13-09-2007)
		CN1578688A	09 February 2005 (09-02-2005)
		CN1578688B	25 April 2012 (25-04-2012)
		CN1602172A	30 March 2005 (30-03-2005)
		CN1658804A	24 August 2005 (24-08-2005)
		CN102343126A	08 February 2012 (08-02-2012)
		EP1411817A2	28 April 2004 (28-04-2004)
		EP1411817A4	22 March 2006 (22-03-2006)
		EP1427482A2	16 June 2004 (16-06-2004)
		EP1427482A4	02 November 2005 (02-11-2005)
		EP1453431A2	08 September 2004 (08-09-2004)
		EP1453431A4	24 May 2006 (24-05-2006)
		EP1501437A1	02 February 2005 (02-02-2005)
		EP1501437A4	04 August 2010 (04-08-2010)
		EP1991673A2	19 November 2008 (19-11-2008)
		EP1991673A4	16 February 2011 (16-02-2011)
		EP1986744A2	05 November 2008 (05-11-2008)
		EP1986744A4	27 May 2009 (27-05-2009)
		IL159579D0	01 June 2004 (01-06-2004)
		IL160505D0	25 July 2004 (25-07-2004)
		IL160505A	24 September 2012 (24-09-2012)
		IL161865D0	20 November 2005 (20-11-2005)
		IL161865A	31 May 2012 (31-05-2012)
		IL164644D0	18 December 2005 (18-12-2005)
		JP2005521432A	21 July 2005 (21-07-2005)
		JP2005503388A	03 February 2005 (03-02-2005)

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
		JP2005512620A	12 May 2005 (12-05-2005)
		JP2009525141A	09 July 2009 (09-07-2009)
		JP2009528853A	13 August 2009 (13-08-2009)
		JP2010047590A	04 March 2010 (04-03-2010)
		KR20040048881A	10 June 2004 (10-06-2004)
		KR20040048888A	10 June 2004 (10-06-2004)
		KR20050044388A	12 May 2005 (12-05-2005)
		MXPA04000187A	27 October 2004 (27-10-2004)
		MXPA04001710A	22 November 2004 (22-11-2004)
		MXPA04004463A	31 March 2005 (31-03-2005)
		MXPA04011187A	14 February 2005 (14-02-2005)
		WO03001984A2	09 January 2003 (09-01-2003)
		WO03001984A3	14 August 2003 (14-08-2003)
		WO03017824A2	06 March 2003 (06-03-2003)
		WO03017824A3	23 October 2003 (23-10-2003)
		WO03039478A2	15 May 2003 (15-05-2003)
		WO03039478A3	16 October 2003 (16-10-2003)
		WO03086215A1	23 October 2003 (23-10-2003)
		WO0032121A1	08 June 2000 (08-06-2000)
		WO0032121A9	17 May 2001 (17-05-2001)
		US2005261750A1	24 November 2005 (24-11-2005)
		US7201765B2	10 April 2007 (10-04-2007)
		US2003004556A1	02 January 2003 (02-01-2003)
		US6676655B2	13 January 2004 (13-01-2004)
		US6283956B1	04 September 2001 (04-09-2001)
		US2006129209A1	15 June 2006 (15-06-2006)
		US2006200213A1	07 September 2006 (07-09-2006)
		US2006184214A1	17 August 2006 (17-08-2006)
		US2006212025A1	21 September 2006 (21-09-2006)
		US2010055789A1	04 March 2010 (04-03-2010)
		US2010174222A1	08 July 2010 (08-07-2010)
		US2010121254A1	13 May 2010 (13-05-2010)
		US2010256550A1	07 October 2010 (07-10-2010)
		US8651112B2	18 February 2014 (18-02-2014)
		US2007191822A1	16 August 2007 (16-08-2007)
		US7494503B2	24 February 2009 (24-02-2009)
		US2002123746A1	05 September 2002 (05-09-2002)
		US6629971B2	07 October 2003 (07-10-2003)
		US2003129154A1	10 July 2003 (10-07-2003)
		US2003060811A1	27 March 2003 (27-03-2003)
		US2003004499A1	02 January 2003 (02-01-2003)
		US6663659B2	16 December 2003 (16-12-2003)
		US6887260B1	03 May 2005 (03-05-2005)
		US2003023283A1	30 January 2003 (30-01-2003)
		US6936044B2	30 August 2005 (30-08-2005)
		WO2007092349A2	16 August 2007 (16-08-2007)
		WO2007092349A3	09 October 2008 (09-10-2008)
		WO2007103132A2	13 September 2007 (13-09-2007)
		WO2007103132A3	31 July 2008 (31-07-2008)
		ZA200400477A	30 August 2006 (30-08-2006)
		ZA200403664A	13 May 2005 (13-05-2005)
CA2809405A1	26 January 2012 (26-01-2012)	CA2809405A1	26 January 2012 (26-01-2012)
		AU2011280265A1	14 March 2013 (14-03-2013)
		GB201012217D0	08 September 2010 (08-09-2010)
		GB201303099D0	10 April 2013 (10-04-2013)
		GB2496805A	22 May 2013 (22-05-2013)
		SG187919A1	28 March 2013 (28-03-2013)
		WO2012011875A1	26 January 2012 (26-01-2012)

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
CA2360202A1	13 July 2000 (13-07-2000)	CA2360202A1	13 July 2000 (13-07-2000)
		CA2360202C	19 February 2013 (19-02-2013)
		EP1140180A2	10 October 2001 (10-10-2001)
		WO0040266A2	13 July 2000 (13-07-2000)
		WO0040266A9	23 November 2000 (23-11-2000)
		WO0040266A3	18 January 2001 (18-01-2001)
		US6183773B1	06 February 2001 (06-02-2001)
		US6600951B1	29 July 2003 (29-07-2003)
		US2004006328A1	08 January 2004 (08-01-2004)
US2008058689A1	06 March 2008 (06-03-2008)	US2008058689A1	06 March 2008 (06-03-2008)
		AU2002315208A1	23 December 2002 (23-12-2002)
		AU2003296475A1	30 June 2004 (30-06-2004)
		AU2003296475A8	30 June 2004 (30-06-2004)
		WO02101847A2	19 December 2002 (19-12-2002)
		WO02101847A3	22 May 2003 (22-05-2003)
		WO2004052238A2	24 June 2004 (24-06-2004)
		WO2004052238A3	14 October 2004 (14-10-2004)
		US2002197050A1	26 December 2002 (26-12-2002)
		US7928278B2	19 April 2011 (19-04-2011)
		US2004166146A1	26 August 2004 (26-08-2004)
		US7304201B2	04 December 2007 (04-12-2007)

(19)中华人民共和国国家知识产权局

(12)发明专利申请

(10)申请公布号 CN 105163759 A
(43)申请公布日 2015.12.16

(21)申请号 201480011433.5

(22)申请日 2014.03.14

(30)优先权数据
61/786,197 2013.03.14 US
61/873,747 2013.09.04 US
14/204,741 2014.03.11 US

(85)PCT国际申请进入国家阶段日
2015.08.31

(86)PCT国际申请的申请数据
PCT/CA2014/000261 2014.03.14

(87)PCT国际申请的公布数据
WO2014/138930 EN 2014.09.18

(71)申请人 克洛克斯科技公司
地址 加拿大魁北克省

(72)发明人 N·卢皮斯 R·皮耶尔加利尼
E·德罗齐埃

(74)专利代理机构 永新专利商标代理有限公司
72002
代理人 苗征 于辉

(51)Int.Cl.
A61K 41/00(2006.01)
A61K 8/02(2006.01)
A61K 9/00(2006.01)
A61L 15/42(2006.01)
A61N 5/06(2006.01)
A61P 17/00(2006.01)
A61P 17/02(2006.01)
A61Q 19/08(2006.01)

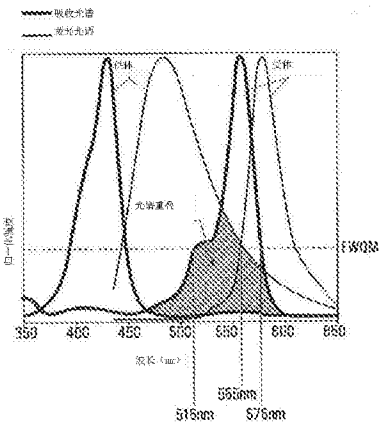
权利要求书6页 说明书34页 附图8页

(54)发明名称

生物光子材料及其用途

(57)摘要

本发明提供用于光疗的局部生物光子材料和方法。特别是，本发明的局部生物光子材料包括粘性基质，及至少一个生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中所述局部生物光子材料是弹性的。本发明的外用生物光子材料和方法用于促进伤口愈合、皮肤更新及治疗痤疮和其它皮肤病。



CN 105163759 A

1. 一种局部生物光子材料，包括：

粘性基质，及

至少一种生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中所述局部生物光子材料是弹性的。

2. 一种局部生物光子材料，包括：

粘性基质，及

至少一种生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中所述局部生物光子材料的撕裂强度与/或拉伸强度大于所述局部生物光子材料与其施用表面的粘合强度。

3. 根据权利要求 1 或 2 所述的局部生物光子材料，其中所述局部生物光子材料是可剥离的膜。

4. 根据权利要求 1 或 3 所述的局部生物光子材料，其中所述局部生物光子材料的撕裂强度与/或拉伸强度大于所述局部生物光子材料与其施用表面的粘合强度。

5. 根据权利要求 2 所述的局部生物光子材料，其中所述局部生物光子材料是刚性的。

6. 根据权利要求 1 至 5 任一项所述的局部生物光子材料，其中所述局部生物光子材料至少基本上是半透明的。

7. 根据权利要求 1 至 6 任一项所述的局部生物光子材料，其中所述局部生物光子材料在可见光范围内的半透明度是至少大约 40％、大约 50％、大约 60％、大约 70％或大约 80％。

8. 根据权利要求 1 至 7 任一项所述的局部生物光子材料，其中所述局部生物光子材料的厚度是大约 0.1mm 至大约 50mm、大约 0.5mm 至大约 20mm，或大约 1mm 至大约 10mm。

9. 根据权利要求 1 至 8 任一项所述的局部生物光子材料，其中所述局部生物光子材料具有预成型配置。

10. 根据权利要求 9 所述的局部生物光子材料，其中所述预成型配置的形状与/尺寸与施用生物光子材料的身体部分的形状与/或尺寸相对应。

11. 根据权利要求 10 所述的局部生物光子材料，其中所述身体部位选自头、头皮、前额、鼻子、脸颊、耳朵、嘴唇、脸、颈、肩、腋窝、臂、肘、手、手指、腹部、胸、肚子、背、骶骨、臀部、生殖器、腿、膝、脚、指甲、头发、脚趾或骨性隆起或它们的组合。

12. 根据权利要求 9 至 11 任一项所述的局部生物光子材料，其中所述局部生物光子材料是遮罩。

13. 根据权利要求 12 所述的局部生物光子材料，其中所述遮罩是一次性的。

14. 根据权利要求 12 或 13 所述的局部生物光子材料，其中所述遮罩是面罩，具有至少一个适用于眼睛、鼻子或嘴巴的开孔。

15. 根据权利要求 9 至 11 任一项所述的局部生物光子材料，其中所述预成型配置的尺寸与/或形状与生物光子材料可以连接的光源或灯的形状与/或尺寸对应。

16. 根据权利要求 1 至 15 任一项所述的局部生物光子材料，其中所述局部生物光子材料可以从施用生物光子材料的表面上清除，而基本上没有任何残留。

17. 根据权利要求 1 至 16 任一项所述的局部生物光子材料，其中所述生色团可以吸收与/或发射可见光范围内的光。

18. 根据权利要求 1 至 17 任一项所述的局部生物光子材料，其中所述生色团可以发射

大约 500nm 至大约 700nm 的光。

19. 根据权利要求 1 至 18 任一项所述的局部生物光子材料，其中所述生色团用光照射时至少部分地发生光漂白。

20. 根据权利要求 1 至 19 任一项所述的局部生物光子材料，其中所述生色团是呫吨染料。

21. 根据权利要求 20 所述的局部生物光子材料，其中所述呫吨染料选自曙红 Y、赤藓红 B、荧光素 B、玫瑰红和荧光桃红 B。

22. 根据权利要求 1 至 21 任一项所述的局部生物光子材料，其中所述至少一个生色团在粘性基质内。

23. 根据权利要求 1 至 22 任一项所述的局部生物光子材料，其中所述粘性基质是颗粒形式。

24. 根据权利要求 1 至 23 任一项所述的局部生物光子材料，其中所述粘性基质包括至少一种聚合物。

25. 根据权利要求 24 所述的局部生物光子材料，其中所述聚合物选自交联聚丙烯酸聚合物、透明质酸盐、水合聚合物、脂溶聚合物和亲水聚合物。

26. 根据权利要求 24 或 25 所述的局部生物光子材料，其中所述粘性基质包括透明质酸钠。

27. 根据权利要求 26 所述的局部生物光子材料，其中透明质酸钠的含量是大约 2wt％至大约 8wt％。

28. 根据权利要求 24 至 27 任一项所述的局部生物光子材料，其中所述粘性基质是脂溶聚合物。

29. 根据权利要求 28 所述的局部生物光子材料，其中生色团溶于水且位于脂溶聚合物的水相内。

30. 根据权利要求 29 所述的局部生物光子材料，其中水相是液体或凝胶。

31. 根据权利要求 28 至 30 任一项所述的局部生物光子材料，其中所述脂溶聚合物是聚硅氧烷。

32. 根据权利要求 28 至 31 任一项所述的局部生物光子材料，进一步包括用于稳定水相的稳定剂。

33. 根据权利要求 1 至 32 任一项所述的局部生物光子材料，进一步包括富氧化合物。

34. 根据权利要求 33 所述的局部生物光子材料，其中富氧化合物选自过氧化氢、过氧化脲和过氧化苯甲酰。

35. 一种局部生物光子材料，包括：

粘性基质，及

至少一种生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中所述局部生物光子材料是遮罩或敷料。

36. 根据权利要求 35 所述的局部生物光子材料，其中所述局部生物光子材料的撕裂强度与 / 或拉伸强度大于所述局部生物光子材料与其施用表面的粘合强度。

37. 根据权利要求 35 或 36 所述的局部生物光子材料，其中所述局部生物光子材料是弹性的。

38. 根据权利要求 37 所述的局部生物光子材料，其中所述局部生物光子材料是可剥离的膜。

39. 根据权利要求 35 或 36 所述的局部生物光子材料，其中所述局部生物光子材料是刚性的。

40. 根据权利要求 35 至 39 任一项所述的局部生物光子材料，其中所述局部生物光子材料至少基本上是半透明的。

41. 根据权利要求 35 至 40 任一项所述的局部生物光子材料，其中所述局部生物光子材料在可见光范围内的半透明度是至少大约 40％、大约 50％、大约 60％、大约 70％或大约 80％。

42. 根据权利要求 35 至 41 任一项所述的局部生物光子材料，其中所述局部生物光子材料的厚度是大约 0.1mm 至大约 50mm、大约 0.5mm 至大约 20mm，或大约 1mm 至大约 10mm。

43. 根据权利要求 35 至 42 任一项所述的局部生物光子材料，其中所述局部生物光子材料具有预成型配置。

44. 根据权利要求 43 所述的局部生物光子材料，其中所述预成型配置的形状与 / 尺寸与施用生物光子材料的身体部分的形状与 / 或尺寸相对应。

45. 根据权利要求 44 所述的局部生物光子材料，其中所述身体部位选自头、头皮、前额、鼻子、脸颊、耳朵、嘴唇、脸、颈、肩、腋窝、臂、肘、手、手指、腹部、胸、肚子、背、骶骨、臀部、生殖器、腿、膝、脚、指甲、头发、脚趾或骨性隆起或它们的组合。

46. 根据权利要求 35 至 43 任一项所述的局部生物光子材料，其中所述遮罩是面罩，具有至少一个适用于眼睛、鼻子或嘴巴的开孔。

47. 根据权利要求 35 至 45 任一项所述的局部生物光子材料，其中所述敷料是伤口敷料。

48. 根据权利要求 35 至 47 任一项所述的局部生物光子材料，其中所述局部生物光子材料是可以重复利用的或一次性的。

49. 根据权利要求 35 至 48 任一项所述的局部生物光子材料，其中所述局部生物光子材料可以从施用生物光子材料的表面上清除，而基本上没有任何残留。

50. 根据权利要求 35 至 49 任一项所述的局部生物光子材料，其中所述生色团可以吸收与 / 或发射可见光范围内的光。

51. 根据权利要求 35 至 50 任一项所述的局部生物光子材料，其中所述生色团可以发射大约 500nm 至大约 700nm 的光。

52. 根据权利要求 35 至 51 任一项所述的局部生物光子材料，其中所述生色团用光照射时至少部分地发生光漂白。

53. 根据权利要求 35 至 52 任一项所述的局部生物光子材料，其中所述生色团是呫吨染料。

54. 根据权利要求 53 所述的局部生物光子材料，其中所述呫吨染料选自曙红 Y、赤藓红 B、荧光素 B、玫瑰红和荧光桃红 B。

55. 根据权利要求 35 至 54 任一项所述的局部生物光子材料，其中所述至少一个生色团在粘性基质内。

56. 根据权利要求 35 至 55 任一项所述的局部生物光子材料，其中所述粘性基质是颗粒

形式。

57. 根据权利要求 35 至 56 任一项所述的局部生物光子材料，其中所述粘性基质包括至少一种聚合物。

58. 根据权利要求 35 至 57 任一项所述的局部生物光子材料，进一步包括富氧化合物。

59. 根据权利要求 58 所述的局部生物光子材料，其中富氧化合物选自过氧化氢、过氧化脲和过氧化苯甲酰。

60. 权利要求 1 至 34，或权利要求 35 至 59 任一项所述局部生物光子材料作为遮罩、敷料或滤波器的用途。

61. 权利要求 1 至 34，或权利要求 35 至 59 任一项所述局部生物光子材料用于组织美容或医学处理的用途。

62. 根据权利要求 61 所途的用途，其中美容处理包括皮肤更新和调理，医学处理包括伤口愈合、牙周炎治疗和皮肤病治疗。

63. 根据权利要求 62 所途的用途，其中皮肤病包括痤疮、湿疹、牛皮癣或皮炎。

64. 权利要求 1 至 34，或权利要求 35 至 59 任一项所述局部生物光子材料用于调节发炎的用途。

65. 权利要求 1 至 34，或权利要求 35 至 59 任一项所述局部生物光子材料用于促进血管生成的用途。

66. 一种用生物光子疗法治疗皮肤病的方法，包括 ：

将局部生物光子材料放在靶向皮肤组织上，其中所述局部生物光子材料是弹性的，包括至少一个生色团和粘性基质 ；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料 ；

其中所述生物光子材料发射波长和强度能促进所述皮肤病痊愈的荧光。

67. 一种用生物光子疗法治疗皮肤病的方法，包括 ：

将局部生物光子材料放在靶向皮肤组织上，其中所述局部生物光子材料包括至少一个生色团和粘性基质，其中所述局部生物光子材料的撕裂强度与 / 或拉伸强度大于所述局部生物光子材料与其施用表面的粘合强度 ；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料 ；

其中所述生物光子材料发射波长和强度能促进所述皮肤病痊愈的荧光。

68. 根据权利要求 66 或 67 所述的方法，其中所述皮肤病选自痤疮、湿疹、牛皮藓或皮炎。

69. 一种用生物光子疗法治疗痤疮的方法，包括 ：

将局部生物光子材料放在靶向皮肤组织上，其中所述局部生物光子材料是弹性的，包括至少一个生色团和粘性基质 ；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料 ；

其中所述局部生物光子材料发射波长和强度治疗痤疮的荧光。

70. 一种用生物光子疗法治疗痤疮的方法，包括 ：

将局部生物光子材料放在靶向皮肤组织上，其中所述局部生物光子材料包括至少一个生色团和粘性基质，其中所述局部生物光子材料的撕裂强度与 / 或拉伸强度大于所述局部生物光子材料与其施用表面的粘合强度 ；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；

其中所述局部生物光子材料发射波长和强度治疗痤疮的荧光。

71. 一种促进伤口愈合的方法，包括：

将局部生物光子材料放在伤口上或伤口内，其中所述局部生物光子材料是弹性的，包括至少一个生色团和粘性基质；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；

其中所述生物光子材料发射波长和强度能促进所述伤口愈合的荧光。

72. 一种促进伤口愈合的方法，包括：

将局部生物光子材料放在伤口上或伤口内，其中所述局部生物光子材料包括至少一个生色团和粘性基质，其中所述局部生物光子材料的撕裂强度与/或拉伸强度大于所述局部生物光子材料与其施用表面的粘合强度；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；

其中所述生物光子材料发射波长和强度能促进所述伤口愈合的荧光。

73. 一种促进皮肤更新的方法，包括：

将局部生物光子材料放在靶向皮肤组织上，其中所述局部生物光子材料是弹性的，包括至少一个生色团和粘性基质；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；

其中所述生物光子材料发射波长和强度能促进皮肤更新的荧光。

74. 一种促进皮肤更新的方法，包括：

将局部生物光子材料放在靶向皮肤组织上，其中所述局部生物光子材料包括至少一个生色团和粘性基质，其中所述局部生物光子材料的撕裂强度与/或拉伸强度大于所述局部生物光子材料与其施用表面的粘合强度；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；

其中所述生物光子材料发射波长和强度能促进皮肤更新的荧光。

75. 根据权利要求 66 至 74 任一项所述的方法，其中所述生物光子材料是遮罩或敷料。

76. 一种促进皮肤更新的方法，包括：

将局部生物光子材料放在靶向皮肤组织上，其中所述局部生物光子材料是遮罩，包括至少一个生色团和粘性基质；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料发射波长和强度能促进皮肤更新的荧光。

77. 根据权利要求 76 所述的方法，其中所述遮罩是面罩，具有至少一个适用于眼睛、鼻子或嘴巴的开孔。

78. 一种促进伤口愈合的方法，包括：

将局部生物光子材料放在伤口上或伤口内，其中所述局部生物光子材料是敷料，包括至少一个生色团和粘性基质；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料发射波长和强度能促进伤口愈合的荧光。

79. 一种预防或治疗疤痕的方法，包括：

将局部生物光子材料放在疤痕或伤口上，其中所述局部生物光子材料是膜，包括至少

一个生色团和粘性基质；及

用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料发射波长和强度能促进伤口愈合的荧光。

80. 根据权利要求 66 至 79 任一项所述的方法，其中所述生物光子材料在照射后被清除。

81. 根据权利要求 66 至 80 任一项所述的方法，其中所述生物光子材料是可以剥离的和被剥离下来。

82. 根据权利要求 66 至 79 任一项所述的方法，其中所述生物光子材料在照射后被留在原位，用于重新照射。

83. 根据权利要求 66 至 82 任一项所述的方法，其中所述生色团在照射后至少部分地发生光漂白。

84. 根据权利要求 66 至 83 任一项所述的方法，其中所述生物光子材料被照射，直到生色团至少部分地发生光漂白。

85. 根据权利要求 66 至 84 任一项所述的方法，其中所述生色团可以吸收与 / 或发射可见光范围内的光。

86. 根据权利要求 66 至 85 任一项所述的方法，其中所述生色团是呫吨染料。

87. 根据权利要求 66 至 86 所述的方法，其中所述呫吨染料选自曙红 Y、赤藓红 B、荧光素 B、玫瑰红和荧光桃红 B。

生物光子材料及其用途

技术领域

[0001] 本发明通常涉及用于光疗的生物光子材料。

背景技术

[0002] 最近，光疗被认为在医疗和美容领域应用广泛，包括用于手术、治疗和检查。例如，光疗已经发展用于治疗癌症和肿瘤，减少侵入性，作为抗菌处理对靶向部位进行消毒，促进伤口愈合，及用于面部皮肤更新。

[0003] 光动力疗法是一种光疗法，涉及向靶向组织施用光敏剂，在期间光敏剂被靶向组织吸收的规定时间后，将靶向组织暴露于光源。但是，这种疗法通常伴随不想要的副作用，包括对患者的全身或局部毒性或损害非-靶向组织。此外，例如，由于施用到靶向组织内的光敏剂选择性较差，这种现有疗法的疗效通常较低。

[0004] 因此，本发明的一个目的是提供用于光疗的性能改善的新的组合物及方法。

发明内容

[0005] 本发明提供用于光疗的局部生物光子材料和方法。

[0006] 特别是，本发明的生物光子材料包括粘性基质，及至少一种生色团，其中至少一种生色团能够吸收和发射来自生物光子材料的光。在上述和下述任一方面的一些实施例中，生物光子材料是弹性材料。

[0007] 另一方面，本发明提供一种局部生物光子材料，包括：粘性基质，及至少一种生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中所述局部生物光子材料是一种可剥离膜。

[0008] 另一方面，本发明提供一种局部生物光子材料，包括：粘性基质，及至少一种生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中所述局部生物光子材料是弹性的。

[0009] 另一方面，本发明提供一种局部生物光子材料，包括：粘性基质，及至少一种生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中所述局部生物光子材料是刚性的。

[0010] 另一方面，本发明提供一种局部生物光子材料，包括：粘性基质，及至少一种生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中所述局部生物光子材料的撕裂强度与/或拉伸强度大于所述局部生物光子材料与其施用表面的粘合强度。

[0011] 另一方面，本发明提供一种局部生物光子材料，包括：粘性基质，及至少一种生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中所述局部生物光子材料在稳态条件下具有定义明确的形状。

[0012] 另一方面，本发明提供一种局部生物光子材料，包括：粘性基质，及至少一种生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中所述局部生物光子材料是遮罩或敷料。在一些实施例中，所述遮罩与/或敷料具有预成型的配置。在一些实施例中，所

述遮罩与/或敷料是弹性的。在一些实施例中，所述遮罩与/或敷料是刚性的。

[0013] 另一方面，本发明提供一种生物光子材料，包括：粘性基质，及至少一种生色团，所述生色团可以吸收和发射来自生物光子材料的光，其中生物光子材料具有预成型配置，所述配置的尺寸与/或形状与生物光子材料可以连接的光源或灯的形状与/或尺寸对应。

[0014] 在上述方面的一些实施例中，生物光子材料是可剥离膜。在一些实施例中，生物光子材料是刚性的。

[0015] 在上述或下述任一方面的一些实施例中，生物光子材料的撕裂强度与/或拉伸强度大于生物光子材料与其施用表面的粘合强度。粘合强度包括克服静摩擦所需的力。

[0016] 在上述或下述任一方面的一些实施例中，生物光子材料至少基本上是半透明的。生物光子材料可以是透明的。在一些实施例中，生物光子材料在可见范围的半透明度是至少大约40％、大约50％、大约60％、大约70％或大约80％。优选的是，通过材料的光的传输是在没有至少一个生色团的条件下测定的。

[0017] 在上述或下述任一方面的一些实施例中，生物光子材料的厚度是大约0.1mm至大约50mm、大约0.5mm至大约20mm、大约1mm至大约10mm。

[0018] 在上述或下述任一方面的一些实施例中，生物光子材料具有预成型配置。在一些实施例中，预成型配置的形状与/尺寸与施用生物光子材料的身体部分的形状与/或尺寸相对应。在一些实施例中，施用生物光子材料的身体部分是头、头皮、前额、鼻子、脸颊、耳朵、嘴唇、脸、颈、肩、腋窝、臂、肘、手、手指、腹部、胸、肚子、背、骶骨、臀部、生殖器、腿、膝、脚、指甲、头发、脚趾或骨性隆起或它们的组合。

[0019] 在上述或下述任一方面的一些实施例中，生物光子材料是遮罩。在一些实施例中，遮罩是面罩，具有至少一个适用于眼睛、鼻子或嘴巴的开孔。在一些实施例中，遮罩是一次性的。遮罩也是可以重复利用的。生色团在单次使用或单次光照射后至少基本上是光漂白的。

[0020] 在上述或下述任一方面的一些实施例中，生物光子材料具有预成型配置，预成型配置的尺寸与/或形状与生物光子材料可以连接的光源或灯的形状与/或尺寸对应。

[0021] 在上述或下述任一方面的一些实施例中，可以将施用生物光子材料的表面上的生物光子材料清除，且基本上没有任何残留。

[0022] 在上述或下述任一方面的一些实施例中，生物光子材料包括的至少一个生色团是荧光团。在一些实施例中，生色团可以吸收与/或发射可见光范围内的光。生色团是可以溶于水的。在一些实施例中，生色团可以发射大约500nm至大约700nm的光。在一些实施例中，生色团或荧光团是咕吨染料。咕吨染料可以选自曙红Y、赤藓红B、荧光素、玫瑰红和荧光桃红B。在一些实施例中，生色团包括在粘性基质中。在上述或下述任一方面的一些实施例中，粘性基质是颗粒形式。

[0023] 在上述或下述任一方面的一些实施例中，生物光子材料的粘性基质包括至少一种聚合物。在一些实施例中，聚合物选自交联聚丙烯酸聚合物、透明质酸盐、水合聚合物、亲水聚合物和脂溶聚合物。在一些实施例中，粘性基质包括透明质酸钠。在一些实施例中，透明质酸钠的含量是大约2％至大约8％。

[0024] 在一些实施例中，粘性基质是脂溶聚合物，如聚硅氧烷。生色团可以溶于水和位于脂溶聚合物的水相内。在这种情况下，生物光子材料包括脂溶聚合物相内含生色团的水相。

水相占脂溶聚合物相的大约 2wt％至大约 40wt％。水相可以是液体或凝胶。生物光子材料可以进一步包括稳定剂，如 CMC 或明胶。

[0025] 在一些实施例中，粘性基质包括明胶或脱乙酰壳多糖。在一些实施例中，生物光子材料进一步包括选自过氧化氢、过氧化脲和过氧化苯甲酰的富氧化合物。

[0026] 在一些实施例中，生色团包括在形成粘性基质的载体介质中。在一些实施例中，当用光照射时，生色团可以吸收和发射粘性基质中的光。在一些实施例中，载体介质是至少一种聚合物或通过聚合、交联或干燥能够形成粘性基质的聚合物前体。

[0027] 另一方面，本发明提供一种局部生物光子材料，包括含水粘性基质中的水溶生色团，其中含水粘性基质分散在脂溶聚合物内。在一些实施例中，脂溶聚合物是聚硅氧烷。水相可以是液体或凝胶。在一些实施例中，含水粘性基质可以是明胶、水或羧甲基纤维素。生色团可以包括荧光团，如呫吨染料，选自曙红 Y、荧光素、赤藓红、荧光桃红 b 和玫瑰红。水相占脂溶聚合物相的大约 2wt％至大约 40wt％。在一些实施例中，局部生物光子材料可用于处理伤口，或处理或预防疤痕。

[0028] 本发明任何方面和实施例的生物光子材料可作为遮罩、敷料或滤波器使用。本发明任何方面或实施例的生物光子材料可用于组织美容或医学处理。在一些实施例中，美容处理是皮肤更新和调理，医学处理是伤口愈合、牙周治疗或痤疮治疗或其它皮肤病，包括痤疮、湿疹、牛皮藓或皮炎的治疗。在一些方面，局部生物光子材料用于调节发炎，或用于促进血管形成。

[0029] 本发明还提供包含本发明各实施例所述生物光子材料或前体材料的容器。在一些实施例中，容器包括用于容纳生物光子材料的密封室，与密封室连接、用于从容器中放出生物光子材料的出口，其中生物光子材料在载体介质中包括至少一个生色团，在从密封室中放出后可以形成粘性基质。在一些实施例中，容器是喷雾罐。容器可以是不透明的。

[0030] 本发明还提供用于制备或提供本发明各实施例所述的生物光子材料或前体材料的试剂盒。在一些实施例中，试剂盒包括含第一生色团的第一容器；包含增稠剂的第二组分，其中增稠剂与第一组分混合时，可以形成粘性基质。在一些实施例中，第二容器可以包含富氧化合物。

[0031] 本发明还提供生物光子治疗的方法，包括将本发明的局部生物光子材料施用到靶向组织上及用光照射所述材料。

[0032] 一方面，本发明提供一种生物光子治疗皮肤病的方法，其中所述方法包括将生物光子材料放在靶向皮肤组织上面或上方，其中生物光子材料是弹性的，包括至少一个生色团和粘性基质；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料发射波长和强度能促进所述皮肤病痊愈的荧光。皮肤病选自痤疮、湿疹、牛皮藓或皮炎。

[0033] 另一方面，提供一种生物光子治疗皮肤病的方法，包括：将局部生物光子材料放在靶向皮肤组织上面或上方，其中生物光子材料包括至少一种生色团和粘性基质，其中局部生物光子材料的撕裂与 / 或拉伸强度大于局部生物光子材料与其施用表面的粘合强度；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料放射荧光，其波长和强度能促进所述皮肤病的愈合。

[0034] 另一方面，提供一种生物光子治疗痤疮的方法，包括：将局部生物光子材料放在靶

向皮肤组织上面或上方，其中生物光子材料是弹性的，包括至少一种生色团和粘性基质；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料放射荧光，其波长和强度治疗痤疮。

[0035] 另一方面，提供一种生物光子治疗痤疮的方法，包括：将局部生物光子材料放在靶向皮肤组织上面或上方，其中生物光子材料包括至少一种生色团和粘性基质，其中局部生物光子材料的撕裂与/或拉伸强度大于局部生物光子材料与其施用表面的粘合强度；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料放射荧光，其波长和强度治疗痤疮。

[0036] 另一方面，提供一种促进伤口愈合的方法，包括：将局部生物光子材料放在靶向皮肤组织上面或上方，其中生物光子材料是弹性的，包括至少一种生色团和粘性基质；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料放射荧光，其波长和强度能促进伤口愈合。

[0037] 提供一种促进伤口愈合的方法，包括：将局部生物光子材料放在靶向皮肤组织上面或上方，其中生物光子材料包括至少一种生色团和粘性基质，其中局部生物光子材料的撕裂与/或拉伸强度大于局部生物光子材料与其施用表面的粘合强度；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料放射荧光，其波长和强度能促进伤口愈合。

[0038] 另一方面，提供一种促进皮肤更新的方法，包括：将局部生物光子材料放在靶向皮肤组织上面或上方，其中生物光子材料是弹性的，包括至少一种生色团和粘性基质；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料放射荧光，其波长和强度能促进皮肤更新。

[0039] 另一方面，提供一种促进皮肤更新的方法，包括：将局部生物光子材料放在靶向皮肤组织上面或上方，其中生物光子材料包括至少一种生色团和粘性基质，其中局部生物光子材料的撕裂与/或拉伸强度大于局部生物光子材料与其施用表面的粘合强度；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料放射荧光，其波长和强度能促进皮肤更新。

[0040] 在一些实施例中，在照射后清除生物光子材料。在一些实施例中，生物光子材料是可以剥离的，在照射后剥离。在一些实施例中，生物光子材料不能剥离，但是可以一片或多片清除。生物光子材料可以是遮罩或敷料，如面罩或伤口敷料。

[0041] 另一方面，提供一种促进皮肤更新的方法，包括：将遮罩的局部生物光子材料放在靶向皮肤组织上面或上方，其中生物光子材料是弹性的，包括至少一种生色团和粘性基质；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料放射荧光，其波长和强度能促进皮肤更新。

[0042] 在一些实施例中，遮罩是至少有一个适用于眼睛、鼻子或嘴巴的开孔的面罩。遮罩可以是一次性的或重复利用的。

[0043] 另一方面，提供一种促进伤口愈合的方法，包括：将敷料局部生物光子材料放在靶向皮肤组织上面或上方，其中生物光子材料是弹性的，包括至少一种生色团和粘性基质；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料放射荧光，其波长和强度能促进伤口愈合。

[0044] 另一方面，提供一种预防或治疗疤痕形成的方法，包括：将膜局部生物光子材料放在靶向皮肤组织上面或上方，其中生物光子材料是弹性的，包括至少一种生色团和粘性基质；用波长与至少一个生色团的吸收光谱重叠的光照射所述生物光子材料；其中所述生物光子材料放射荧光，其波长和强度能促进伤口愈合。

[0045] 在一些实施例中，生物光子材料在照射后被留在原位，用于再次照射。在一些实施例中，生色团在照射后至少部分地发生光漂白。在一些实施例中，生物光子材料照射，直到生色团至少部分地发生光漂白。

[0046] 在一些实施例中，采用可见光照射局部生物光子材料。在上述或下述任一方面的一些实施例中，生物光子材料包括的至少一个生色团是荧光团。在一些实施例中，生色团可以吸收与/或发射可见光范围内的光。生色团是可以溶于水的。在一些实施例中，生色团可以发射大约500nm至大约700nm的光。在一些实施例中，生色团或荧光团是呫吨染料。呫吨染料可以选自曙红Y、赤藓红B、荧光素、玫瑰红和荧光桃红B。在一些实施例中，生色团包括在粘性基质中。

[0047] 在上述或下述任一方面的一些实施例中，生物光子材料至少基本上是半透明的。生物光子材料可以是透明的。在一些实施例中，生物光子材料在可见范围的半透明度是至少大约40％、大约50％、大约60％、大约70％或大约80％。优选的是，通过材料的光的传输是在没有至少一个生色团的条件下测定的。在上述或下述任一方面的一些实施例中，生物光子材料的厚度是大约0.1mm至大约50mm、大约0.5mm至大约20mm、大约1mm至大约10mm。

附图说明

[0048] 参考附图，将更好地了解本发明的其它方面和优点：

[0049] 图1示出了供体和受体生色团的吸收和发射光谱。还示出了受体生色团的吸收光谱与供体生色团的发射光谱之间的光谱重叠情况。

[0050] 图2是雅布隆斯基图的示意图，示出了供体发射和受体吸收之间涉及的耦合跃迁。

[0051] 图3是本发明一个实施例的活化生物光子材料的发射荧光光谱（实例1）。

[0052] 图4是光活化生物光子材料照射成纤维细胞和角化细胞的发射荧光光谱，用于评价蛋白质调节和基因表达（实例2）。

[0053] 图5a和5b分别是曙红Y和荧光素的发射荧光光谱，活化光通过组合物，以不同的生色团浓度（实例4）。

[0054] 图6a和6b分别是凝胶中曙红和荧光素的吸收光谱和发射光谱（实例5）。

[0055] 图7a和7b分别是凝胶中曙红、荧光素和玫瑰红的吸收光谱和发射光谱（实例6）。

[0056] 图8a和8b是本发明实施例所述粘性生物光子材料的应力-应变曲线（实例10）。

具体实施方式

[0057] (1)概述

[0058] 本发明提供生物光子材料及其用途。采用这些材料的生物光子治疗将不涉及本质上治疗靶标直接接触光敏剂（或生色团），包括但不限于皮肤、粘膜、伤口、头发和指甲。因此，可以减少、降低或避免这种直接接触引起的副作用。此外，在一些实施例中，采用本发明

的生物光子材料的光疗将，例如，通过，例如，促进胶原蛋白合成更新皮肤，促进伤口愈合，治疗皮肤病，如痤疮，和治疗牙周炎。

[0059] (2) 定义

[0060] 在继续进一步详细描述本发明之前，应该理解的是，本发明公开并不限于具体的组合物或工艺步骤，因为这些都可能变化。必须指出的是，正如本说明书和所附权利要求书中使用的那样，除非上下文清楚显示，否则，单数形式“一”、“一个”及“该”包括复数指示对象。

[0061] 本发明中给出数值或范围时使用的词语“大约”指的是数值或范围与给出的数值或范围的差别在 20％以内，优选在 10％以内及更优选在 5％以内。

[0062] 本发明中使用的“与 / 或”指的是具体公开了两种规定特征或成分的每一种特征或成分，两者可以同时兼具或者单独具有。例如，“A 与 / 或 B”指的是公开了 (i)A、(ii)B 和 (iii)A 和 B 三种情形，每种情形都是独立的。

[0063] “生物光子性”指的是在生物相关背景中产生、操作、检测和应用光子。换句话说，生物光子组合物和材料主要是由于光子的产生和操作而施加其生理效应。

[0064] “生物光子材料”是一种可被光活化而产生光子，用于生物相关应用的材料。此处所述的生物光子材料可以是粘性胶、半固体或固体。生物光子材料可以是，包括但不限于，膜等形式，用于遮罩、敷料或光连接。生物光子材料可以得复合物，包括纤维、颗粒、肋状物、支撑结构、网、非生物光子层或生物光子层，相同或不同组合物。

[0065] “粘性基质”指的是自支持材料或可以形成自支持材料的介质，例如，在稳态条件下具有规定形状的材料。这可能是由于内部吸引力造成的。材料的粘合性质使材料能够被处理而不被撕开。

[0066] “局部施用”或“局部使用”指的是应用于身体表面，如皮肤、粘膜、阴道、口腔、内部手术伤口部位等。

[0067] 在本发明中，词语“生色团”和“光活化剂”可以互换使用。生色团指的是在受到光照射时能够吸收光的化合物。生色团容易光致激发，然后，将其能量传递给其它分子或以光（荧光）的形式发射。

[0068] “光漂白”指的是生色团的光化学破坏。生色团可以完全或部分光漂白。

[0069] 词语“光化光”指的是特定光源（如灯、LED 或激光器）发出的且能够被物质（例如，生色团或光活化剂）吸收的光能。在优选的实施例中，光化光是可见光。

[0070] “剥离”或“可剥离”膜、膜或基质是在应用后能够，例如，用手机械清除的东西。它可以作为单块或作为少量大块被清除。

[0071] “皮肤更新”指的是减少、消除、延缓或逆转皮肤老化的一个或多个症状或通常改善皮肤状态的过程。例如，增加皮肤亮度、缩小毛孔、减少细纹或皱纹，改善皮肤变薄和透明，改善紧致度，改善皮肤松驰（如骨质疏松引起的松驰），改善干燥皮肤（可能发痒）、减少或逆转斑点，老年斑、蛛状静脉、皮肤粗糙和革质皮肤、拉开时会消失的细纹、皮肤松驰或改善斑点肤质。根据本发明所述，上文所述的一种或多种症状可以通过本发明某些组合物、方法和用途的实施例减少、消除、延缓或甚至逆转。

[0072] “伤口”指的是任何组织的损伤，包括，例如，急性、亚急性、延缓愈合或难以愈合的伤口，以及慢性伤口。伤口的实例包括开放性伤口和闭合性伤口。伤口包括，例如，截肢、烧

伤、切口、切除、损伤、撕裂伤、磨损、刺伤或贯通伤口、手术伤口、擦伤、血肿、压伤、溃疡（如压迫性、糖尿病、静脉或动脉）、牙周炎造成的伤口（牙周发炎）。

[0073] 参考下面的对选定实施例的详细说明（伴有附图说明），本发明主题内容的特征和优点将更为明显。正如将认识到的那样，本发明公开的和权利要求中的主题内容可以在各个方面作出改动，所有改动都不背离权利要求的范围。因此，附图和说明本质上将被视为阐述性的，而并非限制性的，主题内容的完整范围在权利要求书中给出。

[0074] (3) 生物光子材料

[0075] 从广义上来说，本发明提供粘性局部生物光子材料及利用生物光子材料的方法。从广义上来说，生物光子材料可以被特定波长的光（如光子）活化。根据本发明的各种实施例，生物光子材料包含粘性基质和在粘性基质内或粘性基质上的至少一种生色团，被光活化，加速光能的分散，导致光本身具有治疗效果，与/或光化学活化组合物中包含的其它试剂（例如，当组合物中存在此种化合物时或与组合物接触时，加速过氧化物（氧化剂）的分解过程，导致形成氧自由基，如单线态氧）。

[0076] 当生色团吸收某一波长的光子时，生色团被激发。这是一种不稳定的状态，分子将试图返回到基态，释放出多余的能量。对某些生色团来说，当其返回到基态时，最好是以光的形式放出多余的能量。该过程被称为发射荧光。由于转化过程失去能量，与吸收波长相比，所发射的荧光的峰值波长朝更长的波长移动。这种现象被称为斯托克斯频移。在合适的环境中（例如，在生物光子材料中），许多能量被转移给生物光子材料的其它成分或直接转移到治疗部位。

[0077] 人们认为，由于光活化生色团放射的荧光具有被生物细胞和组织认可的飞秒、皮秒或纳秒发射特性，导致有益的生物调节，因此，这种荧光具有治疗特性。但是，并不受限于这种理论。此外，发射的荧光的波长更长，因此，比活化光能更深地穿入组织内部。采用范围如此宽的波长（某些实施例中包括穿过组合物的活化光）照射组织，对细胞和组织具有不同的和互补的效果。换句话说，本发明生物光子材料中使用的生色团对组织具有治疗效果。这是这些光活化剂完全不同的应用，与生色团作为简单的染色剂或作为光-聚合的催化剂的用途完全不同。

[0078] 本发明的生物光子材料具有局部用途，如遮罩或伤口敷料或作为光源的连接，作为波导或作为滤光器。这些生物光子材料的粘性性质使其容易从处理部位清除，因此，处理更迅速和更容易。此外，生物光子材料可以限制生色团和组织之间的接触。这些材料将根据构成组合物的成分进行说明。另外地或替代地，本发明的组合物具有功能和结构性质，这些性质可用于定义和描述组合物。下面将对本发明中的生物光子材料的各组分，包括生色团，增稠剂和其它任选成分进行详细说明。

[0079] 本发明还提供本发明所述材料的前体组合物，所述前体组合物在干燥、加热、光照射、施用于组织或混合时将变得具有粘性。前体组合物在载体介质中包括至少一种生色团，或至少一种生色团和粘性基质。

[0080] (a)生色团

[0081] 合适的生色团可以是荧光化合物（或染色剂）（亦称为“荧光染料”或“荧光团”）。也可以使用其它染料组或染料（生物学和组织学染料、天然染料、食用色素、类胡萝卜素）。合适的光活化剂可以是那些通常被视为安全的光活化剂(GRAS)。有利的是，皮肤或其它组

织耐受性不太好的光活化剂可以包括在本发明的生物光子材料中，正如一些实施例所示，光活化剂包裹在粘性基质内，并不与组织接触。

[0082] 在一些实施例中，本发明的生物光子材料包括第一生色团，在照射光时发生部分或完全光漂白。在一些实施例中，第一生色团在可见光谱范围内的波长处吸收，如在波长大约380-800nm、380-700、400-800或380-600nm处吸收。在其它实施例中，第一生色团在波长大约200-800nm、200-700nm、200-600nm或200-500nm处吸收。在一个实施例中，第一生色团在波长大约200-600nm处吸收。在一些实施例中，第一生色团吸收波长大约200-300nm、250-350nm、300-400nm、350-450nm、400-500nm、450-650nm、600-700nm、650-750nm或700-800nm的光。

[0083] 熟悉本领域的技术人员应该理解的是，具体生色团的光学特性可能根据生色团的周围介质而变化。因此，正如本发明所述，具体生色团的吸收与/或发射波长（或光谱）与本发明中的生物光子材料中所测到的波长（或光谱）相对应。

[0084] 本发明所述生物光子材料可包含至少一种其它生色团。组合生色团可通过组合染料分子而增加光吸收，并增强吸收和光-生物调节的选择性。这就创造了产生新的光敏性与/或选择性生色团混合物的几种可能性。因此，在一些实施例中，本发明的生物光子材料包括一种以上生色团。当用光照射这种多-生色团材料时，在生色团之间可发生能量转移。该过程被称为共振能量转移，是一种广泛流行的光物理过程，通过该过程，被激发的“供体”生色团（此处亦称为第一生色团）将其激发能转移给“受体”生色团（此处亦称为第二生色团）。共振能量转移的效率和导向性取决于供体和受体生色团的光谱特征。特别是，生色团之间的能量流动取决于反映吸收光谱和发射光谱相对位置和形状的光谱重叠。更具体地说，要使能量转移发生，供体生色团的发射光谱应与受体生色团的吸收光谱重叠（图1）。

[0085] 供体发射减少或猝灭和伴随受体发射强度增加的激发态寿命的缩短，都证明了能量转移已经发生。图2是一份雅布隆斯基图，它说明了供体发射和受体吸收之间所涉及的耦合跃迁。

[0086] 为了提高能量转移效率，供体生色团应具有良好的吸收光子和发射光子的能力。此外，供体生色团的发射光谱与受体生色团的吸收光谱之间重叠越多，供体生色团就越能更好地将能量转移给受体生色团。

[0087] 在一些实施例中，本发明的生物光子材料进一步包括第二生色团。在一些实施例中，第一生色团的发射光谱与第二生色团的吸收光谱至少重叠大约80％、50％、40％、30％、20％或10％。在一个实施例中，第一生色团的发射光谱与第二生色团的吸收光谱至少重叠大约20％。在一些实施例中，第一生色团的发射光谱与第二生色团的吸收光谱至少重叠1-10％、5-15％、10-20％、15-25％、20-30％、25-35％、30-40％、35-45％、50-60％、55-65％或60-70％。

[0088] 本发明所述的％光谱重叠指的是在光谱四分之一最大全宽(FWQM)时测量的供体生色团的发射波长范围与受体生色团的吸收波长范围的重叠百分比。例如，图1示出了供体生色团和受体生色团的归一化吸收光谱和发射光谱。受体生色团的吸收光谱的光谱FWQM是大约60nm(515nm至大约575nm)。供体生色团的光谱与受体生色团的吸收光谱重叠大约40nm(从515nm至大约555nm)。因此，重叠％可以计算为40nm/60nm x 100 ＝ 66.6％。

[0089] 在一些实施例中，第二生色团在可见光谱范围内的波长处吸收。在一些实施例

中，第二生色团的吸收波长比第一生色团的吸收波长相对来说更长，波长在大约 50-250、25-150 或 10-100nm 的范围内。

[0090] 第一生色团的含量是生物光子材料重量的大约 0.001-40％。当存在第二生色团时，其含量是生物光子材料重量的大约 0.001-40％。在一些实施例中，第一生色团占生物光子材料重量的大约 0.001-3％、0.001-0.01％、0.005-0.1％、0.1-0.5％、0.5-2％、1-5％、2.5-7.5％、5-10％、7.5-12.5％、10-15％、12.5-17.5％、15-20％、17.5-22.5％、20-25％、22.5-27.5％、25-30％、27.5-32.5％、30-35％、32.5-37.5％或 35-40％。在一些实施例中，第二生色团占生物光子材料重量的大约 0.001-3％、0.001-0.01％、0.005-0.1％、0.1-0.5％、0.5-2％、1-5％、2.5-7.5％、5-10％、7.5-12.5％、10-15％、12.5-17.5％、15-20％、17.5-22.5％、20-25％、22.5-27.5％、25-30％、27.5-32.5％、30-35％、32.5-37.5％或 35-40％。在一些实施例中，生色团或生色团组合的总重量占生物光子材料重量的大约 0.005-1％、0.05-2％、1-5％、2.5-7.5％、5-10％、7.5-12.5％、10-15％、12.5-17.5％、15-20％、17.5-22.5％、20-25％、22.5-27.5％、25-30％、27.5-32.5％、30-35％、32.5-37.5％或 35-40.001％。

[0091] 所用生色团的浓度可以根据生物光子材料的生物光子活性的期望的强度和持续时间，及所达到的医学或美容效果来进行选择。例如，有些染料，如咕吨染料达到“饱和浓度”，在这之后，进一步增加浓度并不能提供显著提高的发射荧光。在饱和浓度之上进一步增加生色团的浓度会减少穿过基质的活化光的数量。因此，如果某一应用所需要的荧光比活化光多，可以使用高“饱和”浓度的生色团。但是，如果在发射荧光和活化光之间要求平衡，可以选择接近或低于饱和浓度的浓度。

[0092] 本发明中的生物光子材料中可以使用的合适的生色团包括但不限于：

[0093] 叶绿素染料

[0094] 示例性叶绿素染料包括但不限于叶绿素 a；叶绿素 b；叶绿酸；油溶叶绿素；菌叶绿素 a；菌叶绿素 b；菌叶绿素 c；菌叶绿素 d；原叶绿素；原叶绿素 a；两亲叶绿素衍生物 1；以及两亲叶绿素衍生物 2。

[0095] 咕吨衍生物

[0096] 示例性咕吨染料包括但不限于曙红 B(4',5'-二溴-2',7'-二硝基-荧光素二价阴离子)；曙红 Y；曙红 Y(2',4',5',7'-四溴-荧光素二价阴离子)；曙红 (2',4',5',7'-四溴-荧光素二价阴离子)；曙红 (2',4',5',7'-四溴-荧光素二价阴离子) 甲酯；曙红 (2',4',5',7'-四溴-荧光素单价阴离子)p-异丙基苄酯；曙红衍生物 (2',7'-二溴-荧光素二价阴离子)；曙红衍生物 (4',5'-二溴-荧光素二价阴离子)；曙红衍生物 (2',7'-二氯-荧光素二价阴离子)；曙红衍生物 (4',5'-二氯-荧光素二价阴离子)；曙红衍生物 (2',7'-二碘-荧光素二价阴离子)；曙红衍生物 (4',5'-二碘-荧光素二价阴离子)；曙红衍生物 (三溴荧光素二价阴离子)；曙红衍生物 (2',4',5',7'-四氯-荧光素二价阴离子)；曙红；曙红联十六烷基吡啶氯离子对；赤藓红 B(2',4',5',7'-四碘-荧光素二价阴离子)；赤藓红；赤藓红二价阴离子；赤藓红 B；荧光素；荧光素二价阴离子；荧光桃红 B(2',4',5',7'-四溴-3,4,5,6-四氯-荧光素二价阴离子)；根皮红 B(四氯-四溴-荧光素)；根皮红 B；玫瑰红 (3,4,5,6-四氯-2',4',5',7'-四碘荧光素二价阴离子)；派若宁 G、派若宁 J、派若宁 Y；罗丹明染料，如罗丹明包括 4,5-二溴-罗丹明甲酯；4,5-二溴-罗丹

明正丁酯；罗丹明 101 甲酯；罗丹明 123；罗丹明 6G；罗丹明 6G 己酯；四溴－罗丹明 123；及四甲基－罗丹明乙酯。

[0097] 亚甲基蓝染料

[0098] 示例性亚甲基蓝衍生物包括但不限于 1- 甲基亚甲基蓝；1,9- 二甲基亚甲基蓝；亚甲基蓝；亚甲基蓝 (16μM)；亚甲基蓝 (14μM)；亚甲紫；溴亚甲基紫；4- 碘亚甲基紫；1,9- 二甲基 -3- 二甲基－氨基 -7- 二乙基－氨基－吩噻嗪；及 1,9- 二甲基 -3- 二乙基氨基 -7- 二丁基－氨基－吩噻嗪。

[0099] 偶氮染料

[0100] 示例性偶氮 (或二偶氮 -) 染料包括但不限于甲基紫、中性红、对位红 (颜料红 1)、苋菜红 (偶氮玉红 S)、酸性红 (偶氮玉红、食品红 3、酸性红 14)、诱惑红 AC(FD&C 40)、酒石黄 (FD&C 黄 5)、橙黄 G(酸性橙 10)、丽春红 4R(食品红 7)、甲基红 (酸性红 2) 及紫脲酸铵－红紫酸铵。

[0101] 在本发明的某些方面，所述生物光子材料的一个或多个生色团可以独立地选自以下任一生色团：酸性黑 1、酸性蓝 22、酸性蓝 93、酸性品红、酸性绿、酸性绿 1、酸性绿 5、酸性洋红、酸性橙 10、酸性红 26、酸性红 29、酸性红 44、酸性红 51、酸性红 66、酸性红 87, 酸性红 91, 酸性红 92, 酸性红 94, 酸性红 101, 酸性红 103, 酸性品红、酸性品红、酸性紫 19、酸性黄 1、酸性黄 9、酸性黄 23、酸性黄 24、酸性黄 36、酸性黄 73、酸性黄 S、吖啶橙、吖啶黄、阿尔新蓝、阿尔新黄、醇溶曙红、茜素、茜素蓝 2RC、茜素卡红、茜素花青 BBS、茜素花青 R、茜素红 S、茜素红紫、试铝灵、酰胺黑 10B、氨基黑、苯胺蓝 WS、蒽蓝 SWR、金胺 O、Azocannine B、偶氮卡红 G、偶氮重氮 (Azoic diazo)5、偶氮重氮 48、天蓝 A、天蓝 B、天蓝 C、碱性蓝 8、碱性蓝 9、碱性蓝 12、碱性蓝 15, 碱性蓝 17、碱性蓝 20、碱性蓝 26、碱性棕 1、碱性品红、碱性绿 4、碱性橙 14、碱性红 2、碱性红 5、碱性红 9、碱性紫 2、碱性紫 3、碱性紫 4、碱性紫 10、碱性紫 14、碱性黄 1、碱性黄 2、比布里希猩红、俾斯麦棕 Y、亮结晶猩红 6R、钙红、胭脂红、胭脂红酸 (酸性 4)、天青石蓝 B、中国蓝、虫红、Coelestine 蓝、铬紫 CG、铬变素 2R、Chromoxane 花青 R、刚果 corinth、刚果红、棉染蓝、棉红、Croceine 猩红、藏花素、结晶丽春红 6R、结晶紫、大丽紫、金刚绿 B、直接靛兰 14、直接蓝 58、直接红、直接红 10、直接红 28、直接红 80、直接黄 7、曙红 B、蓝色曙红、曙红、曙红 Y、黄色曙红、Eosinol、伊利石榴红 B、铬花青 R、赤藓红 B、乙基曙红、乙基绿、乙基紫、伊文思蓝、坚牢蓝 B、坚牢绿 FCF、坚牢红 B、坚牢黄、荧光黄、食品绿 3、焦酚酞、加拉明蓝、倍花青、龙胆紫、氧化苏木精、苏木精、苏木紫、日光坚牢品红 BBL、甲蓝、苏木因、苏木精、苏木紫、霍夫曼紫、皇家红、吲哚菁绿、阿利新蓝、阿利新蓝 1、阿利新黄 1、INT、洋红、胭脂酮酸、Kernechtrot、紫胶、紫胶酸、劳思氏紫、淡绿、丽丝胺绿 SF、Luxol 坚牢蓝、品红 O、品红 I、品红 II、品红 III、孔雀绿、曼彻斯特棕、马休黄、汞溴红、红汞、酸性间胺黄、亚甲基天蓝 A、亚甲基天蓝 B、亚甲基天蓝 C、亚甲基蓝、亚甲基绿、甲基紫、甲基紫 2B、甲基紫 10B、媒染蓝 3、媒染蓝 10、媒染蓝 14、媒染蓝 23、媒染蓝 32、媒染蓝 45、媒染红 3、媒染红 11、媒染紫 25、媒染紫 39、萘酚蓝黑、萘酚绿 B、萘酚黄 S、天然黑 1、天然红、天然红 3、天然红 4、天然红 8、天然红 16、天然红 25、天然红 28、天然黄 6、NBT、天然红、新品红、尼亚加拉蓝 3B、夜蓝、尼罗蓝、尼罗蓝 A、尼罗红、硫酸尼罗蓝、尼罗红、硝基 BT、硝基蓝四唑、核坚牢红、油红 O、橙 G、地衣红、副品红、荧光桃红 B、苦味酸、丽春红 2R、丽春红 6R、丽春红 B、二甲苯胺丽春红、丽春红 S、报春花、红紫素、藻青素、藻红素。藻红蓝蛋白 (PEC)、酞菁、派若宁 G、派若宁 Y、

奎宁、罗丹明B、玫瑰苯胺、玫瑰红、藏红、番红精O、猩红R、猩红、猩红R、紫胶、天狼猩红F3B、砂罗铬花青R、可溶蓝、溶剂黑3、溶剂蓝38、溶剂红23、溶剂红24、溶剂红27、溶剂红45、溶剂黄94、醇溶曙红、苏丹III、苏丹IV、苏丹黑B、硫黄S、瑞士蓝、酒石黄、硫黄素S、硫黄素T、劳氏紫、甲苯胺蓝、甲苯胺红、苯胺黄G、吖啶黄、锥虫蓝、荧光素钠、维多利亚蓝4R、维多利亚蓝B、维多利亚绿B、水溶蓝I、水溶曙红、二甲苯胺丽春红或黄色曙红。

[0102] 在某些实施例中，本发明的生物光子材料包括上文所列生色团中的任何一个生色团，或它们的组合，从而在施用部位提供协同生物光子效用。

[0103] 生色团组合的协同效应指的是生物光子效用大于其各自效用的总和，但并不限于任一具体的理论。有利的是，这可以转化为生物光子材料的反应性增加，速度更快或改进的处理时间。此外，要达到相同的或更好的处理结果，不需要更改处理条件，如暴露于光的时间、所用光源的功率及所用光的波长。换句话说，使用协同的生色团组合可以实现相同的或更好的处理，而并不一定需要延长暴露于光源的时间、提高光源功率或采用不同波长的光源。

[0104] 在一些实施例中，生物光子材料包括曙红Y作为第一生色团及玫瑰红、荧光素、赤藓红、荧光桃红B、叶绿酸中的一种或多种作为第二生色团。人们相信，这些组合具有协同效应，因为，当它们部分地因为与它们的吸收光谱和发射光谱重叠或接近而得到活化时，它们可以将能量从一个生色团转移到另一个生色团。然后，这种转移的能量以荧光形式放出与/或产生反应性的氧。这种吸收和再发射的光被认为在整个组合物中传输，还传输到治疗部位内。

[0105] 在其它实施例中，生物光子材料包括下述协同组合：曙红Y和荧光素；荧光素和玫瑰红；赤藓红和曙红Y、玫瑰红或荧光素；荧光桃红B和曙红Y、玫瑰红、荧光素和赤藓红中的一种或多种。也可以采用其它协同生色团组合。

[0106] 通过生物光子材料中生色团组合的协同效应，通常无法被活化光（例如LED的蓝光）所活化的生色团，可以通过被活化光所活化的生色团的能量转移而得到活化。因此，可以根据要求的美容或医学治疗而利用和定制不同性质的光活化生色团。

[0107] 例如，当玫瑰红在分子氧存在的情况下被活化时，它可产生较高的单线态氧。但是，从发射荧光方面来讲，玫瑰红的量子产率较低。玫瑰红的峰值吸收在540nm附近，因此，它可用绿光进行活化。曙红Y的量子产率高，可以采用蓝光活化。将玫瑰红和曙红Y相结合，得到的组合物蓝光活化时可以发射具有治疗作用的荧光和产生单线态氧。在这种情况下，蓝光光活化曙红Y，曙红Y将其部分能量转移给玫瑰红，并以荧光形式放出部分能量。

[0108] 在一些实施例中，选择一种或多种生色团，从而光活化时其发射荧光是电磁谱中绿光、黄光、橙光、红光及红外光部分内的一种或多种，例如，峰值波长在大约490nm至大约800nm范围之内。在一些实施例中，发射荧光的功率密度是0.005至大约10mW/cm^2、大约0.5至大约5mW/cm^2。

[0109] (b)粘性基质

[0110] 本发明中的生物光子材料包括由一种或多种增稠剂或由某种载体介质制造的粘性基质。换句话说，本发明的生物光子材料包括能够构成粘性基质的一种或多种增稠剂，或某种载体介质。这些试剂的含量和比例应足够提供要求的粘度、柔韧性、刚性、拉伸强度、撕裂强度、弹性和粘合性。期望的性质可能是一种可实现可剥离膜或形成刚性或挠性基质的

性质。增稠剂的选择，要让生色团可以在粘性基质中保持光活性。还根据其将形成的粘性基质的光学透明性来选择增稠剂。粘性基质应能够传输足够的光以活化至少一个生色团；在荧光是由活化生色团发射的实施例中，粘性基质还应能够将发射的荧光传输给组织。熟悉本领域的技术人员应该认识到的是，增稠剂是选择的生色团的合适介质。例如，本发明人已经注意到，有些砧吨染料在非水合介质中并不发荧光，因此，可以使用水合聚合物或极性溶剂。还应根据指定用途选择增稠剂。例如，如果生物光子材料施用到组织上，粘性基质优选是生物相容性材料，或粘性基质具有一个将与组织相接的生物相容性材料外层。

[0111] 增稠剂

[0112] 在一些实施例中，用于制造粘性基质的增稠剂的含量占总重量的大约 0.001％至大约 40％ (w/w％)。在一些实施例中，增稠剂的总含量占大约 0.001-0.01％、大约 0.005-0.05％、大约 0.01-0.1、大约 0.05-0.5％、大约 0.1-1％、大约 0.5-5％、大约 1-5％、大约 2.5-7.5％、大约 5-10％、大约 7.5-12.5％、大约 10-15％、大约 12.5-17.5％、或大约 15-20％、或大约 15-25％、或大约 20-30％或大约 25-35％，或大约 30-40％。熟悉本领域的技术人员应该认识到的是，通过改变增稠剂的含量，可以调节粘度、柔韧性、刚性、拉伸强度、撕裂强度、弹性和粘合性。测定粘度、柔韧性、刚性、拉伸强度、撕裂强度、弹性和粘合性的方法是本领域熟悉的。

[0113] 可用于制备本发明中的生物光子材料的增稠剂包括聚合物、共聚物，单体是：乙烯基吡硌烷酮、甲基丙烯酰胺、丙烯酰胺、N- 乙烯基咪唑、羧基乙烯、乙烯基酯、乙烯醚、硅氧烷、聚环氧乙烷、聚乙二醇、乙烯醇、丙烯酸钠、丙烯酸盐、马来酸、NN- 二甲基丙烯酰胺、双丙酮丙烯酰胺、丙烯酰胺、丙烯酰吗啉、普卢兰尼克、胶原蛋白、聚丙烯酰胺、聚丙烯酸酯、聚乙烯醇、聚亚乙烯基、聚乙烯硅酸盐、糖（例如，蔗糖、葡萄糖、葡糖胺、半乳糖、海藻糖、甘露糖或乳糖）取代聚丙烯酸盐、丙烯酰胺基丙磺酸、四甲氧基原硅酸盐、甲基三甲氧基原硅酸盐、四烷氧基原硅酸盐、三烷氧基原硅酸盐、乙二醇、丙二醇、丙三醇、多糖、藻朊酸盐、葡聚糖、环糊精、纤维素、改性纤维素、氧化纤维素、脱乙酰壳多糖、壳多糖、瓜尔胶、角叉菜胶、透明质酸、菊淀粉、淀粉、变性淀粉、琼脂糖、甲基纤维素、植物胶、hylaronans、水凝胶、明胶、粘多糖、羧甲基纤维素、羟乙基纤维素、羟丙基甲基纤维素、果胶、低 - 甲氧基果胶、交联葡聚糖、淀粉 - 丙烯腈接枝共聚物、淀粉聚丙烯酸钠、甲基丙烯酸羟乙酯、丙烯酸羟乙酯、聚亚乙烯基、聚乙烯基乙醚、聚甲基丙烯酸甲酯、聚苯乙烯、聚氨酯、聚烷羧酸酯、聚乳酸、聚(3- 羟基丁酸)、磺化水凝胶、AMPS(2- 丙烯酰胺基 -2- 甲基 -1- 丙磺酸)，、SEM(甲基丙烯酸乙磺酸酯)、SPM(甲基丙烯酸丙磺酸酯)、SPA(丙烯酸丙磺酸酯)、N,N- 二甲基 -N- 甲基丙烯酰氧乙基 -N-(3- 磺丙基) 铵甜菜碱、甲基丙烯酸酰胺丙基 - 二甲基铵磺基甜菜碱、SPI{ 衣康酸 - 二 (1- 丙基磺酸 -3) 酯二钾盐}、衣康酸、AMBC(3- 丙烯酰胺 -3- 甲基丁酸)、β - 羧乙基丙烯酸酯（丙烯酸二聚体），及巴来酸酐 - 甲基乙烯醚聚合物，及其衍生物、盐、酸，以及它们的组合。

[0114] 增稠剂还包括聚（环氧乙烷）聚合物（如陶氏化学的 POLYOX)、线型 PVP 和交联 PVP、PEG/PPG 共聚物（如巴斯夫 Pluracare L1220)、环氧乙烷 (EO)- 环氧丙烷 (PO) 嵌段共聚物（如巴斯夫公司以商标名 Pluronic 出售的聚合物)、酯胶、虫胶、压敏硅酮胶（如道康宁公司的 BioPSA)，或它们的混合物。在一些实施例中，共聚物包括 (PVM/MA)。在一个实施例中，共聚物包括聚（甲基乙烯醚 / 马来酸酐）。在一些实施例中，共聚物包括聚（甲基乙

烯醚/马来酸)。在一些实施例中,共聚物包括聚(甲基乙烯醚/马来酸)半酯。在一些实施例中,共聚物包括聚(甲基乙烯醚/马来酸)混合盐。

[0115] 增稠剂还可包括卡波姆,卡波姆是丙烯酸与烯丙基蔗糖或季戊四醇的烯丙基醚交联的合成高分子量聚合物,分子量是大约 $3x\ 10^6$。胶凝机理取决于羧酸单元的形成可溶盐的中和作用。聚合物是亲水的,中和时形成光洁透明的凝胶。卡波姆可以是分散在水中而形成低粘度酸性胶态悬浮液的白色细粉末(1%分散液的 pH 大约是 3)。这些悬浮液采用碱(例如,氢氧化钠、氢氧化钾或氢氧化铵)、低分子量的胺和烷醇胺来中和,形成清澈透明的凝胶。

[0116] 在本发明的一个实施例中,卡波姆是Carbopol®。此类聚合物可从 B.F.Goodrich 或 Lubrizol 获得,商品名称是Carbopol® 71G NF、420、430、475、488、493、910、934、934P、940、971PNF、974P NF、980NF、981NF 等。正如 Brock(Pharmacotherapy,14:430-7(1994)) 和 Durrani(Pharmaceutical Res.(Supp.)8:S-135(1991)) 所述,Carbopol 是多用途的控释聚合物,属于与聚烯基聚醚交联的合成高分子量非线性丙烯酸聚合物卡波姆系列。在一些实施例中,卡波姆是Carbopol® 974P NF、980NF、5984EP、ETD2020NF、Ultrez 10NF、934NF、934P NF 或 940NF。在某些实施例中,卡波姆是Carbopol® 980NF、ETD 2020NF、Ultrez 10NF、Ultrez 21 或 1382 聚合物、1342NF、940NF。

[0117] 在一些实施例中,增稠剂或载体介质包括明胶。例如,在粘性生物光子材料中,粘性基质包括至少大约 5%、大约 5 至大约 25wt%、或大约 10 至大约 20wt%明胶。或者,重量百分含量更低的明胶可与化学交联剂或任何其它交联手段一起使用。

[0118] 在一些实施例中,增稠剂或载体介质可以包括透明质酸钠,其含量是大约 2%至大约 14%。

[0119] 本发明所述生物光子材料可以溶于水。或者,本发明中的生物光子材料任选包括不溶于水的基质或脂溶基质。“不溶于水”指的是基质在水中不溶解或在水中不容易分解。在一些实施例中,不溶于水的基质是将处理组合物传输给皮肤或靶向组织的工具或媒介。可作为不溶水基质使用的材料的范围非常广泛。下述非限制性特点可能比较理想:(i) 使用时足够的湿强度,(ii) 足够的柔软度,(iii) 足够的厚度,(iv) 适当的尺寸,(v) 透气性,及 (vi) 亲水性。

[0120] 满足上述标准的合适的不溶于水的基质的非限制性实例包括无纺布基质、织造布基质、水刺缠结基质、空气缠结基质、天然海绵、合成海绵、聚合物网状物等。优选的实施例采用无纺布基质,因为它们经济、材料品种多、容易得到。“无纺布”指的是其层由被制成片、毡、垫层的形式的纤维(而不是由被织造成布料的纤维)所组成。

[0121] 在本发明的一个实施例中,增稠剂或粘性基质可以包括硅胶膜。在此实施例中,一种或多种生色团可以直接包括在硅胶膜内,或者,如果它们是溶于水的,则其作为水相包括在膜的内含物内。例如,水相可以以硅胶中的微乳液的形式出现。水相可以是液体或半固体的。水相可以进一步包括稳定剂,用于稳定乳液,如明胶或 CMC。水相可以包括不超过 40wt%的硅氧烷聚合物相。

[0122] 杀菌剂

[0123] 杀菌剂杀灭微生物或抑制它们的生长或累积,任选包括在本发明的生物光子材料

中。示例性杀菌剂（或抗菌剂）在美国专利申请公开 20040009227 和 20110081530 中引用。本发明方法中使用的合适的杀菌剂包括但不限于过氧化氢、过氧化脲、过氧化苯甲酰、酚类和氯化酚类化合物、间苯二酚及其衍生物、双酚化合物、苯甲酸酯（对羟基苯甲酸酯）、卤代碳酰苯胺、聚合物类杀菌剂、噻唑啉、三氯甲基硫代酰亚胺、天然杀菌剂（亦称为“天然精油”）、金属盐和广谱抗生素。

[0124] 过氧化氢（H_2O_2）是一种强大的氧化剂，分解为水和氧，不会形成任何持久性的有毒残余化合物。生物光子材料中可以使用的过氧化氢的合适的浓度范围是大约 0.1％至大约 3％、大约 0.1 至 1.5％、大约 0.1％至大约 1％、大约 1％，小于大约 1％。

[0125] 过氧化脲（亦称为尿素过氧化物、脲过氧化氢、过碳酰胺）可溶于水，并包含大约 35％过氧化氢。生物光子材料中可以使用的过氧化脲的合适的浓度范围是小于大约 0.25％，或小于大约 0.3％，0.001 至 0.25％，或大约 0.3％至大约 5％。过氧化脲以缓－释方式分解为脲和过氧化氢，该过程可通过加热或光化学反应加速。

[0126] 过氧化苯甲酰由两个与过氧化基团连接的苯甲酰基组成（苯甲酸中的羧酸 H 被脱除）。人们发现，在用于痤疮的治疗中，过氧化苯甲酰的浓度是 2.5％至 10％。释放的过氧化基团在灭菌方面非常有效。过氧化苯甲酰还可以促进皮肤更新和毛孔清除，进一步减少细菌数量和减少痤疮。过氧化苯甲酰与皮肤接触时分解为苯甲酸和氧，这两者都没毒。本发明中的生物光子材料中可以使用的合适的过氧化苯甲酰的浓度是大约 2.5％至大约 5％。

[0127] 根据一些实施例，本发明的生物光子材料可以任选包括一种或多种其它组分，如富氧化合物，作为氧自由基的来源。过氧化物是含有过氧基（R-O-O-R）的氧化剂，具有链状结构，包含两个氧原子，每个氧原子与另一个氧原子和基团或某种元素连接。当本发明包含氧化剂的生物光子材料被光照射时，生色团被激发到更高的能态。当生色团的电子返回到更低的能态时，它们放出能级更低的光子，从而发射出波长更长的光（斯托克斯频移）。在合适的环境中，某些能量被转移给氧或反应性过氧化氢，导致形成氧自由基，如单线态氧。人们认为，生物光子材料活化产生的单线态氧及其它反应性氧是以本能方式操作的。也就是说，通过刺激和调节靶向组织细胞中的应激反应路径，在较少暴露于通常有毒的刺激（如反应性氧）的情况下可以实现有益的健康效果。对外源产生的自由基（反应性氧）的内源性响应得到调节，使其对抗外源性自由基的防御能力增加，从而诱导愈合和再生过程的加速。此外，氧化剂的活化也产生抗菌效果。细菌对暴露于自由基极为敏感，使本发明的生物光子材料实际上是一种杀菌组合物。

[0128] 本发明中可以使用的具体的酚类和氯代酚类杀菌剂包括但不限于：苯酚；2-甲基苯酚；3-甲基苯酚；4-甲基苯酚；4-乙基苯酚；2,4-二甲基苯酚；2,5-二甲基苯酚；3,4-二甲基苯酚；2,6-二甲基苯酚；4-正－丙基苯酚；4-正－丁基苯酚；4-正－戊基苯酚；4-叔戊基苯酚；4-正－己基苯酚；4-正－正庚基苯酚；单－和多－烷基和芳基卤代酚；对－氯苯基；甲基对－氯酚；乙基对－氯酚；正－丙基对－氯酚；正－丁基对－氯酚；正戊基－对－氯酚；仲－戊基对－氯酚；正－己基对－氯酚；环己基对－氯酚；正－庚基对－氯酚；正－辛基对－氯酚；邻－氯酚；甲基邻－氯酚；乙基邻－氯酚；正－丙基邻－氯酚；正－丁基邻－氯酚；正－戊基邻－氯酚；叔－戊基邻－氯酚；正－己基邻－氯酚；正－庚基邻－氯酚；邻－苯甲基对－氯酚；邻－苯甲基－间－甲基对－氯酚；邻－苯甲基－m,m-二甲基对－氯酚；邻－苯基乙基对－氯酚；邻－苯基乙基－间－甲基对－氯酚；3-甲基对－氯酚；3,5-二甲基对－氯

酚；6- 乙基 -3- 甲基对 - 氯酚、6- 正 - 丙基 -3- 甲基对 - 氯酚；6- 异 - 丙基 -3- 甲基对 - 氯酚；2- 乙基 -3,5- 二甲基对 - 氯酚；6- 仲 - 丁基 -3- 甲基对 - 氯酚；2- 异 - 丙基 -3,5- 二甲基对 - 氯酚；6- 二乙基甲基 -3- 甲基对 - 氯酚；6- 异 - 丙基 -2- 乙基 -3- 甲基对 - 氯酚；2- 仲 - 戊基 -3,5- 二甲基对 - 氯酚；2- 二乙基甲基 -3,5- 二甲基对 - 氯酚；6- 仲 - 辛基 -3- 甲基对 - 氯酚；对 - 氯 - 间 - 甲酚对 - 溴苯酚；甲基对 - 溴苯酚；乙基对 - 溴苯酚；正 - 丙基对 - 溴苯酚；正 - 丁基对 - 溴苯酚；正 - 戊基对 - 溴苯酚；仲 - 戊基对 - 溴苯酚；正 - 己基对 - 溴苯酚；环己基对 - 溴苯酚；邻 - 溴苯酚；叔 - 戊基邻 - 溴苯酚；正 - 己基邻 - 溴苯酚；正 - 丙基 -m,m- 二甲基邻 - 溴苯酚；2- 苯基苯酚；4- 氯 -2- 甲基苯酚；4- 氯 -3- 甲基苯酚；4- 氯 -3,5- 二甲基苯酚；2,4- 二氯 -3,5- 二甲基苯酚；3,4,5,6- 四溴 -2- 甲基苯酚；5- 甲基 -2- 戊基苯酚；4- 异丙基 -3- 甲基苯酚；对 - 氯 - 间二甲苯酚 (PCMX)；氯百里酚；苯氧乙醇；苯氧异丙醇；及 5- 氯 -2- 羟基二苯甲烷。

[0129] 间苯二酚及其衍生物也可用作杀菌剂。具体的间苯二酚衍生物包括但不限于：甲基间苯二酚；乙基间苯二酚；正 - 丙基间苯二酚；正 - 丁基间苯二酚；正 - 戊基间苯二酚；正 - 己基间苯二酚；正 - 庚基间苯二酚；正 - 辛基间苯二酚；正 - 壬基间苯二酚；苯基间苯二酚；苯甲基间苯二酚；苯乙基间苯二酚；苯丙基间苯二酚；对 - 氯苯甲基间苯二酚；5- 氯 -2,4- 二羟基二苯甲烷；4’- 氯 -2,4- 二羟基二苯甲烷；5- 溴 -2,4- 二羟基二苯甲烷；及 4’- 溴 -2,4- 二羟基二苯甲烷。

[0130] 本发明中可以使用的具体的双酚抗菌剂包括但不限于：2,2’- 亚甲基双 -(4- 氯苯酚）；2,4,4’- 三氯 -2’- 羟基 - 二苯醚，Ciba Geigy（地址：美国新泽西州 Florham Park）以商品名 Triclosan® 销售的产品；2,2’- 亚甲基双 -(3,4,6- 三氯苯酚）；2,2’- 亚甲基双 -(4- 氯 -6- 溴苯酚）；双 -(2- 羟基 -3,5- 二氯对 - 己基）硫化物；及双 -(2- 羟基 -5- 氯苯甲基）硫化物。

[0131] 本发明中可以使用的具体的苯甲酸酯（对羟基苯甲酸酯）包括但不限于：对羟基苯甲酸甲酯；对羟基苯甲酸丙酯；对羟基苯甲酸丁酯；对羟基苯甲酸乙酯；对羟基苯甲酸异丙酯；对羟基苯甲酸异丁酯；对羟基苯甲酸苄酯；对羟基苯甲酸甲酯钠；及对羟基苯甲酸丙酯钠。

[0132] 本发明中可以使用的具体的卤代碳酰苯胺包括但不限于：3,4,4’- 三氯碳酰苯胺，如 3-(4- 氯苯基）-1-(3,4- 二氯苯基）脲，Ciba-Geigy（地址：美国新泽西州 Florham Park）以商品名 Triclocarban® 销售的产品；3- 三氟甲基 -4,4’- 二氯碳酰苯胺；及 3,3’,4- 三氯碳酰苯胺。

[0133] 本发明中可以使用的具体的聚合物抗菌剂包括但不限于：聚六亚甲基双胍盐酸盐；及聚（亚胺基酰亚胺羰基亚胺基酰亚胺羰基亚胺基六亚甲基盐酸盐），以商品名 Vantocil® IB 销售。

[0134] 本发明中可以使用的具体的噻唑啉包括但不限于：以商品名 Micro-Check® 销售的产品；及 2- 正 - 辛基 -4- 异噻唑啉 -3- 酮，以商品名 Vinyzene® IT-3000DIDP 销售。

[0135] 本发明中可以使用的具体的三氯甲基硫代酰亚胺包括但不限于：N-（三氯甲基硫代）邻苯二甲酰亚胺，以商品名 Fungitrol® 销售；及 N- 三氯甲基硫代 -4- 环己烯 -1,2- 二

甲酰亚胺，以商品名Vancide®销售。

[0136] 本发明中可以使用的具体的天然抗菌剂包括但不限于下述物质的油：大茴香；柠檬；柑桔；迷迭香；鹿蹄草；百里香；熏衣草；丁香；酒花；茶树；枫茅；小麦；大麦；芸香草；雪松叶；杉木；肉桂；旋复花草（fleagrass）；老鹳草；檀香；紫罗兰；越橘；桉树；马鞭草；薄荷；安息香胶；罗勒；茴香；枞树；凤仙花；薄荷醇；牛至（ocmea origanuin）；黄连碱；角叉菜（carradensis）；小檗科（Berberidaceac daceae）；拉坦尼根（Ratanhiae longa）；及姜黄。归入天然抗菌剂一类的还可包括人们发现的植物油中能够提供抗菌好处的关键化学成分。这些化学物质包括但不限于：茴香脑；儿茶酚；茨烯；百里酚；丁香酚；桉叶醇；阿魏酸；法尼醇；扁柏酚；草酚酮；柠檬烃；薄荷醇；水杨酸甲酯；香芹酚；松油醇；马鞭草烯酮；小檗碱；拉坦尼根（ratanhiae）精华；丁香烯氧化物；香茅酸；姜黄；橙花叔醇；及香叶醇。

[0137] 本发明中可以使用的具体的金属盐包括但不限于元素周期表3a-5a、3b-7b和8族金属的盐。金属盐的具体实例包括但不限于以下金属的盐：铝；锆；锌；银；金；铜；镧；锡；汞；铋；硒；锶；钪；钇；铈；镨；钕；钜；钐；铕；钆；铽；镝；钬；铒；铥；镱；镏；及它们的混合物。金属离子类抗菌剂的一个实例是HealthShield Technology（地址：美国马萨诸塞州Wakefield）生产、以商品名HealthShield®销售的一种抗菌剂。

[0138] 本发明可以使用的具体的广谱抗菌剂包括但不限于本发明其它抗菌剂类别中引用的那些抗菌剂。

[0139] 本发明方法中可以使用的其它抗菌剂包括但不限于：吡硫翁，特别是吡硫翁-包括锌络合物，如以商品名Octopirox®销售的产品；二甲基羟甲基乙内酰脲，以商品名Glydant®销售的产品；甲基氯异噻唑啉酮/甲基异噻唑啉酮，以商品名Kathon CG®销售的产品；亚硫酸钠；亚硫酸氢钠；咪唑烷基脲，以商品名Germall 115®销售的产品；二唑烷基脲，以商品名Germall 11®销售的产品；苯甲醇v2-溴-2-硝基丙烷-1,3-二醇，以商品名Bronopol®销售的产品；福尔马林或甲醛；碘代丙烯基丁氨基甲酸酯，以商品名Polyphase P100®销售；氯乙酰氨；六亚甲基四胺；甲基二溴腈戊二腈（1,2-二溴-2,4-二氰基丁烷），以商品名Tektamer®销售；戊二醛；5-溴-5-硝基-1,3-二恶烷，以商品名Bronidox®销售；苯乙醇；邻-苯基苯酚/钠邻-苯基苯酚钠羟甲基甘氨酸盐，以商品名Suttocide A®销售；聚甲氧基双环恶唑烷，以商品名Nuosept C®销售；二甲氧烷；硫柳汞；二氯苯甲醇；克菌丹；chlorphenenesin；双氯酚；氯丁醇；月桂酸甘油酯；卤代二苯醚；2,4,4'-三氯-2'-羟基-二苯醚，以商品名Triclosan®销售，并且可从Ciba-Geigy（地址：美国新泽西州Florham Park）获得；及2,2'-二羟基-5,5'-二溴-二苯醚。

[0140] 本发明方法中可以使用的其它抗菌剂包括美国专利Nos.3,141,321；4,402,959；4,430,381；4,533,435；4,625,026；4,736,467；4,855,139；5,069,907；5,091,102；5,639,464；5,853,883；5,854,147；5,894,042；和5,919,554，及美国专利申请公开Nos.20040009227和20110081530中公开的那些抗菌剂。

[0141] (4)生物光子材料的光学性质

[0142] 在一些实施例中，本发明的生物光子材料是基本上透明的或半透明的。例如，可以利用Perkin-Elmer Lambda 9500系列UV-可见分光光度计在波长250nm至800nm范围测量生物光子材料的透光率%。在一些实施例中，测定可见光范围的透光率并对数据进行平

均。在一些实施例中，在将生色团脱除的情况下测定生物光子材料的透光率。由于透光率取决于厚度，在将样品装到分光光度计中之前，采用卡规测量每个样品的厚度。可根据下式对透光率数据进行归一化

[0143] $$F_{T-corr}(\lambda, t_2) = [e^{-\sigma_t(\lambda)t_1}]^{\frac{t_2}{t_1}} = [F_{T-corr}(\lambda, t_1)]^{\frac{t_2}{t_1}},$$

[0144] 式中，t_1＝试样实际厚度，t_2＝透光率测定归一化的厚度。在本领域中，透光率测定通常归一化为 1cm。

[0145] 在一些实施例中，生物光子材料基本上是不透明的。在这些实施例中，生物光子材料可以包括采用可以传输光的材料制造的光传输结构，如纤维、颗粒、网。光传输结构可以是波导，如光纤。

[0146] 在一些实施例中，生物光子材料在可见光范围内的透光率是大于大约 20％、30％、40％、50％、60％、70％或 75％。在一些实施例中，生物光子材料在可见光范围内的透光率超过 40％、41％、42％、43％、44％或 45％。

[0147] (5) 生物光子材料的形式

[0148] 本发明中的生物光子材料可以是包含至少一个生色团的粘性膜或基质的形式。粘性膜或基质可以是粘性凝胶，或膏、腻子、半固体或固体。

[0149] 本发明的生物光子材料可以是能变形的。它们可以是弹性的或非弹性的（即挠性或刚性）。例如生物光子材料可以是可剥离的形式（“可剥离”），令其使用简单、迅速。在一些实施例中，剥离形式的撕裂强度与／或拉伸强度大于其粘合强度。这一点有助于材料的可操作性。本领域技术人员应该认识到的是，剥离生物光子材料的性质，如粘结性、柔韧性、弹性、拉伸强度、撕裂强度，可以采用本领域技术人员熟悉的方法测定与／或调节，例如，通过选择合适的增稠剂和调节其相对比例来实现。

[0150] 生物光子材料可以是预成型形状。在一些实施例中，预成型形状是（包括但不限于）膜、面罩、补片、敷料或绷带。在一些实施例中，针对个人用户，预成型形状可以通过修改尺寸进行定制。在一些实施例中，在预成型形状的周边设有孔，以方便修剪。在一些实施例中，预成型可以通过手动或通过机械手段（如 3-D 打印）来实现。若采用 3-D 打印，待处理区域尺寸可以成像，如伤口或面部，然后，对 3-D 打印机进行配置，构造或形成与成像处理区尺寸和形状匹配的粘性生物光子材料。

[0151] 本发明的生物光子材料可以配置为具有适用于所要求的受试者身体部位的形状与／或尺寸。例如，生物光子材料的形状和尺寸可以与接受生物光子处理的身体部位相对应。这种要求的皮肤部位可以选自（包括但但不限于）皮肤、头部、前额、头皮、鼻子、脸颊、嘴唇、耳朵、脸、颈、肩、腋窝、臂、肘、手、手指、腹部、胸、肚子、背、臀部、骶骨、生殖器、腿、膝、脚、脚趾、指甲、头发、任何骨性隆起，及它们的组合等。因此，本发明的生物光子材料的形状和尺寸可以适用于受试者身体任何部位的皮肤。例如，生物光子材料可以呈袜、帽、手套或连指手套的形状。在生物光子材料是弹性或刚性的实施例中，它可以被剥离下来并且在组织上没有任何残留。

[0152] 在一些实施例中，生物光子材料是可以预成型的弹性可剥离面罩形式。在其它实施例中，生物光子材料是也可以预成型的非弹性（刚性）面罩的形式。面罩有适用于一只或两只眼睛、鼻子和嘴巴的开孔。在另一个实施例中，开孔用遮盖物保护；鼻子、嘴唇或眼

睛的暴露的皮肤采用例如可可油来保护。在一些实施例中，预成型面罩是由几部分组成，例如，脸上部分和脸下部分。在一些实施例中，面部对光源的不均匀接近性通过下列方式进行补偿：例如调节面罩的厚度，或调节面罩不同部位的生色团的含量，或在离光最近的地方遮蔽皮肤。在一些实施例中，预成型形状只有一个尺码，它适合所有人使用。

[0153] 在一些方面，面罩（或补片）不是预成型的，例如，通过在皮肤或靶向组织上摊涂构成面罩（或补片）的组合物来施用，或通过将组合物喷、抹、拍或滚到靶向组织上来施用。然后，在施用到皮肤或组织上以后，通过（例如但不限于）干燥、光照射、改变温度或 pH，转化为可以剥离的形式。所述面罩（或补片）然后可以剥离下来而不在皮肤或组织上残留任何薄片，优选不进行擦除或清洗。

[0154] 在一些方面，生物光子材料具有形状记忆特性。例如，生物光子材料可包括形状记忆材料，例如光活化时其原形状被恢复的形状记忆聚合物。原形状可以是平坦状或凹面状，使膜 / 基质容易从组织上剥离下来。形状记忆材料可以作为一个与生物光子材料相连接，或与生物光子材料相集成的层而包括进来。

[0155] 在一些方面，生物光子材料构成复合材料的一部分，可以包括纤维、颗粒、非生物光子层，或组成部分相同或不同的多重生物光子层。

[0156] 在一些实施例中，生物光子材料可以包括几个波导，至少部分地延伸通过生物光子材料，或至少部分地包含在生物光子材料之内。波导可以与光源连接，从而从内部照射生物光子材料。生物光子材料可以进一步包括与波导连接的光源。波导可以是不仅从其两端，而且从其纤体传输光的光纤。例如，采用聚碳酸酯或聚甲基丙烯酸甲酯或任何其它合适材料制造的光纤。

[0157] 在不同的实施例中，生物光子材料包括一层织造或无纺布敷料或面罩。波导或光源可以包括在敷料或面罩织物内。例如，敷料或面罩织物可以是接收生物光子材料的包袋的形式，包括至少一个光发射表面。

[0158] 在一些方面，生物光子材料是滤波器。例如，生物光子材料可以制造为具有某种形状和尺寸，可以与一盏灯的光发射表面相连接或与其相间隔。在一个实施例中，灯可以是手持式灯，如手电筒或牙科医生固化灯。带生物光子滤波器的灯可用于以接触或非接触的方式处理患者的组织部位。在此实施例中，滤波器具有一个本体，本体有一个第一端，其尺寸和形状可以与光发射表面连接；另有一个第二端，其形状被做成适合用于处理组织。

[0159] 在一些方面，生物光子材料是波导。在一些实施例中，至少一个生色团被包括在具有良好的光传播性质和合适的机械性能的长固体基质中。波导可以是挠性的。波导可以是光纤的形状。这样的光纤可以与光源连接，及与被光源活化的粘性基质中的至少一个生色团相连接，从而将具有治疗效果的荧光传输到难以到达的地方，如内部腔体和牙周袋。聚甲基丙烯酸甲酯是作为生物光子波导使用的合适粘性基质的一个实例。这种光导另外还可包括一种防止光沿其长度消散的涂层。

[0160] 在其它方面，包括至少一个生色团和粘性基质的生物光子材料是颗粒形式。可以采用本领域熟悉的材料加工技术来形成任何形状或尺寸的颗粒。这些颗粒可以包含在半固体或液体制剂中。例如，所述生物光子颗粒可以在皮肤制剂中，如霜、乳液中使用，为皮肤提供治疗效果。在此案中，使用一种生物相容固体基质，该基质可用于包裹所有类型的生色团，甚至那些皮肤对其耐受性不那么好的生色团。

[0161] 本发明中的生物光子材料的厚度是大约 0.1mm 至大约 50mm，大约 0.5mm 至大约 20mm，或大约 1mm 至大约 10mm。应该认识到的是，生物光子材料的厚度将根据指定用途而变化。在一些实施例中，生物光子材料的厚度是大约 0.1-1mm。在一些实施例中，生物光子材料的厚度是大约 0.5-1.5mm、大约 1-2mm、大约 1.5-2.5mm、大约 2-3mm、大约 2.5-3.5mm、大约 3-4mm、大约 3.5-4.5mm、大约 4-5mm、大约 4.5-5.5mm、大约 5-6mm、大约 5.5-6.5mm、大约 6-7mm、大约 6.5-7.5mm、大约 7-8mm、大约 7.5-8.5mm、大约 8-9mm、大约 8.5-9.5、大约 9-10mm、大约 10-11mm、大约 11-12mm、大约 12-13mm、大约 13-14mm、大约 14-15mm、大约 15-16mm、大约 16-17mm、大约 17-18mm、大约 18-19mm、大约 19-20mm、大约 20-22mm、大约 22-24mm、大约 24-26mm、大约 26-28mm、大约 28-30mm、大约 30-35mm、大约 35-40mm、大约 40-45mm、大约 45-50mm。

[0162] 生物光子材料的拉伸强度将根据指定用途而变化。拉伸强度可以通过开展拉伸试验和记录力度和位移而测定。然后，这些可以转化为应力（利用截面面积）和应变；应力-应变曲线的最高点是“极限拉伸强度”。在一些实施例中，拉伸强度采用 500N 桌上型机械试验系统 (#5942R4910, Instron®)，5N 最大静态负载传感器 (#102608, Instron) 进行表征。可采用气动边作用夹固定样品 (#2712-019, Instron)。在一些实施例中，应用恒定的伸长率（例如、大约 2mm/min)，直到失败，根据应力对应变数据图来计算拉伸强度。在一些实施例中，拉伸强度可以采用美国材料试验学拉伸试验方法，如ASTM D638、ASTM D882和ASTM D412 中描述的方法或与这些方法相当的方法进行测定。

[0163] 在一些实施例中，生物光子材料的拉伸强度是大约 1-50kPa、1 至大约 1000kPa、1 至大约 500kPa、50kPa 至大约 600kPa。在一些实施例中，生物光子材料的拉伸强度是大约 75kPa 至大约 500kPa、大约 100kPa 至大约 200kPa，100-300kPa，400kPa、大约 150kPa 至大约 350kPa，或大约 200kPa 至大约 300kPa。

[0164] 在一些实施例中，拉伸强度是至少大约 50kPa，至少大约 75kPa，至少大约 100kPa，至少大约 150kPa，至少大约 200kPa，至少大约 250kPa，至少大约 300kPa，至少大约 350kPa，至少大约 400kPa，至少大约 450kPa，至少大约 500kPa，至少大约 550kPa 或至少大约 600kPa。

[0165] 在一些实施例中，生物光子材料的拉伸强度不超过大约 8MPa。

[0166] 生物光子材料的粘合强度将根据指定用途而变化。生物光子材料的撕裂强度可以采用 500N 桌上型机械试验系统 (#5942R4910, Instron®)，5N 最大静态负载传感器 (#102608, Instron) 进行测定。可采用气动边作用夹固定样品 (#2712-019, Instron)。样品可以采用恒定拉伸率（例如、大约 2mm/min) 进行测试，直到失败。根据本发明，撕裂强度可以计算为失败时的力度除以平均厚度 (N/mm)。

[0167] 在一些实施例中，生物光子材料的撕裂强度是大约 0.1N/mm 至大约 1N/mm。在一些实施例中，生物光子材料的撕裂强度是大约 0.20N/mm 至大约 0.40N/mm、大约 0.25N/mm 至大约 0.35N/mm、大约 0.25N/mm 至大约 0.45N/mm、大约 0.35N/mm 至大约 0.535N/mm、大约 0.45N/mm 至大约 0.65N/mm、大约 0.55N/mm 至大约 0.75N/mm、大约 0.65N/mm 至大约 0.85N/mm、大约 0.75N/mm 至大约 0.95N/mm。

[0168] 在一些实施例中，生物光子材料的撕裂强度是至少大约 0.10N/mm，至少大约 0.15N/mm，至少大约 0.20N/mm，至少大约 0.25N/mm，至少大约 0.30N/mm，至少大约 0.35N/

mm，至少大约 0.40N/mm，至少大约 0.45N/mm，至少大约 0.55N/mm 或至少大约 1N/mm。

[0169] 生物光子材料的粘合强度将根据指定用途而变化。粘合强度可以根据 ASTM D-3330-78，PSTC-101 来测定，它是对于按特定角度和以特定脱除速度从试板上清除生物光子材料所需的力度的测量。在一些实施例中，将预定尺寸的生物光子材料施用到干净的玻璃试板的水平表面上。采用坚硬的橡胶辊将试板压紧，消除所有不连续的地方和夹带的空气。然后，将生物光子材料试板的自由端对折，差不多接触到本身，让从玻璃板脱除生物光子的角度是 180 度。生物光子材料试板的自由端与粘附试验仪刻度表相连（如 Instron 拉伸试验仪或 Harvey 拉伸试验仪）。然后，将试板夹在拉伸试验机的夹子内，将试板按预定恒定速率从刻度表拉开。当生物光子材料被从玻璃表面剥离时，记录刻度读数，单位 kg。

[0170] 在一些实施例中，粘合强度可以通过考虑生物光子材料的静摩擦来进行测定。对于本发明中的粘性生物材料的一些实施例来说，粘合性质与其静摩擦力（即静态阻力）有关。在这些情况下，将样品放在一个试验表面，按大约 0° 的角度（基本上与表面平行）拉样品的一端，同时在样品上施加向下的已知力（如使用一个砝码），测定样品从表面滑落时的重量，这样就可测得粘合强度。法向力 F_n 是每个表面施加在与所述表面垂直（法向）的另一个表面上的力，计算方法为样品和砝码的总重量乘以重力常数 (g)(9.8m/s^2)。然后，将顶部有砝码的生物光子材料拉离天平，直到生物光子材料从表面滑落，重量被记录在刻度尺上。刻度尺上记录的重量与克服摩擦所需的力相当。然后，将刻度尺上记录的重量乘以 g，计算出摩擦力 F_f)。由于 $F_f \leq \mu F_n$（库仑摩擦定律），将 F_f/F_n 可以得到摩擦系数 μ。然后，μ 将材料重量乘以摩擦系数，可以计算出从表面剪切材料所需的应力（粘合强度）。

[0171] 在一些实施例中，生物光子材料的粘合强度小于其拉伸强度。在一些实施例中，生物光子材料的粘合强度小于其撕裂强度。

[0172] 在一些实施例中，生物光子材料的粘合强度是大约 0.01N/mm 至大约 0.60N/mm。在一些实施例中，粘合强度是大约 0.20N/mm 至大约 0.40N/mm，或大约 0.25N/mm 至大约 0.35N/mm。在一些实施例中，粘合强度小于大约 0.10N/mm，小于大约 0.15N/mm，小于大约 0.20N/mm，小于大约 0.25N/mm，小于大约 0.30N/mm，小于大约 0.35N/mm，小于大约 0.40N/mm，小于大约 0.45N/mm，小于大约 0.55N/mm 或小于大约 0.60N/mm。

[0173] (6) 使用方法

[0174] 本发明的生物光子材料具有美容与 / 或医学益处。它们可用于促进皮肤更新和皮肤调理，促进皮肤病治疗，如痤疮、湿疹或牛皮癣，促进组织修复，及促进伤口愈合，包括牙周袋。它们可用于治疗急性炎症。急性炎症本身呈现疼痛、发热、发红、肿胀和丧失功能。它包括虫咬等变态反应的那些症状，如蚊子、蜜蜂、黄蜂叮咬、毒常春藤刺伤、消融治疗术后等。

[0175] 因此，在某些实施例中，本发明提供一种治疗急性炎症的方法。

[0176] 在一些实施例中，本发明提供一种皮肤更新或改善皮肤状况、治疗皮肤病、预防或治疗疤痕，与 / 或加速伤口愈合与 / 或组织修复的方法，所述方法包括：将本发明的生物光子材料施用到需要治疗的皮肤或组织部位，用波长与生物光子材料中的生色团的吸收光谱重叠的光照射生物光子材料。

[0177] 在本发明方法中，可以使用任何光化光光源。任何类型的卤素灯、LED 或等离子弧灯或激光器都是合适的。合适的光化光光源的主要特点是其发射一个（或多个）波长适合

活化组合物中一个或多个光活化剂的光。在一个实施例中，使用氩激光器。在另一个实施例中，使用磷酸钛氧钾 (KTP) 激光器（如 GreenLight™ 激光器）。在另一个实施例中，光化光光源是 LED 灯，如光固化设备。在另一个实施例中，光化光光源是波长大约 200 至 800nm 的光源。在另一个实施例中，光化光光源是波长大约 400 至 600nm 的可见光光源。在另一个实施例中，光化光光源是波长大约 400 至 700nm 的可见光光源。在另一个实施例中，光化光的光源是蓝光。在另一个实施例中，光化光的光源是红光。在另一个实施例中，光化光的光源是绿光。此外，光化光光源应具有合适的功率密度。非准直光源 (LED、卤素灯或等离子灯）合适的功率密度是大约 0.1mW/cm^2至大约 200mW/cm^2。激光器光源合适的功率密度是大约 0.5mW/cm^2至大约 0.8mW/cm^2。

[0178] 在本发明方法的一些实施例中，照射到受试者皮肤表面的光的能量是大约 0.1mW/cm^2至大约 500mW/cm^2，或 0.1-300mW/cm^2，或 0.1-200mW/cm^2，其中施用的能量至少取决于待处理的状态、光的波长、皮肤与光源之间的距离及生物光子材料的厚度。在一些实施例中，受试者皮肤处的光是大约 1-40mW/cm^2，或 20-60mW/cm^2，或 40-80mW/cm^2，或 60-100mW/cm^2，或 80-120mW/cm^2，或 100-140mW/cm^2，或 30-180mW/cm^2，或 120-160mW/cm^2，或 140-180mW/cm^2，或 160-200mW/cm^2，或 110-240mW/cm^2，或 110-150mW/cm^2，或 190-240mW/cm^2。

[0179] 生物光子材料中生色团的活化在照射时几乎立即发生（飞秒或皮秒）。延长暴露时，对开发本发明中的生物光子材料的吸收、反射和重新发射的光的协同效应及其与待处理组织的相互作用来说，可能是有益的。在一个实施例中，光化光照射组织或皮肤或生物光子材料的时间是 1 分钟至 5 分钟。在另一个实施例中，光化光照射组织或皮肤或生物光子材料的时间是 1 分钟至 5 分钟。在其它一些实施例中，生物光子材料被照射 1 分钟至 3 分钟。在一些实施例中，光照射的时间是 1-30 秒、15-45 秒、30-60 秒、0.75-1.5 分钟、1-2 分钟、1.5-2.5 分钟、2-3 分钟、2.5-3.5 分钟、3-4 分钟、3.5-4.5 分钟、4-5 分钟、5-10 分钟、10-15 分钟、15-20 分钟或 20-30 分钟。处理时间可以是不超过大约 90 分钟、大约 80 分钟、大约 70 分钟、大约 60 分钟、大约 50 分钟、大约 40 分钟或大约 30 分钟。应该理解的是，可以通过调节传输给处理部位的能量密度的传输速率来调节处理时间，以保持剂量。例如，传输的积分能量是大约 4 至大约 60J/cm^2、大约 10 至大约 60J/cm^2、大约 10 至大约 50J/cm^2、大约 10 至大约 40J/cm^2、大约 10 至大约 30J/cm^2、大约 20 至大约 40J/cm^2、大约 15J/cm^2至 25J/cm^2，或大约 10 至大约 20J/cm^2。

[0180] 在一些实施例中，生物光子材料可以按某一间隔重新照射。在另一个实施例中，光化光的光源是在处理部位上方连续移动适当的照射时间。在另一个实施例中，照射生物光子组合物，直到生物光子组合物至少部分地发生光漂白或完全光漂白。

[0181] 在某些实施例中，粘性基质中的生色团可以通过包括日光和顶部照明的环境光进行光激发。在一些实施例中，生色团可以通过电磁谱可见范围内的光光活化。这种光可以由任何光源发射，例如日光、灯泡、LED 设备、电子显示器，例如电视、计算机、电话、移动装置、移动装置上的电筒。在本发明方法中，可以使用任何光源。例如，可以结合使用环境光和直射光或人工直射光。环境光包括顶部照明，例如 LED 灯泡、荧光灯等，及非直射日光。

[0182] 在本发明的方法中，在光照射后将生物光子材料从皮肤处清除。在一些实施例中，在光照射后从皮肤处将生物光子材料清除。在一些实施例中，生物光子材料在光照射后作为单件从皮肤处清除。在其它实施例中，生物光子材料被留在组织上较长的时间，在合适的

时间采用直射或环境光重新活化，从而处理状况。

[0183] 在本发明方法的一些实施例中，生物光子材料可按每周一次、两次、三次、四次、五次或六次，每天或以任何其它频次施加到组织上，如脸上。总的治疗时间可以是一周、两周、三周、四周、五周、六周、七周、八周、九周、十周、十一周、十二周或认为合适的任何其它时间长度。在一些实施例中，待处理的总组织可以分为独立的区域（面颊、前额），每个区域分别处理。例如，所述组合物可以局部施用到第一部分，并用光照射该部分，然后清除所述生物光子组合物。然后，将所述组合物施用到第二部分、对其进行照射和清除。最后，将所述组合物施用到第三部分，对其进行照射和清除。

[0184] 在一些实施例中，生物光子材料可在伤口闭合后使用，用于优化疤痕修复。在这种情况下，可以定期施用生物光子材料，例如，一周一次，或医生认为合适的间隔。

[0185] 在某些实施例中，生物光子材料可在痤疮治疗后使用，以保持治疗皮肤的状态。在这种情况下，可以定期施用生物光子材料，例如，一周一次，或医生认为合适的间隔。

[0186] 在某些实施例中，生物光子材料可在烧蚀性皮肤再生治疗后使用，以保持治疗皮肤的状态。在这种情况下，可以定期施用生物光子材料，例如，一周一次，或医生认为合适的间隔。

[0187] 在本发明所述方法中，在生物光子材料中可任选包括其它组分或其它组分可与生物光子材料一起使用。这种其它组分包括，但不限于，愈合因子、抗菌剂、富氧试剂、皱纹填充剂，如肉毒杆菌毒素，透明质酸和聚乳酸、真菌剂、抗菌剂、抗病毒剂与／或促进胶原蛋白合成的试剂。这些其它组分可在局部施用本发明的生物光子材料之前、同时与／或之后以局部方式施用到皮肤上。合适的愈合因子包含促进或增强施用部位组织愈合或更新过程的化合物。在本发明中的生物光子材料光活化期间，治疗部位处皮肤或粘膜对此种其它组分的分子的吸收增加。在一些实施例中，一段时间内，观察到治疗部位血液流动增加。加入愈合因子，因自由基级联的动态交互作用所引起的淋巴引流增加及可能的渗透平衡变化，都会得到改善或甚至被强化。愈合因子还可以调节生物光子组合物的生物光子产量，如光漂白时间和特性，或调节组合物中的某种组分的漂白。合适的愈合因子包括但不限于葡糖胺、尿囊素、藏红花、促进胶原蛋白合成的试剂、抗真菌剂、抗菌剂、抗病毒剂和伤口愈合因子，如生长因子。

[0188] (i) 皮肤更新 (skin rejuvenation)

[0189] 本发明的生物光子材料可用于促进皮肤更新或改善皮肤状态和外观。真皮是皮肤的第二层，含有皮肤的结构性元素结缔组织。真皮内有具有不同功能的各种类型的结缔组织。弹性纤维赋予皮肤弹性，胶原蛋白赋予皮肤强度。

[0190] 真皮和表皮之间的接合处是一个非常重要的结构。真皮－表皮接合处连结形成与手指类似的表皮嵴。表皮细胞从真皮内的血管接收其营养物质。表皮嵴增加表皮暴露于这些血管和所需营养物质的表面积。

[0191] 皮肤的老化伴随皮肤的显著生理学变化。新皮细胞的产生减缓，真皮－表皮接合处的表皮嵴变平。虽然弹性纤维的数量增加，但是，其结构和凝聚性下降。此外，胶原蛋白的数量和真皮的厚度随着皮肤老化而降低。

[0192] 胶原蛋白是皮肤细胞外基质的主要成分，提供结构性框架。在老化过程期间，胶原蛋白合成下降及胶原蛋白纤维不溶解，导致真皮变薄，丧失皮肤的生物力学性质。

[0193] 皮肤的生理学变化导致出现显著的老化症状，通常被称为时序老化、内在老化和光老化。皮肤变得更干燥、粗糙和脱屑增加，外表变得更暗淡无光，出现明显的细纹和皱纹。皮肤老化的其它症状包括但不限于：皮肤变薄和透明、底层脂肪流失（导致双颊凹陷和眼睛深陷，以及手部和颈部明显失去紧致度）、骨质疏松（由于骨质疏松，骨骼与皮肤分离，导致皮肤松驰）、皮肤干燥（可能发痒）、无法排汗充分冷却皮肤、面部长毛、雀斑、老年斑、蛛状静脉、皮肤粗糙和革质皮肤、拉开时会消失的细纹、皮肤松驰或长斑。

[0194] 真皮－表皮接合处是基底膜，将表皮中的角化细胞与位于表皮下面的细胞外基质分离。该基底膜由两层组成：与角化细胞接触的基底层及与细胞外基质接触的下层网状层。基底层富含 IV 型胶原蛋白和层粘连蛋白，这些分子在为细胞连接而提供结构性网络和生物粘合特征方面起到作用。

[0195] 层粘连蛋白是糖蛋白，仅存在于基底膜内。它由三种多肽链（α、β 和 γ）组成，以不对称交叉形状布置，通过二硫键保持在一起。这三种链以不同的亚型存在，导致层粘连蛋白有十二种不同的同分异构体，包括层粘连蛋白 -1 和层粘连蛋白 -5。

[0196] 真皮通过 VII 型胶原蛋白纤维被锚定在基底膜角化细胞的半桥粒处，半桥粒是位于角化细胞上的特异性接合点，由 α－整联蛋白和其它蛋白组成。层粘连蛋白，特别是层粘连蛋白 -5，在基底角化细胞中的半桥粒跨膜蛋白及 VII 型胶原蛋白之间构成实际的锚定点。

[0197] 已经证明，在老化皮肤中，层粘连蛋白 -5 合成和 VII 型胶原蛋白表达减少。这导致真皮和表皮之间的接触丧失，导致皮肤失去弹性和松驰。

[0198] 最近，通常称为表情纹的另一种类型的皱纹得到了普遍认可。这些皱纹要求弹性丧失，尤其是在真皮中，因此，当产生面部表情的面部肌肉施加应力到皮肤上时，皮肤不再能够恢复其原来状态，导致表情纹。

[0199] 本发明的生物光子材料和方法促进皮肤更新。在一些实施例中，本发明的生物光子材料和方法改善皮肤状态，如皮肤亮度，缩小毛孔，减少斑点，使肤色均匀，减少皮肤干燥和使皮肤紧致。在一些实施例中，本发明的生物光子材料和方法促进胶原蛋白合成。在一些实施例中，本发明的生物光子材料和方法可以减少、消除、延缓或甚至逆转一种或多种皮肤老化的症状，包括但不限于出现细纹或皱纹、皮肤变薄和透明、底层脂肪流失（导致双颊凹陷和眼睛深陷，以及手部和颈部明显失去紧致度）、骨质疏松（由于骨质疏松，骨骼与皮肤分离，导致皮肤松驰）、皮肤干燥（可能发痒）、无法排汗充分冷却皮肤、面部长毛、雀斑、老年斑、蛛状静脉、皮肤粗糙和革质皮肤、拉开时会消失的细纹、皮肤松驰或长斑。在一些实施例中，本发明的生物光子材料和方法可以诱导毛孔缩小、增强皮肤各部分的紧致性，与 / 或增强皮肤半透明性。

[0200] 在一些实施例中，生物光子材料可与胶原蛋白促进剂一起使用。促进胶原蛋白合成的试剂（即原胶原蛋白合成试剂）包括氨基酸、缩氨酸、蛋白质、类脂；小化学分子、天然产品及天然产品提取物。

[0201] 例如，人们发现，摄入维生素 C、铁和胶原蛋白可有效提高皮肤或骨骼中胶原蛋白的数量。参见，例如，美国专利申请公开 20090069217。维生素 C 的实例包括抗坏血酸的衍生物，如 L- 抗坏血酸或 L- 抗坏血酸钠，利用乳化剂等涂敷抗坏血酸得到的抗坏血酸制剂，及含任意比例的两种或多种维生素 C 的混合物。此外，也可以使用含维生素 C 的天然产品，

如金虎尾和柠檬。铁制剂的实例包括：无机铁，如硫酸亚铁、柠檬酸亚铁钠，或焦磷酸铁；有机铁，如血红素铁、铁蛋白铁，或乳铁蛋白铁；含任意比例的两种或多种这些铁制剂的混合物。此外，还可以使用含铁天然产品，如菠菜或动物肝脏。此外，胶原蛋白的实例包括：用酸或碱处理哺乳动物（如牛或猪）的骨头、皮肤获得的提取物；用蛋白酶，如胃蛋白酶、胰蛋白酶或糜蛋白酶水解获得的缩氨酸；及含任意比例的两种或多种这些胶原的混合物。还可以使用从植物提取的胶原蛋白。

[0202] 例如，在美国专利7598291、7722904、6203805、5529769等及美国专利申请公开20060247313、20080108681、20110130459、20090325885、20110086060等中对其它原胶原蛋白合成剂进行了描述。

[0203] (ii)皮肤病

[0204] 本发明的生物光子材料和方法可用于治疗皮肤病，包括但不限于红斑、毛细管扩张、光化毛细血管扩张、牛皮癣、皮肤癌、天疱疮、晒斑、皮炎、湿疹、疹子、脓疱病、单纯慢性苔癣、肥大性酒渣鼻、口周皮炎、须部假性毛囊炎、药疹、多形红斑、结节性红斑、环形肉芽肿、光化性角化病、紫癜、斑秃、口疮性口炎、药物皮炎、干性皮肤、皲裂、干燥病、寻常性鱼鳞癣、真菌感染、单纯疱疹、擦烂、瘢瘤、角化症、粟丘疹、触染性软疣、玫瑰糠疹、瘙痒症、荨麻疹和血管瘤和各种变形。皮炎包括接触性皮炎、特异反应性皮炎、脂溢性皮炎、钱币状皮炎、全身剥落性皮炎及静态性皮炎。皮肤癌包括黑色素瘤、基底细胞癌和鳞状细胞癌。

[0205] (iii)痤疮和痤疮疤痕

[0206] 本发明的生物光子材料和方法还可用于治疗痤疮。本发明所述“痤疮”指的是皮肤腺或毛囊炎症引起的皮肤病。本发明的生物光子材料和方法可用于在早期萌前阶段或痤疮引起的损伤可见的后期阶段治疗痤疮。本发明的生物光子组合物和方法实施例可用于治疗轻度、中度和重度痤疮。痤疮早期萌前阶段通常开始于皮脂分泌过度，或由位于毛皮脂内的皮脂腺所分泌的皮肤油。皮脂通过毛囊管到达皮肤表面。管道中和皮肤上存在过多皮脂会阻塞或淤塞毛囊管的正常的皮脂流动，从而使皮脂增厚和固化，形成称为粉刺的固体塞。在痤疮形成的正常顺序中，刺激毛囊孔形成过度角质化，从而完全堵住管道。通常的结果是丘疹、脓疱或囊肿，通常被细菌污染，导致继发性感染。痤疮的特征尤其在于存在粉刺、炎性丘疹或囊肿。痤疮的外观可能是轻微的皮肤刺激性至坑点，甚至可能发展成影响容貌的疤。因此，本发明的光子材料和方法可用于治疗一种或多种与痤疮有关的皮肤刺激、坑点、疤痕发展、粉刺、炎性丘疹、囊肿、角质化及皮脂增厚和硬化。

[0207] 例如，痤疮的一些类型，包括寻常痤疮、囊性痤疮、萎缩性痤疮、溴痤疮、氯痤疮、聚合性痤疮、美容性痤疮、去污剂痤疮、流行痤疮、表皮痤疮、夏季痤疮、暴发性痤疮、卤素痤疮、硬结性痤疮、碘痤疮、瘢痕瘤性痤疮、机械性痤疮、丘疹性痤疮、发蜡痤疮、月经前座疮、脓疱性痤疮、坏血病性痤疮、结核性痤疮、荨麻疹性痤疮、痘样痤疮、中毒性痤疮、丙酸痤疮、人工痤疮、革兰氏阴性痤疮、类固醇痤疮及结节囊性痤疮。

[0208] 某些皮肤病具有不同的症状，包括发红、变红、灼痛、脱屑、疙瘩、丘疹、脓疱、粉刺、斑点、节结、囊、水泡、毛细管扩张、蛛状静脉、疮、表面刺激或疼痛、痒、炎症、红、紫或蓝斑或变色、痣与/或肿瘤。

[0209] 本发明的生物光子材料和方法可用于治疗各种类型的痤疮。例如，痤疮的一些类型，包括寻常痤疮、囊性痤疮、萎缩性痤疮、溴痤疮、氯痤疮、聚合性痤疮、美容性痤疮、去污

剂痤疮、流行痤疮、表皮痤疮、夏季痤疮、暴发性痤疮、卤素痤疮、硬结性痤疮、碘痤疮、瘢痕瘤性痤疮、机械性痤疮、丘疹性痤疮、发蜡痤疮、月经前座疮、脓疱性痤疮、坏血病性痤疮、结核性痤疮、荨麻疹性痤疮、痘样痤疮、中毒性痤疮、丙酸痤疮、人工痤疮、革兰氏阴性痤疮、类固醇痤疮及结节囊性痤疮。

[0210] 在一些实施例中，本发明的生物光子材料与全身或局部抗生素治疗一起使用。例如，用于治疗痤疮的抗生素包括四环素、红霉素、米诺环素、强力霉素，它们也可与本发明的组合物和方法一起使用。使用生物光子材料可以缩短抗生素治疗所需的时间或减少剂量。

[0211] (iv) 伤口愈合

[0212] 本发明中的生物光子材料和方法可用于治疗伤口，促进伤口愈合，促进组织修复与/或消除或减少对美容的需要，包括改善运动机能（如关节运动）。本发明的生物光子材料和方法可以治疗的伤口包括，例如，不同方式引发的皮肤和皮下组织的伤口（如卧床时间太长引起的压迫性溃疡、外伤引起的伤口、牙周炎等症状引起的伤口）及具有不同特点的伤口。在一些实施例中，本发明提供治疗，例如灼伤、切口、切除术、撕裂、磨损、刺伤或贯通伤口、手术伤口、挫伤、血肿、压伤、疮和溃疡与/或促进这些伤口的愈合的生物光子材料和方法。

[0213] 本发明的生物光子材料和方法可用于治疗慢性皮肤溃疡或伤口与/或促进这些伤口的愈合，这些伤口无法通过有序及时的系列事件实现持久结构性的、功能性的及美观的闭合。、绝大多数慢性伤口可以根据其病原学分为三类：压迫性溃疡、神经病变性（糖尿病足部）溃疡及血管性（静脉或动脉）溃疡。

[0214] 例如，本发明提供用于治疗糖尿病溃疡与/或促进糖尿病溃疡愈合的生物光子材料和方法。由于神经和血管并发症，糖尿病患者容易患足部溃疡和其它溃疡。周围神经病变会导致足部与/或腿部感觉改变或完全丧失。晚期神经病变的糖尿病患者完全丧失了辨别剧痛的能力。患神经病变的患者足部出现任何伤口或创伤时，他们可能数天或数周都完全没注意到。晚期神经病变患者丧失了感觉持续压力刺激的能力，结果，可能出现组织缺血和坏疽，导致，例如，足底溃疡。微血管疾病是糖尿病显著的并发症之一，也会导致溃疡。在一些实施例中，本发明提供了治疗慢性伤口的生物光子材料和方法，其中慢性伤口的特征在于因糖尿病神经病变与/或血管并发症而引起的糖尿病足部溃疡与/或溃疡。

[0215] 在其它实例中，本发明提供用于治疗压迫性溃疡与/或促进压迫性溃疡愈合的生物光子材料和方法。压迫性溃疡包括褥疮、褥疮性溃疡和坐骨结节溃疡，这些溃疡会给患者带来巨大的痛苦和不适。压迫性溃疡是由长期施加到皮肤上的压力引起的。因此，由于个人的重量或质量，压力可以施加到患者的皮肤上。当皮肤一个区域供血阻塞或中断两小时或三小时以上时，会形成压迫性溃疡。受影响的皮肤区域会变红、疼痛及坏死。如果不进行治疗，皮肤会露出来，受到感染。因此，压迫性溃疡是因长期卧床、坐轮椅与/或戴管型造成的压力下皮肤某一区域发生的皮肤溃疡。当一个人卧床不起、失去意识、无法感觉疼痛或不能动时，会发生压迫性溃疡。压迫性溃疡通常发生在身体的骨头突出部分，如臀部区（骶骨或髂嵴）或足跟。

[0216] 本发明的生物光子材料和方法可以治疗的其它类型的伤口包括美国专利申请公开 No. 20090220450 中披露的那些伤口，该专利通过引用而并入本发明中。

[0217] 伤口愈合过程有三个明显的阶段。首先，在炎症阶段，通常从伤口出现到两天至五

天，血小板聚集从而沉积肉牙，促进纤维蛋白的沉积及刺激生长因子的释放。白血球迁移到伤口部位，开始消解伤口处的碎片和将碎片运走。在此炎症阶段，单核细胞还转化为巨噬细胞，后者释放出生长因子，刺激血管的形成和成纤维细胞的产生。

[0218] 其次，在增生阶段，通常发生在两天至三周，肉牙组织形成，开始上皮形成和收缩。成纤维细胞是该阶段的关键细胞类型，它们通过增生和合成胶原蛋白来填充伤口，提供强大的基质供上皮细胞生长。当成纤维细胞产生胶原蛋白时，从附近血管延伸形成血管，导致形成肉牙组织。肉牙组织通常从伤口底部生长。上皮形成涉及上皮细胞从伤口表面迁移，从而封住伤口。上皮细胞被接触类似细胞的需求推动，并受到充当网格作用的纤维蛋白链网络的引导，这些细胞在网格上迁移。在伤口处出现称为肌成纤维细胞的收缩细胞，帮助伤口闭合。这些细胞显示出胶原蛋白合成和收缩性，并且在肉牙性伤口中比较常见。

[0219] 再次，重塑阶段，即伤口愈合的最后阶段，从三周到几年，伤疤中的胶原蛋白经历反复降解和重新合成。在此阶段，新形成的皮肤的拉伸强度提高。

[0220] 但是，当伤口愈合速度增加时，通常伤疤形成相应增加。结疤是大多数成年动物和人类组织愈合过程的结果。疤痕组织与其代替的组织不同，其功能质量通常更差。疤痕的类型包括但不限于萎缩性疤痕、增生性疤痕和瘢痕瘤(keloidal scar)，以及瘢痕挛缩。萎缩性疤痕呈扁平，其表面低于周围皮肤下，形成谷或洞。增生性疤痕是留在原损伤边界内的隆起疤痕，通常含有以异常方式布置的过多的胶原蛋白。瘢痕瘤(keloidal scar)是在原伤口边缘外扩散的隆起疤痕，以位点特异性方式侵入到正常皮肤附近，通常含有以异常方式布置的胶原蛋白螺旋。

[0221] 与此相反的是，正常皮肤由以网织篮式方式布置的胶原蛋白纤维，有助于真皮的强度和弹性。因此，为了使伤口愈合过程更顺利，需要一种方法，不仅刺激胶原蛋白的产生，而且还以减少疤痕形成的方式刺激胶原蛋白的产生。

[0222] 本发明的生物光子材料和方法通过促进基本上均匀的上皮形成、促进胶原蛋白合成、促进控制收缩与/或减少疤痕组织形成而促进伤口愈合。在一些实施例中，本发明的生物光子材料和方法可以通过促进基本上均匀的上皮形成而促进伤口愈合。在一些实施例中，本发明的生物光子材料和方法促进胶原蛋白合成。在一些实施例中，本发明的生物光子材料和方法促进控制性收缩。在一些实施例中，本发明的生物光子材料和方法，例如，通过减少疤痕组织的形成而促进伤口愈合。

[0223] 在本发明的方法中，本发明的生物光子材料还可与负压辅助闭锁装置和系统一起使用。

[0224] 在其它一些实施例中，所述生物光子材料的保留时间高达一周、两周或三周，并以不同的间隔采用包括环境光的光进行照射。在这种情况下，所述组合物在两次暴露于光的间隔期间可以用不透明材料盖起来或任其在光下暴露。

[0225] (6)试剂盒

[0226] 本发明还提供制备本发明中的生物光子材料的试剂盒与/或提供形成本发明中的生物光子材料所需的任何组分的试剂盒。

[0227] 在一些实施例中，试剂盒包括容器，容器内包含用于制备本发明中的生物光子材料的组分或组合物。在一些实施例中，试剂盒包括本发明的生物光子材料。制备本发明中的生物光子材料的不同组分可以放置在独立的容器内。例如，如果生物光子材料包括富氧

试剂，富氧试剂优选放在与生色团不同的容器内。容器的实例有双室注射器、配可移动分隔的双室容器、带小袋的袋子和多隔泡罩包装。另一个实例是其中一个组分放置在注射器中，可以直接注射到另一个组分的容器内。

[0228] 在其它实施例中，试剂盒包括用于增强本发明中的生物光子材料治疗效果的全身性药物。例如，试剂盒包括全身性或局部性抗生素，激素治疗药物（例如，用于治疗痤疮或伤口愈合），或负压装置。

[0229] 在一些实施例中，试剂盒包括含第一生色团的第一组分；含至少一种增稠剂的第二组分，其中增稠剂与第一组分混合时，将混合物施用到皮肤上时，或当采用光照射时，可以形成粘性基质。

[0230] 在其它实施例中，试剂盒包括施用生物光子材料各组分的手段。

[0231] 在一些方面，提供一个容器，包含一个容纳生物材料的室，一个与所述室连接、用于从容器放出生物光子材料的出口，其中生物光子材料在载体介质中包含至少一个生色团，在从密封室中放出后，例如，与皮肤接触或光照射时，可形成生物光子材料。容器可以是带压或不带压喷雾罐。

[0232] 在一些实施例中，试剂盒包括第一组分，它包含生物光子材料或非粘性形式的生物光子材料（“前体”）；以及第二组分，它包含敷料或遮罩。所述敷料或遮罩可以是多孔或半多孔结构，用于接收生物光子材料。敷料或遮罩可以包含机织或无纺纤维材料。生物光子材料或其前体可以，在生物光子材料在敷料或遮罩内呈粘性形式之前通过例如注射的方式来包括到敷料中。

[0233] 在试剂盒的一些实施例中，试剂盒可进一步包含光源，如波长适合活化生物光子材料中的生色团的便携式灯。便携式灯可以用电池或可以充电。

[0234] 试剂盒中可以包含关于如何使用本发明中的生物光子材料的书面说明书，或者书面说明书可以标示在包含本发明生物光子材料的容器上或与容器相关联的地方。说明书包括如何利用试剂中提供的增稠剂或基质前体形成粘性基质的资料。

[0235] 根据本发明的教导，识别相当的生物光子材料、方法和试剂盒是本领域技术人员熟悉的，除常规试验外不再需要进行其它实验。

[0236] 对于熟悉本领域的技术人员来说，阅读本发明后能够对本发明做出各种改变和改造。此处公开的特点可以以具有此处所述的一个或多个其它特点的任何组合和分组合（包括几个依赖性组合和分组合）实施。上面所述的各种特点，包括它们的任何部件，可以组合或集成到其它系统中。此外，某些特点可以省略或不实施。熟悉本领域的技术人员可以对这些实例进行改变、替换和更改，只要不背离本发明的范围即可。此处引用的所有参考文献通过引用均整体并入到本申请中，并构成本申请的一部分。

[0237] 根据下述实例，将更全面地了解本发明，这些实例仅作解释之用，无论如何都不应视为限制本发明。

[0238] 实例

[0239] 实例 1- 示例性粘性生物光子材料的制备

[0240] 按照本发明一个实施例制备了粘性生物光子材料并总结在表 1 中。

[0241] 表 1、本发明一个实施例粘性生物光子材料的组成

[0242]

组分	组成中的%含量 (wt/wt)
水	60-95
丙三醇	5-15
丙二醇	2-6
透明质酸钠	2-8
过氧过脲	1-5
硫酸盐葡萄糖胺	0.5-4
聚羧乙烯	0.1-2
第一生色团	0.001-0.01
第二生色团	0.001-0.01

[0243] 将水、曙红 Y、玫瑰红和硫酸盐葡萄糖胺混合制备 A 相。然后，向 A 相中加入 B 相（水、丙三醇、丙二醇、过氧化脲、聚羧乙烯），混合，直到得到略稠的液体。然后，向混合物中加入C相（透明质酸钠），混合，直到得到均匀粘稠的粘性凝胶。将这种均匀的粘性凝胶涂到平坦的表面上，用铝片盖好，干燥 24 小时。24 小时后，得到的膜很容易操作，可以施用到皮肤上，剥离后几乎没有或没有任何残留。干燥 24 小时后，材料总重量损失是 5-20％。膜可以储存在两层保鲜膜、石蜡之间等。在距离光源 5cm 的地方采用光（峰值波长 400-470nm，功率密度大约 30-150mW/cm^2）照射 5 分钟，薄膜发射荧光，荧光被光谱仪 SP-100 分光辐射谱仪 (SP-100,ORB Optronix) 捕获，以测量功率密度谱图 vs 波长，如图 3 所示。发射的荧光是电磁谱中的绿光、黄光和橙光部分。在照射 5 分钟后，发现生色团至少部分地发生光漂白。

[0244] 实例 2- 生物光子组合物的血管生成潜力

[0245] 采用含成纤维细胞和角化细胞的人体皮肤模型对生物光子组合物的血管生成潜力进行评价。组合物是包含荧光生色团、曙红 Y 和赤藓红的透明凝胶。简单地说，将生物光子组合物放在人体皮肤模型顶部，它们被孔径 20 微米的尼龙网隔开。然后，在距离光源 10cm 处用蓝光（“活化光”）照射组合物 5 分钟。活化光由 LED 灯发射的光组成，光的平均峰值波长是大约 400-470nm，功率密度是 30-150mW/cm^2。在距 LED 10cm 处，活化光在峰值波长处的功率是大约 2-3mW/cm^2/nm（大约 2.5mW/cm^2/nm），平均功率是大约 55-65mW/cm^2，5 分钟照射时间内的能量密度是大约 15-25J/cm^2（大约 16-20J/cm^2）。在采用活化光照射后，生物光子组合物发射荧光，荧光采用 SP-100 分光辐射谱仪 (SP-100,ORB Optronix) 测定，结果如图 4 所示。由于所述组合物允许活化光穿过，皮肤模型基本上同时被活化光和荧光照射。

[0246] 由于生物光子组合物与细胞的接触受限，成纤维细胞与角化细胞主要暴露于活化光和生物光子组合物发射的荧光。然后，向之前平板接种在 Matrigel™中的糖尿病患者的

人体主动脉内皮细胞上和有病的微脉管内皮细胞上涂覆来自经过处理的人体 3D 皮肤模型的条件培养液。24 小时后通过显微镜观察和监测内皮细胞管的形成情况。来自光照射处理 3D 皮肤模型的条件培养液诱导体外内皮管的形成，表明通过成纤维细胞和角化细胞的生长因子，光处理（蓝光和荧光）对血管形成存在间接效用。采用未处理皮肤样品的普通培养液及条件培养液作为对照，它们都没有诱导内皮管的形成。

[0247] 实例 3- 生物光子组合物的蛋白质分泌和基因表达谱

[0248] 采用受伤的和未受伤的 3D 人体皮肤模型 (EpiDermFT™, MatTek Corporation) 用于评价本发明组合物引发明显的蛋白质分泌和基因表达谱的潜力。生物光子组合物包括荧光生色团曙红 Y 和赤藓红。将组合物放在在不同条件下（生长因子、50％生长因子和没有生长因子）培养的受伤和未受伤 3D 人体皮肤模型的顶部。利用孔径 20 微米的尼龙网将皮肤模型和组合物分开。然后，用特性与实例 2 所述类似的蓝光（“活化光”）照射每个皮肤模型 - 组合物组合 2 分钟。荧光发射如图 4 所示。对照样由未采用光照射的 3D 皮肤模型组成。

[0249] 光照射 24 小时后测量基因表达谱和蛋白质分泌谱。通过抗体阵列 (RayBio Human Cytokine 抗体阵列）分析细胞因子的分泌，通过 PCR 阵列 (PAHS-013A, SABioscience) 分析基因表达，并通过 GAPDH 和 LDH 释放测定细胞毒性。结果（表 2 和表 3）表明，在受伤皮肤插入片段上、在非饥饿状态中，光处理能提高伤口愈合初期炎症阶段的蛋白质分泌和基因表达水平。令人感兴趣的是，在细胞水平上，光处理对未受伤皮肤模型的影响远低于其对受伤皮肤插入片段的影响，表明光处理具有细胞水平上的影响。似乎可以调节与发炎有关的介体。在光处理中未观察到细胞毒性。

[0250] 表 2 -

[0251] 在第 3 天时，经处理样品和未经处理对照样品之间的分泌比具有统计学显著差异的蛋白质的清单。双箭头表示分泌比超过 2 倍。

[0252]

	介质 1 X	**介质 0.5 X**	**介质 0 X**
增加		**ENA78 p=0.04 ↑↑** **Il-1R4/ST2 p=0.02 ↑↑** **MMP3 p=0.01 ↑↑** **MCP-2 p=0.04 ↑↑**	血管生成素 p=0.03↑ CXCL16 p=0.04 ↑
递减	BMP6 p=0.01 ↓ TNFα p=0.005 ↓	BMP6 p=0.02 ↓	

[0253] 表 3 -

[0254] 第一个 24 小时期间经处理样品和未经处理对照样品的表达比具有统计学显著差异的基因的清单。双箭头表示分泌比超过 2 倍。

[0255]

	介质 1 X	**介质 0.5 X**	**介质 0 X**
增加	CTGF p=0.02 ↑ ITGB3 p=0.03 ↑ MMP1 p=0.03 ↑ MMP3 p=0.01 ↑ THBS1 P=0.02 ↑	CTGF P=0.04 ↑ ITGB3 p=0.05 ↑ **MMP1 p=0.02 ↑↑** **MMP10 p=0.003 ↑↑** **MMP3 p=0.007 ↑↑** **MMP8 p=0.02 ↑↑** THBS1 p=0.03 ↑	**MMP3 p=0.007 ↑↑** LAMA1 p=0.03 ↑ ITGA2 p=0.03 ↑
递减	HAS1 p=0.009 ↓↓ NCAM1 p=0.05 ↓↓ VCAM1 p=0.03 ↓↓ COL7A1 p=0.04 ↓ CTNNA1 p=0.03 ↓	**NCAM1 p=0.02 ↓↓** VCAN p=0.02 ↓ LAMC1 p=0.002 ↓ COL6A1 p=0.007 ↓ MMP7 p=0.003 ↓	

[0256] 实例 4- 选择组合物中的生色团的浓度

[0257] 采用分光光度计和活化蓝光，对生色团浓度不同的生物光子材料的荧光光谱进行了研究。曙红 Y 和荧光素的示例性荧光光谱分别如图 5a 和 5b 所示。从图中发现，这些生色团发射的荧光随浓度增加而迅速增加，但是，当浓度进一步增加时，荧光增加速度减慢，达到一个平台。随着生色团含量的增加，更多的光被生色团吸收，因此，穿过组合物的活化光随生色团的含量的增加而下降。因此，根据本实例，可以根据处理组织要求的活化光和荧光素的比例和水平，选择本发明中的生物光子材料中生色团的浓度。还可以通过调节生物光子材料的厚度来控制所处理的组织的光，以及组合物的光学性质（如透明性）。

[0258] 实例 5- 曙红 Y 和荧光素的协同作用

[0259] 对凝胶（包含大约 12％过氧化脲）中 (i) 浓度大约 0.09mg/mL 的荧光素钠盐，(ii) 浓度大约 0.305mg/mL 的曙红 Y，及 (iii) 浓度大约 0.09mg/mL 的荧光素钠盐和浓度大约 0.305mg/mL 的曙红 Y 的混合物的光动力学性质进行了评价。采用 flexstation 384II 分光光度计，参数如下 :模式 :荧光，激发 :460nm，发射光谱 :465-750nm。吸收光谱和发射光谱分别示于图 6a 和 6b 中，图中表明，组合中生色团之间发生了能量转移。可以合理推断的是，本发明中的生物光子材料中也会发生这种能量转移。

[0260] 实例 6- 曙红 Y、荧光素和玫瑰红的协同作用

[0261] 对凝胶（含大约 12％过氧化脲）(A 组）中的 (i) 浓度大约 0.085mg/mL 的玫瑰红，(ii) 终浓度大约 0.44mg/mL 的荧光素钠盐，(ii) 浓度大约 0.305mg/mL 的曙红 Y，及 (iv)

(i)、(ii) 和 (iii) 的混合物的光动力学性质进行了评价。采用 flexstation 384II 分光光度计，参数如下：模式：荧光，激发：460nm，发射光谱：465-750nm。吸收光谱和发射光谱分别示于图 7a 和 7b 中，图中表明，生色团组合中生色团之间发生了能量转移。可以合理推断的是，本发明中的生物光子材料中也会发生这种能量转移。

[0262] 在下述生色团之间也出现了能量转移：曙红 Y 和玫瑰红；荧光桃红 B 和曙红 Y；荧光桃红 B、曙红 Y 和荧光素，以及其它组合。可以合理推断地是，本发明中的生物光子材料中也会发生这种能量转移。

[0263] 实例 7- 生物光子组合物的胶原蛋白形成潜力

[0264] 对包含位于载体基质 (1.8％卡波姆凝胶) 中的 0.01％曙红 Y 和 0.01％荧光素的生物光子组合物诱导胶原蛋白形成的潜力进行了评价。将真皮人成纤维细胞平板接种在带孔玻底培养皿 (MatTek®) 内。每孔内有大约 4000 个细胞。48 小时后，将玻底培养皿倒过来，通过玻璃底 (i) 无光照射 (对照)，(ii) 在中午利用日光照射大约 13 分钟 (对照)，(iii) 将组合物施用到细胞另一侧的玻璃孔底部 (无光照射)，(iv) 将组合物施用到细胞另一侧玻璃孔底部，中午日光照射大约 13 分钟，及 (v) 将组合物施用到细胞另一侧玻璃孔底部并用蓝光照射。在 (iii)、(iv) 和 (v) 的情况下，细胞和组合物之间不存在直接接触。在 (iv) 的情况下，当照射日光时，细胞暴露于来自和穿过曙红 Y 和荧光素组合物的光。在 (iv) 中观察到部分光漂白，在 (v) 中观察到完全光漂白。在处理后，洗涤细胞，并在普通培养液中培养 48 小时。然后，采用苦味酸 - 天狼星红方法，对上层清液开展胶原蛋白分析。这包括将天狼星红染料的苦味酸溶液加到上清液中，轻轻振荡培养 30 分钟，然后离心分离，形成颗粒。首先用 0.1N HCl，然后用 0.5N NaOH 洗涤颗粒，脱除游离染料。离心分离后，对 I 型胶原蛋白来说，读取悬浮液在 540nm 处的读数。结果见表 4。

[0265] 表 4 -

[0266] 暴露于下述条件的真皮人成纤维细胞上清液中 I 型胶原蛋白浓度的定性对比：(i) 无光照射 (对照)，(ii) 中午日光照射大约 13 分钟 (对照)，(iii) 任何曙红 Y 和荧光素组合物发射的穿过玻璃隔离物的光 (无活化光照射)，(iv) 中午日光照射大约 13 分钟时，曙红 Y 和荧光素组合物发射的和穿过曙红 Y 和荧光素组合物，穿过玻璃隔离物的任何光，及 (v) 蓝光照射时组合物发射的和穿过组合物，穿过玻璃隔离物的光。++ 表示胶原蛋白含量是 + 的两倍，+++ 表示胶原蛋白含量是 + 的三倍。

[0267]

	无光照射 (对照)	仅日光 (单独)	曙红 Y 和荧光素 - 无光	曙红 Y 和荧光素 - 日光	曙红和荧光素 - 蓝光
胶原蛋白形成	+	+	++	+++	+++

[0268] 照射日光的曙红 Y 和荧光素组合物诱导的胶原蛋白含量与无光和仅日光的对照样相比存在统计学上的显著差别。照射蓝光的曙红 Y 和荧光素组合物诱导的胶原蛋白含量与无光和仅日光的对照样相比也存在统计学上的显著差别。胶原蛋白的产生指示了组织修

复的潜力，包括肉芽组织的稳定及伤口尺寸的变小。还与细纹减少、毛孔收缩、完好皮肤的质地改善及拉伸强度的改善相关联。

[0269] 可以合理预期的是，采用光发射特性与实例 2、3 和 7 中组合物基本上类似或相当的本发明的粘性生物光子材料，可以得到相同的或类似的生物光子效应。

[0270] 实例 8 - 基于聚硅氧烷的示例性粘性生物光子材料的制备

[0271] 根据本发明实施例，制备了包含聚硅氧烷膜（其中含有生色团，特别是溶于水的生色团曙红 Y 和荧光素）的粘性生物光子膜。生物光子膜基于胶体系统，胶体系统包括固体聚硅氧烷相之内的溶解生色团水相（微 - 乳液）。粘性生物光子膜是通过以下方法制备的：将乙苯中的基质 (B)，包括 (i) 二甲基乙烯封端的二甲基硅氧烷，(ii) 二甲基乙烯化和三甲基化二氧化硅，(iii) 四（三甲氧基硅氧基）硅烷，和乙苯中的固化剂 (C)，包括 (i) 二甲基，甲基氢硅氧烷，(ii) 二甲基乙烯封端的二甲基硅氧烷，(iii) 二甲基乙烯化和三甲基化二氧化硅，及 (iv) 四甲基四乙烯基环四硅氧烷（两者都是液体形式，来源于Sylgard® 184 硅酮弹性体试剂盒，Dow Corning Corp, Ltd）。当按 10(B):1(C) 比例混合时，混合物固化为弹性材料。得到的材料是一种柔韧透明 / 半透明的弹性体。还采用稳定剂来稳定乳液和防止相分离。在一个实例中，采用羧甲基纤维素 (CMC) 作稳定剂（大约 2%）。在另一个实例中，采用明胶作稳定剂。

[0272] 在一个实施例中，将 9.4g 基质与 0.94g 固化剂混合，向此混合物中加入含 0.327mg(0.011wt%，水相中）曙红 Y 和 0.327mg(0.011wt%，水相中）荧光素的 2mL 2% CMC 溶液 (18wt%)。将整个混合物剧烈乳化大约 15 分钟，并浇铸在培养皿上，在 35℃固化大约 16 小时，形成包含硅氧烷基质及 CMC 相中嵌入生色团液滴的半透明 / 透明膜。在另一个实施例中，采用 2mL 明胶溶液 (5%) 取代 CMC 作为稳定剂。这也形成包含包含硅氧烷基质及明胶相中嵌入生色团液滴的半透明 / 透明膜。在这两种情况下，得到 2mm 厚的膜，虽然应该了解的是，膜的厚度可以通过浇铸溶液的体积来控制。在这两种情况下，膜可以单张的形式施用到组织（人体皮肤）上和从组织上清除。

[0273] 应该了解的是，可以使用其它稳定剂，包括但不限于甲基纤维素或羟乙基纤维素。可以使用其它浓度的明胶，如大约 1 至大约 20wt%。水相的总重量百分数是大约 2wt%至大约 40wt%。

[0274] 当用蓝光照射生物光子膜时，生色团吸收和发射光。随着照射时间延长，发现生色团至少部分地发生光漂白。当在硅氧烷中直接包含溶于水的荧光生色团时（即作为单一相），它们并不吸收或发射光。本发明人认为，生色团作为水相包含在硅氧烷膜中时提供了合适的介质，从而让其具有生物光子活性。除液相之外，溶于水的生色团也可以直接被任何其它允许光的吸收和发射的介质所包围，如凝胶或水，或吸附在细的固体颗粒上，例如但不限于二氧化硅和羟基磷灰石颗粒。

[0275] 采用任何其它脂溶聚合物或基质来取代硅氧烷，也证明了上面的实例。

[0276] 实例 9 - 基于明胶的示例性粘性生物光子材料的制备

[0277] 根据本发明另一个实施例，制备了粘性生物光子材料，其中包含粘性明胶基质，明胶基质内含有生色团。在典型的制备中，将 10g 明胶分散到 50mL 去离子水中，然后在连续搅拌下在热水水浴中加热到大约 65℃，直到明胶完全溶解。当温度下降到大约 40℃时，向明胶溶液中加入 0.5mL 曙红 Y 溶液 (10.9mg/mL)，将得到的包含曙红 Y 的明胶溶液 (20% w/

v) 浇到培养皿上，冷却到室温，形成含曙红 Y 的水凝胶膜。得到厚 2mm 的透明弹性膜。该膜可作为单张施用到组织上和从组织上清除。当采用蓝光照射明胶膜时，生色团吸收和发射光。照射后，观察到粘性膜内生色团至少部分地发生光漂白。采用超过 5wt％的明胶基质，同样可以得到可剥离的膜。加入化学交联剂，如戊二醛或乙二醛，可以得到含＜大约 5wt％明胶的可剥离生物光子膜。用脱乙酰壳多糖作为粘性基质取代明胶，也可以得到类似的结果。

[0278] 实例 10- 拉伸强度的测量

[0279] 按照下述方法测定按照实例 8 和 9 所形成的硅氧烷和明胶类粘性生物光子材料的某些实施例的拉伸强度。基于实例 8 和 9 的硅氧烷和明胶膜及不含生色团的膜制备了 50mm x 10mm、厚 2mm 的矩形试样。采用游标卡尺测定样品的长度、宽度和厚度（每个尺寸测定 3 个点），用以计算样品的截面积。

[0280] 样品的每端紧紧固定在夹具之间，夹具有一个与 1/16 英寸的钢缆连接的 15mm 橡胶爪。将该样品 / 夹具组件垂直装在由钢管制造的刚性支架内。顶部电缆从手动棘轮装置悬挂，用于绞起顶部电缆远离底部电缆，底部电缆与一个砝码相连。砝码被加载到精密天平上，天平垂直安装在手动棘轮装置的下面。然后，夹具之间的样品用棘轮以稳定缓慢的速率拉伸。通过天平上测定的砝码的减少，测定样品变形（相对基线长度）所需的力。通过放松样品来测定基线，从而天平所测定的重量是最大的。然后，通过棘轮机制将顶部电缆拉离底部电缆，直到在天平上观察到重量下降。此点被视为基线，记录天平上的读数，用游标卡尺测定样品的长度（夹具之间的距离）。此长度被定义为样品的初始长度。然后，逐步启动棘轮，以拉伸样品，在每一步记录天平的读数和样品的长度，直到样品被撕裂。通过检查测定的砝码的稳定化和使用样品上的目视指示器，来确认不存在夹具滑落。

[0281] 硅氧烷类和明胶类膜的典型应力 - 应变曲线分别如图 8a 和 8b 所示。含有不同增稠剂的包含和未包含生色团的硅氧烷膜的拉伸性能基本上类似。包含和未包含生色团的明胶膜也具有基本上类似的拉伸性能。明胶类膜的拉伸强度是大约 0.01MPa(±10％)(100kPa)，弹性模量（应力 / 应变曲线的斜率）是大约 0.01MPa(±10％)(100kPa)。硅氧烷类膜的刚性比明胶类膜大，平均弹性模量是大约 1.11MPa(±10％)(1110kPa)。这一数值位于文献报导的大约 1.2-1.8MPa 的范围之内。由于夹具滑落，测定的拉伸强度是 0.405MPa(826g)，但是，根据文献中关于固化硅氧烷的报导，拉伸强度预期达到大约 8MPa。

[0282] 这种方法依据的原理与美国材料试验学会拉伸试验方法，如 ASTM D638、ASTM D882 和 ASTM D412 类似。但是，在本发明实例中，用重力代替气动力来进行样品拉伸。

[0283] 实例 11- 粘合强度的测定

[0284] 按照下述方法测定根据实例 8 和实例 9 形成的生物光子材料的某些实施例的粘合强度。根据实例 10 所述制备样品。将每个样品的一端与固定于夹具内，夹具有一个与 1/16 钢缆一端连接的 15mm 橡胶爪。钢缆的另一端通过低摩擦滑轮与放置在天平上的砝码连接。样品平放在一名志愿者的前臂内侧皮肤上。然后，为了在与皮肤接触的样品上施加均匀的已知向下力，将表面积与样品匹配的已知砝码放到样品上。法向力 F_n（每个表面施加在与所述表面垂直（法向）的另一个表面上的力）按照样品和样品上砝码的总重量乘以重力常数 (g)(9.8m/s^2) 来计算。然后，在负载砝码的样品条件下，将前臂拉离钢缆，直到样品从皮肤表面滑落。此时天平上记录的砝码乘以 g，得到摩擦力 (F_f)（克服样品和皮肤之间摩擦所

需要的力）。然后，利用 $F_f \leq \mu F_n$（库仑摩擦定律），计算样品的摩擦系数。

[0285] 平均说来，硅氧烷膜的摩擦系数是大约 1.43，明胶膜的摩擦系数是大约 1.04。将摩擦系数乘以样品的重量，可以转化为将样品从试验表面剪断所需的重量。因此，对于硅氧烷膜来说，将膜从皮肤上剪下，需要的重量是 1.50g。根据图 8a，这相当于伸长大约 0.1%，远低于其拉伸强度。对明胶膜来说，将膜从皮肤上剪下，需要的重量是大约 1.04g。根据图 8b，这相当于伸长大约 1.5%，远低于其拉伸强度（相当于 24.12g）。因此，实例 8 和实例 9 的所有硅氧烷膜和明胶膜是可以剥离的。

[0286] 实例 12 - 本发明粘性生物光子材料的可剥离性质证明

[0287] 将实例 1、8 和 9 所述的生物光子材料施用于志愿者的皮肤上，用手将其剥离，对它们的剥离性进行评价。所有膜都可以剥下来，重新施用再重新剥离下来，而膜没有损坏，未在志愿者皮肤上有任何残留。

[0288] 实例 13 细胞研究

[0289] 对实例 8 的粘性生物光子材料的某些实施例调节炎症，特别是细胞因子 IL6 和 IL8 的能力进行了评价。HaCaT 细胞作为接受的体外模块，用于评价这些炎性细胞因子的调节性。无毒的 $IFN_{\gamma\ w}$ 被用于调节 HaCaT 细胞的 IL6 和 IL8 分泌。

[0290] 对包含曙红 y 和荧光素水相的硅氧烷膜及水相中包括 CMC 或明胶的情况进行了评价。采用浓度 5μM 的地塞米松的消炎效果作为阳性对照。在距离 5cm 处，以能量密度大约 11.5J/cm^2 的蓝光照射材料 90 秒。在处理后 24 小时，通过培养上清液上的细胞因子免疫试剂，开展细胞因子定量。分泌的细胞因子的数量归一化为细胞活性。在处理后 24 小时采用分光光度计评价活细胞数，衡量细胞活性，所有试验样品均未观察到毒性效应。所有试验膜均在 IFN_γ 刺激的 HaCaT 细胞上产生向下的 IL6 和 IL8 调节。

[0291] 应该理解的是，本发明并不限于此处描述和阐明的具体实施例，而是包括所附权利要求书中定义的本发明范围之内的所有变动和更改。

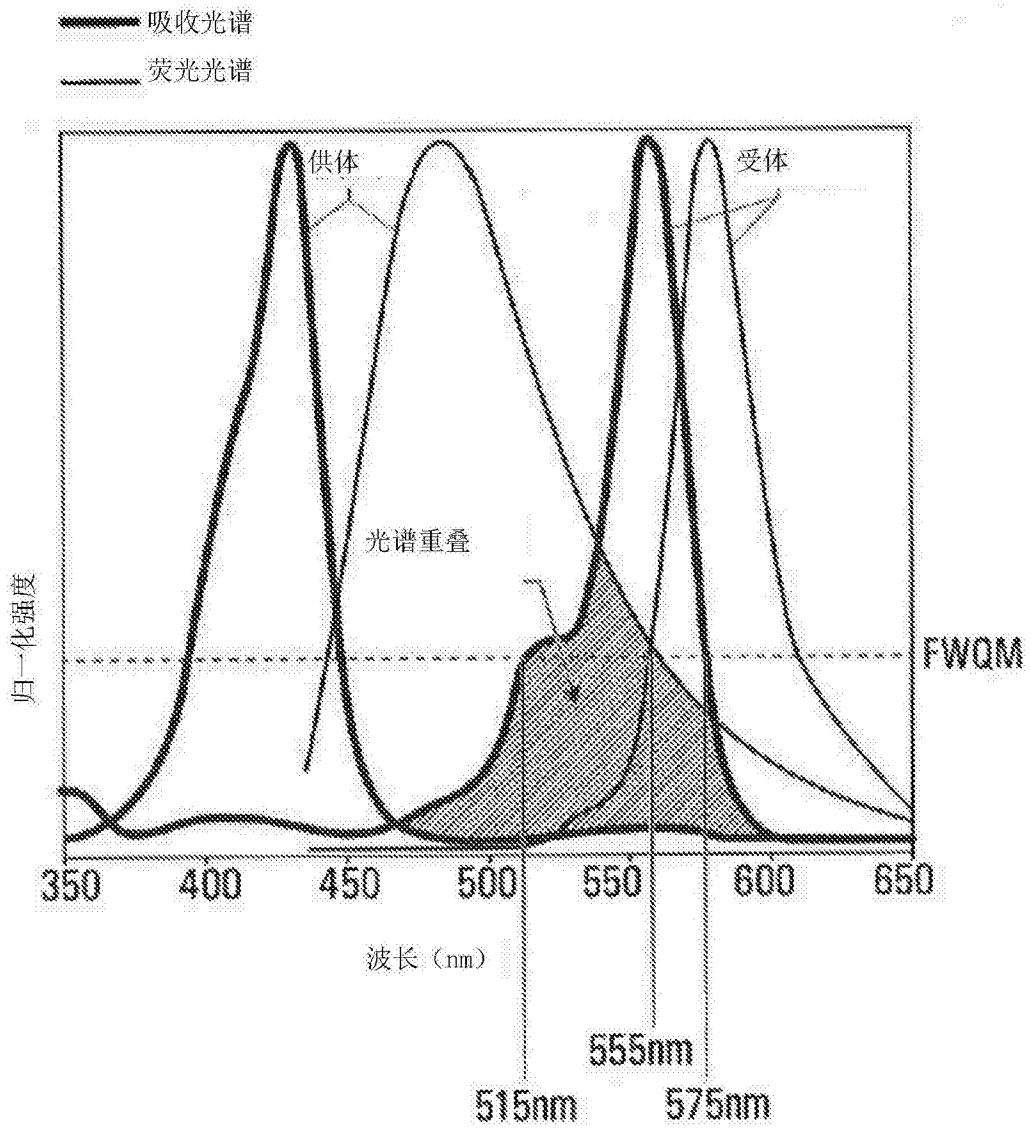

吸收光谱
荧光光谱
供体
受体
光谱重叠
FWQM
归一化强度
350
400
450
500
550
600
650
波长（nm）
515nm
555nm
575nm

图 1

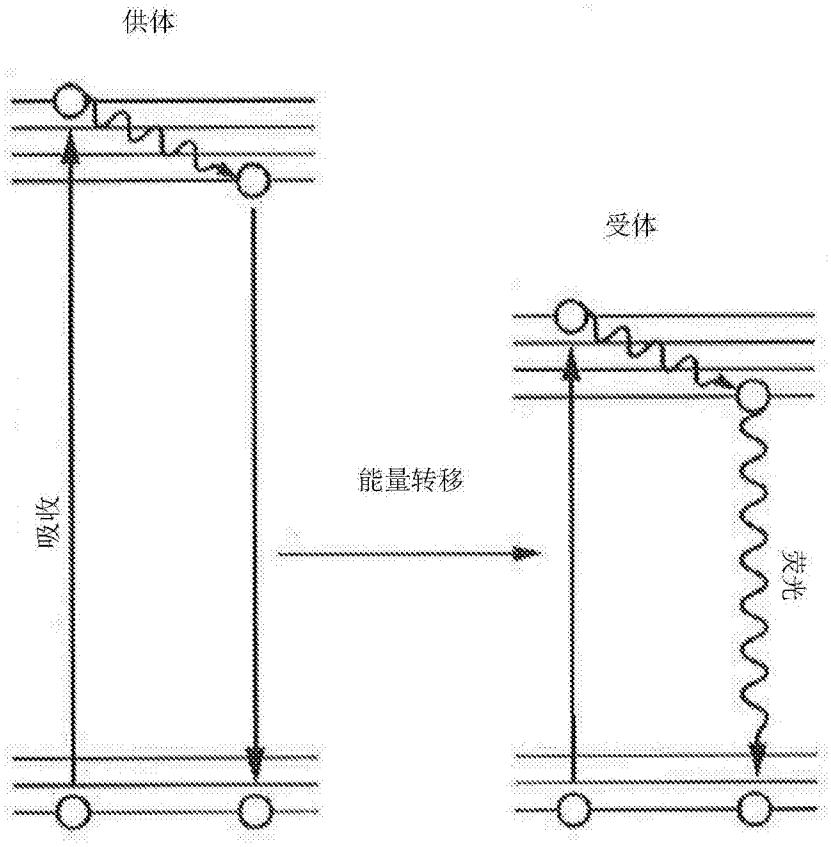


图 2

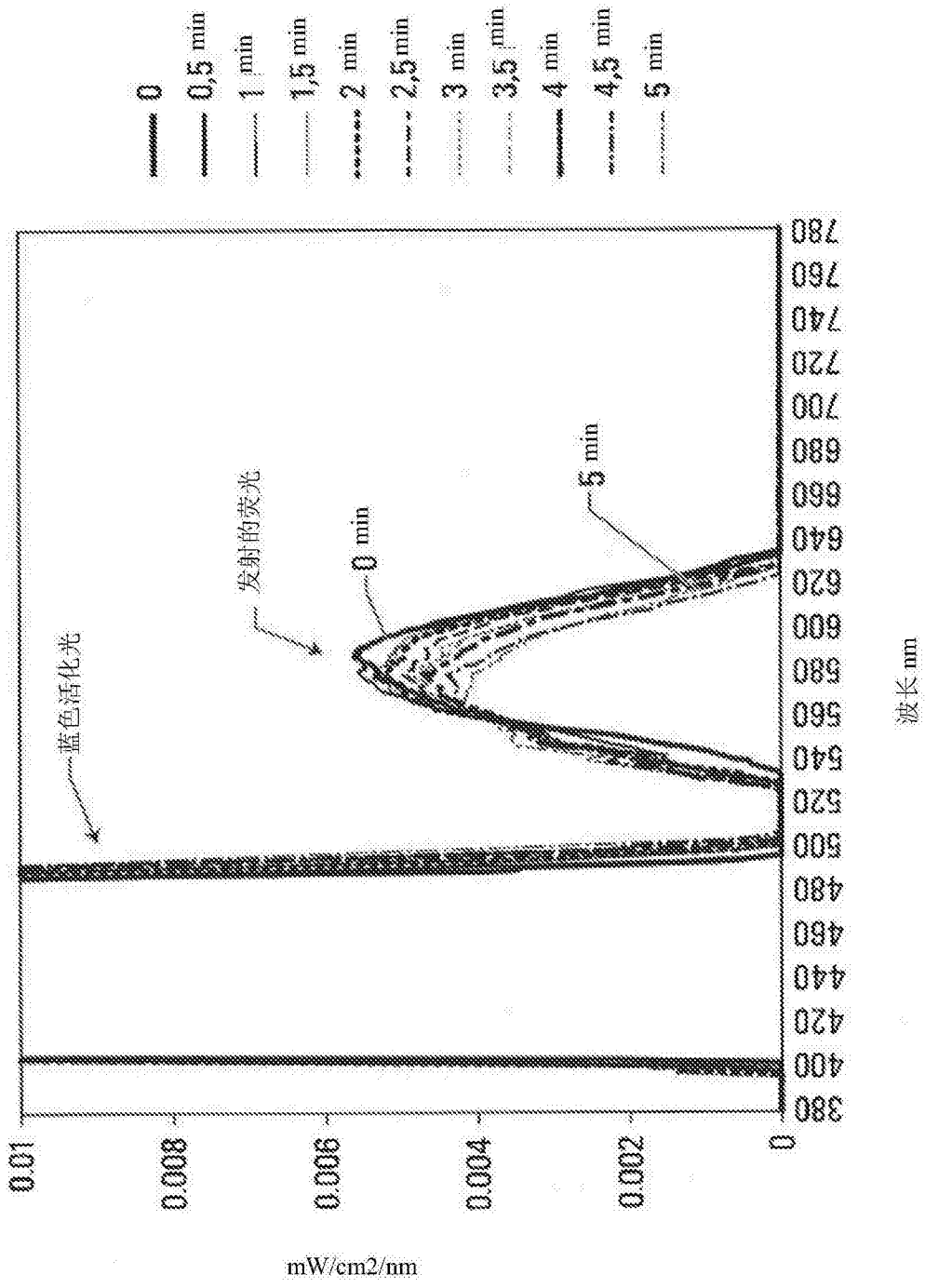

0
0,5 min
1 min
1,5 min
2 min
2,5 min
3 min
3,5 min
4 min
4,5 min
5 min
蓝色活化光
发射的荧光
0 min
5 min
0.01
0.008
0.006
0.004
0.002
0
mW/cm2/nm
380
400
420
440
460
480
500
520
540
560
580
600
620
640
660
680
700
720
740
760
780
波长 nm

图 3

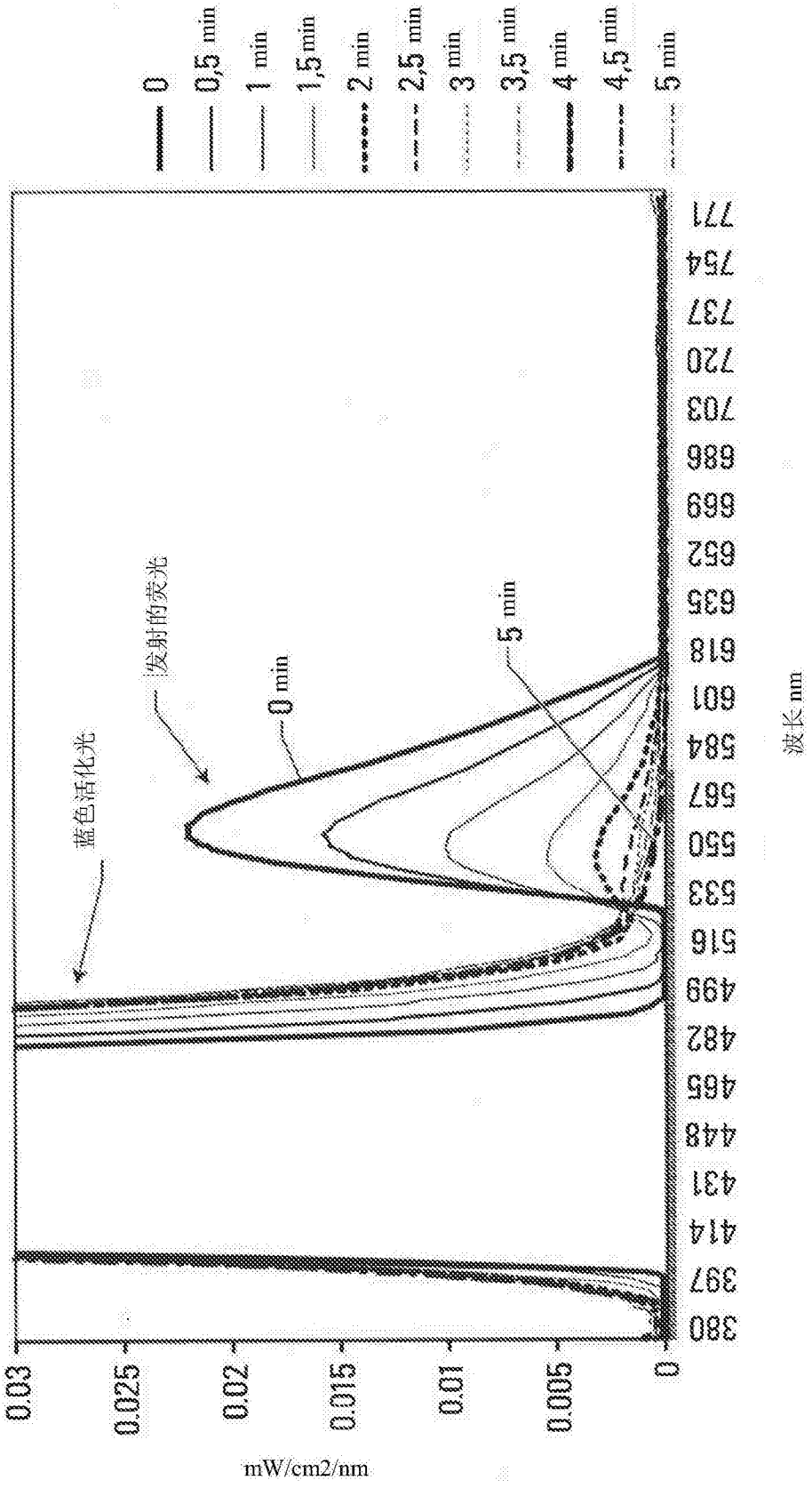

0
0,5 min
1 min
1,5 min
2 min
2,5 min
3 min
3,5 min
4 min
4,5 min
5 min
771
754
737
720
703
686
669
652
635
618
601
584
567
550
533
516
499
482
465
448
431
414
397
380
波长 nm
0.03
0.025
0.02
0.015
0.01
0.005
0
mW/cm2/nm
蓝色活化光
发射的荧光
0 min
5 min

图 4

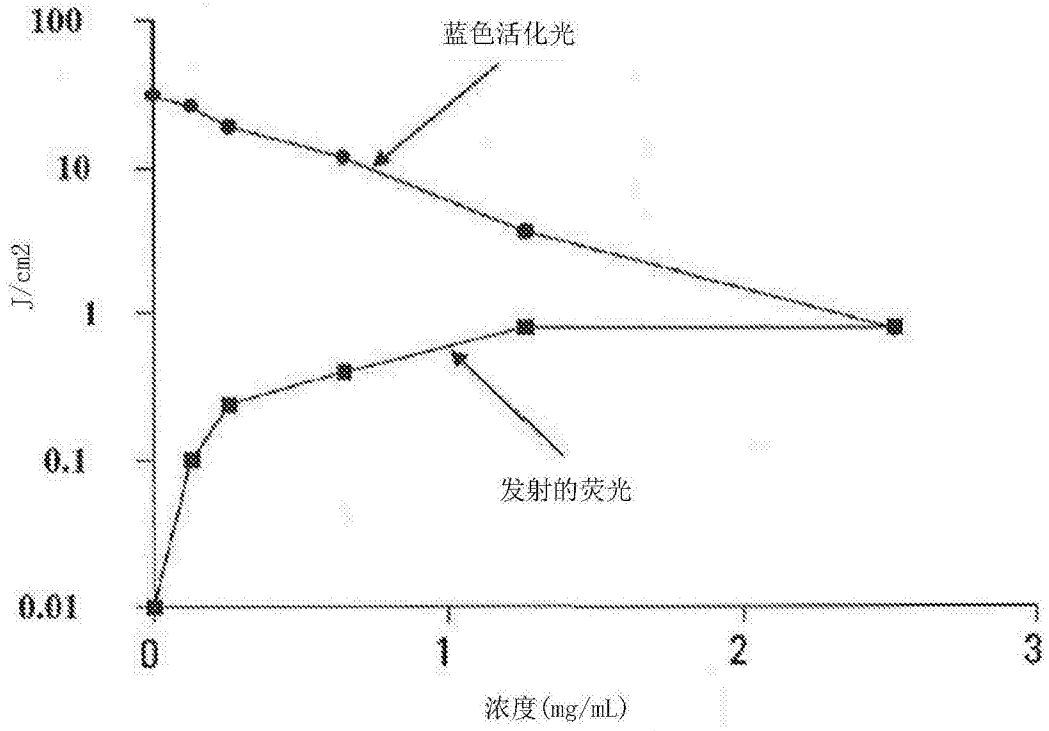

100
10
1
0.1
0.01
J/cm2
蓝色活化光
发射的荧光
0
1
2
3
浓度(mg/mL)

图 5A

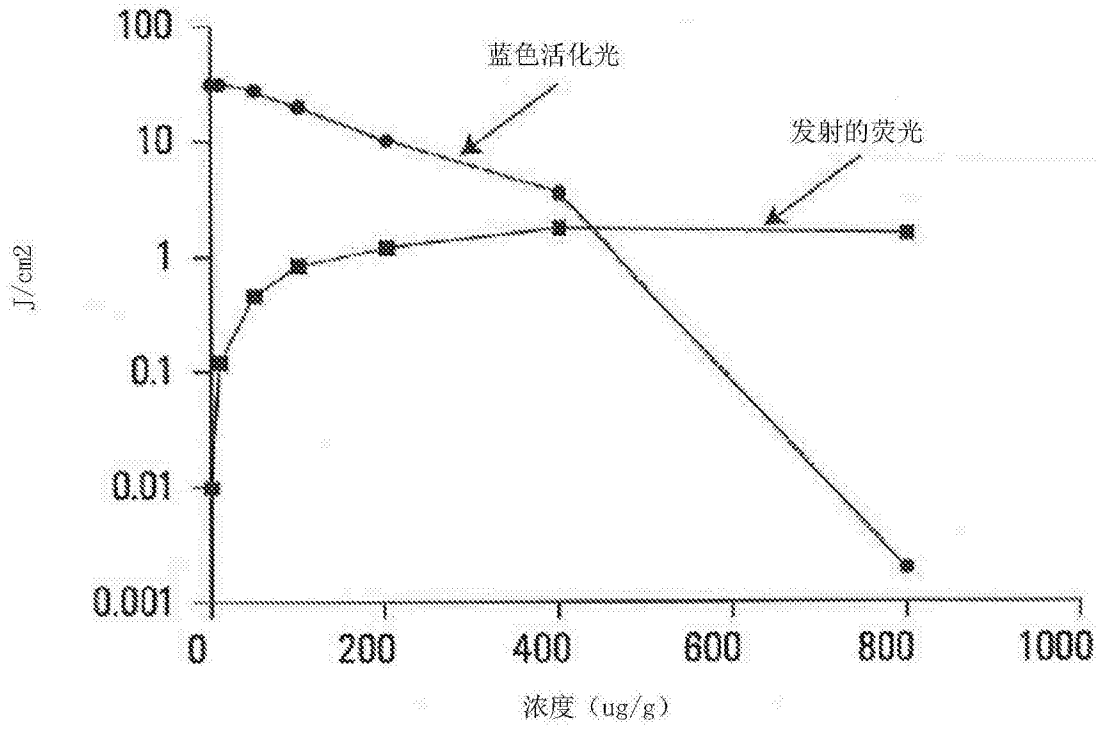

100
10
1
0.1
0.01
0.001
J/cm2
蓝色活化光
发射的荧光
0
200
400
600
800
1000
浓度（ug/g）

图 5B

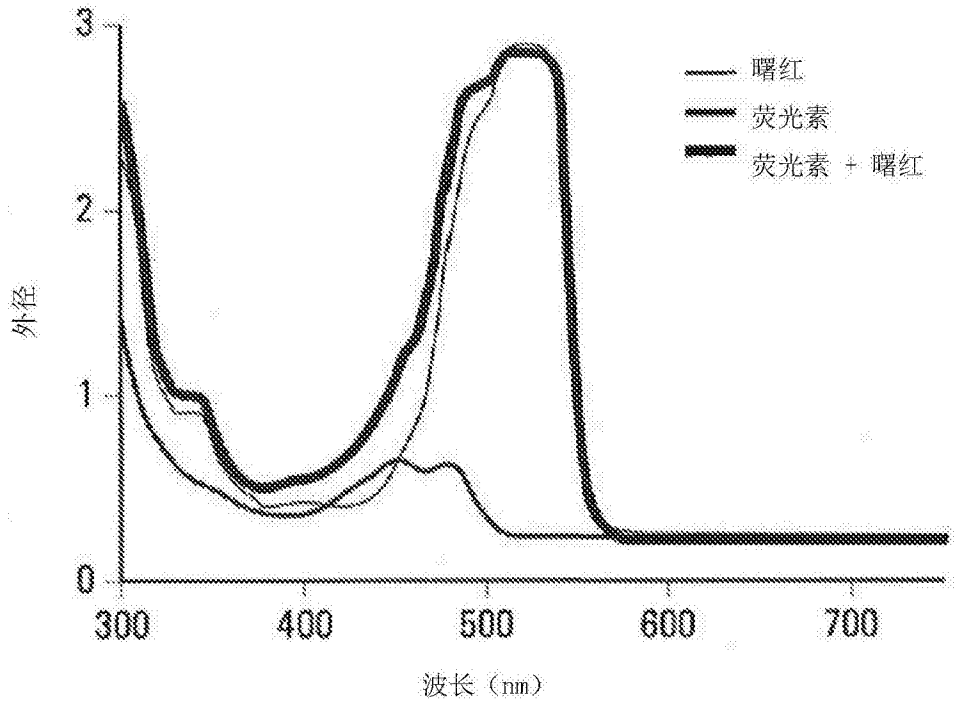

3
2
1
0
外径
300
400
500
600
700
波长（nm）
曙红
荧光素
荧光素 + 曙红

图 6A

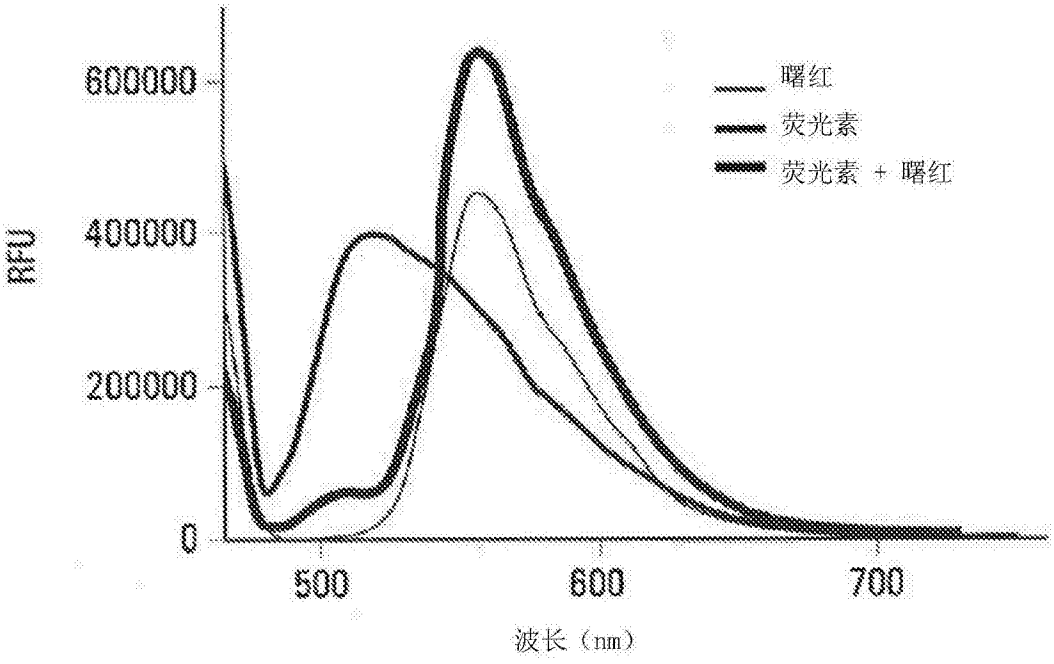

600000
400000
200000
0
RFU
500
600
700
波长（nm）
曙红
荧光素
荧光素 + 曙红

图 6B

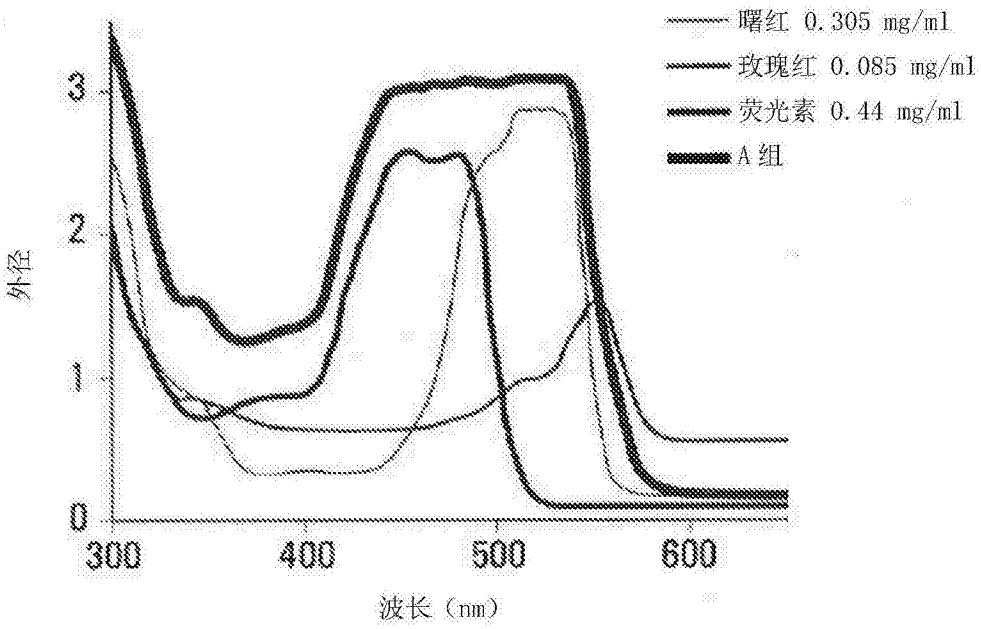

曙红 0.305 mg/ml
玫瑰红 0.085 mg/ml
荧光素 0.44 mg/ml
A 组
外径
0
1
2
3
300
400
500
600
波长（nm）

图 7A

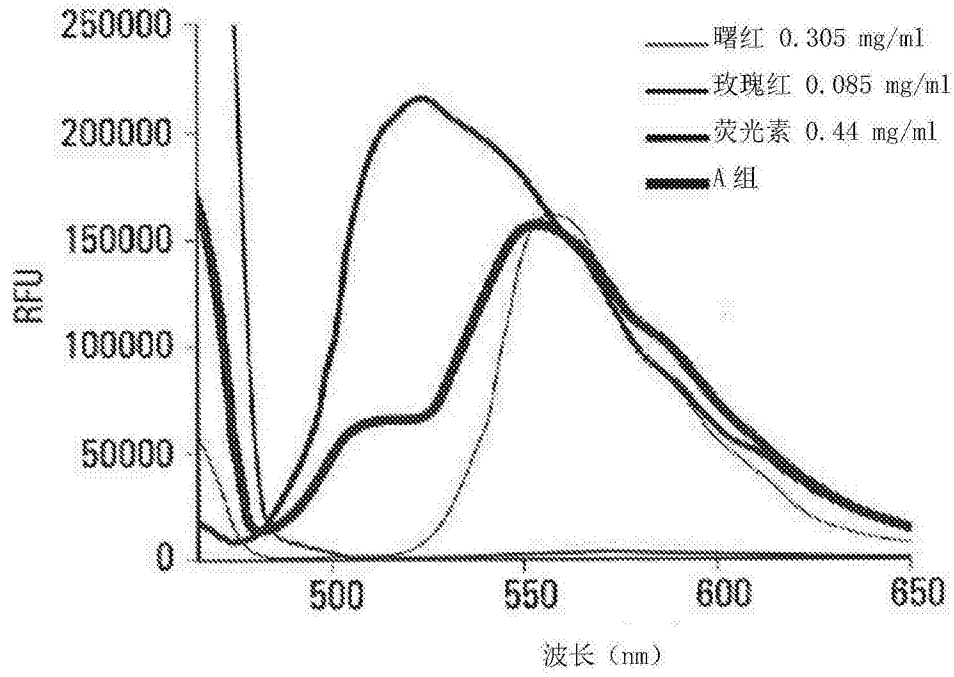

曙红 0.305 mg/ml
玫瑰红 0.085 mg/ml
荧光素 0.44 mg/ml
A 组
RFU
0
50000
100000
150000
200000
250000
500
550
600
650
波长（nm）

图 7B

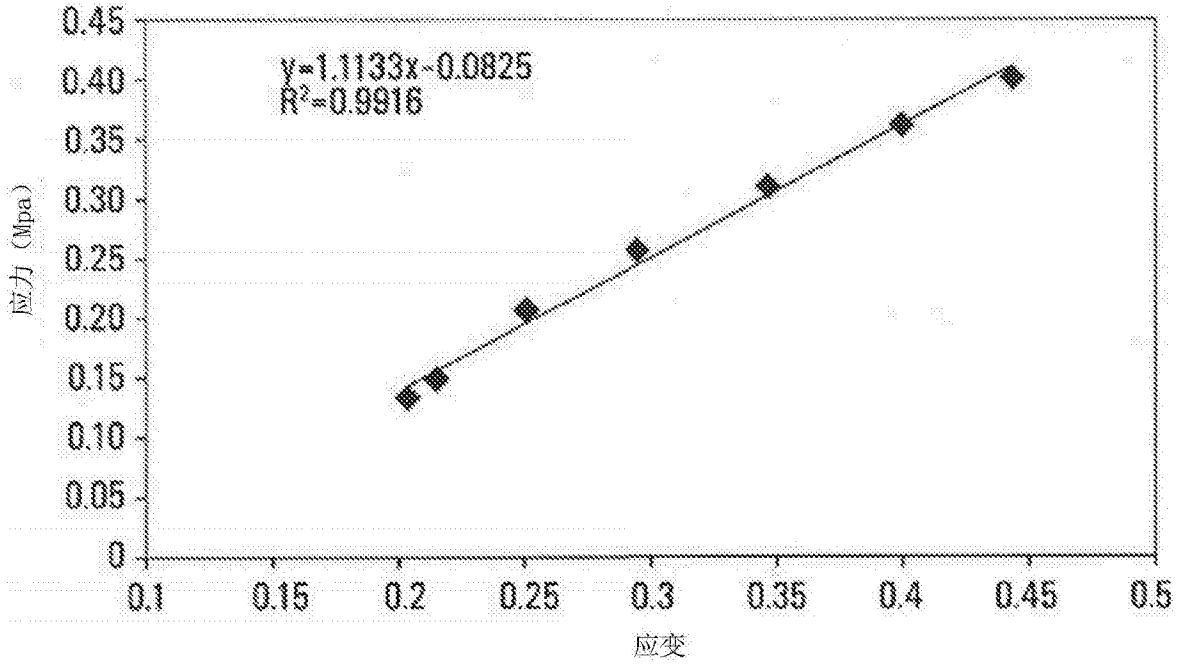

y=1.1133x-0.0825
R²=0.9916
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
应力（Mpa）
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
0.5
应变

图 8A

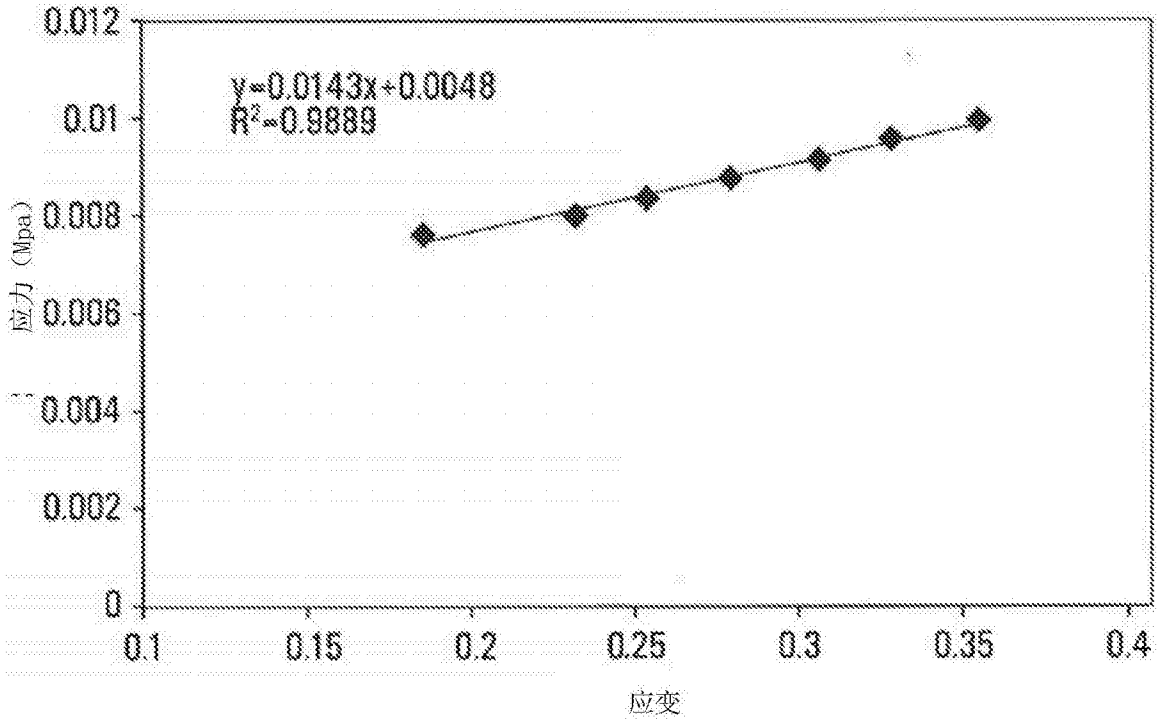

y=0.0143x+0.0048
R²=0.9889
0.012
0.01
0.008
0.006
0.004
0.002
0
应力（Mpa）
0.1
0.15
0.2
0.25
0.3
0.35
0.4
应变

图 8B