Title: POLYPODIUM LEUCOTOMOS EXTRACT PREPARATION AND USE THEREOF

Abstract: Provided herein are methods and products for use in reducing photoaging of the skin. The products can include a purified extract from a fern of the genus Polypodium in a form suitable for formulation into creams and lotions. Such products can be supplemented with one or more of the following components: biologically active botanical extracts, vitamins and growth factors. The products also can include physical and/or chemical sunscreen agents and/or cosmetic agents. The products often have photoprotective, antioxidant, anti-inflammatory and cell stimulation properties.
POLYPODIUM LEUCOTOMOS EXTRACT PREPARATION AND USE THEREOF

BACKGROUND

Cross Reference to Related Applications

[001] This application claims the benefit of U.S. provisional patent applications 62/017,131, filed June 25, 2014 and 62/182,382, filed June 19, 2015, the entire disclosures of which are incorporated by reference herein.

Field

[002] The technology relates in part to compositions for topical administration to a subject that can inhibit photoaging of skin. The technology also relates in part to methods for preparing an active component of a fern (e.g., Polypodium leucotomos) suitable for formulation in a cream or lotion and/or for topical administration to skin of a subject.

Description of the Related Art

[003] Photoaging or premature skin aging from ultraviolet light exposure results in many deleterious clinical symptoms including rhytids, lentigines, mottled hyperpigmentation, loss of translucency and decreased elasticity. Polypodium leucotomos (P. leucotomos) has been shown to be an effective prevention and treatment for skin damage from UV exposure in animals and humans when administered orally.

[004] Thus there is a need for an effective anti-aging extract. There is also a need for a topical anti-aging composition.

Summary

[005] A skin treatment is described including the topical application of creams and lotions that avoids the use of lower alky alcohols. In addition a composition is described for use in topical applications. A process for preparing an extract is described comprising extracting P. leucotomos material with C₂ - C₅ polyol in a ratio of about 1 gram of dried P. leucotomos plant material to about 5 grams to about 100 grams of a C₂ to C₅ polyol, thereby preparing a leucotomos polyol extract, and filtering the leucotomos polyol extract, thereby providing a filtered polyol extract. In some embodiments, the process further includes heating the polyol extract to about 60 degrees Celsius to about 90 degrees Celsius. In some embodiments, the
process further includes stirring the polyol extract for between 30 minutes and 4 hours. In some embodiments, the filtering of the polyol extract is through a fluted paper filter.

[006] In an embodiment, a process for preparing an extract is described, the process comprising extracting dried P. leucotomos material with vegetable glycerin in a ratio of about 1 gram of dried P. leucotomos extract to about 1 gram to about 100 grams of vegetable glycerin, thereby preparing a leucotomos polyol extract, heating the polyol extract to about 60 degrees Celsius to about 90 degrees Celsius, stirring the polyol extract for between 30 minutes and 4 hours; and filtering the polyol extract through a fluted paper filter, thereby providing a filtered polyol extract.

[007] In some embodiments, a composition is described, the composition comprising a filtered polyol extract made as described herein. In some embodiments, a topical composition is described, the composition comprising a P. leucotomos polyol extract. In some embodiments, a topical composition is described, the extract comprises a C2-C5 polyol and a P. leucotomos polyol extract. In some embodiments, a topical composition is described, the C2-C5 polyol can be a vegetable glycerin.

[008] These and other embodiments are described in greater detail below.

Brief Description of the Drawings

[009] FIG. 1 is a graph depicting the viability of fibroblasts in control medium, control medium supplemented with 1.0 wt% glycerin, or in treatment medium supplemented with a low, medium or high concentration of polyol extract for 12 hours.

[010] FIG. 2 is a graph depicting the viability of fibroblasts in control medium, control medium supplemented with 1.0 wt% glycerin, or in treatment medium supplemented with a low, medium or high concentration of polyol extract for 24 hours.

[011] FIG. 3 is a graph depicting the viability of fibroblasts in control medium, control medium supplemented with 1.0 wt% glycerin, or in treatment
medium supplemented with a low, medium or high concentration of polyol extract for 48 hours.

[012] FIG. 4 is a graph depicting the viability of fibroblasts in control medium, control medium supplemented with 1.0 wt% glycerin, or in treatment medium supplemented with a low, medium or high concentration of polyol extract for 72 hours.

[013] FIG. 5 is a graph depicting the viability of fibroblasts in control medium, control medium supplemented with 1.0 wt% glycerin, or in treatment medium supplemented with a low, medium or high concentration of polyol extract for 96 hours.

[014] FIG. 6 is a graph depicting fold changes in the expression of inflammatory genes TNFa relative to an internal control (GAPDH) in fibroblasts after growth in control medium, control medium containing 1.0% glycerol, or in treatment medium containing a low of active for 96 hours.

**Detailed Description**

[015] The term "lower alkyl alcohol" refers to C1-C5 alkyl alcohols having one hydroxyl substituent group attached to a C1-C5 alky group, including, but not limited to, ethanol, methanol, n-propanol, isopropanol, n-butanol, etc.

[016] The term photoaging refers to premature aging (dermatoheliosis) of the skin caused by repeated exposure to ultraviolet radiation (UV) primarily from the sun, but also from artificial UV sources. This includes the UV damage to the skin that continues in the dark immediately after exposure for up to six hours that allows "evening-after" treatment. Photoaging can be determined by a visual assessment of the subjects' skin's fine wrinkling, coarse wrinkling, mottled hyperpigmentation and/or yellowing (sallowness).

[017] The term "plant material" refers to portions of a plant, including, but not limited to stems, leaves, roots, buds, flowers, rhizomes and/or branches.

[018] The term "polyol" refers to an alcohol having more than one hydroxyl functional group.
The technology relates in part to methods for preparing an active component of a fern, e.g., *Polypodium leucotomos* (otherwise can be known as *Phlebodium aureum*, golden polypody, golden serpent fern, cabbage palm fern, gold-foot fern, hare-foot fern, and/or *Polypodium aureum*) suitable for formulation in a cream or lotion and/or for topical administration to skin of a subject. The active component can be utilized to inhibit skin photoaging, and sometimes is administered topically to prematurely aged skin of a subject. Preparation methods often do not involve use lower alkyl alcohols, for example in the extraction solution and/or in the topical formulation. In some embodiments, pharmacologic action of the active component is enhanced by co-formulation with an anti-inflammatory agent and/or anti-oxidative vitamins that have been synthetically modified. In certain embodiments, compositions that include the active component also can include one or more therapeutic botanical extracts, and sometimes can include one or more growth factors.

Thus, provided in certain aspects is a process for isolating an active component of a fern (e.g., *Polypodium leucotomos* [P. leucotomos]), to a form which has sufficient activity, purity and/or physical suitability for topical administration in a lotion or cream (e.g., administered to photoaged skin). In some embodiments, the process includes isolating the active component as a glycerol solution from dried fern powder or from fern extract powder. Dried fern powder and fern extract powder often contain a mixture of undesirable particulates, fatty solids, insoluble tannins, high molecular weight cellulose, oxidized P. leucotomos and the desired active component. The resulting glycerol extract often is filtered to yield a clear solution rich in active component that is administered alone or is combined with one or more other components (other formulants).

Also provided in certain aspects is a method for preparing a lotion or cream comprising the active component of P. leucotomos and one or more anti-inflammatory and/or anti-oxidative components. The one or more anti-inflammatory and/or anti-oxidative components sometimes are (1) selected botanical extracts or are from such extracts, (2) synthetic products that contain chemically modified vitamins or isolated modified vitamins, (3) the like, or (4) a combination of the foregoing.
[022] Provided also in some aspects is a method for stimulating photoaged cells in combination with P. leucotomos active component that use 1) Growth Factors to enhance cell signaling and/or 2) the Growth Factors have been independently formulated so as to protect the growth factors tertiary structure to further formulation and also to make the growth factors bioavailable to the live skin cells. The P. leucotomos active component and formulated Growth Factors are used in combination with the botanical extract and synthetic modified vitamin in lotions and creams.

[023] Technology described herein can be utilized for application to photoaged skin directly or in a cream or lotion with or without the addition of synthetically altered vitamins and botanical extracts; and with or without formulated growth factors. Various aspects and embodiments of the technology are described hereafter.

[024] A process for preparing an extract is described comprising extracting dried P. leucotomos material with C$_{2-5}$ polyol in a ratio of about 1 gram of dried P. leucotomos plant material to about 5 to about 100 grams of a C$_2$ to C$_5$ polyol, thereby preparing a leucotomos polyol extract, and filtering the leucotomos polyol extract, thereby providing a filtered polyol extract. In some embodiments, the process further includes heating the polyol extract to about 60 degrees Celsius to about 90 degrees Celsius. In some embodiments, the process further includes stirring the polyol extract for between 30 minutes and 4 hours. In some embodiments, the filtering of the polyol extract is through a fluted paper filter.

[025] In an embodiment, a process for preparing an extract is described, the process comprising extracting dried P. leucotomos plant material with a vegetable glycerin in a ratio of about 1 gram of dried P. leucotomos plant material to about 1 gram to about 100 grams of vegetable glycerin, thereby preparing a leucotomos polyol extract, heating the polyol extract to about 60 degrees Celsius to about 90 degrees Celsius, stirring the polyol extract for between 30 minutes and 4 hours; and filtering the polyol extract through a fluted paper filter, thereby providing a filtered polyol extract.

[026] In some embodiments, a composition is described, the composition comprising a filtered polyol extract made as described herein. In some
embodiments, a topical composition is described, the composition comprising a P. leucotomos polyol extract. In some embodiments, a topical composition is described, the P. leucotomos polyol extract comprises a C_2-C_5 polyol. In some embodiments, a topical composition is described, the topical composition comprises a C_2-C_5 polyol. In some embodiments, a topical composition is described, the C_2-C_5 polyol can be a vegetable glycerin.

[027] The names for several moieties used herein are indicated with the corresponding structures below.

\[
\begin{align*}
\text{Glycerin, glycerol, glycerine} & \quad \text{propylene glycol} \\
\text{Diethylene glycol}
\end{align*}
\]

Active component of P. leucotomos

[028] In some embodiments, a process is described comprising extracting a fern source, e.g., P. leucotomos, with a solution comprising C_2-C_5 polyol, thereby generating a fern, e.g., P. leucotomos, polyol extract; and filtering the fern polyol extract, thereby yielding a filtered polyol extract.

[029] In one embodiment, a process for preparing a filtered polyol extract from the fern P. leucotomos, is described, the process comprising: combining dried P. leucotomos plant material and vegetable glycerin in a ratio of about 1 gram of dried P. leucotomos plant material to about 1 gram to about 100 grams of vegetable glycerin, thereby preparing a polyol extract, heating the polyol extract to about 70 degrees Celsius to about 75 degrees Celsius, stirring the polyol extract for about 1 hour, cooling the polyol extract to about room temperature over about 2 hours, and
filtering the polyol extract through a fluted paper filter, thereby providing a filtered polyol extract.

[030] In some embodiments, a C₂-C₅ polyol can be used to extract the active agent from the plant material. In some embodiments a C₂-C₅ polyol can be mixed with the plant material. In some embodiments the extracting solution comprises a C₂-C₅ polyol. In some embodiments the polyol comprises at least 2, at least 3, and/or at least 4 hydroxyl functional groups. In some embodiments, the polyol is an extracting agent. In some embodiments, the polyol is a moisturizing agent. In some embodiments, the polyol is both a moisturizing agent and an extracting agent. In some embodiments, the polyol can be glycerol (glycerin, glycerine), propylene glycol, diethylene glycol and/or pentylene glycol. In some embodiments the glycerol can be an animal, vegetable and/or synthetic glycerol. In some embodiments the glycerol can be a vegetable glycerol. In some embodiments, the vegetable glycerol can be from soybeans. In some embodiments, about 0.1 to 10 gm of dried plant material can be extracted with about 100 ml of glycerin/glycerol.

Glycerin is commonly used in lotions, creams and skin treatments and it has been determined that it can be used to extract P. leucotomos active component, and after filtration, the active component can be used to treat photoaging. This polyol extract can also be used as the sole treatment for sun damaged skin or it can be used in combination with other natural or synthetic supplements either alone or in lotions or creams. In some embodiments, a ratio of 1:5 to 1:100 of the extract source to the polyol, e.g., 1 gm dried P. leucotomos material to 10 ml (about 12.6 g) or 40 ml (about 50.4 gm) of polyol.

[031] In some embodiments, the extracting solution is exclusive of lower alkyl alcohols. The term exclusive of can refer to being substantially free or free of the respective material. In some embodiments, the extracting solution is substantially free or free from lower alkyl alcohols. The term lower alcohol refers to C₁-C₅ alcohols having one hydroxyl functional group. In some embodiments, C₁-C₅ mono-hydroxy alcohols can be methanol, ethanol, n-propanol, isopropanol, n-butanol. In this regard, the term "substantially" means that the lower alkyl alcohol content in the extracting medium, e.g., glycerin above, can be 1.0% to 0.01 % by weight or less and/or 0.005% by weight or less lower alkyl alcohol content. P. leucotomos alcohol extracts can exhibit free radical inhibitor activity (S.Gonzalez et. al.,...
al., Photochem. Photo. Biol Sci. 9, 559-563 (2010)) with mild antiinflammatory activity but they can lack acute in vivo activity in inflammation models induced by carrageenam and arachidonic acid. (A. Brieva Inlammo Pharmacology 9, (4), 361-371 (2008). In this regard, the term "substantially" can mean that the lower alkyl alcohol content in the polyol extract and/or the extracting solution or media can be 1.0% to 0.01% by weight or less and/or 0.005% by weight or less lower alkyl alcohol content.

[032] In some embodiments, the filtering comprises passing the fern polyol extract through a filter. In some embodiments, the filter can be paper. In some embodiments, the filter can comprise a porous ceramic, polymeric and/or metal. In some embodiments, the filter can comprise a wire mesh. In some embodiments, the filter can remove particulates greater than 10.0, 5.0, 3.5, and/or 2.0 microns.

[033] In some embodiments, the filtered polyol extract comprises an active fraction that inhibits or treats skin photoaging when administered topically to a subject. A suitable method for determining the photoaging is by punch biopsy (3 mm). Alternative methods for determining photoaging can be by measuring skin conductivity, trans-epidermal water loss (TEWL) and/or skin topography analysis.

[034] In some embodiments, the polyol extract can be substantially free, or free, from particulates, fatty solids, oxidized P. leucotomos plant material or a combinations thereof. In this regard, the term "substantially" means that the content of particulates, fatty solids, oxidized P. leucotomos or a combination thereof in the polyol extract can be 0.01% by weight or less and preferably 0.005% by weight or less.

[035] In some embodiments, the filtered polyol extract is substantially free, or free, of a lower alkyl alcohol. In this regard, the term "substantially" means that the content of lower alkyl alcohols in the extract is less than 1.0% by weight, 0.01% by weight, and/or 0.005% by weight.

[036] In some embodiments, the filtered polyol extract can be substantially free, or free, of particulate. The term particulate can refer that known by those skilled in the art. The filtered polyol extract is preferably and substantially free from particulate matter. In this regard, the term "substantially" means that the content of

8
particulates in the filtered extract can be less than 5% by weight, 1.0% by weight, 0.01 % by weight and/or 0.005% by weight. In some embodiments the particulates have a maximum size of less than 100 microns, 50 microns, 25 microns, 20 microns, and/or 8 microns.

[037] In some embodiments, the filtered polyol can be substantially free or free, of phenolic acid esters. In some embodiments the phenolic acid ester can be the ester of para-coumaric acid. In this regard, the term "substantially" means that the content of phenolic acid esters in the extract or extraction solution is less than 1.0% by weight, 0.01 % by weight and/or 0.005% by weight. In this regard, the term "substantially" means that the content of lower alkyl alcohols in the extract or extraction solution is less than 1.0% by weight, 0.01 % by weight and/or 0.005% by weight. Suitable methods for determining the amount of the respective materials in the extract or extracting solution can be with liquid chromatography / mass spectroscopy (LCMS). While not wanting to be limited by theory, it is believed that skin irritation can be a result of a covalent linkage between a skin nucleotide and an aldehyde or Michael acceptor. These aldehydes or Michael acceptors can be generated by high pressure/temperature ethanolic extraction. It is believed that glycerol extraction reduces the amount or presence of these acceptors and thus reduces the covalent linkage with skin nucleotides, reducing irritation. In some embodiments, the extract provides a less irritating topical adjuvant. In some embodiments, the extract can be taken orally. In some embodiments, the exposure to stomach acid can rehydrolyze the inactive acid acceptor, reducing the amount of Michael acceptors available to covalently bond with skin nucleotides.

[038] In some embodiments, the filtered polyol extract has a color with a lightness that lies between 5 and 10 on the Munsell value scales as defined by the Munsell Color System. The lightness of the extract powder can be determined by those known methods in the art, e.g., ASTM D1535. In some embodiments, the filtered polyol extract is substantially free, or free, of brown discoloration and/or black discoloration. In some embodiments, the filtered polyol extract is "light colored" and/or not "dark colored". The term "dark-colored" when used with respect to a stain means that the stain has an L* value less than 60 as determined by casting a 25 .mu.m dry thickness coating film over the white part of a BYK-Gardner No. PA-2811 opacity drawdown chart (from BYK-Gardner USA) and measuring L* as defined in
the ASTM International Standards on Color and Appearance Measurement: 8th Edition. In some embodiments, the filtered polyol is substantially clear or clear. The term "clear" refers to without coloration, cloudiness. In some embodiments, the filtered polyol extract can be straw colored. In some embodiments, the filtered polyol can have a color of straw yellow (sRGBB of about 228 ± 20, 217 ± 20, 111 ± 20).

[039] In some embodiments, the filtered extract can inhibit or treat skin photoaging when administered topically, in a composition comprising the active ingredient, to a subject. In some embodiments, 0.005 to 10 gm of filtered extract applied topically twice daily.

[040] In some embodiments, the process further comprises agitating the polyol extract. In some embodiments the agitating can be by sonicating the polyol extract at about 15-60 khz for about 5 minutes to about 3 hours. In some embodiments, the agitation can be by mechanically stirring the polyol extract. In some embodiments, the mechanical stirring can be between about 50 to 1000 rpm, e.g., at about 250 rpm, for about 30 minutes to about 4 hours. In some embodiments, the polyol extract can be stirred at about 250 rpm for about 1 hour to about 4 hours.

[041] In some embodiments, the process further comprises heating the polyol extract to a temperature between about 55 °C, 60 °C, 70° C to about 75° C, 80°, 90° C. In some embodiments the heating temperature can range between any combination of the above mentioned temperatures. In some embodiments, the heating temperature is ramped up from room temperature to the desired heating temperature within a period of about 2 hours, 1.5 hours, 1 hour, 30 minutes, 15 minutes and/or 5 minutes. While not wanting to be bound by theory, it is believed that temperatures above 90° C can darken the extract and/or can undesirably affect the efficacy of the extract.

[042] In some embodiments, the process further comprises cooling the polyol extract. In some embodiments, the polyol is cooled to room temperature. In some embodiments, the polyol is cooled to about 20 °C to about 25 °C. In some embodiments, the polyol extract is cooled over a time period between about 20 minutes to about 24 hours. In some embodiments, the polyol extract is cooled from about 1 hour to about 4 hours. In some embodiments, the cooling can be performed
without addition artificial cooling/refrigeration and/or cooling with ice or other lower temperature materials or compounds.

[043] In some embodiments, the process is performed under a reducing and/or inert atmosphere. In some embodiments, the process further comprises contacting the polyl extract with an inert atmosphere. In some embodiments, the reducing and/or inert atmosphere comprises nitrogen (N₂) gas and/or argon gas or mixtures thereof.

[044] In some embodiments, the process further comprises contacting the polyl extract with carbon in amount effective to reduce coloring in the polyl extract. In some embodiments, about one gram of carbon is combined with about 10 milliliters to about 100 milliliters of the polyl extract. In some embodiments, the carbon can be activated carbon.

[045] In some embodiments, the polyl extract can be filtered through a filter compatible with polyl for a time period of about 1 hour to about 96 hours. In some embodiments, the filtering is performed under normal gravity. In some embodiments, the compatible filter comprises filter paper. In some embodiments, the filter paper can have a medium flow rate. The term Medium flow rate is as known by those skilled in the art, e.g., 10 to 100 ml in 10.5 sec per square inch. In some embodiments, the filter paper can remove particulates of greater than 20-25 microns, 15 microns, and/or 11 microns. A suitable example can be Grade 1, Grade 2 and/or Grade 3 paper filter paper (Whatman filter paper, Sigma, St. Louis, MO).

PHARMACOLOGIC ACTIVE BOTANICAL EXTRACTS SUPPLEMENT

[046] In some embodiments, the composition, topical composition or polyl extract can comprise fern material and/or polyl extracted materials therefrom. In some embodiments, the composition, topical composition or polyl extract can comprise fern material extracted with a C₂ to C₅ polyl. In some embodiments, the fern material can comprise polypodium material. In some embodiments, the fern material can comprise the leaves, stems, branches, and or roots of the fern material. In some embodiments, the polypodium material can comprise polypodium leucotomos material. In some embodiments, the polypodium material can comprise dried polypodium leucotomos material. In some embodiments, a composition is
described, the composition comprising any of the filtered polyol extracts described herein. In some embodiments the filtered polyol comprises a polyol extract of a fern plant. In some embodiments, the fern can be a P. leucotomos. In some embodiments, the composition comprises a filtered polyol extract prepared by a process of any one of embodiments described herein. In some embodiments, the composition comprises one or more components having anti-inflammatory activity and/or antioxidative activity. In some embodiments, a 1 % solution in polyol of the above polypodium extract can give an increased cell viability in fibroblasts of at least two fold, at least three fold, at least four fold, and/or at least five fold. In some embodiments, a 0.01 % solution in polyol of the above polypodium extract can give at least a 1.5 fold, two fold, and/or at least a three fold decrease of the inflammatory marker TNF alpha (a) at 0.01 % concentration after 96 hours.

[047] In some embodiments, the composition can further comprise an oil, an emulsifying agent, an aqueous component, one or more botanical extracts and/or modified vitamins.

[048] In some embodiments, the oil can comprise a fragrance. In some embodiments, the oil can be an apricot kernel oil, jobjoba oil, coconut alkanes, butyrospermum or petrolatum. In some embodiments, the formulation can comprise 0.00005 wt% to about 10 wt% oil/fragrance, e.g., 4.3 ml in 2052.0 ml (0.00209 wt%), 0.001 wt % and/or 0.01 wt %.

[049] Supplements can be added that are designed to augment antiinflammatory and antioxidative activity of an active component in a polyol extract. These additional antiinflammatory and antioxidative activities can be from pharmacologically active botanical extracts and/or from synthetic compounds.

[050] Lotions or creams that contain polyol extracts of P. leucotomos can be supplemented with botanical extracts that have anti-inflammatory or antioxidant properties. In some embodiments, the composition/formulation can comprise 0.00001 wt%, 0.0001 wt%, 0.0005 wt% to 0.5 wt%, 1.0 wt%, 5 wt% and/or10 wt %, and/or any combinations of the previously described values, of additional botanical extracts, e.g., 4.3 ml in 2052.9 ml (see examples). In some embodiments, the composition can further comprise at least one botanical extract. In some embodiments, non-limiting examples of botanical extracts include those that come

[051] In some embodiments, the botanical extract can include Osmanthus Fragrans, that has also shown anti-inflammatory activity (S. De-Gyeong et al., Arch Pharm Res 34(12) 2029-2035, (2011)) as well as antioxidative and UV protective properties (S.Huang et. al., Med. Chem. Res. 20, 475-481 (2011)). In one embodiment, the dried flower of Osmanthus Fragrans can be extracted with water, e.g., as a tea which can be used as the basis of a lotion or added into a cream and the variability in components resulting from growth in different regions or method of extraction (C-D. Hu et al., Molecules, 15, 3683-3693 (2010)).

[052] In some embodiments, the Osmanthus Fragrans extract can be supplemented by addition of other botanical extracts with the missing components. In some embodiments, the botanical extract can further comprise Boronia Megastigma extract. An example of this is the varied megastigmas composition of Osmanthus Fragrans which is compensated for by addition of Boronia Megastigma extract. In a typical procedure 70g of dried Osmanthus Fragrans flowers are added to 1liter of reverse osmosis purified water (RO water) and bought to a temperature of 98°C for 10-30mins and then cooled to room temperature. The extract is first filtered through a mesh sieve then passed through a paper filter. Active carbon (1g to 250ml) can be added for further clarification of the Osmanthus Tea before filtration. To this tea 0.1 to 1ml of a CO₂ extract of Boronia Megastigma can be added. Approximately 600-800ml of an aqueous base is formed by this procedure and is suitable for combining with the glycerol extract of P. leucotomos that contains the active component and can be converted into lotions or creams. In some embodiments, in some embodiments, a suitable amount of the filtered extract, e.g., 1 gram of dried P. leucotomos plant material to about 1 gram to about 100 grams of
vegetable glycerin, can be added to this aqueous base to provide the 0.001 wt%, 0.001 wt%, 0.001 wt% to about 2.5 wt%, 5.0 wt%, and/or 10 wt% filtered polyol extract and/or any combination of the above described values, e.g., 1 wt%, in the final topical application.

[053] Other botanical extracts can also be added that impart important properties or fragrance to the lotion or cream. In some embodiments, the composition can comprise further botanical extracts. For example this can be a Lavender extract or Rosmarinus officinalis extract that impart antiseptic properties but also can stimulate Nerve Growth Factor (K.Kunio et. al.; Biological & Pharmaceutical Bulletin 26 (11): 1620-1622 (2003)).

MODIFIED VITAMIN SUPPLEMENTS

[054] In some embodiments, the composition can comprise modified vitamin supplements. In some embodiments, the composition/formulation can comprise 0.0001 wt% to 10 wt % modified vitamin supplements. Synthetic derivatives can also be used as a supplement to the topical use of P. leucotomos active component. Vitamin C-palmitate which has antioxidative properties as well as some UV protection (L. Chen, e.t al., Journal of the American Academy of Dermatology, 67( 5), 1013-1024 (2012)). Other examples of vitamin C derivatives include but are not limited to Aminopropyl Ascorbyl Phosphate (H.H. Kang et al., Bull. Korean Chem. Soc, 24(8) 1169-1172 (2003) which also has skin whitening effects. Other vitamins include vitamin E acetate is a stable form of vitamin E that have antioxidative effects. Other modified vitamins which could be added include but are not limited to Vitamin A derivatives including Vitamin A-palmitate.

GROWTH FACTOR SUPPLEMENTS

[055] In some embodiments, the composition can comprise growth factors. In some embodiments, the composition/formulation can comprise 0.0001 wt% to 10 wt % growth factors. Growth factors have been clinically shown to reverse photoaging (R.E. Fitzpatrick et. al., Journal of Cosmetic and Laser Therapy,5(1), 25-34 (2003)) when applied topically. An example of a growth factor supplement to P. leucotomos active component is carefully formulated human Epidermal Growth Factor formed into microspheres so as to maintain the growth factors tertiary
structure. Some suitable growth factors that can be used in conjunction with P. leucotomos active component are: Transforming growth factor beta (TGF-B), Vascular endothelial growth factor (VEGF) Hepatocyte growth factor (HGF) Keratinocyte growth factor (KGF) Basic fibroblast growth factor (bFGF) Insulin-like growth factor 1 (IGF1) Platelet-derived growth factor AA (PDGF-AA) Transforming growth factors (TGF-B2 & B3) and Epidermal Growth Factor. Microspheres containing the growth factors are formed by suspending the growth factor in a neutral phosphate buffer and the following added: sodium oleate or sodium stearate, PEG 100, cetyl alcohol and petrolatum and then hand shaken until a white emulsion. The high shear strength of mechanical mixing can be avoided to maintain the tertiary structure of the protein. This white emulsion can be added to lotions or creams containing P. leucotomos active component.

[056] In some embodiments, the composition can be a solution, cream, gel or paste, or lotion. The present P. leucotomos active components and supplements are generally employed as a solution, cream, gel or paste, or lotion. Typically 0.1-10% (e.g., by weight) of the P. leucotomos active component, P. leucotomos material extracted with a \textit{C_{2-C_{5}}} polyol and/or supplements are present in the end formulation.

[057] In some embodiments, the compositions can also include other standard adjuvants such as an emollient, moisturizer, thickener, emulsifier, neutralizer, coloring agent, UV absorber or filter, preservative, skin conditioner and/or gelling agent such as those described below. In some embodiments, when employed in the formulation, each of these adjuvants can be present in an amount of between about 0.1 to 10 wt % of the formulation.

EMOLLIENT

[058] Suitable emollients for use herein include, optionally hydroxy-substituted \textit{C_{3-C_{10}}} unsaturated fatty acids and esters thereof, \textit{C_{24}} esters of \textit{C_{8-C_{10}}} saturated fatty acids such as isopropyl myristate, cetyl palmitate and octyldecylmyristate (Wickenol 142), beeswax, saturated and unsaturated fatty alcohols such as behenyl alcohol and cetyl alcohol, hydrocarbons such as mineral oils, petrolatum, squalane, fatty sorbitan esters, lanolin and lanolin derivatives, such as lanolin alcohol ethoxylated, hydroxylated and acetylated lanolins, cholesterol and
derivatives thereof, animal and vegetable triglycerides such as almond oil, peanut oil, wheat germ oil, linseed oil, jojoba oil, oil of apricot pits, walnuts, palm nuts, pistachio nuts, sesame seeds, rapeseed, cade oil, corn oil, peach pit oil, poppyseed oil, pine oil, castor oil, soybean oil, avocado oil, safflower oil, coconut oil, hazelnut oil, olive oil, grapeseed oil, and sunflower seed oil and C1-C24 esters of dimer and trimer acids such as diisopropyl dimerate, diisostearylmalate, diisostearyl dimerate and tri isostearyl trimerate.

[059] Preferred emollients are selected from hydrocarbons such as isohexadecane, mineral oils, petrolatum, squalane, lanolin alcohol, oil of apricot pits and stearyl alcohol. In some embodiments, these emollients may be used independently or in mixtures and may be present in the composition of the present invention in an amount from about 1% to about 30% by weight, and/or in an amount from about 5% to about 15% by weight of the total composition.

EMULSIFIER

[060] Suitable emulsifiers for use herein include but are not limited to glyceryl stearate and laureth 23, PEG 20, cetearyl alcohol/ cetearl glucoside, dimethyldodecylammonium chloride and minkamidopropyl dimethyl 2-hydroxyethylammonium chloride. Preferred emulsifiers are cetearyl alcohol/ cetearl glucoside.

MOISTURIZER

[061] Typical moisturizers are glycerin, petrolatum and maleated vegetable oil.

Thickener

[062] The compositions of the invention can also contain a hydrophilic gelling agent at a level from about 0.01 wt% to about 10 wt%, preferably from about 0.02 wt% to about 2 wt%, and especially from about 0.02 wt% to about 0.5 wt%. Suitable hydrophilic gelling agents can generally be described as water-soluble or colloidally water-soluble polymers, and include cellulose ethers (e.g. hydroxyethyl cellulose, methyl cellulose, hydroxypropyl methyl cellulose), polyvinyl alcohol, polyquaternium-10, guar gum, hydroxypropyl guar gum and xanthan gum.
Among suitable hydrophilic gelling agents are acrylic acid/ethyl acrylate copolymers and the carboxyvinyl polymers. The resins consist essentially of a colloidally water-soluble polyalkenyl polyether crosslinked polymer of acrylic acid crosslinked with from 0.75% to 2.00% of a crosslinking agent such as polyallyl sucrose or polyallyl pentaerythritol. Examples include Carbopel 934, Carbopel 940, Carbopel 950, Carbopel 980, Carbopel 951 and Carbopel 981. Carbopel 934 is a water-soluble polymer of acrylic acid crosslinked with about 1% of a polyallyl ether of sucrose having an average of about 5.8 allyl groups for each sucrose molecule. Also suitable for use herein are hydrophobically-modified crosslinked polymers of acrylic acid having amphipathic properties available under the Trade Name Carbopol 1382, Carbopel 1342 and Pemulen TR-1 (CTFA Designation: Acrylates/1-10-30 Alkyl Acrylate Crosspolymer). A combination of the polyalkenyl polyether cross-linked acrylic acid polymer and the hydrophobically modified crosslinked acrylic acid polymer is also suitable for use herein. Other suitable gelling agents suitable for use herein are oleogels such as trihydroxy stearin and aluminum magnesium hydroxy stearate.

**NEUTRALIZER**

Neutralizing agents suitable for use in neutralizing acidic group containing hydrophilic gelling agents herein include sodium hydroxide, potassium hydroxide, ammonium hydroxide, monoethanolamine, diethanolamine and triethanolamine, and aminomethyl propanol.

**SKIN CONDITIONER**

Hyaluronic Acid is known to be a constituent of cells and is incorporated into various cosmetic preparations for the skin. In this role it is proposed that the addition of hyaluronic acid to the skin is able to raise the level of hyaluronic acid present in the cells and coats the dermal layers thereby improving the condition of the skin. Typical concentrations vary between 0.1-1 % w/v. Ceramides are a family of waxy lipid molecules and are found in high concentrations within the cell membrane of cells. Formulations containing lipids could improve disturbed skin conditions.

**Other Optional Components**
Another optional but preferred component of the composition is one or more preservatives. The preservative concentration in the composition, based on the total weight of that composition, is in the range of between about 0.05% and about 1.0% by weight, preferably between about 0.1% and about 0.4% by weight. Typical preservatives that can be used include sodium benzoate benzyl alcohol, salicylic acid, glycerin, sorbic acid and propyl paraben, and mixtures thereof.

The composition may also contain additional materials such as, for example, fragrances, fillers such as nylon, sun-screens, electrolytes such as sodium chloride, proteins, antioxidants and chelating agents as appropriate.

To enhance absorption of one or more components into live skin cells an absorption enhancer can be used. Examples include but are not limited to dimethyl sulfoxide or pentylene glycol. Pentylene glycol is preferred.

Another optional component is one or more ultraviolet absorbing agents. Ultraviolet absorbing agents, often described as sun-screening agents, can be present in a concentration in the range of between about 1% and about 25% by weight, based on the total weight of composition. Preferably, the UV absorbing agents constitute between about 2% and 15% by weight. More preferably, the UV absorbing agents can be present in the composition in a concentration range of between about 4% and about 10% by weight. Of the ultraviolet absorbing agents suitable for use herein, benzophenone-3, benzophenone-4, octyl dimethyl PABA (Padimate O), octyl methoxy cinnamate, octyl salicylate, octocrylene, p-methylbenzyldene camphor, butyl methoxy dibenzoyl methane (Parol 1789), titanium dioxide, zinc oxide and mixtures thereof are particularly preferred.

In some embodiments, the topical formulation can comprise a ratio of 1.0 to 10 top part materials to 1.0 part base mix. In some embodiments, the topical formulation can comprise about 10 g polyol extract dissolved into about 100 ml glycerin, e.g., vegetable glycerin. In some embodiments the topical formulation can comprise about 0.001 wt% to about 10 wt%, about 0.01 wt% to about 7.5 wt% polyol extract and/or about 0.1 wt% to about 5 wt% polyol extract or any combination of the above described values, e.g., about 1 wt% polyol extract. In some embodiments, the polyol extract can be about 1 g of dried p. leucotomos material extracted by about 10 ml, about 40 ml, and/or about 100 ml of polyol. In some embodiments, the final
topical product comprises from about 0.01 wt% to about 10 wt% of the extracted polyol extract, e.g., about 1 wt%.

[071] In some embodiments, the relative amounts of each ingredient may be adjusted such that a final topical product comprises about 0.01 wt% to about 10 wt% of the extracted polyol extract, e.g., about 1 wt% of an extract starting with about 100 g leucotomos plant material in 100 ml of polyol. In some embodiments, the relative amounts of each ingredient may be adjusted such that a final topical product comprises about 0.001 wt% to about 10 wt% of the original extracted plant material, e.g., about 0.1 wt%.

[072] In some embodiments, the topical formulation in vivo can inhibit reactive oxygen species (ROS), preventing DNA damage as well as inhibiting Nuclear Factor-kappa Beta (NF-kBeta); specifically decreases apoptosis and necrosis when topically applied to the skin as described therein. In some embodiments, 0.1 gram, 1 gm, 2.5 gms, and/or 5 gms of polyol extract can be applied safely to the skin (including hair) per 24 hours. In some embodiments, 0.001 ml, 0.01 ml, 0.1 ml, 0.2 ml of the 1 wt% extract described herein can be topically applied to the skin. In some embodiments, (10mg-500mg) of polyol extract P. leucotomos material can be applied topically every 4 hours to all areas of the skin (including hair). In some embodiments, the topical formulation can have a lack of toxicity effect in in vitro and in vivo studies.

[073] In some embodiments a method for inhibiting, preventing and/or treating skin photo-damage is described, the method can comprise administering topically to the skin of a subject a composition of any one of embodiments described herein in an amount described herein effective to inhibit, prevent, reduce and/or treat skin photo-damage. In some embodiments, the amount effective to inhibit, prevent, reduce and/or treat skin photo-damage can be an amount sufficient to reduce fine wrinkling, coarse wrinkling, mottled hyperpigmentation and/or Yellowing, and/or combinations thereof. (Griffith, et al, A Photonumeric Scale for the assessment of cutaneous photodamage, Arch Dermatology, 128:347 (1992)). In some embodiments, the subject can be a human subject. In some embodiments, the subject self-administers the composition. In some embodiments, the skin of the subject is photo-damaged. In some embodiments, the topical composition's effective
amount can be about 0.01 wt% to about 10 wt% polyol extract. In some embodiments, the amount effective can be about 1 gm of plant material to about 1 gm to about 100 gm C2-C5 polyol and/or amounts described elsewhere herein. In some embodiments, the effective amount can be topically applied at least once weekly, every other day, once daily, every 12 hours, every 8 hours and/or every 4 hours. In some embodiments, the effective amount can be topically applied for at least once, at least one day, at least 48 hours, at least 72 hours, at least for one week, at least for two weeks, at least for one month, at least for two months, and our at at least for six months. In some embodiments, the effective amount can be formulated for topical application to the skin, such as the skin surrounding or including the eyes, mouth, nose, forehead, ears, neck, hands, feet, hair, and/or overall body.

[074] The following embodiments are contemplated:

A1. A process for preparing an extract comprising extracting P. leucotomos material with C2 to C5 polyol in a ratio of about 1 gram of P. leucotomos material to about 10 to about 100 grams of a C2 to C5 polyol, thereby preparing a leucotomos polyol extract; and filtering the leucotomos polyol extract, thereby providing a filtered leucotomos polyol extract.

A2. The process of embodiment A1, wherein the P. leucotomos material is Polypodium leucotomos (P. leucotomos) material.

A3. The process of embodiment A1 or A2, wherein the leucotomos polyol extract comprises an active component that inhibits or treats skin photoaging when administered topically to a subject.

A4. The process of embodiment A3, wherein the C2-C5 polyol is in an amount effective to separate the active component from particulates, fatty solids, oxidized P. leucotomos or a combination thereof.

A5. The process of any one of embodiments A1 to A4, wherein the polyol extract is substantially free, or free, from particulates, fatty solids, oxidized P. leucotomos or a combination thereof.
A6. The process of any one of embodiments A1 to A5, wherein the polyol extract is substantially free, or free, from phenolic acid esters.

A7. The process of any one of embodiments A1 to A6, wherein no lower alkyl alcohol is combined with the fern material, fern powder, fern extract, polyol extracting media, polyol extract and/or filtered leucotomos polyol extract.

A8. The process of any one of the embodiments of A1 to A6, wherein the fern material, fern powder, fern extract, polyol extracting media, polyol extract and/or filtered leucotomos polyol extract are exclusive of lower alkyl alcohol.

A9. The process of any one of embodiments A1 to A8, wherein the filtered polyol extract is substantially free, or free, of a lower alkyl alcohol.

A10. The process of any one of embodiments A1 to A9, wherein the filtered polyol extract is substantially free, or free, of particulate.

A11. The process of any one of embodiments A1 to A10, wherein the filtered polyol extract is substantially free, or free, of brown discoloration and/or black discoloration.

A12. The process of any one of embodiments A3 to A11, wherein the polyol extract inhibits or treats skin photoaging when administered topically, in a composition comprising the polyol extract to a subject.

A13. The process of A12, wherein 0.1 to 5 ml of the polyol extract is topically applied at least once or twice daily to the affected areas.

A14. The process of any one of embodiments A1 to A13, wherein a ratio of the C2- C5 polyol to the plant material, dried plant or dried plant extract is about 1:1 to about 100:1.
A15. The process of any one of embodiments A1 to A14, wherein a ratio of the polyol to the dried plant or dried plant extract is about 1 gram of *P. leucotomos* material to about 10 grams to about 100 gms of C$_2$-C$_5$ polyol.

A16. The process of any one of embodiments A1 to A15, which comprises mechanically stirring the polyol extract.

A17. The process of any one of embodiments A1 to A16, which comprises heating the polyol extract to a temperature of about 60 degrees Celsius to about 90 degrees Celsius.

A18. The process of embodiment A17, wherein the polyol extract is heated to a temperature of about 70 degrees Celsius to about 75 degrees Celsius.

A19. The process of any one of embodiments A1 to A18, which comprises contacting the polyol extract with an inert atmosphere.

A20. The process of any one of embodiments A1 to A18, wherein the polyol extract is not contacted with an inert atmosphere.

A21. The process of any one of embodiments A1 to A20, wherein the polyol extract is stirred for about 30 minutes to about 4 hours.

A22. The process of any one of embodiments A1 to A21, wherein the polyol extract is stirred for about 1 hour to about 4 hours.

A23. The process of any one of embodiments A1 to A22, which comprises cooling the polyol extract.

A24. The process of embodiment A23, wherein the polyol extract is cooled to about 20 degrees Celsius to about 25 degrees Celsius.

A25. The process of embodiment A23 or A24, wherein the polyol extract is cooled over a time period of about one hour to about four hours.
A26. The process of any one of embodiments A1 to A25, which comprises contacting the polyol extract mixture with carbon in amount effective to reduce coloring in the polyol extract.

A27. The process of embodiment A26, wherein about one gram of carbon is combined with about 10 milliliters to about 100 milliliters of the polyol extract.

A28. The process of any one of embodiments A1 to A27, wherein the C_2 to C_5 polyol is vegetable glycerin.

A29. The process of any one of embodiments A1 to A28, wherein the glycerin is vegetable glycerin.

A30. The process of embodiments A28 to A29, wherein the vegetable glycerin is substantially pure.

A31. The process of embodiments A28 to A30, wherein the vegetable glycerin is soybean vegetable glycerin.

A32. The process of any one of embodiments A1 to A31, wherein the glycerin mixture is filtered through a filter compatible with glycerin for a time period of about 24 hours to about 96 hours.

A33. The process of any one of embodiments A1 to A32, wherein the filtering comprises filtering the glycerin mixture through fluted filter paper.

A34. The process of any one of the embodiments A1 to A33, wherein the filtering removes particulates of greater than at least 20 to 25 microns.

A35. The process of any one of embodiments A1 to A34, wherein the filtered glycerin extract is clear or substantially clear.
A36. The process of any one of embodiments A1 to A35, wherein the filtered glycerin extract is straw colored.

A37. A process for preparing a filtered glycerin extract from the fern P. leucotomos, comprising:

- extracting dried P. leucotomos material with vegetable glycerin in a ratio of about 1 gram of dried P. leucotomos extract to about 25 to about 75 grams of vegetable glycerin, thereby preparing a leucotomos glycerin extract,
- heating the glycerin mixture to about 60 degrees Celsius to about 90 degrees Celsius,
- stirring the glycerin mixture for between 30 minutes and 4 hours,
- cooling the glycerin mixture to about room temperature over about 2 hours, and
- filtering the glycerin mixture through a fluted paper filter, to remove particulates greater than about 20 microns, thereby providing a filtered glycerin extract.


B2. The composition of B1 wherein the fern plant is a Polypodium plant.

B3. The composition of embodiment B1 to B2, wherein the fern is P. leucotomos.

B4. A composition comprising a filtered polyol extract prepared by a process of any one of embodiments A1 to A37.

B5. The composition of any one of embodiments B1 to B4, which comprises one or more components having antiinflammatory activity and/or antioxidative activity.

B6. The composition of any one of embodiments B1 to B5, which comprises one or more botanical extracts.

B7. The composition of embodiment B6, wherein the one or more botanical extracts are from a plant of the genus Araliaceae, Actinidiaceae, Lardizabalaceae,

B8. The composition of embodiment B6, wherein one of the one or more botanical extracts is from Osmanthus fragrans.

B9. The composition of embodiment B6, wherein one of the one or more botanical extracts is from Boronia megastigma.

B10. The composition of embodiment B6, wherein one of the one or more botanical extracts is from Rosmarinus officinalis.

B11. The composition of any one of embodiments B1 to B10, which comprises one or more vitamin supplements.

B12. The composition of embodiment B11, wherein at least one of the one or more vitamin supplements is a modified vitamin supplement.

B13. The composition of embodiment B12, wherein the modified vitamin supplement is chosen from vitamin C-palmitate, vitamin A-palmitate and vitamin E acetate.

B14. The composition of any one of embodiments B1 to B13, which comprises one or more growth factors.

B15. The composition of embodiment B14, wherein the one or more growth factors independently are chosen from epidermal growth factor (EGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), hepatocyte growth factor...
(HGF), keratinocyte growth factor (KGF), basic fibroblast growth factor (bFGF), insulin-like growth factor 1 (IGF1), and platelet-derived growth factor AA (PDGF-AA).

B16. The composition of embodiment B15, wherein the TGF is chosen from TGF-beta, TGF-beta2 and TGF-beta3.

B17. The composition of any one of embodiments B14 to B16, wherein at least one of the one or more growth factors is encapsulated.

B18. The composition of embodiment B17, wherein the at least one of the one or more growth factors is encapsulated in a microsphere.

B19. The composition of embodiment B18, wherein the microsphere comprises one or more components chosen from sodium oleate or sodium stearate, PEG 100, cetyl alcohol and petrolatum.

B20. The composition of any one of embodiments B1 to B19, which comprises one or more adjuvants.

B21. The composition of embodiment B20, wherein at least one of the one or more adjuvants is chosen from an emollient, moisturizer, thickener, emulsifier, neutralizer, hyaluronic acid, coloring agent, ultraviolet absorber, ultraviolet filter, preservative and gelling agent.

B22. The composition of embodiment B20 or B21, wherein the one or more adjuvants are cosmeceutically acceptable adjuvants.

B23. The composition of any one of embodiments B1 to B22, which is a solution, cream, gel or paste, or lotion.

B24. The composition of any one of embodiments B1 to B23, wherein the composition is about 0.1% to about 10% by weight of the filtered glycerin extract.
B25. The composition of any one of embodiments B20 to B24, wherein the composition is about 0.1 % to about 10% by weight of each of the one or more adjuvants.

C1. A composition comprising a filtered polyol extract from a fern plant, an oil, an emulsifying agent, an aqueous component, one or more botanical extracts and/or modified vitamins.

C2. The composition of embodiment C1, which comprises a fragrance.

C3. The composition of embodiment C1 or C2, wherein the oil is an apricot kernel oil.

C4. The composition of any one of embodiments C1 to C3, wherein the emulsifying agent is a quaternary ammonium compound, detergent or a non-ionic emulsifier.

C5. The composition of embodiment C4, wherein the non-ionic emulsifier is a cetearyl alcohol or cetearyl glucoside.

C6. The composition of any one of embodiments C1 to C5, wherein the aqueous component contains a fragrance.

C7. The composition of any one of embodiments C1 to C6, wherein the one or more botanical extracts are chosen independently from plants chosen from one or more of Osmanthus fragrans, Boronia megastigma, Rosmarinus officinalis and Rosa damascene.

C8. The composition of any one of embodiments C1 to C7, wherein the aqueous component comprises a skin smoothing component.

C9. The composition of embodiment C8, wherein the skin smoothing component is sodium salt of hyaluronic acid.
C10. The composition of any one of embodiments C1 to C9, wherein the modified vitamins are chosen from vitamin C palmitate, vitamin E acetate, vitamin A palmitate and combinations thereof.

C11. The composition of any one of embodiments C1 to C10, which comprises a non-ionic emulsifier.

C12. The composition of any one of the embodiments of C1 to C11, which comprises a growth factor.

C12. The composition of embodiment C11, wherein the growth factor is epidermal growth factor.

C13. The composition of embodiment C11 or C12, wherein the growth factor is encapsulated in microspheres.

C14. The composition of embodiment C13, wherein the growth factor is suspended in a neutral phosphate buffer and the microspheres comprise sodium oleate or sodium stearate, PEG 100, cetyl alcohol and petrolatum.

C15. The composition of any one of embodiments C1 to C14, wherein the fern is P. leucotomos.

C16. The composition of any one of embodiments C1 to C15, wherein the filtered glycerin extract prepared by a process of any one of embodiments A1 to A29.

C17. The composition of any one of embodiments C1 to C16, which is a solution, cream, gel or paste, or lotion.

D1. A method for inhibiting, preventing and/or treating skin photo-damage, comprising administering topically to the skin of a subject a composition of any one of embodiments B1 to B24 or C1 to C17 in an amount effective to inhibit, prevent and/or treat skin photo-damage.
D2. The method of embodiment D1, wherein the subject is a human subject.

D3. The method of embodiment D2, wherein the subject self-administers the composition.

D4. The method of any one of embodiments D1 to D3, wherein the skin of the subject is photo-damaged.

D5. The method of any one of embodiments D1-D4, wherein the amount effective is about 0.01 wt% to about 10 wt% polyol extract.

D6. The method of any one of embodiments D1-D5, wherein the amount effective is about 1 gm to about 10 gm plant material to about 1 gm to about 100 gm C2-C5 polyol.

EXAMPLES

Extraction of Polypodium leucotomos (Example 1)

[075] Polypodium Leucotomos extract (1 g) (dried leaf material of P. leucotomos, Parchem Fine & Specialty Chemicals, New Rochelle, NY, USA) was mixed in about 40 ml of pure vegetable glycerol (ParChem Fine & Specialty Chemicals) and heated to 75°C ± 5°C with rapid stirring for about 1 h. The resulting mixture was then allowed to cool unaided without additional ice or refrigerated cooling to room temperature over 2h. This mixture was then gravity filtered through a paper filter (Whatman filter paper No 2, 8 micrometer (micron) pore size, Sigma Aldrich, Wisconsin, USA) over two days in a covered container at room temperature. The filter paper, after completion of the separation, contained about 200-400mg of a black brown residue and the filtrate produced was a clear to light straw colored solution that contained the active component.

EXTRACT ACTIVITY

Cell based assays using skin cells can show the extracts have significant and useful biological activity that improve the lifetime of the cells compared to untreated cells. Also the extracts can modify the inflammatory messengers within the cell.
These assays also aid in the preparation of the extracts by giving a measurable method of monitoring biological activity.

IN VIVO TESTING

PREPARATION OF THE ACTIVE FOR CELL CULTURE:

[076] The active (glycerol extract), prepared as described above, was stored in the dark at room temperature. Dilutions of the active (0.01%, 0.1% and 1.0%) were aseptically added to appropriate culture media, then filter sterilized through a 0.22µm filter and stored in the dark at 4°C, until used.

CELL CULTURE:

[077] Fibroblasts were cultured in Dulbecco's Modified Eagle's Medium (DMEM) + 10% fetal bovine serum (complete growth medium). Keratinocytes were cultured in serum-free keratinocyte complete growth medium. Both cell types were grown to 70%-80% confluence. Cells were cultured in complete medium alone (Control or C), complete medium supplemented with 1.0% glycerol (Control + 1.0% glycerol or CG), complete medium supplemented with 0.01% active (Low), 0.1% active (Medium), or 1.0% active (High) for specific amounts of time. For cell viability studies, 96-well plates were seeded with 5,000 cells/cm² of fibroblasts for the Control (buffer only), Control + 1.0% Leucotomos Glycerol Extract, Low (0.01% leucotomos Glycerol extract), Medium (0.1% leucotomos glycerol Extract) and High (1.0% Glycerol extract) (1.0% refers to 1% solution of the filtered extract [1 gm of P. leucotomos extracted with 40 ml glycerin] dissolved in 100% glycerin) concentration of Poldodium lecotomutus extract in an XTT assay and with 3,500 cells/cm² of keratinocytes for the WST-8 assay. For the collagen assay, 24-well plates were seeded with 5,000 cells/cm² of fibroblasts. For the gene expression study, T75 flasks were seeded with 5,000 cells/cm² of fibroblasts. At the specific time point, cultures were taken through the appropriate assay.

XTT CELL VIABILITY ASSAY:

[078] The cell proliferation colorimetric assay (Sigma-Aldrich, St. Louis, Missouri) was used to determine cell viability of fibroblasts after growth in after 12, 24, 48, 72 and 96 hours. XTT assay working stock solution was prepared as filter
sterile 1 mg/ml XTT ((2,3-Bis(2-methoxy-4-nitro-5-sulfophenyl)-2H- tetrazolium-5-carboxanilide inner salt)) and 32 µM PMS (phenazine methosulfate) in appropriate culture medium. The XTT assay was performed at each appropriate time point. 50 µl XTT/PMS was added to wells containing 200 µl media and the plates were incubated at 37°C in 5% CO2 for 1.5-2 hours. The optical density (OD) was read at 450nm and 650nm and the data were analyzed. The results are shown in FIGS. 1-5. The XTT assays indicated that the extracts exhibited comparable cell viability with those cells having been exposed to the controls.

WST-8 Assay

[079] The WST-8 assay was used to determine cell viability of keratinocytes after growth in Control, Control + 1.0% Glycerol, Low and High medium after 24, 48 and 96 hours. 10 µl of Cyto-X solution (Cell Applications, San Diego, CA) was added to wells containing 200 µl media and the plates were incubated at 37°C in 5% CO2 for 1-4 hours. The optical density (OD) was read at 450nm and the data were analyzed. The presence of (0.01 %) concentration of the extract overcomes the glycerol control effect after 96 hours of growth with the cell viability assay (WST-8). The control shows an absorbance at 450nm of 1.8 absorption units whereas the 0.01 % concentration of active shows an absorbance of 2.1 absorption units.

Real-time PCR

[080] Fibroblasts were cultured in T75 flasks in appropriate treatment and grown to 70-80% confluence, then trypsinized. Cells were centrifuged and the pellet was gently resuspended in 500 µl RNALater and then stored at -80°C until the RNA was extracted. Total RNA was extracted with Trizol and first strand cDNA was synthesized. Samples were analyzed in triplicate and the average Ct value was used to calculate fold change (increase or decrease) in gene expression using the AACt method (Kenneth J. Livak and Thomas D. Schmittgen; METHODS 25, 402-408 (2001) ). The results are shown in FIG. 6. "0.01 % active (high) vs CG" represents fold change in expression of TNFa in cells grown in high concentration of active compared to control and 1.0% glycerol cells. The results show that the extract described herein modify the inflammatory signaling within the cell.
EXTRACTION FORMULATIONS

[081] Typical formulations of the lotion are represented but not limited by the following Table 1 below (about 76.91 %wt water (items 1, 12, and 23); 1.05 %wt preservatives (items 2 and 14); 3.0 wt% absorption enhancer (item 4); 2.55 wt% thickeners (items 3, 5, 10 and 17); 3.5 wt% moisturizers (items 8, 11, 15, 19); 8.75 wt% emulsifier (items 6-8, and 10); PE extract 1.0 wt% (item 18); 2.2 wt% antipigmentation agent (item 16 and 24); 0.01 wt% fragrance (21, 22); pH adjuster 0.03 wt % (13); UV blocking agent 1.0 wt% (20):

Table 1
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<td>Cetearyl Alcohol,</td>
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<td></td>
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<td>11</td>
<td>C</td>
<td>Soline</td>
<td>Expanscience</td>
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<td></td>
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<td>Helianthus Annus</td>
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<td></td>
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<td>(Sunflower) Seed Oil</td>
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<tr>
<td>Item #</td>
<td>Phase</td>
<td>Trade Name/INCI Name</td>
<td>Supplier</td>
<td>% WT</td>
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<td>12</td>
<td>D</td>
<td>Deionized Water</td>
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<td>Sodium Hydroxide, Pellets, NF Sodium Hydroxide</td>
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<td>Phenoxyethanol, Caprylyl Glycol, Hexylene</td>
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<td>Glycol, Ethylhexylglycerin</td>
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<td>SK-Influx V</td>
<td>Evonik</td>
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<td>16</td>
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<td>Simulgel NS</td>
<td>Seppic</td>
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<td>Hydroxyethyl Acrylate/Sodium Acryloyldimethyl</td>
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<td>Taurate Copolymer, Water (Aqua), Squalane, Polysorbate 60, Sorbitan Isostearate</td>
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<td></td>
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<tr>
<td>18</td>
<td>E</td>
<td>PLE Extract in Glycerin</td>
<td>Paris Therapeutics</td>
<td>1.0000</td>
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</table>
Formulation Procedure

(A) Into the main processing tank (about 100 liters), equipped with a propeller mixer and side sweep, was added item #1 (Di Water) and begin moderate-speed. Added item #2 and mix until uniform. Added item #3 and heat to about 80°C to about 85°C. The composition was mixed until uniform while maintaining the temperature at 80°C- 85°C. (B) In a separate vessel, items #4 and #5 were premixed. Once dispersed, added to the main processing tank and mix until uniform. Cooled to 75°C- 80°C. (C) In a separate vessel, items #6-#11 were added. The resulting mixture was heated to about 75°C to about 80°C and mixed until uniform. This mixture was slowly added to the main processing tank and mixed until uniform. The temperature was maintained at 75°C- 80°C. (D) In a separate vessel, items #12 and #13 were premixed. Once dissolved, this was added to the main processing tank and mixed until uniform. This was cooled to about 35°C to about 40°C. (E) At 35°C- 40°C, items #14- #22 were added to the main processing tank in the order given, mixing well after each addition. This was mixed until uniform. (F) In a separate vessel, items #23 and #24 were premixed. Once dispersed, add to the main processing tank and mix until uniform. Continue mixing and cooling to 35°C.
A top note anti-inflammatory fragrance solution was prepared by combining the materials in Table 2 below.

Table 2

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Relative Volume</th>
<th>Reference Volume</th>
<th>Source (Sigma-Aldrich)</th>
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<tr>
<td>β-Linalool / C10H18O</td>
<td>346.5</td>
<td>231</td>
<td>W263508-Sample-K</td>
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<tr>
<td>β-Ionol / C13H220</td>
<td>180</td>
<td>120</td>
<td>00468-5ML (Aldrich)</td>
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<tr>
<td>α-Ionol / C13H220</td>
<td>43.5</td>
<td>29</td>
<td>00469-5ML</td>
</tr>
<tr>
<td>Methylhexadecanoate / C17H30O2</td>
<td>10.5</td>
<td>7</td>
<td>P51 77-1 G</td>
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<tr>
<td>Acetoin</td>
<td>7.5</td>
<td>5</td>
<td>W200808-SAMPLE-K</td>
</tr>
<tr>
<td>trans-Geraniol / C10H18O</td>
<td>60</td>
<td>40</td>
<td>W250708-Sample-K</td>
</tr>
<tr>
<td>α-Ionone</td>
<td>15</td>
<td>10</td>
<td>E-Bay</td>
</tr>
<tr>
<td>β-Ionone / C13H20O</td>
<td>82</td>
<td>55</td>
<td>W259500-Sample-K</td>
</tr>
<tr>
<td>D-Limonene / C10H16</td>
<td>7.5</td>
<td>5</td>
<td>W263303-Sample-K</td>
</tr>
<tr>
<td>6-methyl-5-hepten-2-one</td>
<td>7.5</td>
<td>5</td>
<td>W270709-SAMPLE-K</td>
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<tr>
<td>β-Myrcene / C10H16</td>
<td>4.5</td>
<td>3</td>
<td>W276200-Sample-K</td>
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<td>Nerol / C10H18O</td>
<td>2.1</td>
<td>14</td>
<td>W277002-Sample-K</td>
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<td>Nonanal / C9H180</td>
<td>16.5</td>
<td>11</td>
<td>W278203_Sample_K</td>
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<td>a-Terpineol / C10H18O</td>
<td>67.5</td>
<td>45</td>
<td>W304506_Sample-K</td>
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<td>cis-3-hexenyl acetate</td>
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<td>W31 7101-SAMPLE-K</td>
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<th>Ingredients</th>
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<th>Source (Sigma-Aldrich)</th>
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<tr>
<td>δ-Undecalactone / C11H20O2</td>
<td>39</td>
<td>W329401-Sample-K</td>
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<tr>
<td>cis-β-Ocimene / C10H16</td>
<td>7.5</td>
<td>W353901-Sample</td>
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<tr>
<td>Dihydro-β-ionone / C13H22O</td>
<td>16.5</td>
<td>W362603-Sample</td>
</tr>
<tr>
<td>cis-Linalool oxide / C10H18O2</td>
<td>7.5</td>
<td>W374600-SAMPLE-K</td>
</tr>
<tr>
<td>α-Farnesene / C15H24</td>
<td>22.5</td>
<td>W383902-Sample_K</td>
</tr>
<tr>
<td>3-Nonen-2-one / C9H16</td>
<td>34.5</td>
<td>W395500-SAMPLE-K</td>
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<tr>
<td>8-β-H-Cedran-8-ol / C15H26O</td>
<td>12</td>
<td>W521418-Sample_K</td>
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<tr>
<td>Boronia Megastigma</td>
<td>20</td>
<td>High Altitude Organics</td>
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<tr>
<td><strong>Total</strong></td>
<td>1036.5</td>
<td>678</td>
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A base solution was prepared from botanical extracts according to Table 3 below:
**Middle / Base Note**

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<tr>
<th>Ingredient</th>
<th>Drops</th>
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<tr>
<td>Bergamot</td>
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<td>Simplers Botanicals</td>
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<tr>
<td>Rosemary</td>
<td>20</td>
<td>Simplers Botanicals</td>
</tr>
<tr>
<td>Sandlewood</td>
<td>20</td>
<td>Simplers Botanicals</td>
</tr>
<tr>
<td>Benzoin</td>
<td>12</td>
<td>Simplers Botanicals</td>
</tr>
<tr>
<td>Oak Moss</td>
<td>4</td>
<td>Simplers Botanicals</td>
</tr>
</tbody>
</table>

1 drop = about 0.05 mL

[085] An alternative formulation based upon Apricot Kernel oil is given below. 1.6 L of deionized water, 200 mL of Apricot Kernel Oil, 40 g Vaseline, 40 g of cetearyl alcohol and cetearyl glucoside (non-ionic emulsifier) were mixed at 80 degrees centigrade at about 250 RPM on a turbo stirrer for about 60 minutes. The stirred mixture was then cooled to about 40 degrees centigrade. About 100 mL of DI water was added to the cooled mixture and stirred for about 1 hr at room temperature to provide about 2.0 L of cooled lotion base.

[086] To the 2.0 L of cooled lotion base was added 20.0 mL of PLE extract in glycerin prepared as described in Example 1 above, 8.6 mL of the top note solution prepared above, 4.3 mL of base material solution prepared as described above, 10 mL of artichoke C02 extract (Sigma, St. Louis MO, USA), 10 mL Vitamin C Palmitate (Sigma-Aldrich, St Louis, Missouri); and 10 mL (4000 IU) vitamin E acetate in glycerin / soy oil (Vendor). The concentration of the glycerol extract made as described in Example 1, was about was about 1% in the resulting lotion base.

[087] The active component from the glycerol extraction was then combined into a lotion that is used for sun damaged or sun damage preventative topical applications. The lotion contains oil, such as apricot kernel oil (~100g), an emulsifying agent such as quaternary ammonium compound or a detergent or a non-ionic emulsifier such as cetearyl alcohol and cetearyl glucoside (~1 : 1 5g). The lotion is made with an aqueous component (~650mL) which may contain a fragrance; water based therapeutic agent or a botanical agent that imparts therapeutic advantages such as the tea from Osmanthus fragrants. In some embodiments, the fragrant can be fragrant solutions, e.g., top note fragrant solutions, middle note. This tea can be made from purified water and dried
Osmanthus fragrans flowers and the tea supplemented with other botanical components that compensate for the poor extraction ability of water. Such other botanical components can include Boronia megastigma to replace missing or partially extracted megastigmas.

[088] The aqueous component can also be supplemented with a skin smoothing component such as the sodium salt of Hyaluronic acid (0.1 - 1% wt to volume).

[089] The resulting lotion is supplemented with vitamins such as vitamin C palmitate, vitamin E acetate with or without vitamin A and its derivatives. In addition when a non-ionic emulsifier is used the lotion can be enhanced with a cell signaling component such as epidermal growth factor. Typically the factor is formed into microspheres by suspending the growth factor in a neutral phosphate buffer and the following added: sodium oleate or sodium stearate, PEG 100, cetyl alcohol and petrolatum and then hand shaken until a white emulsion is formed. Typically 50 micrograms of the cell signaling factor is used and this is then added to the lotion as the last step in the formulation by gently hand mixing.

[090] In addition other botanical extracts, fragrances and preservatives can be added to the lotion. Preferably botanical extracts that provide both a fragrance and a preservative effect are used. Non-limiting examples include Rosmarinus officinalis and/or Rosa damascene.

IN VITRO TESTING

[091] Topical application of the lotion made as described in the examples above to the hands of the human body. Daily topical applications of the lotions by way of contact occlusion to the desired areas were made.

21 Day cumulative patch testing

[092] Consumer products or raw materials designed for consistent reapplication to areas of the skin may, under proper conditions, prove to be contact irritants in certain individuals. This study was intended to determine cumulative dermal irritation potential of the test material by the use of predictive patch test techniques.
Twenty subjects (18, Female; 2, Male; 15 Caucasian; 4 Hispanic, 1 Asian) were requested to bathe or wash as usual before arrival at the facility (AMA Laboratories, New City, New York). 0.2 ml of the test material (0.1 wt% filtered polyol extract without additional adjuvants) was dispensed onto an occlusive, hypoallergenic patch (2 cm X 2 cm square Parke-Davis Hypoallergenic Readi Bandages). The patch was then applied directly to the skin of the infrascapular regions of the back, to the right or left of the midline and the subject was dismissed with instructions not to wet or expose the test area to direct sunlight. After 24 hours the patch was removed at the facility. Prior to each reapplication, the test sites were evaluated. Skin responses were evaluated according to the following scale by a technical associate of AMA Laboratories (scorer) trained in the evaluation of skin using consistent ambient lighting. All reasonable attempts were made to ensure that the same individual did all of the scoring of reactions to the test articles during the course of the study, and was blinded to the treatment assignments and any previous scores. The scoring was as follow:

0 - No evidence of any effect
1 - Pink uniform erythema covering most of the contact site
2 - Pink-red erythema visibly uniform in entire contact site
3 - Bright red erythema with or without petechiae or papules
4 - Deep red erythema with vesiculation or weeping with or without edema.

All scorers were required to take and pass a visual discrimination examination conducted by a board certified ophthalmologist using the Farnsworth-Munsell 100 Hue test. This test, which determines a person's ability to discern color against a black background, was modified to incorporate a flesh tone background (instead of black) to simulate the actual use conditions.

The test material was applied five days weekly for 21 days to the same site, or until irritation scores of 3 or 4 were observed. In this case application of the test product was discontinued and the score attained was entered for the balance of the 21 day test. The same test articles were applied to the test sites after visual evaluation.
The maximum potential score for a test material was calculated by multiplying the maximum potential daily score by the number of panelists completing the study by the number of days of evaluation.

In the event of an adverse reaction, the area of erythema and edema was measured. The edema was estimated by the evaluation of the skin with respect to the contour of the unaffected normal skin accompanying edema (swelling) at any test site was recorded with an "e" and was described as mild, moderate or severe as compared with the normal surface of surrounding skin.

No adverse reactions of any kind were noted during the course of this study.

Hand study

The subject's hands were examined before the topical application of the polyol extract and rated on a scale of 0-9 (0 = none, 1-3 mild, 4-6 moderate, and 7-9 severe) for fine wrinkling, course wrinkling, Mottled hyperpigmentation and yellowing (sallowness). "Fine wrinkling" was a visual assessment of the number and depth of superficial wrinkles (i.e., shallow indentations or lines). Fine wrinkles typically appear in periorbital and perioral regions and are usually found further from the eyes and mouth than are coarse wrinkles. "Coarse wrinkling" was a visual assessment of the number and depth of coarse wrinkles (i.e., deep lines, furrows, or creases). Coarse wrinkles appear on the forehead, galabelia, chin, and nasolabial and periorbital areas, and they tend to be located closer to the eyes and mouth than fine wrinkles. "Mottled hyperpigmentation" was a visual assessment of light patchy, mottled hyperpigmentation and solar freckling (including melisma) based on quantitative and qualitative criteria such as the area/density of pigment, color intensity (dark vs. light) and uniformity of distribution (i.e., the more uneven or blotchy, the greater the score), Lentigines, nevi, and other pigmented lesions are not to be included in this assessment. "Yellowing" (Sallowness) was a visual assessment of color tone from very pink or rosy to very sallow or pale. (Griffith, et al, A Photonumeric Scale for the assessment of cutaneous photodamage, Arch Dermatology, 128:347 (1992)).
[0100] 1 mL of polyol extract formulation as described in Tables 1, 2, and 3 above was applied topically to the back of the hand of a 55 year old human female once a day for 2 weeks. After two weeks, the hands were examined and assessed for the same visual assessments. The results are shown in Table 4.

Table 4

<table>
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<tr>
<th>Assessment</th>
<th>Before topical administration</th>
<th>After topical administration</th>
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<tbody>
<tr>
<td>Fine Wrinkles</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Coarse Wrinkles</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Mottled hyperpigmentation</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Yellowing (sallowness)</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

The topical application of the polyol extract resulted in a reduction of the fine wrinkles, coarse wrinkles, mottled hyperpigmentation and yellowing.

[0101] Unless otherwise indicated, all numbers expressing quantities of ingredients, properties such as molecular weight, reaction conditions, and so forth used in the specification and claims are to be understood as being modified in all instances by the term "about." Accordingly, unless indicated to the contrary, the numerical parameters set forth in the specification and attached claims are approximations that may vary depending upon the desired properties sought to be obtained. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of the claims, each numerical parameter should at least be construed in light of the number of reported significant digits and by applying ordinary rounding techniques.

[0102] The terms "a," "an," "the" and similar referents used in the context of describing the invention (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context. All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly
contradicted by context. The use of any and all examples, or exemplary language (e.g., "such as") provided herein is intended merely to better illuminate the invention and does not pose a limitation on the scope of any claim. No language in the specification should be construed as indicating any non-claimed element essential to the practice of the invention.

[0103] Groupings of alternative elements or embodiments disclosed herein are not to be construed as limitations. Each group member may be referred to and claimed individually or in any combination with other members of the group or other elements found herein. It is anticipated that one or more members of a group may be included in, or deleted from, a group for reasons of convenience and/or patentability. When any such inclusion or deletion occurs, the specification is deemed to contain the group as modified thus fulfilling the written description of all Markush groups used in the appended claims.

[0104] Certain embodiments are described herein, including the best mode known to the inventors for carrying out the invention. Of course, variations on these described embodiments will become apparent to those of ordinary skill in the art upon reading the foregoing description. The inventor expects skilled artisans to employ such variations as appropriate, and the inventors intend for the invention to be practiced otherwise than specifically described herein. Accordingly, the claims include all modifications and equivalents of the subject matter recited in the claims as permitted by applicable law. Moreover, any combination of the above-described elements in all possible variations thereof is contemplated unless otherwise indicated herein or otherwise clearly contradicted by context.

[0105] In closing, it is to be understood that the embodiments disclosed herein are illustrative of the principles of the claims. Other modifications that may be employed are within the scope of the claims. Thus, by way of example, but not of limitation, alternative embodiments may be utilized in accordance with the teachings herein. Accordingly, the claims are not limited to embodiments precisely as shown and described.
WHAT IS CLAIMED IS:

1. A process for preparing an extract comprising:
   extracting P. leucotomos material with C₂ to C₅ polyol in a ratio of about 1 gram of P. leucotomos material to about 10 to about 100 grams of a C₂ to C₅ polyol, thereby preparing a leucotomos polyol extract; and
   filtering the leucotomos polyol extract, thereby providing a filtered leucotomos polyol extract.

2. The process of claim 1, further including heating the leucotomos polyol extract to about 60 degrees Celsius to about 90 degrees Celsius.

3. The process of claim 1 further including stirring the leucotomos polyol extract for between 30 minutes and 4 hours,

4. The process of claim 1, wherein the filtering of the leucotomos polyol extract is through a fluted paper filter.

5. The process of claim 1, wherein preparing a leucotomos polyol is exclusive of a lower alkyl alcohol.

6. A composition comprising a filtered polyol extract made according to claim 1.

7. The composition of claim 6, further comprising a growth factor.

8. A process for preparing an extract comprising:
   extracting dried P. leucotomos material with vegetable glycerin in a ratio of about 1 gram of dried P. leucotomos extract to about 5 to about 100 grams of vegetable glycerin, thereby preparing a leucotomos polyol extract,
   heating the leucotomos polyol extract to about 60 degrees Celsius to about 90 degrees Celsius;
   stirring the leucotomos polyol extract for between 30 minutes and 4 hours; and
   filtering the leucotomos polyol extract through a filter to remove particulates greater than about 20 microns, thereby providing a filtered polyol extract.


10. The topical composition of claim 9, wherein the extract comprises a C₂-C₅ polyol

11. The topical composition of claim 10, wherein the C₂-C₅ polyol is vegetable glycerin.

12. The topical composition of claim 9, wherein the topical composition has a phenolic acid ester concentration of less than 0.01%.
13. A method for providing anti-inflammatory activities to the skin, comprising the steps of topically applying the topical composition of claims 1-12 to the skin.

14. A method for providing anti-oxidative activities to the skin, comprising the steps of topically applying the topical composition of claims 1-12 to the skin.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

INV. A61Q19/08 A61K8/97 A61K8/34

ADD.

According to International Patent Classification (IP) into both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

A61Q A61K

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

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

EPO-Internal, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
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<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
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<td>X</td>
<td>US 2006/03690 AI (ALMAGR0 ELISE0 Q [ES]) 4 May 2006 (2006-05-04) paragraphs [0013], [0026], [0032], [0038]</td>
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<td>X,P</td>
<td>wo 2014/106638 A2 (GOLÜKE TIMM [DE]) 10 July 2014 (2014-07-10) page 4, lines 22-29; examples 1-5</td>
<td>6,7,9-12</td>
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</table>

[X] Further documents are listed in the continuation of Box C.  
[X] See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"A" document member of the same patent family

Date of the actual completion of the international search: 21 August 2015

Date of mailing of the international search report: 11/09/2015

Name and mailing address of the ISA:

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016

Authorized officer: Vayssié, Stephane

Form PCT/ISA/210 (second sheet) (April 2005)
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<td>GONZALEZ SALVADOR ET AL: &quot;Mechanistic insights in the use of a Polypodium leucotomos extract as an oral and topical photoprotective agent&quot;, PHOTOCHEMICAL &amp; PHOTobiological SCI EnCES, vol. 9, no. 4, 2010, pages 559-563, XP002743535, ISSN: 1474-905X cited in the application Title; paragraph [06.1]</td>
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