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(54) Title: SUNSCREEN COMPOSITIONS AND METHODS

(57) Abstract: Sunscreen compositions are provided for protecting skin from sun-induced damage comprising (i) at least one UV-B or UV-A/UV-B sunblock active, (ii) at least one meroterpene and (iii) a dermatological acceptable carrier. Preferably, the sunblock active will be a UV-A/UV-B sunblock active or said sunscreen compositions will further comprise at least one UV-A sunblock active. Suitable meroterpenes include plant extracts having one or more meroterpene-enriched fractions, especially suited are Bakuchiol and derivatives of Bakuchiol. These skin protective compositions may optionally include an effective amount of one or more skin protective ingredients such as antioxidants, vitamins, anti-inflammatory agents, self-tanning agents and mixtures thereof.

SUNSCREEN COMPOSITIONS AND METHODS

FIELD OF THE INVENTION

[0001] This invention relates to sunscreen compositions for protecting skin from sun-induced damage comprising (i) at least one UV-B or UV-A/UV-B sunblock active, (ii) at least one meroterpene and (iii) a dermatological acceptable carrier. Most preferably, the sunblock active will be a UV-A/UV-B sunblock active or said sunscreen compositions will further comprise at least one UV-A sunblock active. Suitable meroterpenes include plant extracts having one or more meroterpene-enriched fractions. Especially suited are Bakuchiol and derivatives of Bakuchiol. These skin protective compositions may optionally include an effective amount of one or more skin protective ingredients such as antioxidants, vitamins, anti-inflammatory agents, self-tanning agents, and mixtures thereof.

BACKGROUND OF THE INVENTION

[0002] As the outermost barrier of the body, the skin is directly exposed to a pro-oxidative environment. The effects of ultraviolet (UV) radiation from sun exposure can induce or exacerbate oxidative attack leading to the generation of reactive oxygen species (ROS) and other free radicals. The most prominent short-term effect of such skin exposure is a reddening of the skin (erythema): the most common consequence and evidence of sunburn. The most severe long-term consequence of photo-damage is skin cancer. Less severe long term photo-aging changes result in wrinkling, scaling, dryness, and uneven pigmentation consisting of hyper- and hypo-pigmentation (SR Pinnell, "Cutaneous Photodamage, Oxidative Stress, and Topical Antioxidant Protection", *J Am Acad Dermatol*, 48: 1-19, 2003; J Wenk, P Brenneisen, C Meewes, M Wlaschek, T Peters, R Blaudschwun, W. Ma, L. Kuhr, L Schneider, and K. Scharftetter-Kochanek, UV-Induced Oxidative Stress and Photoaging, in J Thiele and P. Elsner, Eds. Oxidants and Antioxidants in Cutaneous Biology. *Current Prob. Dermatol.* Basel, Karger, 29: 2001, pp 83-94; M Berneburg, H Plettenberg, and J Krutmann, Photoaging of Human Skin, *Photodermatol Photoimmunol Photomed*, 16: 239-244, 2000).

[0003] Extended life-span, more spare time and excessive exposure to UV radiation from sunlight or tanning devices, especially in the western population, has resulted in an ever increasing demand to protect human skin against the detrimental effects of UV-exposure. Sunscreens - the current gold standard of photo-protection - are useful, but their

protection is most often inadequate due to improper and/or non-optimal application. Furthermore, most sunscreens are not suitably effective against long wave UV-A light due to the poor selectivity of most sunblock actives for UV-A and because UV-A is especially efficient at generating reactive oxygen species (ROS) (M Wlaschek, K Briviba, GP Stricklin, H Sies, K Scharfetter-Kochanek, *J Invest Dermatol*, 104: 194-198, 1995; M Berneburg, S Grether-Beck, V Kurten, T Ruzicka, K Briviba, H Sies and J Krutmann, Singlet Oxygen Mediates the UV-induced Generation of the Photoaging-Associated Mitochondrial Common Deletion, *J Biol Chem*, 274: 15345-15349, 1999; R Haywood, P Wardman, R Sanders and C Linge, Sunscreens Inadequately Protect Against Ultraviolet-A-Induced Free Radicals in Skin: Implications for Skin Aging and Melanoma, *J Invest Dermatol,* 121: 862-868, 2003). Although the principal focus of sunscreen products has traditionally been on UV-B due to its highly damaging nature, UV-A is being recognized increasingly as an important cause of photo-aging and skin cancer.

[0004] Furthermore, because, photo-aging of skin is a complex biological process affecting various layers of the skin with major changes seen in the connective tissue of the dermis, the natural shift toward a more pro-oxidant state in intrinsically aged skin can be significantly enhanced following UV-irradiation. Through the evaluation of punch biopsies of human skin following UV irradiation, Brennan et. al. have identified MMP-1 as the major collagenolytic enzyme responsible for collagen damage in photoaging (M Brennan, H Bhatti, KC Nerusu, N Bhagavathula, S Kang, GJ Fisher, J Varani and JJ Voorhees, Matrix Metalloproteinase-1 Is The Major Collagenolytic Enzyme Responsible for Collagen Damage in UV-Irradiated Human Skin, *Photochem Photobiol*, 78: 43-48, 2003). In contrast, the synthesis of tissue inhibitory metalloprotease –1 (TIMP-1), the natural inhibitor of matrix metalloprotease, increases only marginally. This imbalance is one of the causes of severe connective tissue damage resulting in photo aging of the skin. Although collagen content decreases, collagen synthesis in sun-damaged skin appears to remain similar to that of sun-protected sites (A Oikarinen, M. Kallionen, Biochemical and Immunohistochemical Study of Collagen in Sun-Exposed and Protected Skin, *Photodermatology*, 6: 24-31, 1989; E Schwartz, FA Crickshank, CC Christensen, JS Perlish, and M Lebwohl, Collagen Alterations in Chronically Sun-Damaged Human Skin, *Photochem Photobiol*, 58: 841-844, 1993). Thus, evidence suggests that the decrease in collagen content in photo-damaged skin results from increased collagen degradation, by

matrix metalloprotease, without significant changes in collagen production (EF Bernstein and J Uitto, The Effect of Photodamage on Dermal Extracellular Matrix, *Clinics in Dermatology*, 14: 143-151, 1996).

[0005] The damage caused by excessive MMP on the ECM proteins does not appear overnight, but results from the accumulation of successive instances of molecular damage, especially in the case of overexposure to UV light. The skin repercussion on the degradation of the ECM proteins may then be revealed in many ways depending on age, genetic predisposition, and life-style and, of course, on the general health status of the individual (A Oikarinen, The Aging of Skin: Chronoaging Versus Photoaging, Photderm. *Photoimmun. Photomed.*, 43: 3-4, 1990).

[0006] Whether extrinsic or intrinsic, these factors result in visible signs of skin aging and environmental damage, such as wrinkling and other forms of roughness (including increased pore size, flaking and skin lines), and other histological changes associated with skin aging or damage. The elimination of wrinkles has become a booming business in youth-conscious societies. Extrinsic or intrinsic factors may result in the thinning and general degradation of the skin. For example, as the skin naturally ages, there is a reduction in the cells and blood vessels that supply the skin. There is also a flattening of the dermal-epidermal junction which results in weaker mechanical resistance of this junction. See for example, Oikarinen, "The Aging of Skin: Chronoaging Versus Photoaging," *Photodermatol. Photoimmunol. Photomed.*, vol. 7, pp. 3-4, 1990, which is incorporated by reference herein in its entirety.

[0007] Many sunscreen preparations are sold commercially or are described in cosmetic or pharmaceutical literature. Ideally, sunscreen compositions should be nontoxic and non-irritating to the skin tissue and be capable of convenient application in a uniform continuous film. The product should be chemically and physically stable so as to provide an acceptable shelf life upon storage; and, it is particularly desirable that the preparation should retain its protective effect over a prolonged period after application. In general, sunscreen preparations are formulated as creams, lotions, oils or sprays containing, as the active agent, an inorganic additive that physically blocks the UV rays or an organic compound that absorbs ultra violet radiation, or combinations thereof. The sunscreen preparation works by blocking, physically or chemically, passage of ultra violet radiation thereby preventing its penetration into the skin.

[0008] According to Zecchino et al. (U.S. Pat. No. 5,008,100), sunblock active agents may be characterized in the order of decreasing effectiveness as either highly chromophoric (monomeric organic compounds and inorganic compounds such as titanium dioxide) and minimally chromophoric (polymeric organic solids).

[0009] Organic sunscreens are classified into UV-A filters, UV-B filters or broad spectrum filters (UV-A and UV-B functionality in a single molecule) depending on the type of radiation they absorb. UV-A sunscreens absorb radiation in the 320 to 400 nm regions of the ultra violet spectrum and UV-B sunscreens absorb radiation in the 290 to 320 nm regions of the ultra violet spectrum (See Sunscreens, Regulations and Commercial Development, Third Edition, Ed Nadim A. Shaath, Taylor & Francis, 2005). Broad-band sunscreens (UV-A and UV-B functionality) absorb radiation in the 290 to 400 nm region of the ultra violet spectrum and have two maximums, one in the UV-B region and the other in the UV-A region. Representative references relating to UV sunscreens include Gonzalez et. al. - US 7,186,404; Aust et. al. - US 7,175,834; Roseaver et. al.– US 7,172,754; Simoulidis et. al. - US 7,175,835; Mongiat et. al. - US 7,101,536; Maniscalco – US 7,078,022; Chaudhuri et. al. - US 6,165,450; Forestier et. al. US 5,175,340; and Wang et. al. US 5,830,441.

[0010] Unfortunately, some of the highly chromophoric monomeric organic compounds employed in sunscreen compositions are not photostable and the protection from sun damage is lost after only a short period of time. For example, Avobenzone, a UV-A sunscreen, is generally photo-unstable. Furthermore, photo-instability of Avobenzone increases significantly when combined with Octyl methoxycinnamate (a UV-B organic sunscreen). In most studies, Octyl methoxycinnamte (OMC) has been regarded as relatively photostable. The absorption maxima of Avobenzone (about 360 nm) and OMC (about 310 nm) do not overlap sufficiently to allow directly excited singlet-singlet energy transfer to occur. However, transfer from one excited triplet-state to another is possible provided the energy levels are suitable. Techniques for stabilizing UV absorbent compositions are known. Representative disclosures in this area include Forestier et. al. - US 5,567,418, US 5,538,716, and US 5,951,968; Deflandre et. al. – US 5,670,140; Chaudhuri - US 7,150,876, US 6,831,191, US 6,602,515, US 7,166,273, US 6,936,735, US 6,831,191,and US 6,699,463; Chaudhuri et. al. - US 7,150,876; and Bonda et. al. US 6,962,692.

[0011] In an effort to address some of the shortcomings of typical sunscreen compositions, certain manufacturers have added antioxidants. Antioxidants are believed to provide protection from free-radical damage by quenching or sequestering free radicals generated by UV exposure. Photo-protective products combining sunscreens and an antioxidant or antioxidant mixtures have been touted as providing increased efficacy and safety relative to UV exposure (SR Pinnell, Cutaneous Photodamage, Oxidative Stress, and Topical Antioxidant Protection, *J Am Acad Dermatol*, 48: 1-19, 2003). To be an effective quencher, it is believed that the antioxidant must be present in an adequate concentration at the site of free radical generation. However, since antioxidants are used in relatively low concentrations and are a separate ingredient, they may not be available at the site of free radical generation. Consequently, the level of skin protection may be reduced and, oftentimes, less than desired.

[0012] While the general use of antioxidants in sunscreen formulations is advocated, it is often disregarded that these compounds not only function as antioxidants, but intrinsically have pro-oxidant action as well, especially in the presence of transition metals (See e.g., "Role of Antioxidants in Sun Care Products" by R. Chaudhuri in Sunscreens, NA Shaath, editor, Taylor and Francis, p603-638, 2005). There is pro-oxidant action even in well-known antioxidants, such as, vitamin C (ascorbate), vitamin E (tocopherols), glutathione and proanthocyanidins (from pine and grape). The pro-oxidant activity of vitamin C results from the reduction of Fe^{3+} to Fe^{2+} and its reaction with H_2O_2 to generate OH radicals. Pro-oxidant effects are not unique to vitamin C: they can be demonstrated with many reducing agents, including vitamin E, glutathione and several plant phenolic compounds, in the presence of transition metal ions. Thus, if vitamin C's pro-oxidant effects are relevant, the pro-oxidation effects of these other reductants may also be expected to occur.

[0013] While the objective of sunscreens is, in general, to prevent skin damage due to UV exposure, such also prevents, in many instances, the skin darkening effect, or tanning, desired by many sunbathers. So as not to completely disappoint those desirous of a bronze look, formulators oftentimes add self-tanning agents such as dihydroxyacetone (DHA) to their sunscreen compositions. DHA is an intermediate of carbohydrate metabolism in higher plants and animals: commonly present as the dihydroxyacetone monophosphate in glycolysis. In crystalline form, DHA is a mixture of one monomer and four dimers:

though an all monomer form may be generated by heating or melting dimer DHA or by dissolving it in water.

[0014] The reaction product of DHA and the skin protein that produces the "tan" color has been shown to provide protection against UV-A in animals and humans (Self-Tanners: Formulating with Dihydroxyacetone, R. Chaudhuri & C Hwang, *Cosmetics & Toiletries*, 116:87-96, 2001; Dihydroxyacetone: Chemistry and Applications in Self-Tanning Products, R. Chaudhuri, in The Chemistry and Manufacture of Cosmetics, Ed. M Schlossman, Allured publishing, 3rd Edition, 383-402, 2002). Experimental and clinical evidence show that skin that has been treated topically with 3 % DHA solution overnight has a Sun Protection Factor (SPF) of at least 3 in the UV-B region. Likewise, a photoprotection factor of 10 in the UV-A region has been observed with 15% solution of DHA. Unfortunately, DHA is photochemically very unstable and it takes a long time to get a very little skin protection against sun-induced skin damage (Self-Tanners: Formulating with Dihydroxyacetone, R. Chaudhuri & C Hwang, *Cosmetics & Toiletries*, 116:87-96, 2001).

[0015] Despite all the efforts that have been undertaken to formulate effective sunscreen compositions and despite the constant reminders of the importance of proper and adequate application, current sunscreen products are not entirely effective. Either the formulation is not fully effective or its application is faulty or improper: most often a little of both. Presently available sunscreen compositions are, for the most part, ineffective against Reactive Oxygen Species induced and/or enzyme induced skin damage. Furthermore, it is merely a matter of reality that those who apply the sunscreen often do so improperly or ineffectively: particularly when it comes to the timely re-application of the sunscreen product and/or its re-application following certain activities, such as swimming, washing face and hands, etc. Consequently, the user oftentimes finds oneself with a sunburn, and the concomitant underlying damage manifested by the sunburn inducing UV exposure, despite their best efforts.

[0016] Thus, there is a continuing need and effort to formulate sunscreen compositions that are more effective and more forgiving.

[0017] Furthermore, since sunscreens are not utopian and there is and always will be the human factor relative to their application, it would also be especially desirable to provide a sunscreen product that not only protects one's skin from the damaging effects

of UV exposure, but also improves the health and/or physical appearance of the skin and/or repairs past skin damage, whether due to UV exposure or merely as a result of natural aging.

[0018] Surprisingly, it has now been found that effective sunscreen compositions having many, if not most, of the desired attributes of the utopian, or nearly utopian, sunscreen composition may be prepared by the further incorporation therein of an effective amount of one or more purified meroterpenes or meroterpene enriched extracts.

[0019] Furthermore, it has now been found that the combination of traditional sunblock actives and meroterpenes or enriched meroterpene extracts in a sunscreen composition provide a performance synergy in preventing damage due to UV exposure as well as in mitigating the manifestation of said damage, particularly in the short term time frame.

SUMMARY

[0020] According to the present invention there are provided novel sunscreen compositions for protecting skin from sun-induced damage comprising (i) at least one UV-B or UV-A/UV-B sunblock active, (ii) at least one meroterpene, and (iii) a dermatologically acceptable carrier wherein the meroterpene is free or substantially free of coumarins, especially furocoumarins. Preferably, the sunblock active will be a UV-A/UV-B sunblock active or said sunscreen compositions will further comprise at least one UV-A sunblock active. Suitable meroterpenes include purified meroterpenes as well as plant extracts having one or more purified meroterpene-enriched fractions. Especially preferred sunscreen compositions are those based on the meroterpene Bakuchiol or derivatives of Bakuchiol and which are free or substantially free of psorlens, especially psoralene and isopsoralene.

[0021] The sunscreen compositions of the present invention will typically comprise the sunblock actives in their conventional amounts and the meroterpene in an amount of from about 0.1 to about 10 wt %, preferably from about 0.5 to about 5 wt % based on the total weight of the sunscreen composition. Additionally, these sunscreen compositions may optionally include an effective amount of one or more skin protective and/or treatment ingredients such as antioxidants, vitamins, anti-inflammatory agents, self-tanning agents, moisturizers, emollients, humectants, and the like, and mixtures thereof, in their conventional amounts.

[0022] The sunscreen compositions of the present invention are applied topically and may take the form of a lotion, spray, ointment, gel, or other topically applicable form.

[0023] The present invention is also directed to a method of preventing skin damage arising from exposure to UV radiation, said method comprising the step of applying a sunscreen composition comprising (i) at least one UV-B or UV-A/UV-B sunblock active, (ii) at least one meroterpene, and (iii) a dermatologically acceptable carrier wherein the meroterpene is free or substantially free of coumarins, especially furocoumarins to the exposed skin. Preferably, the method comprises the step of applying the sunscreen composition to the skin prior to exposing it to sunlight, most preferably at least 15 minutes prior to said exposure. Furthermore, the method may also, and preferably does, include the step of re-applying the sunscreen composition periodically, preferably at least every couple of hours, and/or following participation in those activities that may wash or wear away the sunscreen composition already applied to the skin.

[0024] The present invention also relates to a method of preventing skin damage due to UV exposure concurrent with the treatment of skin damage due to various disease conditions and/or aging and/or long-term exposure to UV light said method comprising the step of applying a sunscreen composition comprising (i) at least one UV-B or UV-A/UV-B sunblock active, (ii) at least one meroterpene, and (iii) a dermatologically acceptable carrier wherein the meroterpene is free or substantially free of coumarins, especially furocoumarins to those areas of the skin showing evidence of the disease condition and/or prior damage from UV exposure.

[0025] These and other features, aspects, and advantages of the present invention will become evident to those skilled in the art from reading of the present disclosure.

DESCRIPTION OF THE INVENTION

[0026] As used herein and in the appended claims, the phrase "substantially free of" means that the recited compound or component, if present, is present at an inconsequential level, generally less than 0.1 wt% based on the weight of the meroterpene, and does not interfere with the performance of the sunblock additive or the meroterpene. Most preferably, the amount, if present will be insufficient to manifest any visible skin damage, including erythema, following exposure to UV light at levels which would manifest such damage with the same formulation containing the recited compound at its conventional concentration. The term "dermatologically-acceptable", as used herein, means that the

compositions or components thereof so described are suitable for use in contact with human skin without undue toxicity, incompatibility, instability, allergic response, and the like. Finally, all publications and patents references, including published patent applications, referenced herein are hereby incorporated herein in their entirety.

[0027] The first of the two critical ingredients of the sunscreen compositions of the present invention is the presence of a sunblock active that either absorbs or physically blocks UV-B radiation, e.g., UV-B and/or UV-A/UV-B sunblock actives. UV-B is the most damaging of ultraviolet radiation and, therefore, is the most important one to address. Also, because there are those who still desire a "natural" tan, the absence of a significant amount of UV-A sunblock active or a strongly UV-A type UV-A/UV-B sunblock active will still provide some protection against the harmful effects of UV exposure while still allowing the "tanning" waves to do their stuff. Indeed, such formulations may also contain an active ingredient that promotes tanning by amplifying the effects of UV light, e.g., melanin, L-tyrosine, tea oil, and green tea extracts. Most preferably, though, particularly since self-tanning agents such as DHA can be added to the sunscreen compositions, the sunscreen compositions of the present invention will be effective against both UV-A and UV-B and have either strong UV-A/UV-B sunblock actives or the presence of an additional UV-A sunblock active.

[0028] As noted earlier, sunblock actives are of two types, inorganic actives that work by reflecting the UV light and organic actives that work, predominately, by absorbing UV energy. The amount of the sunblock active to be incorporated into the sunscreen formulations is that which is conventional in the art. Typically, the amount is dependent upon, among other factors, the delivery means, e.g., is it applied as a spray or lotion; the stability of the active; the efficacy of the selected sunblock active itself; and the application rate, as well as the particular SPF desired. From the commercial perspective, another factor influencing the level of such sunblock actives in the sunscreen formulations is the regulatory limitations on their use. In the United States, for example, strict controls are placed upon the maximum level at which approved sunblock actives may be present. Similar regulatory/governmental controls may also dictate which sunblock actives may be used and at what amount in other countries as well.

[0029] Suitable organic sunblock actives include include, for example, avobenzone, butyl methoxydibenzoylmethane, cinoxate, benzophenone-8, dioxybenzone, homosalate,

octylsalate, menthyl anthranilate, octocrylene, ethyhexyl methoxycinnamate, octyl methoxycinnamate, octyl salicylate, oxybenzone, padimate O, ethylhexyl salicylate, benzophenone-3, p-aminobenzoic acid (PABA), ethylhexyl dimethyl PABA, glyceryl PABA, phenylbenzimidazole sulfonic acid, sulfisobezone, trolamine salicylate, 4-methylbenzylidene camphor, bisoctrizole, bemotrizinol, ecamsule, drometrizole trisiloxane, disodium phenyl dibenzimidazole tetrasulfonate, diethylamine hydroxybenzoyl hexyl bezoate, octyl triazone, hexyl benzoate, benzophenone-4, ethyhexyl triazone, diethylhexyl butamido triazone, bisimidazylate, polysilicone-15, etc.

[0030] Inorganic sunscreens include, but are not limited to, microfine surface treated titanium dioxide and microfine untreated and surface treated zinc oxide. The titanium dioxide in the sunscreen compositions preferably has a mean primary particle size of between 5 and 150 nm, preferably between 10 and 100 nm. Titanium oxide may have an anatase, rutile, or amorphous structure. The zinc oxide in the sunscreen compositions preferably has a mean primary particle size of between 5 nm and 150 nm, preferably between 10 nm and 100 nm. Examples of suitable hydrophobically modified titanium dioxide compositions include but are not limited to the following:

[0031] UV Titans® X161, M160, M262 (surface treated with stearic acid and alumina) (Kemira)

[0032] Eusolex ® T-2000 (surface treated with alumina and simethicone) (Merck KGaA)

[0033] T-Cote® (surface treated with dimethicone) (BASF)

[0034] Mirasun® TiW60 (surface treated with silica and alumina) (Rhodia)

[0035] Tayaca MT100T (surface treated with aluminum stearate) (Tayaca)

[0036] Tayaca MT-100SA (surface treated with silica and alumina) (Tayaca)

[0037] Tayaca MT-500SA (surface treated with silica and alumina) (Tayaca)

[0038] Tioveil® EUT, FIN, FLO, FPT, GCM, GPT, IPM, MOTG, OP, TG, TGOP (surface treated with silica and alumina, 40% dispersion in a range of cosmetic vehicle) (ICI)

[0039] Eusolex® T-45D (surface treated with alumina and simethicone, 45% dispersion in isononoylnonaoate) (Merck KGaA)

[0040] Eusolex® T-Aqua (surface treated with aluminum hydroxide, 25% dispersion in water) (Merck KGaA)

[0041] Examples of suitable untreated and hydrophobically modified zinc oxide include but are not limited to the following:

[0042] Z-Cote® (uncoated microfine zinc oxide) (BASF)

[0043] Z-Cote® HP-1 (surface treated with dimethicone) (BASF)

[0044] Sachtotec® LA 10 (surface treated with lauric acid) (Sachtleben)

[0045] Sachtotec® (uncoated microfine zinc oxide) (Sachtleben)

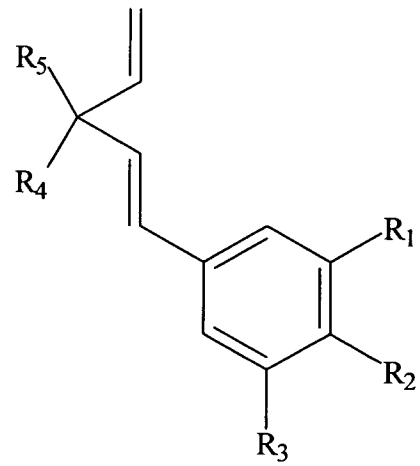
[0046] Spectraveil® FIN, IPM, MOTG, OP, TG, TGOP (uncoated, 60% dispersion in a range of cosmetic vehicle) (ICI)

[0047] Z-sperse® TN (untreated, dispersion in C_{12-15} alkyl benzoate) (Collaborative)

[0048] Z-sperse® TN (untreated, dispersion in octydodecyl neopentanoate) (Collaborative)

[0049] Most preferably, the sunscreen compositions of the present invention will comprise a combination of such sunblock actives. In this respect, it is well known that certain sunblock actives have better stability, hence longevity, than others; while others have better absorptive capabilities, whether in reference to selectivity for certain UV energy of certain wavelength(s) or cumulative absorptive capabilities. Hence, by using combinations of such UV sunblock actives, one is able to provide greater protection. Suitable combinations are well known in the art and within the skill of a typical artisan in the field.

[0050] The second critical component of the sunscreen compositions of the present invention is the meroterpene. Meroterpenes are terpenes having an aromatic ring and are generally of the following chemical structure (I):



wherein R_1, R_2, and R_3 are each independently selected from the group consisting of H, OH, OR_6 or CH_2R_6 where R_6 is linear or branched C_1 to C_8 alkyl; and R_4 and R_5 are each independently a linear or branched, C_1 to C_{20} alkyl or alkenyl group. Exemplary meroterpenes include Bakuchiol wherein R_1=R_3=H; R_2=OH, R_4=CH_3; R_5=CH_2CH_2CH=$C(CH_3)_2$ and Corylifolin wherein R_1=R_3=H; R_2=OH, R_4= R_5=CH_3.

[0051] Meroterpenes are typically derived from plants and plant extracts, though they have also been obtained from fungi as well as produced synthetically. Plants and plant extracts, though, remain the most common source of these compounds with *Psoralea coryfolia, Psoralea grandulosa,* and *Otholobium pubescens* (Fabaceae) being the more common of such plant sources. In the practice of the present invention, the meroterpene may be added as an isolated or purified material of at least 60% purity w/w, preferably at least 95% pure w/w, or it may be added in the form of a purified plant extract containing 1 to about 70% or more by weight meroterpene based on the total weight of the extract. As used herein the phrases "purified plant extract" and "purified extract" means that the extracts are purified to remove coumarins and other deleterious constituents, as discussed below, without specific isolation and recovery of the specific meroterpene and/or multiple fractions are combined or the collection time and temperatures for a given fraction are longer than would be used to isolate a specific meroterpene. Regardless of the nature or form of the meroterpene, the meroterpene must be free or substantially free of coumarins, especially furocoumarins like psoralene and iso-psoralene, and other like compounds that are skin sensitizers and/or enhance the detrimental effect of UV exposure. Because such materials are also found in the same plants and extracts, they are typically present in commercial grade meroterpenes and meroterpene extracts. For example, psorlens and iso-psoralens typically comprise 0.1 to 2% of the dry weight of the plant and seed source materials and from 1.0 to 20% by weight of the crude extracts thereof in organic solvents such as ethanol.

[0052] The preferred meroterpene for use in the practice of the present invention is Bakuchiol. Bakuchiol is a known bio-active material and has been used as an anti-tumor agent, an antimicrobial agent, an anti-inflamatory agent, a skin whitening agent, etc. It, in combination with pyridine aldehyde, has also been used in the treatment of pimples, acne, blackheads, herpes, and other skin disorders. However, its use is limited or at least tempered by the presence of high levels of psoralene and other furocoumarins. Although

psoralene is also a strong bio-active agent, - it is used in combination with UVA for the treatment of psoriasis and eczema – it greatly enhances the sensitivity of skin to the effects of UV exposure, significantly increasing the potential for sunburn. Consequently, the use of Bakuchiol and other meroterpenes, particularly those derived from plant sources, as a treatment has been limited to circumstances where sun exposure is not of concern or where precautions are taken to avoid sun exposure following treatment.

[0053] Recent developments, however, have been made in meroterpene production and recovery enabling one to prepare meroterpenes that are free or substantially free of coumarins, especially furocoumarins like psoralene and isopsoralene. For example, Indian patent publication # 00570/KOL/2005, (filed June 29, 2005 and published on January 13, 2006) which is incorporated herein by reference in its entirety, describes a method of purifying Bakuchiol from the extract of *Psoralea corylifolia* seeds. The method involves extraction of the plant material (powdered seeds) with a non-polar solvent like hexane or heptane. The extract solution is then treated with an alkali solution such as an alkali metal carbonate, bicarbonate or hydroxide to provide a 3-layered volume liquid, an organic layer, an emulsion layer and an aqueous layer. The organic layer is washed with water and dilute HCl and concentrated to a viscous mass. Concurrently, the emulsion layer is dissolved in a polar solvent like ethyl acetate and separated to remove the so-formed aqueous layer. The aforementioned viscous mass is then mixed with the ethyl acetate solution and concentrated to remove ethyl acetate and traces of the non-polar solvent. The concentrated mass is then subjected to high vacuum distillation, generally 1 mm to 0.1 mm at 139°C to 175° C. That fraction collected between the oil bath temperature of 190-270° C and vapor temperature range of 140-180° C is found to contain pure Bakuchiol, free or substantially free of psoralene and isopsoralene as well as other known constituents of such plant extracts such bavachicin, bavachin, angelicin, isobavachalcone, bakuchcin, and the like.

[0054] A similar method for the preparation of Bakuchiol that is free or substantially free of impurities, particularly furocoumarin impurities, is described in Jia et. al. – US 2006/0251749, which is incorporated herein by reference in its entirety. Jia et. al. describes a method wherein the plant source materials are subjected to an extraction and the extract solutions are then subject to hydrolysis with a basic solution such as aqueous sodium hydroxide. The resultant product is then purified by one of column

chromotography, extraction followed by crystallization, solvent partition, recrystallization, and combinations of the foregoing. Crude extracts purified in this way are said to be essentially free of furocoumarins such as psoralene and isopsoralene.

[0055] Other publications or patents that describe isolation or synthesis of meroterpenes include:

[0056] CN Backhouse, CL Delporte, RE Negrete, S Erazo, A Zuniga, A Pinto, BK Cassels, *J Ethnopharmacology*, 78(1):27-31, 2001.

[0057] H Haraguchi, J Inouye, Y Tamara, K Mizutani, *Planta Medica*, 66(6):569-571, 2000.

[0058] JM Krenisky, J Luo, MJ Reed, JR Carney, *Biol Pharm Bull*, 22(10):1137-1140, 1999.

[0059] H Katsura, R Tsukiyama, A Suzuki, M Kobayashi, *Antimicrobial Agents and Chemotherapy*, 45(11):3009-3013, 2001.

[0060] S Adhikari, R Joshi, BS Patro, TK Ghanty, GJ Chintalwar, A Sharma, S Chattopadhaya, T Mukherjee, *Chem Res Toxicol*, 16:1062-1069, 2003.

[0061] JB Perales, NF Makino, DL Van Vranken, *J Org Chem*, 67:6711-6717, 2002,

all of which are incorporated herein by reference in their entirety. These purified meroterpenes, especially the purified bakuchiol, may be obtained from Sytheon Ltd., of Lincoln Park, NJ, USA and Unigen Pharmaceuticals, Inc. of Lacey, WA, USA.

[0062] The meroterpene is present in the sunscreen compositions in an effective amount, that is, in an amount that reduces erythema from UV exposure as compared to the same formulation without the meroterpene. Generally speaking, sunscreen compositions according to the present invention will contain from about 0.1 to about 10, preferably from about 0.5 to about 5, weight percent of the meroterpene based on the total weight of the sunscreen composition. With this level of use, the visual manifestation of erythema following short term exposures to UV light may be avoided altogether as compared to sunscreen formulations without the meroterpene; whereas, longer exposures will result in erythema, but less pronounced and/or shorter lived as compared to sunscreen formulations without the meroterpene. When the meroterpene is added as a purified plant extract or as a purified material that also contains other components, the weight percent is based on the meroterpene content itself.

[0063] The third and final key component of the sunscreen compositions of the present invention is the carrier. The carrier is that material or combination of materials that is used to essentially carry or deliver the sunblock active(s) and meroterpenes to the skin. The specific carrier material will depend upon the delivery method itself. For example, as mentioned earlier, the sunscreen compositions may be in the form of lotions, creams, gels, foams, emulsions, dispersions, sprays, liposomes, coacervates, etc. Each composition will typically include any of the known topical excipients and like agents necessary for achieving the particular form, such excipients include, e.g., mineral oils and emulsifying agents. In its most simplest of embodiments, the carrier may be water, alcohol or water/alcohol combinations, or other solvent(s) or solvent systems in which the aforementioned actives may be, e.g., soluble, dispersed, emulsified, etc. Preferably, though, the sunscreen compositions will include excipients and the like that create a substantially stable, homogenous sunscreen compositions and/or provide body and viscosity to the sunscreen composition so that the actives do not merely run off the skin once applied. Typically, the carrier will comprise from about 30 to about 99 % by weight of the sunscreen composition.

[0064] Generally speaking, any known carrier or base composition employed in traditional sunscreen compositions may be used in the practice of the present invention. Suitable carriers and carrier compositions are described at length in, for example, Gonzalez et. al. - US 7,186,404; Aust et. al. - US 7,175,834; Roseaver et. al.– US 7,172,754; Simoulidis et. al. - US 7,175,835; Mongiat et. al. - US 7,101,536; Maniscalco – US 7,078,022; Forestier et. al. US 5,175,340, US 5,567,418, US 5,538,716, and US 5,951,968; Deflandre et. al. – US 5,670,140; Chaudhuri - US 6,831,191, US 6,602,515, US 7,166,273, US 6,936,735, and US 6,699,463; Chaudhuri et. al. - US 6,165,450 and US 7,150,876; Bonda et. al. US 6,962,692; and Wang et. al. US 5,830,441, all of which are incorporated herein by reference in their entirety. Those skilled in the art will readily recognize and appreciate what carriers may be employed in light of the intended form and/or delivery method for the inventive sunscreen compositions.

[0065] Though a carrier by itself is sufficient, the inventive sunscreen compositions of the present invention may, and preferably will, contain various other components typically associated with skin care products. For example, various skin care agents including, but not limited to, conventional skin care excipients as well as additional photoprotective

agents and skin lightening agents may be present. Such agents include, but are not limited to antioxidants, vitamins, anti-inflammatory agents, self-tanning agents, moisturizers, emollients, humectants, and the like, and mixtures thereof, in their conventional amounts. Exemplary agents and additive materials are described briefly below as well as in the aforementioned patents, especially Maniscalco – US 7,078,022.

[0066] Suitable antioxidants include, but are not limited to, water-soluble antioxidants such as sulfhydryl compounds and their derivatives (e.g., sodium metabisulfite and N-acetyl-cysteine), lipoic acid and dihydrolipoic acid, resveratrol, lactoferrin, and ascorbic acid and ascorbic acid derivatives (e.g., ascorbyl palmitate and ascorbyl polypeptide). Oil-soluble antioxidants suitable for use in the compositions of this invention include, but are not limited to, butylated hydroxytoluene, retinoids (e.g., retinol, tretinoin, and retinyl palmitate), tocopherols (e.g., tocopherol acetate), tocotrienols, alkylresorcinols, curcurmin and its derivatives and ubiquinone. Natural extracts containing antioxidants suitable for use in the compositions of this invention, include, but not limited to, extracts containing flavonoids and isoflavonoids and their derivatives (e.g., genistein and diadzein), extracts containing resveratrol and the like. Examples of such natural extracts include grape seed, green tea, pine bark, *Phyllanthus emblica* and propolis. Other examples of antioxidants may be found on pages 1612-13 of the ICI Handbook as well as in Ghosal – US 6,124,268, both of which are incorporated herein by reference in their entirety.

[0067] The sunscreen compositions of the present invention may also include one or more vitamins and/or their derivatives. Vitamins and vitamin derivatives include, for example, vitamin A, vitamin A propionate, vitamin A palmitate, vitamin A acetate, retinol, vitamin B, thiamine chloride hydrochloride (vitamin B.sub.1), riboflavin (vitamin B.sub.2), nicotinamide, vitamin C and derivatives (for example ascorbyl palmitate, magnesium ascorbyl phosphate, ascorbyl acetate), vitamin D, ergocalciferol (vitamin D.sub.2), vitamin E, DL-.alpha.-tocopherol, tocopherol E acetate, tocopherol hydrogensuccinate, vitamin K.sub.1, esculin (vitamin P active ingredient), thiamine (vitamin B_1), nicotinic acid (niacin), pyridoxine, pyridoxal, pyridoxamine, (vitamin B_6), pantothenic acid, biotin, folic acid and cobalamine (vitamin B_{12}). Preferred vitamins are, for example, vitamin A palmitate, vitamin C and derivatives thereof, DL-α-tocopherol, tocopherol E acetate, nicotinic acid, pantothenic acid and biotin. Vitamin E, which is often added to cosmetic and personal care products is also preferably stabilized by the

compounds according to the invention. Additional preferred vitamins are Vitamin C and K and derivatives thereof.

[0068] Suitable emollients include those agents known for softening the skin which may be selected from hydrocarbons, fatty acids, fatty alcohols and esters. Petrolatum is a common hydrocarbon type of emollient conditioning agent. Other hydrocarbons that may be employed include alkyl benzoate, mineral oil, polyolefins such as polydecene, and paraffins, such as isohexadecane. Fatty acids and alcohols typically have from about 10 to 30 carbon atoms. Illustrative are myristic, isostearic, hydroxystearic, oleic, linoleic, ricinoleic, behenic and eruicic acids and alcohols. Oily ester emollients may be those selected from one or more of the following, triglyceride esters, acetoglyceride esters, ethoxylated glycerides, alkyl esters of fatty acids, ether esters, polyhydric alcohol esters and wax esters. Additional emollients or hydrophobic agents include C_{12} to C_{15} alkyl benzoate, dioctyladipate, octyl stearate, octyldodecanol, hexyl laurate, octyldodecyl neopentanoate, cyclomethicone, dicapryl ether, dimethicone, phenyl trimethicone, isopropyl myristate, capriylic/capric triglycerides, propylene glycol dicaprylate/dicaprate and decyl oleate.

[0069] Suitable humectants include various polyhydric alcohols, especially polyalkylene glycols and, more preferably, alkylene polyols and their derivatives. Exemplary humectants include propylene glycol, dipropylene glycol, polypropylene glycol, polyethylene glycol, sorbitol, 2-pyrrolidone-5-carboxylate, hydroxypropyl sorbitol, hexylene glycol, ethoxydiglycol 1,3-butylene glycol, 1,2,6-hexanetriol, glycerin, ethoxylated glycerin, propoxylated glycerin, compatible solutes, such as ectoin, hydroxectoin, taurines, carnithine, acetyl carnithine and mixtures thereof. When employed in effective amounts, generally from 1 to 30%, preferably from 2 to 20%, by weight of the sunscreen composition, these additives serve as skin moisturizers as well as reduce scaling and stimulate the removal of built-up scale from the skin.

[0070] Examples of ant-inflammatory ingredients include, but are not limited to, bisabolol, curcurmin and its derivatives, retinoids, flavonoids and other polyphenolics etc. These and other anti-inflammatory agents, as well as additional anti-oxidants and the like, are disclosed in Gupta et. al. – US 2005/0048008A1, which is incorporated herein by reference in its entirety.

[0071] Examples of self-tanning ingredients include, but are not limited to, dihydroxyacetone and erythrulose.

[0072] The sunscreen compositions of the present invention may also include one or more skin penetrants. These are additives that, when applied to the skin, have a direct effect on the permeability of the skin barrier: increasing the speed with which and/or the amount by which certain other compounds are able to penetrate into the skin layers. Exemplary organic penetration enhancers include dimethyl sulfoxide; isopropyl myristate; decyl, undecyl or dodecyl alcohol; propylene glycol; polyethylene glycol; C_{9-11}, C_{12-13} or C_{12-15} fatty alcohols; azone; alkyl pyrrolidones; lecithin; etc. Surfactants can also be used as penetration enhancers. In the case of meroterpenes, penetrants have the benefit of carrying the meroterpene into the skin faster than it might otherwise penetrate on its own: thereby expediting and, possible, enhancing the benefit of the meroterpene.

[0073] Other optional adjunct ingredients for the sunscreen compositions of the present invention include preservatives, waterproofing agents, fragrances, anti-foam agents, plant extracts (Aloe vera, witch hazel, cucumber, etc), opacifiers, stabilizers, skin conditioning agents colorants, and the like, each in amounts effective to accomplish their respective functions.

[0074] The sunscreen compositions of the present invention are effective in reducing or preventing skin damage due to UV exposure, especially exposure to the sun. As such, the present invention also pertains to a method of protecting skin from damage due to UV exposure said method comprising the step of applying of the aforementioned sunscreen compositions to skin. In particular, the present invention provides a method of reducing or preventing erythema resulting from exposure to UV light. Generally speaking, the method comprises the step of applying the sunscreen composition to areas of the skin that are or may be exposed to the sun. It may also be desirable to apply the sunscreen composition to areas that are not typically exposed to the sun but that nevertheless have exposure to the penetrating UV rays. For example, tee shirts and other light fabrics offer minimal protection against sun exposure, especially to UV rays. Thus, conceivably, the inventive sunscreen compositions may be applied to essentially all areas of the body, including those typically covered by clothing.

[0075] The amount of the sunscreen composition that is to be applied to the skin is consistent with that amount applied with respect to sunscreen formulations without the

meroterpene. To some extent, the amount depends upon the form of the sunscreen composition and its mode of application. For example, a spray formulation may be applied so as to provide a light, even coat on the skin. Lotions, creams, gels and the like are typically applied at a rate of about 1 to 2 ounces (29.6 to 59.2 ml) for the entire body, i.e., for the exposed skin of a "average individual" wearing a swimsuit and standing 5 feet 4 inches (1.63 m) tall, weighing 150 pounds (68.3 kg), and having a 32 inch (0.81 m) waist. This translates to an application rate of about 2 mg/cm^2 of skin. On the face, a typical application rate is ¼ to 1/3 of a teaspoon (1.2 to 1.7 ml). Generally speaking, the application rate will be from about 0.1 to about 10 mg/cm^2, preferably from about 1 to about 3 mg/cm^2, of skin.

[0076] To be most effective, the sunscreen composition should be applied before sun exposure, preferably at lest 15 minutes before, and reapplied at least every 2 hours or more frequently, especially if the individual engages in activities/actions that may cause the sunscreen composition to wear or wipe off, e.g., swimming; washing dishes, windows, etc.; washing hands and/or face; contact sports activities; activities that promote substantial sweating; etc.

[0077] In addition to the above-mentioned photo-protective benefits of the inventive sunscreen compositions, the continual, preferably daily, use of the sunscreen compositions of the present invention, regardless of whether one anticipates UV exposure or not, provides a number of additional benefits to ones skin. For example, the continual use of these sunscreen compositions will delay the appearance of fine lines, enhance extracellular matrix cohesion, reduce the appearance of spider veins, improving skin firmness and elasticity: skin effects that are not only a result of exposure to the sun but also the natural aging process. In essence, the long-term benefits of the continual use of the sunscreen compositions of the present invention include the lessening or delayed manifestation, possibly even the prevention or repair, of skin damage and will manifest itself in an overall improved skin quality as compared to skin on which meroterpene-free sunscreens had been applied and, most especially, to which no sunscreen product had been applied on an on-going basis. For example, the long-term use of the inventive sunscreen compositions may help with thickening the keratinous tissue (i.e., building the epidermis and/or dermis layers of the skin), thereby preventing and/or retarding atrophy of human skin; preventing and/or retarding the appearance of spider veins and/or red blotchiness on

human skin; preventing and/or retarding the appearance of dark circles under the eye; preventing and/or retarding sallowness and/or sagging of human skin; soften and/or smooth lips; preventing and/or relieving itch of human skin, regulating skin texture (e.g. wrinkles and fine lines), improving skin color (e.g. redness, freckles); and the like.

[0078] **EXAMPLES**

[0079] Having described the invention in general terms, Applicants now turn attention to the following examples in which specific formulations and applications thereof are evaluated. In the foregoing and in the following examples, unless otherwise indicated, all temperatures are set forth in degrees Celsius and all parts and percentages are by weight.

[0080] **Bakuchiol and Corylifolin**

[0081] Purified Bakuchiol and Corylifolin for use in the following examples were obtained by the method described by RK Tikare and P Pujari (Indian patent application 00570/KOL/2005; publication date January 13, 2006). Specifically, seeds of *Psoralea Corylifolia* were powdered and subjected to extraction using a non-polar solvent, hexane, in a ratio of 3 ml solvent for each gram of powdered seed. The mix was stirred with heating at 60° C for 4 hrs and then filtered to separate the extract solution. The extraction was repeated three more times, for a total of four extractions on each sample of the powdered seed material, to increase the yield. Extract solution collected from all four batches was combined and the total volume reduced by distilling off excess solvent until the remaining volume was about one-half the original volume. The concentrated solution was then treated/washed with 7.5 L of an alkali solution (5 % NaOH) twice. The alkali treatment produced three layers: an organic layer, an emulsion layer and an aqueous layer. The organic layer was washed with an equal volume of water and dilute HCl and subsequently concentrated to produce a viscous mass. The emulsion layer from the alkali washing was dissolved in a polar solvent, ethyl acetate, to isolate and remove any water that may have been present in the original emulsion layer. The remaining ethyl acetate solution was then combined with organic layer viscous mass, produced above, and the mixture concentrated by distillation to remove ethyl acetate and any remaining hexane. The concentrated mass was then subjected to high vacuum distillation and various fractions collected. Those fractions collected between oil bath temperatures of 190°C and 270°C and vapor temperature of from 140°C to 180°C were found to contain pure Bakuchiol with less than 0.05% by weight psoralene and isopsoralene. Those fractions

collected between oil bath temperatures of 140 °C and 190°C and vapor temperature of from 90°C to 150°C were subjected to column chromatographic purification to obtain pure Corylifolin with less than 0.1% psoralene. Purity was determined by HPLC analysis using a sample concentration of ≈ 0.5 mg/ml in acetonitrile , using a mobile phase composition of acetonitrile and water (70/30) with a flow rate of 1.0 ml/min., and a UV detector set at λ_{max}261 nm.

[0082] **Example 1**: Reduction of UV-induced Erythema

[0083] Erythema, the most familiar manifestation of UV radiation exposure, occurs in a biphasic manner. UV-A mediates the early part of this reaction, known as immediate pigment darkening (IPD) and lasts for about half-hour. Delayed erythema, a function primarily of UV-B dosages, begins 2-8 hours after exposure and reaches a maximum in 24-36 hours, with erythema, pruritius, and pain in the sun-exposed areas.

[0084] Microscopically, changes are detectable as early as 30 minutes after UV radiation exposure. Epidermal changes include intracellular edema, vacuolization and swelling of melanocytes, and the development of characteristic sunburn cells. In the dermis, UV radiation initially leads to interstitial edema and endothelial cell swelling. Later, there is perivenular edema, degranulation, and loss of mast cells, a decrease in the number of Langerhans cells, neutrophil infiltration, and erythrocyte extravasation.

[0085] In order to evaluate the anti-erythematic properties of the sunscreen compositions of the present invention, a sample lotion, free of sunscreen actives, but containing the purified bakuchiol, was applied to subjects who were then subjected to prolonged UV exposure. The sunscreen active was omitted so as expedite/exaggerate the manifestation of erythema that might otherwise be found with the sunscreen actives present. The lotion evaluated comprised the formulation set forth in Table 1.

[0086] The lotion was prepared by combining the Phase 1 ingredients, and then dispersing the Phase A-2 ingredient in the combined Phase A-1 composition while stirring and heating to a temperature of 75°C. Concurrently, the ingredients of Phase B were combined and heated to 75°C. Phase B was then added to Phase A with good mixing. Thereafter, the combined Phase A and B were homogenized at moderate speed, while adding Phases C and D. The complete mixture was allowed to cool to room temperature with constant propeller agitation until a homogeneous mixture was attained. The resultant

mixture was found to have a pH of 6.20 and viscosity of 20,000 mPas (Brookfield RVT, Spindle C, 10 rpm) at 25°C.

TABLE 1

Ingredient	Trade Name / Supplier	wt%
Phase A-1		
Water	Water(demineralized)	78.70
Disodium EDTA	Versene Na/Dow	0.10
Glycerine	Emery 916/Cognis	3.00
Phase A-2		
Xanthan Gum	Vanzan NF/Vanderbilt	0.20
Phase B		
Caprylic /Capric Triglyceride	Myritol 318/Cognis	6.00
Squalane	Fitoderm/Centerchem	1.00
Cetyl Esters	Crodamol SS/Croda	1.00
Cetyl Alcohol	Crodacol C-70/Croda	1.00
Dimethicone	Dow Corning 200,50 cst/Dow Corning	2.00
Glyceryl Stearate, PEG-100 Stearate	Arlacel 165/Uniquema	3.50
Bakuchiol	***Sytenol™ A / Sytheon***	1.00
Phase C		
Hydroxyethyl Acrylate/Sodium Acryloyldimethyl Taurate Copolymer & Squalane & Polysorbate 60	Simulgel NS/Seppic	1.50
Phase D		
phenoxyethanol, Methylparaben, propylparaben,Ethylparaben	Phenonip XB.Clariant	1.00
Total		100.00

[0087] In preparing for the erythema test, a 50 cm^2 test site on the backs of eleven human volunteers was subjected to seven UV exposures: the first lasting 25 seconds and each subsequent exposure lasting 25% longer than the previous, each exposure being made to a different portion of the test site. 16 to 24 hours later, the exposed areas of the human volunteers were evaluated using a chromameter to assess their MEDs (Minimal Erythematic Dose). Thereafter, the test lotion was applied at a rate of 2 mg/cm^2 twice a day for seven days to a test site measuring 4 cm x 2.5 cm on the backs of each human volunteer. Following the completion of the application protocol, the test site and an untreated site of each volunteer were irradiated at 2x their MED. 16 to 24 hours following irradiation, the L and b parameters on both the treated and untreated sites were measured using a Chromameter. The changes in L values and ITA.degree (Individual Topology

Angle – COLIPA SPF test method) were determined to assess erythema. ITA.degree. was calculated using the formula:

ITA.degree.=[Arc Tangent(L*-50)/b*)]180/3.1416

wherein L*value—lightness and b*--color in blue-yellow axis. Table 2 presents the average L and ITA values of the treated and untreated skin for all human volunteers prior to irradiation or UV exposure ("Pre-Irr") and following irradiation or UV exposure ("Post-Irr"). Table 2 also sets forth the delta or change in these values.

TABLE 2

	Pre-Irr	**Post-Irr**	**Δ L or ΔITA value**
L-value (treated)	65.69	66.25	0.56
L-value (untreated)	66.45	60.71	-5.74
ITA (treated)	43.97	46.83	-2.86
ITA (untreated)	46.05	36.76	9.29

[0088] As indicated by the results shown in Table 2, the degree of erythema as measured by a mechanical chromometer was markedly reduced in those areas that were treated with the bakuchiol containing lotion as compared to the untreated areas. To the naked eye, erythema in the treated areas was barely detectable though readily visible in the untreated areas. These results were surprising inasmuch as commercial grade Bakuchiol when used in skin treatments for, e.g., psoriasis, is shown to increase erythema.

[0089] **Example 2**: Collagenase Inhibitory Activity

[0090] In order to ascertain whether other benefits may be attained by the use of meroterpenes in sunscreen formulations, a study was conducted on the impact, if any, the presence of bakuchiol may have on collagenase: a collagenolytic enzyme responsible for much of the collagen damage associated with UV exposure and photoaging in general. Collagenase activity was measured with an Enzcheck kit from Molecular Probes (Carlsbad, CA, USA) using quenched fluorescent gelatin and Clostridium collagenase IV, a generic metalloproteinase. Test material (aqueous solutions 1000ug/ml, 100ug/ml, 10ug/ml and 1ug/ml made from 10mg/ml stock in DMSO) was incubated in the presence of collagenase substrate - quenched fluorescin-linked gelatin and in the presence of the proteolytic enzyme. Phenanthroline, a potent metalloprotease (MP) inhibitor was used as

positive control at 100ug/ml. The kinetics of the release of the digested, fluorescent gelatin were measured at excitation/emission wavelengths of 485/530nm with Millipore Cytofluor 2350 microfluorometer. Collagenase inhibitory concentration 50% (IC_{50}) for the purified Bakuchiol was found to be ~0.1% (w/w).

[0091] These results indicate that the sunscreen formulations in accordance with the present invention would be expected to offer significant inhibition of collagenase as well as other damaging metalloproteiniase arising from UV exposure.

[0092] **Example3**: Elastase Inhibitory Activity

[0093] While collaginase is perhaps the enzyme most responsible for the manifestation of skin damage due to exposure to UV light, another enzyme whose activity is induced by UVA irradiation and other inflammatory processes, and which is a likely contributor to the process of photoaging, is elastase. Elastase is a protease capable of breaking down connective tissue components, especially elastin, an elastic fiber that, together with collagen, determines the mechanical properties of connective tissue. Overproduction of elastase by dermal fibroblasts has been associated with skin diseases such as cutis, laxa, acquired cutis laxa, mild dermal elastolysis, pseudoxanthoma elasticum and solar elastosis.

[0094] In an effort to ascertain whether the use of meroterpenes in sunscreen formulations would also affect elastase production and/or activity, a comparative study was conducted evaluating the impact of Retinol, a known skin enhancing compound, and bakuchiol on elastase activity. Stock solutions of the two actives were prepared by dissolving bakuchiol (Sytenol A, available from Sytheon Ltd of Lincoln Park, NJ, US) and Retinol 50C (available from BASF of Florham Park, NJ, US) in DMSO to a concentration of 10 mg/ml. Test solutions of each active (aqueous solutions 25 ug/ml, 5 ug/ml and 1 ug/ml made from the 10 mg/ml stock solutions in DMSO) were incubated with pure human neutrophil elastase (Elastase, Human Neutrophil, Cat. No. 324681, available from Calbiochem of San Diego, CA, US) and its substrate (Elastase Substrate VIII, Colorimetric (Suc-Ala-Ala-Ala-pNA), Cat. No. 03-32-0009, available from Calbiochem of San Diego, CA, US): each system was tested in triplicate. Controls were also employed: the first, Type 1 water served as the negative control and Elastase Inhibitor III (Cat. No. 324745, available from Calbiochem of San Diego, CA, US) served as the positive control at a concentration of 150 ug/ml. The proteolytic activity of elastase in the presence of the

test materials was measured by following the generation of a chromophoric reaction product at 410 nm using a BioRad microplate reader.

[0095] The results of the comparative study are presented in Table 3. Elastase activity is presented as the percent (%) of the positive control, with the negative control (water) as the 100% of control. In the table, the results are further presented as the average of the three individual test runs. As indicated, Retinol had no statistically significant elastase inhibitory effect at all concentrations tested: indeed, at all but the lowest levels tested, elastase activity appeared greater than if no active were present at all. Conversely, the use of bakuchiol, in accordance with the practice of the present invention demonstrated a clear elastase inhibition at all concentrations tested. The positive control, Elastase Inhibitor III, showed complete inhibition of elastase activity. Based on these results, it appears that the theoretical Effective Dose 50% (ED50) for Sytenol is between 1 and 5 ug/ml. Interesting, both actives showed a reverse dose-response trend. These results, together with the results of Example 2 above indicate that the sunscreen formulations in accordance with the present invention would be expected to offer significant inhibition of skin damaging enzymatic activities, especially those associated with elastase, collagenase as well as other damaging metalloproteiniase, arising from UV exposure.

Table 3 - Elastase Activity (% of Control)

Active	Control	25 ug/ml	5 ug/ml	1 ug/ml
EI III* (150 ug/ml)	0			
Retinol		416	138	87
Bakuchiol		77	65	31
Type 1 Water	100			

* Elastase Inhibitor III

Example 4: Skin Sensitivity

[0096] Given the known sensitivity issues associated with commercial grade bakuchiol, evaluation of the skin sensitivity to the purified bakuchiol was also evaluated. Skin sensitivity was evaluated following the method cited in the reference Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics, published by The Association of Food and Drug Officials of The United States. The method employs nine inductive patching and not the ten cited in the reference under occlusive patch conditions.

[0097] Samples were prepared for evaluation by diluting the purified Bakuchiol in corn oil to a 5% concentration, with dilutions freshly prepared on each application day.

0.2 ml or 0.2 g of the diluted test material was dispensed onto the occlusive, hypoallergenic patch and the treated patch applied directly to the skin of the infrascapular regions of the back, to the right or left of the midline of each subject: one hundred and eleven subjects were employed. After application of the patch, each subject was dismissed with instructions not to wet or expose the test area to direct sunlight. The patch was removed by the subject after 24 hours. This procedure was repeated every Monday, Wednesday and Friday for three consecutive weeks until a series of nine consecutive 24 hour exposures had been made. During the test period, the test area on the subjects' backs were observed for evidence of edema or erythema just before applications two through nine and the next test date following application nine. If evidence of a reaction was found, the area of edema and/or erythema was then measured and recorded: edema being estimated by an evaluation of the skin with respect to the contour of the unaffected normal skin. The subjects were then given a 10 - 14 day rest period after which a challenge or retest dose was applied once to a previously unexposed test site. The retest dose was equivalent to any one of the original nine exposures. Reactions were scored 24 and 48 hours after application. Based on the test results, the 5% dilution in corn oil of the purified bakuchiol was determined to be a NON-PRIMARY IRRITANT and a NON-PRIMARY SENSITIZER according to the reference.

[0098] **Example 5**: Sunscreen Formulations 5A – 5J

[0099] The following tables set forth various formulations and embodiments of sunscreens according to the present invention. Following each table is a brief description of the process by which each formulation is made.

[0100] Formulation 5A: Sunscreen Lotion

INCI Name	Trade Name / Supplier	% W/W
Phase A		
Water (demineralized)		57.25
Disodium EDTA		0.10
Propylene Glycol		2.00
Sorbitol	Sorbo (70% soln.)/Uniqema	2.00
Sodium Lauryl Sulfate	Stepanol ME-Dry/Stepan	0.15
Phase B		
Glyceryl Stearate	Tegin M/Goldschmidt	5.00
Stearic acid	Emersol 132/Cognis	1.00
Persea Gratissima (Avocado) oil Unsaponifiables	Crodarom Avocadin/Croda	15.00

Avobenzone (sunscreen)	Eusolex 9020 / EMD	2.00
Diethylhexyl syringylidene malonate (photostabilizer)	Oxynex ST / EMD	2.00
Homosalate (sunscreen)	Eusolex HMS / EMD	10.00
Beeswax	White Bleached NF Beeswax Prills/Ross	1.50
Bakuchiol	Present Invention	1.00
Phase C		
Triethanolamine	TEA 99%/Union Carbide	qs
Phase D		
Propylene glycol, DMDM Hydantoin, Methylparaben	Paragon/McIntyre	1.00
Total		100.00

[0101] Formulation 5A is prepared by separately combining the ingredients of Phases A and B and heating each mixture to 70-75°C. Thereafter, Phases A and B are combined while stirring. The pH is adjusted to 5.0-6.0 by the addition of Phase C to the mixture of Phases A and B. Subsequently, Phase D is added with mixing until a uniform, substantially homogenous mixture is attained.

[0102] Formulation 5B – Daily Sunscreen Lotion

INCI Name	**Trade Name / Supplier**	**% W/W**
Phase A-1		
Water (demineralized)		48.18
Disodium EDTA		0.05
Propylene Glycol		5.00
Niacinamide		2.00
Phase A-2		
Xantham Gum	Vanzan NF/Vanderbilt	0.25
Magnesium aluminum stearate	Veegum Ultra granules/Vanderbilt	0.40
Phase B		
Cetearyl alcohol and cetearyl glucoside	Montanov 68/Seppic	7.00
Apricot kernel oil	Lipovol P/Lipo	5.00
Octyl stearate	Cetiol 868/Cognis	3.00
Dimethicone	Dow Corning 200 fluid 10cst/Dow Corning	6.00
Octinoxate (sunscreen)	Eusolex 2292 / EMD	7.5
Homosalate (sunscreen)	Eusolex HMS / EMD	12.5
***Psoralea corylifolia* purified plant extract containing 65% Bakuchiol**	**Present Invention**	**2.00**
Phase C		
Triethanolamine	TEA 99%/Union Carbide	0.12

Phase D		
Phenoxyethanol, Isopropylparaben, Isobutylparaben, butylparaben	Liquapar PE/Sutton	1.00
Total		100.00

[0103] Formulation 5B is prepared by separately combining the constituents of each of Phases A-1 and A-2. Thereafter, Phase A-2 is dispersed in Phase A-1 and heated to 70-75°C. The mixture of Phase B is then heated to 70-75°C and added to the Phase A-1/A-2 dispersion with constant stirring. The mixture is homogenized until it cools to 60°C. Thereafter the pH is adjusted to 4.0-5.0 using Phase C. Thereafter, Phase D is added to the mixture and the mixture continually mixed until uniform, substantially homogeneous lotion is achieved.

[0104] Formulation 5C: Skin Rejuvenating Sunscreen Lotion

INCI Name	**Trade Name / Supplier**	**% W/W**
Phase A-1		
Water (demineralized)		43.65
Disodium EDTA		0.05
Propylene Glycol		5.00
Phase A-2		
Xanthan Gum	Vanzan NF/Vanderbilt	0.20
Phase B		
PEG-6 stearate, ceteth-20, glyceryl stearate, steareth-20, stearic acid	Tefose 2561/Gattefosse	10.00
Stearic Acid	Emersol 132/Cognis	1.00
Hydrogenated castor oil	Cutina HR/Cognis	1.00
Octyldodecyl myristate	M.O.D./Gattefosse	8.00
Dimethicone	Dow Corning 200, 50cst/Dow Corning	4.00
Phenyltrimethicone	Dow Corning 556 Wax/Dow Corning	2.00
Avobenzone (sunscreen)	Eusolex 9020	3.00
Octocrylene (sunscreen)	Eusoloex OCR	7.00
Homosalate (sunscreen)	Eusolex HMS	10.00
Phase C		
Sweet Almond oil	Cropure Almond/Croda	3.00
Bakuchiol	**Present Invention**	**1.00**
Phase D		
Triethanolamine	TEA 99%/Union Carbide	0.10
Phase E		
Phenoxyethanol, Isopropylparaben, Isobutylparaben, butylparaben	Liquapar PE/Sutton	1.00
Total		100.00

[0105] Formulation 5C is made by dispersing Phase A-2 in the pre-mixed Phase A-1 and heating to 70-75°C. Concurrently, the ingredients of Phase B are combined and heated to 70-75°C and then that mixture added to the Phase A-1/A-2 mixture while stirring. The combined mix is homogenized until the mixture cools to 60°C. Phase C is then added at 40°C. The pH is then adjusted to 5.0-6.0 with phase D. Thereafter, Phase E is added and mixed until a uniform, substantially homogeneous mixture is attained.

[0106] Formulation 5D: Broad-Spectrum Sunscreen

INCI Name	Trade Name	% W/W
Phase A		
Avobenzone (sunscreen)	Eusolex 9020	1.00
Glyceryl Stearate, Cetareth-15	Tego Care 215, Pellets	3.00
Decyl Oleate	Cetiol V	5.00
Isopropyl Palmitate	-	5.00
Dimethicone	Mirasil DM 350	0.50
Stearyl Alcohol	Lanette 18	2.00
Carbomer	Carbopol ETD 2050	0.10
Phase B		
Glycerin (about 87%)	Glycerol	3.00
Ectoin	RonaCare Ectoin	0.50
Preservative		1.00
Water, Ethyhexyl methoxycinnamate (sunscreen), Silica, PVP, Chlorphenesin, BHT	Eusolex UV-Pearls OMC	15.00
Water	Water, deminaralized	q.s
Phase C		
Corylifolin	Present Invention	0.50
Phase D		
Sodium hydroxide	Sodium hydroxide, 10% solution	0.45
Phase E		
Perfume	Fragrance "Delicat"	0.20
Total		100.00

[0107] The ingredients of Phase A and Phase B are separately combined and each mixture heated to 80°C. Phases A and B are then combined with constant stirring. The combined mix is homogenized until the mixture cools to 60°C. Phase C is then added at 40°C. The pH is then adjusted to 5.0-6.0 with phase D. Thereafter, Phase E is added and mixed until a uniform. Substantially homogeneous mixture is attained.

[0108] Formulation 5E: Sunburn Responsive and Skin Rejuvenating Sunscreen

INCI Name	**Trade Name / Supplier**	**% w/w**
Phase A-1		
Water (demineralized)		42.20
Disodium EDTA		0.05
Propylene Glycol		5.00
Phase A-2		
Xantham Gum	Vanzan NF/Vanderbilt	0.20
Phase B		
PEG-6 stearate, ceteth-20, glyceryl stearate, steareth-20, stearic acid	Tefose 2561/ Gattefosse	10.00
Stearic Acid	Emersol 132/Cognis	1.00
Hydrogenated castor oil	Cutina HR/Cognis	1.00
Octyldodecyl myristate	M.O.D./Gattefosse	8.00
Dimethicone	Dow Corning 200, 50cst/Dow Corning	4.00
Phenyltrimethicone	Dow Corning 556 Wax/Dow Coning	2.00
Avobenzone (sunscreen)	Eusolex 9020 / EMD	1.00
Octocrylene (sunscreen)	Eusolex OCR / EMD	2.00
Homosalate (sunscreen)	Eusolex HMS / EMD	10.00
Phase C		
Sweet Almond oil	Cropure Almond/Croda	3.00
Bisabolol	Bisabolol/Rona	1.00
Corylifolin	**Present invention**	**2.00**
Phase D		
Phyllanthus emblica fruit extract	Emblica / EMD	0.50
Water (dimineralized)		5.00
Phase E		
Aminomethyl propanol		0.05
Phase F		
Phenoxyethanol, Isopropylparaben, Isobutylparaben, Butylparaben	Liquapar PE/Sutton	1.00
Total		100.00

[0109] Formulation 5E is made by separately combining the components of Phase A-1 and Phase A-2. Phase A-2 is then dispersed in Phase A-1 and heated to 70-75°C. Concurrently, the ingredients of Phase B are combined and heated to 70-75°C and then that mixture added to the Phase A-1/A-2 dispersion while stirring. The combined mix is homogenized until the mixture cools to 60°C. Phase C is then added at 30°C with constant stirring using a propeller mixer. The pH is then adjusted to 5.0-6.0 with phase D.

Thereafter, Phases E and F are sequentially added and mixed under dark conditions until a uniform mixture is attained.

[0110] Formulation 5F: Anhydrous Oil-Free Sunscreen Gel

INCI Name	**Trade Name / Supplier**	**%W/W**
Phase A		
Ozokerite	White Ozokerite SP-1020/Strahl & Pitsch	3.00
Cyclomethicone	Dow Corning 345 Fluid/Dow Corning	20.00
Cyclomethicone (and) Polysilicone-11	Gransil GCM/Grant Industries	52.50
Octinoxate (sunscreen)	Eusolex 2292 / EMD	7.50
Homsalate (sunscreen)	Eusolex HMS / EMD	5.00
Phase B Bismuth Oxychloride	Biron® LF-2000/Rona	2.00
Phase C Cyclomethicone	Dow Corning 345 Fluid/Dow Corning	3.60
Cyclomethicone (and) Dimethicone Crosspolymer	Dow Corning 9040 Silicone Elastomer Blend/Dow Corning	5.40
Bakuchiol	**Present Invention**	**1.00**
Total		100.00

[0111] Formulation 5F is prepared by blending the Phase A ingredients while heating to 70-75°C and mixing until clear and uniform mixture is obtained. Phase B is then dispersed in the Phase A mixture with mixing. The Phase C ingredients are separately blended until the mixture is smooth and substantially free of lumps. The Phase A/B mixture is then cooled to 50 - 60° C and Phase C added with mixing until a substantially uniform mixture is obtained.

[0112] Formulation 5G: Self-Tanning Sunscreen Spray Lotion

INCI Name	**Trade Name / Supplier**	**% w/w**
Phase A		
Glyceryl Stearate, Ceteareth-20, Cetearyl Alcohol, Ceteareth-12, Cetyl Palmitate	Emulgade SE/Henkel	4.50
Ceteareth-20	Eumulgin B2/Henkel	1.00
Dicapryl Ether	Cetiol OE/Henkel	5.00
Coco Caprylate/Caprate	Cetiol LC/Henkel	5.00
Octinoxate (sunscreen)	Eusolex 2292 / EMD	7.00
Octisalate (sunscreen)	Eusolex OS / EMD	5.00
Oxybenzone (sunscreen)	Eusolex 4360 / EMD	2.00
Phase B		
Demineralized water		39.45
Disodium EDTA		0.05
Phase C		
3-Hydroxy Bakuchiol	**Present invention**	**1.50**
Phase D		
Demineralized water		20.00
Propylene glycol		2.50
Dihydroxyacetone	Dihydroxyacetone/EMD	6.00
Propylene Glycol (and) DMDM Hydantoin (and) Methylparaben	Paragon/McIntyre	1.00
Total		100.00

[0113] Formulation 5G is prepared by combining the Phase A ingredients while stirring and heating to 80-85°C. Phase B is heated to 80-85°C and slowly Phase A is added to Phase B while stirring with a propeller mixer. Homogenize the Phase A/B mixture and allow the mixture to cool to around 40°C. Phase C is then added and mixed well. Separately, the ingredients of Phase D are combined at room temperature by stirring. Once the Phase A/B/C mixture is cooled to 30°C, Phase D is then added with mixing. If necessary, the pH may be adjusted to 3.5-4.0 using citric acid. The mixture should have a viscosity < 100 cps as measured by a Brookfield RV#1, 50 rpm @ 23 °C.

[0114] Formulation 5H: Sunscreen Cream

INCI name	**Trade Name/Supplier**	**% w/w**
Phase A		
Titanium Dioxide (sunscreen), Alumina, Simethicone	Eusolex® T-2000/Rona	10.00
Polyglyceryl-2 Dipolyhydroxystearate	Dehymuls PGPH/Cognis	4.00
Polyglyceryl-3 Diisostearate	Lamaform TGI FL/Cognis	2.00
Beeswax	Beeswax White SP 422/Strahl & Pitsch	3.00
Isostearic Acid	Emersol 871/Cognis	1.00
Zinc Stearate	Unichem ZS/Universal Preser-A-Chem	1.00
Dicaprylyl Carbonate	Cetiol CC/Cognis	11.00
Tocopherol (antioxidant)	Vitamin E/Hoffmann- La Roche	2.00
3-Hydroxy Bakuchiol	**Present Invention**	**5.00**
Propylparaben	Nipasol M/Clariant	0.05
Phase B		
Water (demineralized)		44.30
Magnesium Sulfate	Magnesium Sulfate Heptahydrate/Rona	1.00
Methylparaben	Nipagin M/Clariant	0.15
Glycerin	Emery 916/Cognis	5.00
Phase C		
Bisabolol	RonaCare® Bisabolol/Rona	0.50
Total		100.00

[0115] Formulation 5H is prepared by separately combining the ingredients of Phase A and Phase B and heating each mixture to 80°C. Phase B is then added slowly to phase A while stirring. The mixture is homogenized at 65-55°C and then cooled while stirring. Once the temperature reaches 40°C, Phase C is added and the mixture mixed until uniform.

[0116] Formulation 5I: Broad Spectrum Sunscreen Lotion

INCI name	Trade Name/Supplier	% w/w
Phase A-1		
Deionized water		64.95
Disodium EDTA		0.10
Propylene Glycol		3.00
Glycerin		2.00
Phase A-2		
Acrylates/C10-30 Alkyl Acrylate Copolymer	Carbopol EDT 2020/Goodrich	0.15
Xanthan Gum	Vanzan NF/Vanderbilt	0.15
Phase B		
Cetyl alcohol, glyceryl stearate, PEG-75, ceteth-20 and steareth-20	Emolium Delta / Gattefosse	4.00
Bakuchiol	**Present invention**	**1.00**
Dimethicone	DC200 fluid, 100cst/Dow	0.50
C30-38 Olefin/Isopropyl Maleate / MA Copolymer	Performa V1608 / New Phase Technologies	1.00
C12-15 Alkyl benzoate	Finsolv TN / Finetex	10.00
Avobenozne (sunscreen)	Eusolex 9020 / RONA	2.00
Diethylhexyl syringylidene malonate (photostabilizer)	Oxynex ST / RONA	2.00
Homosalate (sunscreen)	Eusolex HMS/RONA	8.00
Phase C		
Triethanolamine (99%)	TEA 99% / Union Carbide	0.15
Phase D		
Phenoxyethanol (and) Isopropylparaben (and) Isobutylparaben (and) Butylparaben	Liquapar PE/ISP	1.00
Total		**100.00**

[0117] Formulation 5I is prepared by separately combining the ingredients of Phase A-1 Phase A-2. Phase A-2 is then dispersed in the Phase A-1 mixture with agitation and heated to 75°C. Separately, the Phase B ingredients are combined and heated to 75°C. The Phase B mixture is then added to the Phase A-1/A-2 dispersion with continuous stirring. The mixture is homogenized for 10 min and cooled to 45°C. Phases C and D are then sequentially added and mixed until uniform.

[0118] Formulation 5J: Self-Tanning Sunscreen Lotion

INCI Name	**Trade Name / Supplier**	**% w/w**
Phase A		
Deionized Water		39.15
Xanthan Gum	Keltrol/Kelco	0.75
Propylene Glycol	Propylene Glycol	5.00
Methylparaben		0.20
Propylparaben		0.10
Phase B		
Steareth-10	Brij 76/ICI	0.70
Glyceryl Stearate (and) PEG-100 Stearate	Arlacel 165/ICI	1.20
PEG-40 Stearate	Myrj 52-S/ICI	0.40
Cetearyl Alcohol (and) Ceteareth-20	Cosmowax J/Croda	1.00
Cetearyl Alcohol		1.50
Cyclomethicone	Dow Corning 344 Fluid/Dow Corning	5.00
Dimethicone	Dow Corning 200 Fluid 100 cst/Dow Corning	0.50
Octyldodecyl Neopentanoate	Elefac I-205/Bernel	16.50
Avebenzone (sunscreen)	Eusolex 9020 / EMD	1.00
Diethyhexylsyringyledene malonate (photostabilizer)	Oxynex ST / EMD	1.00
Homosalate (sunscreen)	Eusolex HMS / EMD	5.00
Octisalate (sunscreen)	Eusolex OS / EMD	5.00
Phase C		
Bakuchiol	**Present invention**	**2.00**
Phase D		
Deionized Water		10.00
Dihydroxyacetone	Dihydroxyacetone/Rona	5.00
Total		100.00

[0119] Formulation 5J is prepared by charging the Phase A water component to a mixing vessel. Under low homogenization, the Phase A xanthan gum is sprinkled in and mixed to uniformity. The remaining Phase A ingredients are then added while maintaining homogenization and the mixture heated 75-80°C. The Phase B ingredients are mixed in a separate vessel and heated to 85°C. An emulsion is prepared by adding Phase B to Phase A and adjusting the homogenizer speed as necessary to ensure adequate batch turnover. The homogenized mixture is then held at 85°C for 10 minutes after which mixing is then switched from homogenization to impeller mixing at 60°C. The mixture is allowed to cool and Phase C is added at around 40°C and mixed well. The Phase D

ingredients are separately mixed at room temperature with constant mixing to ensure uniformity. The Phase D mixture is then added to Phase A/B/C mixture at 40°C and continually mixed until the mixture reaches room temperature.

[0120] In any of the formulations set forth above, the meroterpene identified could just as readily be susbstituted with another meroterpene such as baukchiol, corylifolin, hydroxy-bakchiol, etc. Additionally, these formulations are preferably stored and packaged in tinted vessels/containers so as to prevent their exposure to light, especially UV light, until use. This is especially important for those formulations employing organic UV absorbers that are chemically altered and/or rendered inactive once a given amount of UV light is absorbed.

[0121] Similarly, while the foregoing formulations contain many ingredients other than the critical ingredients including surfactants, stabilizers, self-tanning agents, antioxidants and the like, these additional ingredients could just as easily have been omitted without compromising the sunscreen and anti-erythema properties thereof.

[0122] Without further elaboration, it is believed that one skilled in the art can, using the preceding description, can utilize the present invention to its fullest extent. Furthermore, while the present invention has been described with respect to aforementioned specific embodiments and examples, it should be appreciated that other embodiments utilizing the concept of the present invention are possible, and within the skill of one in the art, without departing from the scope of the invention. The preceding preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

What is claimed is:

1. A sunscreen composition for preventing or lessening sun-induced damage to human skin comprising (i) at least one UV-B or UV-A/UV-B sunblock active in a conventional amount, (ii) from about 0.1 to about 10 weight percent of at least one meroterpene and (iii) a dermatological acceptable carrier, said meroterpene being free or substantially free of coumarins.

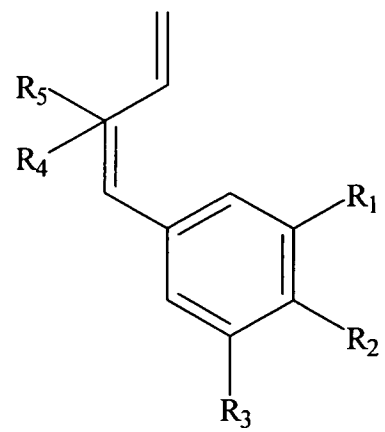
2. The sunscreen composition of claim 1 wherein the meroterpene is free or substantially free of furocoumarins.

3. The sunscreen composition of claim 1 or 2 wherein the meroterpene is free or substantially free of psoralenes.

4. The sunscreen composition of any of claims1 thru 3 further comprising at least one UV-A sunblock active.

5. The sunscreen composition of any of claims 1 thru 4 wherein the meroterpene is present in an amount of from about 0.5 to 5 percent by weight.

6. The sunscreen composition of any of claims 1 thru 5 wherein the meroterpene is a compound having the structure:



wherein R_1, R_2, and R_3 are each independently selected from the group consisting of H, OH, OR_6 or CH_2R_6 where R_6 is linear or branched C_1 to C_8 alkyl; R_4 and R_5 are each independently a linear or branched, C_1 to C_{20} alkyl or alkenyl group.

7. The sunscreen of any of claims 1 thru 6 wherein the meroterpene is selected from the group consisting of bakuchiol, hydroxybakuchiol, corylifolin, a derivative of bakuchiol, a derivative of corylifolin, or a combination or any two or more thereof.

8. The sunscreen composition of any of claims 1 thru 7 wherein the meroterpene is bakuchiol or a derivative thereof.

9. The sunscreen composition of any of claims 1 thru 8 wherein the merotepene is added as a meroterpene enriched plant extract containing from 85 to 99.99% by weight of the meroterpene.

10. The sunscreen composition of claim 9 wherein the merotepene-enriched plant extracts is derived from *Psoralea corylifolia, P. grandulosa,* or *Otholibium pubescens.*

11. The sunscreen composition of any of claims 1 thru 10 further comprising one or more skin protective and/or treatment ingredients.

12. The sunscreen composition of any of claims 1 thru 11 further comprising one or more ingredients selected from the group consisting of antioxidants, vitamins, anti-inflammatory agents, self-tanning agents, moisturizers, emollients, humectants, and mixtures thereof.

13. An improved sunscreen composition wherein the improvement comprises the presence of from about 0.1 to about 10 weight percent of at least one meroterpene that is free or substantially free of coumarins.

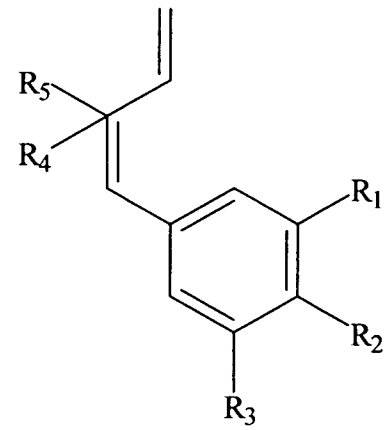
14. The sunscreen composition of claim 13 wherein the meroterpene is free or substantially free of furocoumarins.

15. The sunscreen composition of claim 13 or 14 wherein the meroterpene is free or substantially free of psoralenes.

16. The sunscreen composition of any of claims 13 thru 15 further comprising at least one UV-A sunblock active.

17. The sunscreen composition of any of claims 13 thru 16 wherein the meroterpene is present in an amount of from about 0.5 to 5 percent by weight.

18. The sunscreen composition of any of claims 13 thru 17 wherein the meroterpene is a compound having the structure:



wherein R_1, R_2, and R_3 are each independently selected from the group consisting of H, OH, OR_6 or CH_2R_6 where R_6 is linear or branched C_1 to C_8 alkyl; R_4 and R_5 are each independently a linear or branched, C_1 to C_{20} alkyl or alkenyl group.

19. The sunscreen composition of any of claims 13 thru 18 wherein the meroterpene is bakuchiol or a derivative thereof.

20. The sunscreen composition of any of claims 13 thru 19 further comprising one or more skin protective and/or treatment ingredients.

21. The sunscreen composition of any of claims 13 thru 20 further comprising onr or more ingredients selected from the group consisting of antioxidants, vitamins, anti-

inflammatory agents, self-tanning agents, moisturizers, emollients, humectants, and mixtures thereof.

22. A method of preventing or lessening UV-induced skin damage and/or preventing or lessening skin erythema due to exposure to sunlight, said method involving the step of applying a sunscreen composition comprising (i) at least one UV-B or UV-A/UV-B sunblock active in a conventional amount, (ii) from bout 0.1 to about 10 weight percent of at least one meroterpene and (iii) a dermatological acceptable carrier to the skin wherein the meroterpene is free or substantially free of coumarins.

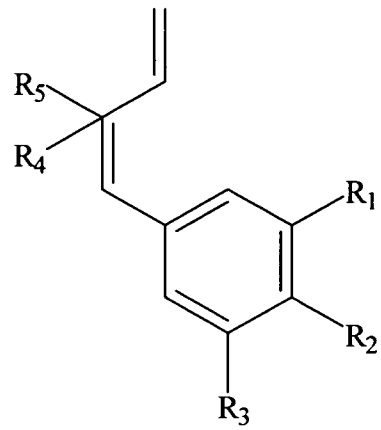
23. The method of claim 22 wherein the meroterpene is free or substantially free of furocoumarins.

24. The method of claim 22 or 23 wherein the meroterpene is free or substantially free of psoralenes.

25. The method of any of claims 22 thru 24 wherein the sunscreen composition further comprises at least one UV-A sunblock active.

26. The method of any of claims 22 thru 25 wherein the meroterpene is present in an amount of from about 0.5 to 5 percent by weight.

27. The method of any of claims 22 thru 26 wherein the meroterpene is a compound having the structure:



wherein R_1, R_2, and R_3 are each independently selected from the group consisting of H, OH, OR_6 or CH_2R_6 where R_6 is linear or branched C_1 to C_8 alkyl; R_4 and R_5 are each independently a linear or branched, C_1 to C_{20} alkyl or alkenyl group.

28. The method of any of claims 22 thru 27 wherein the sunscreen composition further comprises one or more skin protective and/or treatment ingredients.

29. The method of any of claims 22 thru 28 wherein the sunscreen composition further comprises one or more additional ingredients selected from the group consisting of antioxidants, vitamins, anti-inflammatory agents, self-tanning agents, moisturizers, emollients, humectants, and mixtures thereof.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 08/05461

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/37 (2008.04)
USPC - 424/59, 424/60
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC: 424/59, 424/60

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 424/70.9 (text search)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST(USPT,PGPB,EPAB,JPAB); DialogWeb; Google Scholar
Search Terms Used: meroterpene, bakuchiol, coumarin,furocoumarin, furancoumarin, psoralen, sunscreen, UVA, UVB, sunblock.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6,878,381 B2 (COLLINGTON) 12 April 2005 (12.04.2005); col 7, ln 10-21 and 30-35; col 8, ln 33-35; col 9, ln 46-51; col 10, ln 51-57; col 12, ln 7-20.	1-3, 13-15 and 22-24
Y	US 2006/0251749 A1 (JAI et al.) 09 November 2006 (09.11.2006); abstract; para [0012], [0021]-[0024], [0044], [0050], [0053].	1-3, 13-15 and 22-24

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

* 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	Date of mailing of the international search report
24 July 2008 (24.07.2008)	06 AUG 2008
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 08/05461

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of 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. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims 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. ☒ Claims Nos.: 4-12, 16-21 and 25-29
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 claims 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 claims 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.