REVIEW ARTICLE

Molecular mechanisms of skin photoaging and plant inhibitors

Chanchal Garg, Priyanka Khurana, Munish Garg

Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, Haryana, India

Abstract

Skin ageing is a complex multifactorial process occurring in all living beings. It generally comprises two independent and distinct processes, i.e., intrinsic, age-dependent or chronological aging and premature aging, or photoaging which is the result of undue exposure of the skin to ultraviolet (UV) radiations. Photoaging can be prevented or the effects of photoaging can be reduced by the use of certain anti-aging and anti-wrinkle agents. The extracellular matrix (ECM) which forms the outermost part of skin comprises fibroblasts and proteins such as collagen and elastin. Degradation of ECM is directly linked to skin aging and is responsible for the increase in activity of certain enzymes such as collagenase, elastase, and hyaluronidase (HYAL) that are involved in skin aging. With aging there is decrease in the levels of elastin, collagen, and hyaluronic acid which leads to loss of strength and flexibility of skin and appear as wrinkles on the skin. Further, the increase in the activity of collagenase, elastase, and HYAL is triggered by the high levels of reactive oxygen species produced when the skin is exposed to excessive UV radiations leading to skin aging. Today, in the age of modern science and advanced technology, although many techniques such as laser rejuvenation, plastic surgery, and lots of synthetic products such as sunscreen lotions, creams are available yet, there is a place for natural, herbal anti-aging cosmetics. Various botanical extracts have the power to reduce the appearance of skin aging and enhance the beauty of the skin. Medicinal plants have several phytoconstituents such as polyphenols, alkaloids, tannins, saponins, carotenoids, and terpenoids which possess antioxidant properties and can be used in treating the signs of aging. Some plants contain phenolic compounds which have free-radical scavenging property and can suppress aging. Some plants or their extracts possess several other constituents that may have the capability of inhibiting various enzyme such as HYAL, elastase, and matrix metalloproteinases enzyme that play a major role in skin aging. Some of them may possess the free radical scavenging or antioxidant property to fight against the signs of aging. This review focuses on the compilation of medicinal plants and natural compounds as anti-aging and anti-wrinkling agents along with their chemical constituents based on their possible molecular mechanism of action. The present review will facilitate the scientists working in this area for the development of new anti-aging and anti-wrinkle formulations with better efficiency and safety.

Key words: Collagenases, elastases, herbs, hyaluronidases, matrix metalloproteinases, photoaging, plant inhibitors, wrinkles

INTRODUCTION

Skin aging is a complex multifactorial process occurring in all living beings that are generally influenced by two independent and distinct processes. One being the unpreventable, unavoidable, intrinsic, age-dependent, or chronological aging which influences the skin and all other organs of the body in the similar way.[1] It may be due to changes in the levels of hormones with age,[2] production of sex hormones and altered levels of estrogen and progesterone associated with menopause leading to the degradation of collagen, loss of elasticity and appearance of wrinkles in the skin.[3] However, the aging occurred due to the excessive exposure of the skin to the ultraviolet (UV) irradiations is generally referred to as premature aging or photoaging which results in hyperpigmentation of the skin. Furthermore, the skin appears leathery with deep furrows and wrinkles.[4,5] There have been innumerable studies conducted

Address for correspondence:
Dr. Chanchal Garg, Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, Haryana, India. Phone: +91-8059488857.
E-mail: cgarg72@gmail.com

Received: 21-01-2017
Revised: 11-04-2017
Accepted: 25-04-2017

to spell out the various molecular mechanisms underlying the cause of aging and its preventive strategies. This review focuses on the molecular mechanism underlying the skin aging and the plant inhibitors that can be used for their treatment.

CLINICAL MANIFESTATION OF PHOTOAGING

Skin is comprised three distinct layers; epidermis, dermis, and subcutaneous tissue. The extracellular matrix (ECM) which forms the outermost part of skin comprises fibroblasts and proteins such as collagen and elastin.[6] Degradation of ECM is directly linked to skin aging and is responsible for the increase in activity of certain enzymes such as collagenase, elastase, and hyaluronidase (HYAL) that are involved in skin aging.[5,7,8] With aging there is decrease in the levels of elastin, collagen, and hyaluronic acid (HA) which leads to loss of strength and flexibility of skin and appear as wrinkles on the skin. Further, the increase in the activity of collagenase, elastase, and HYAL is triggered by the high levels of reactive oxygen species (ROS) produced when the skin is exposed to excessive UV radiations leading to skin aging.[9-11] The skin shows hypertrophic features with deep wrinkles, leathery appearance, dark/light pigmentation, sallowness, premalignant lesions, irregular dryness, and lentigines.[12] Other signs of aging include elastosis (a coarse, yellow, cobblestoned effect is on the skin) and actinic purpura (easy bruising corresponding to vascular wall fragility in dermis).[13] Figure 1 outlines the possible molecular mechanism of skin aging that takes place in the skin.

MOLECULAR MECHANISMS AND PLANT INHIBITORS

In an ancient system of traditional medicine, various botanical extracts have the power to reduce the appearance of skin aging and enhance the beauty of the skin. Medicinal plants have several phytoconstituents such as polyphenols, alkaloids, tannins, saponins, carotenoids, and terpenoids which possess antioxidant properties and can be used in treating the signs of aging. Some plants contain phenolic compounds which have free-radical scavenging property and can suppress aging.[14] The various skin care product that contain natural constituents are rapidly absorbed by the outermost layer of the skin and are mainly hypoallergenic in nature. Some plants or their extracts possess several other constituents that may have the capability of inhibiting various enzyme such as HYAL, elastase, and matrix metalloproteinases (MMP) enzyme that play a key role in skin aging.[15] Some of them may possess the free radical scavenging or antioxidant property to fight against the signs of aging. Following sections explains the detailed mechanism involved in skin aging.

MOLECULAR MECHANISMS IN SKIN AGING

MMP/Collagenases

MMPs are a group of zinc-containing extracellular proteinases, also referred as matrixins or collagenases, which help in remodeling the extracellular matrix (ECM).[16-25] MMP expression is induced and activated only after the exposure of skin to UVB radiations.[26] Fisher *et al*., 2002[4] suggested that the UV radiations trigger various growth factors and cytokine receptors existing on the cell surface. This stimulates mitogen-activated protein kinase signal transduction which further upregulates activator protein-1 (AP-1), the transcription factor comprised c-Jun and c-Fos proteins and nuclear factor kappa B (NF-κB) in the nucleus. The induction of AP-1 leads to the elevation of MMP expression along with the elevation of MMP-1 (collagenase), MMP-3 (stromelysin - 1), and MMP-9 (gelatinases). This further leads to the degradation of the

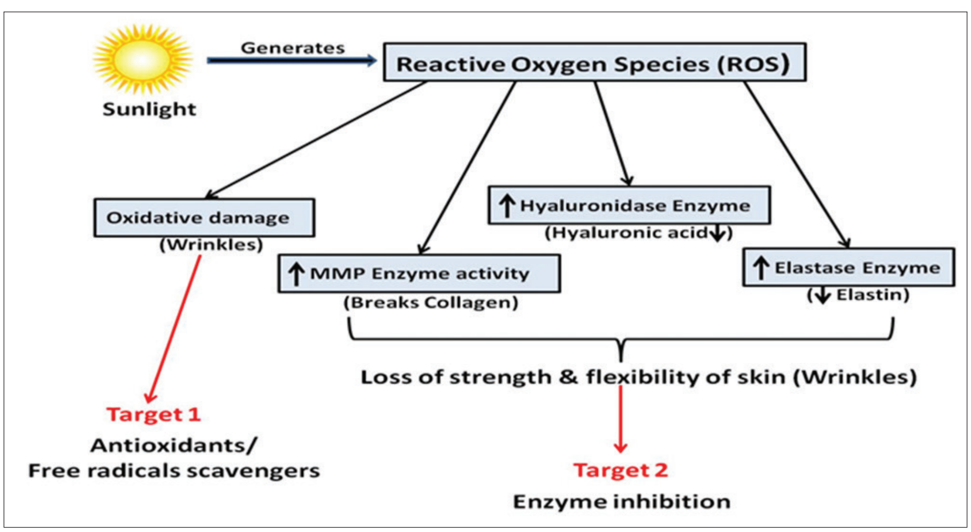

Figure 1: Schematic representation of molecular mechanisms of skin aging

components of extracellular matrix in human skin *in vivo*.[4,27] As the result of degradation, there is an accumulation of fragmented, disorganized collagen fibrils. These disrupted collagen products downregulate the synthesis of new collagen. Thus, collagen synthesis is negatively regulated by collagen breakdown.[28,29] The joined actions of MMP-1, MMP-3, and MMP-9 degrade most of the Types - I and III dermal collagen. Furthermore, the procollagen biosynthesis is inhibited by AP-1 by suppressing the Types - I and III procollagen gene expression in the dermis leading to the reduced collagen content.[30]

HYALUROINIDASES

Skin aging is also correlated with loss of skin moisture that is maintained by hyaluronan or HA, a glycosaminoglycan, having the unique property of binding and retaining water molecules.[31] HA is most abundant in the skin,[32-36] accounting for 50% of total body HA.[37] HA is mainly produced by mesenchymal cells but can also be produced by other cell types.[38-43] It keeps the body smooth, moist and lubricated. During aging, HA present in the skin diminishes leading to the dry and wrinkled skin. HA is degraded by the enzyme HYAL by hydrolyzing the hexosaminidic β (1-4) linkages between N- acetyl-D-glucosamine and D- glucuronic acid residues. HA is hydrolyzed by HYAL by lowering its viscosity and increasing the permeability.[44]

ELASTASES

Extracellular matrix also contains elastin which is responsible for maintaining the elasticity and resilience.[45] During aging, the elasticity of the skin is reduced by the enzyme elastase which leads to sagging. Elastin, an insoluble elastic fiber protein, which along with collagen influences the mechanical properties of connective tissue, is only degraded by the enzyme elastase.[46] Elastase belongs to the family of chymotrypsin, an enzyme that is capable of hydrolyzing materials such as elastin and fibrillin (which are the fiber materials found within the ECM). The secretion and activation of elastase from dermal fibroblasts in response to UV irradiation and/or to cytokines released by keratinocytes are responsible for the degeneration of the three-dimensional structure of elastic fibers during the formation of wrinkles. Elastase has a significant impact in the metabolism of elastic fibers in skin tissues during photoaging. It was also found that the transcriptional activity of NF-kB is induced by UV irradiation and greatly contributes to the photoaging process.[47]

FREE RADICAL SCAVENGERS/ ANTIOXIDANTS

When the skin is continuously exposed to the UV radiations, the production of free radicals which damage the biological skin cell membranes is induced. Free radicals are the highly ROS which contain one or more unpaired electrons that are formed as a result of cellular oxidative metabolic reactions.[48] Skin is a prime target of oxidative stress as it is rich in lipids, proteins, carbohydrates, and DNA which are highly vulnerable to oxidative processes and the effects of ROS generated as a result of oxidative stress.[49] The oxidative processes induced by ROS results in lipid peroxidation, DNA mutations and damage of membrane protein that play a key role in skin aging.[50] Lipid peroxidation causes the alteration in the fluidity of plasma membrane and leakage of molecules and the consequent disruption of their primary roles.[51] The enzymes can be directly inactivated by ROS that may lead to protein degradation.[49] ROS also cause an oxidative damage of DNA such as modifications or loss of bases and DNA breakage, which may end up in various adverse processes and even cancer.[51] This oxidative stress appears as uneven, blotchy pigmentation, and disturbs the basic structural framework of the skin, consequently giving rise to wrinkles and sagging skin.[52] Although the epidermis of skin possesses an effective natural antioxidant defenses which includes different antioxidant enzymes such as peroxidases, catalases, and glutathione, the protective cover offered by them may be restricted due to huge production of ROS. This leads to cellular oxidative stress because of the imbalance between antioxidant and oxidant species of living organisms. Therefore, antioxidants with free radical scavenging activity may have great significance in defense and therapeutics of age-related diseases involving free radicals.[50,53,54]

PLANT INHIBITORS

In recent times, there has been an increase in the scientific interest in minimizing the effects of aging.[55] Although now a day's curing of aging skin is more efficient by the use of modern technology that involves more invasive procedures, the use of herbs and herbal products is still relevant. Combining these herbal preparations with molecular techniques will assist in maximizing their results and help in maintaining the desired anti skin aging benefits. Plants produce a great variety of compound broadly classified as terpenoids, alkaloids, and phenolic compounds.[56] This article intends to review the plants and plant extracts and their constituents along with their action mechanisms which have been reported to exhibit anti-aging and potential.

Aloin A and B present in *Aloe vera* have been shown to inhibit *Clostridium histolyticum* collagenase reversibly and noncompetitively. Aloe gel and aloin are also effective inhibitors of stimulated granulocyte MMPs.[57] UV-B induced MMP-1 expression and increased Type - I procollagen expression is suppressed by Xanthorrhizol present in *Curcuma xanthorrhiza*.[58] The extracts plant Wild Yam (*Dioscorea villosa*) shows anti collagenase activity making its use in anti-aging products.[59] Diosgenin present in it shows advantageous effects on aging skin especially to reduce the effects of climacteric issues.[60] *Camellia japonica* oil has been reported to have anti-aging property.[61] It induces the synthesis of human Type - I procollagen and inhibits the MMP-1 activity. The oil of *C. japonica* is also reported to hold transepidermal water loss without causing any adverse effects. The roots of *Panax ginseng* have been demonstrated to induce the synthesis of Type - I collagen via Smads (series of proteins that perform downstream functions from the serine/threonine kinase receptors of the TGF-β family) activation pathway.[62] Fruit extract of *Emblica officinalis* has been reported to stimulate the proliferation of fibroblasts and production of procollagen. It shows the decrease in the production of MMP-1 from fibroblasts whereas the TIMP-1 was increased significantly.[63]

There are certain plant metabolites which inhibits HYAL. Quercetin, gallotannins, tannic acid, ascorbic acid, and glycyrrhizin from *Glycyrrhiza glabra*, polyphenols from blackberry, glycoproteins from *Withania somnifera* and certain alkaloids are reported to be good HYAL inhibitors.[64] Glycyrrhizin also exhibits excellent free radical quenching activity and also act as a blocking agent to stop lipid peroxidation chain reactions.[65] Thus, *G. glabra* shows powerful antioxidant activity by ROS scavenging, hydrogen donating, and metal ion chelating.[66] Tagetes erecta flowers contain provitamin A "β-carotene" which is responsible for photoprotection as inhibits HYAL, elastase, and MMP-1.[5]

Curcumin present in *Curcuma longa*,[67] procyanidins extracted from *Vitis vinifera*,[68] phenolic compounds such as epicatechin, resveratrol,[69] and flavonoidal components such as galangin, kaempferol, quercetin, and myricetin exhibits potential elastase inhibition.[70] The condensed tannin pentagalloylglucose and ellagic acid are reported to prevent the degradation of elastin and helps to bind it also.[71] *Peucedanum graveolens* (Dill) extract improves the skin elasticity, skin feels more elastic, wrinkles appear smooth, and the face contours are remodeled.[72] *Zanthoxylum bungeanum* is used as a functional cosmetic ingredient to bring about the temporary improvement of skin wrinkles.[73]

A large number of plants and their extracts are evaluated for their antioxidant action. Flavonoids like Rutin and other phenolic compounds show antioxidant activities.[48] The polyphenols derived from Green tea and Yerba mate helps in preventing lipid peroxidation in mammals and other adverse effects caused by UV radiation by reducing the oxidative damage and production of metalloproteinase.[48] Extracts of Mulberry (*Morus alba*) show superoxide scavenging activity which is involved in the protection against auto-oxidation.[74,75] The antioxidant activity of Basil, Oregano, and Thyme essential oils has been evaluated through various *in vitro* tests.[76] Thymus species exhibits their antioxidant activity through different mechanisms such as decomposition of peroxides, free radical scavenging, and prevention of continuous hydrogen abstraction.[77] Fruits of *Vaccinium uliginosum* (bog blueberry) reduces ROS production and act as an antioxidant.[78] Plants with their chemical constituents and possible molecular mechanisms are listed in Table 1.

DISCUSSION

In the field of cosmetics, the herbal cosmetic as anti-aging agents plays a key role in reversing the adverse effects of aging caused due to excessive exposure to UV radiations. The ingredients present in herbal cosmetics not only show the biological action but also provide the required nutrition to the skin. The use of herbal anti-aging products has increased

Table 1: Plant inhibitors with their possible molecular mechanisms as antiaging agents

Botanical name	Family	Part used	Active constituents	Possible mechanism of action	References
Aloe vera	Liliaceae	Leaves	Aloe-emodin, barbaloin, aloin A and aloin B	By increasing Type - I procollagen and its decreasing the MMP-1 gene expression. Inhibits tyrosine hydroxylase and 3,4-dihydroxyphenylalanine oxidase	[57,79,80]
Angelica archangelica L.	Apiaceae	Root	Furanocoumarins	Inhibits elastase and collagenase	[81]
Astragalus membranaceus	Fabaceae	Leaves	It contains saponin, amino acids, polysaccharide, trace elements	Increases the content of hyaluronic acid	[82,83]
Alpinia katsumadai	Zingiberaceae	seed	Chalcone, flavonoids, sesquiterpenoids	Inhibitory effect on leukocyte elastase, hyaluronidase and lipid peroxidation	[84]

(Contd...)

Table 1: *(Continued)*

Botanical name	Family	Part used	Active constituents	Possible mechanism of action	References
Arctium lappa L	Asteraceae	Root	Sulfur containing polyacetylenes in roots including artinal and lappaphens	Inhibits elastase	[81]
Areca catechu	Arecaceae	Seeds	Tannins, polyphenols	Inhibits elastase	[85]
Allium sativum	Amaryllidaceae	Plant's bulb	Homocysteine, allicin (diallyl thiosulfinate or diallyl disulfide)	Antioxidant	[86]
Acanthopanax koreanum	Araliaceae	Leaves, root	Acanthopanic acid, rutin, and saponins	Free radical scavenging activity	[87]
Alnus formosana	Betulaceae	Leaves	Phenolic compounds	Free radical scavenging activity and inhibit matrix metalloproteinases in human skin fibroblasts	[88]
Ananas comosus	Bromeliaceae	Peel	Β- carotene, citronic, ascorbic acid	Free radical scavenging activity	[89]
Berberis aristata	Berberidaceae	Berries	Berbamine, berberine, oxycanthine, epiberberine, palmatine, aromoline, dehydrcaroline, columbamine, karachine	Regulates MMP-1 and Type - I procollagen expression in human dermal fibroblasts by inhibiting MMp-9 and IL-6	[90,91]
Biophytum sensitivum	Oxalidaceae	Leaves	Amentoflavone, cupressuflavone, and isoorientin	Inhibits hyaluronidase	[92]
Boswellia species	Burseraceae	Resin	Boswellic acid, phenolic compounds	Anti-elastase activity	[93]
Brassica oleracea	Brassicaceae	Leaves	Vitamin C, indole-3-carbinol	Antioxidant	[94]
Brassica campestris	Cruciferae/ Brassicaceae	Stem, flower, root	Flavonoids, hydroxycinnamic acid derivatives	Free radical scavenging activity	[87]
Calendula officinalis	Asteraceae	Flower	Triterpenoids and flavonoids (patuletin and Patulitrin) and saponins	Inhibits the activity/ secretion of MMP-2 and MMP-9, decreases transdermal water loss	[95]
Camellia japonica	Theaceae	Oil	Phenolic and flavonol glycoside triterpenoids, camellenodiol, camelledionol	Inhibits MMP1 activity and induces type-I procollagen synthesis, free radical scavenging activity, and elastase inhibition	[61,87]
Camellia sinensis	Theaceae	Leaves	Epicatechin, epicatechin gallate, epigallocatechin gallate, quercetin, kaempferol, caffeic acid	Inhibits UV - induced erythema, inhibits the activity of collagenases and increase the collagen synthesis rate of human fibroblasts, antioxidant effect, inhibits elastase and collagenase	[81,96-102]

(Contd...)

Table 1: *(Continued)*

Botanical name	Family	Part used	Active constituents	Possible mechanism of action	References
Capsicum annum	Solanaceae	Whole plant	Carotenoids, ascorbic acid	Free radical scavenging activity, inhibition of elastase activity and MMP-1 expression	[87]
Curculigo orchioides	Hypoxidaceae	Rhizome	Two phenolic glycosides, curculigosides,orcinol- beta-D-glucoside and two cycloartane saponins, curculigosaponin G, curculigosaponin I, mucilage, tannins, oxalate of calcium	Inhibits MMP-1 expression	[9,103]
Curcuma longa L.	Zingiberaceae	Rhizome	Curcuminoids, curcumin, demethoxycurcumin, bisdimethoxycurcumin	Inhibits MMP-2 expression, inhibits elastase, hyaluronidase and lipid peroxidation	[67,104,105]
Curcuma xanthorrhiza Roxb	Zingiberaceae	Rhizome	Curcuminoids, xanthorrhizol	Inhibits MMP-1 expression and Type - I procollagen –inducing effect	[58,106]
Centella asiatica L	Umbelliferae	Whole plant	Triterpenoids, omposi acid, asiaticoside, madecassic acid, madecassoside, brahmic acid, brahminoside	Induces Type - I collagen synthesis	[107-109]
Cinnamomum cassia	Lauraceae	Bark	Phenols, isoeugenol, cinnamic aldehyde, coumarin	Inhibitory effect on leukocyte, elastase, hyaluronidase and lipid peroxidation	[84]
Cucumis sativus	Cucurbitaceae	Fruit juice	Ascorbic acid	Antioxidant activity and inhibitory effect on hyaluronidase and elastase activity	[110]
Citrus sinensis L.	Rutaceae	Fruit	Ascorbic acid	Inhibits elastase	[111]
Callistemon lanceolatus	Myrtaceae	Stem	Betulinic acid, pyracrenic acid, arjunolic acid, catechin	Elastase inhibition and free radical scavenging activity	[112]
Cocos nucifera	Arecaceae	Fruit and all parts	Vitamin B, vitamin C, etc.	Antioxidant	[113]
Citrus limonum	Rutaceae	Fresh fruits	α-pinene, camphene, β-pinene, limonene, ascorbic acid	Inhibits free radical-mediated reactions	[88,114]
Caesalpinia pulcherrima	Caesalpiniaceae	Flower	Gallic acid, catechin, rutin and ellagic acid	DPPH radical scavenging and ABTS cation radical scavenging activity	[115]
Carica papaya	Caricaceae	Fruit pulp	Vitamin A, E, and C, beta- carotene enzymes		[89]
Dioscorea villosa	Dioscoreaceae	Rhizome	Sponins (diosgenin, dioscin]) and an alkaloid (dioscorin)	Increased bromodeoxyuridine uptake and intracellular cAMP level in keratinocytes	[116]

(Contd...)

Table 1: *(Continued)*

Botanical name	Family	Part used	Active constituents	Possible mechanism of action	References
Diospyros discolor	Ebenaceae	Leaves	Phenolic compounds	Inhibits matrix metalloproteinase in human skin fibroblasts	[117,118]
Dryopteris crassirhizoma	Dryopteridaceae	Entire plant	Dryopteroside, [+] catechin-6-C-beta-D-} glucopyranoside	Inhibitory effect on leukocyte elastase, hyaluronidase, lipid peroxidation and free radical scavenging activity	[84,87]
Distylium racemosum	Hamamelidaceae	Leaves, stem	Catechin derivatives, gallic acid derivatives, tyrosol, flavonoids, lupeol	Free radical scavenging activity and inhibits elastase	[87,119]
Daucus carota	Apiaceae	Leaves	Anthocyanins, caffeic acid, carotenoids, ferulic acid and cinnamic acid derivatives, Sitosterol, vitamin A, laserine, epilaserine	Free radical scavenging activity	[87,120]
Emblica officinalis	Euphorbiaceae	Fruit	Tannins, gallic acid, chebulic acid, ascorbic acid, citric acid	By promoting procollagen production and inhibiting MMP-1 in human skin fibroblasts	[63,121,122]
Eucommia ulmoides	Eucommiaceae	Bark and leaves	Lignans, iridoids, terpenes and phenols, aucubin	Inhibits MMP-1	[123]
Euonymus fortune	Celastraceae	Fruits	Flagelignanins A, lupeol, b- sitosterol glycoside	Inhibits elastase	[87]
Fraxinus chinensis	Oleaceae	Bark	Coumarins such as esculin and esculetin secoiridoids, phenylethanoids, flavonoids	Free radical scavenging activity and decreases the MMP-1 mRNA expression	[124,125]
Fucus vesiculosus	Fucaceae	Thallus	Alginic acid, alginates, volatile oils	Inhibits elastase and collagenase	[81,126]
Garcinia indica	Clusiaceae/ Guttiferae	Fruits	Garcinol, iso garcinol, cyanidin, 3- glucoside, cyaniding, coumarins, 3- sambubioside cambogia	Inhibits hyaluronidase and elastase enzyme	[89,127]
Glycirrhiza glabra	Fabaceae	Root and rhizome	Glycyrrhizin, hyaluronic acid	Antioxidant inhibits hyaluronidases	[64,92,128]
Galium aparine L.	Rubiaceae	Leaves, stem	Tannins, phenolic acids, flavonoids, iridoid glycosides	Inhibits elastase and collagenase	[81]
Glycine max L.	Fabaceae/ leguminoceae	Seeds (bean)	Isoflavones, anthocyanins	Enhance collagen and elastin synthesis, antioxidant activity and prevent caspase-3 pathway activation	[89,129-132]
Ginkgo biloba	Ginkgoaceae	Leaves	Ginkgolides, bilobalide kaempferol, quercetin	Antioxidant and free radical scavenging activity	[133,134]
Impatiens parviflora DC	Balsaminaceae	Leaves	Phenols, flavonoids, coumarins, triterpenes, saponins, carotenoids, sterols, and lipids	Inhibits hyaluronidase	[135]

(Contd...)

Table 1: *(Continued)*

Botanical name	Family	Part used	Active constituents	Possible mechanism of action	References
Illicium verum	Illiaceae	Fruit	Essential oil consisting of trans- anethol, anisaldehyde, methyl chavicol and other monoterpenoids	Inhibits elastase and collagenase	[81]
Leucas aspera	Lamiaceae	Leaves	Ursolic acid, phenolic compounds, alkaloids	Inhibits hyaluronidase	[92,136]
Lastrea japonica	Filicales	Entire plant	Phenolic compound	Inhibits elastase	[137]
Luffa cylindrica	Cucurbitaceae	Seeds	Oil contains fatty acids like stearic acid and linoleic acid and phenolic compounds	Antioxidant and free radical scavenging activity	[138,139]
Machilus thunbergii		Stem bark	Procyanidin, epicatechin-(4β-8)-epicatechin (4β-6), meso-dihydroguaiaretic acid and licarin A	Inhibition of MMP-1	[140]
Melothria heterophylla	Cucurbitaceae	Roots	1,2,4,6- tetra-O- galloyl-beta-(D)-glucopyranose and 3,4,5-trihydroxybenzoic acid	Inhibition of MMP-1 activity and antioxidant	[141]
Macrocystis pyrifera	Laminariaceae	Algae	Uronic acids, α-linolenic acid, eicosapentaenoic acid, docosahexaenoic acid, arachidonic acid	Inhibits MMP-1 and MMP-2	[142-144]
Myristica fragrans	Myristicaceae	Seed kernels	Volatile oil, myristicin and myristic, epicatechin and cyaniding	Inhibitory effect on leukocyte elastase, hyaluronidase and lipid peroxidation	[84]
Nardostachys jatamansi	Valerianaceae	Roots	Sesquiterpenes and coumarins	Inhibition of MMP-1	[145]
Nelumbo nucifera	Nelumbonaceae	Leaves, seed, and flower	Kaempferol, glucopyranose, sitosterol flavonoids	Inhibits elastase and free radical scavenging activity	[115]
Panax ginseng	Araliaceae	Leaves, roots	Ginsenosides and panaxosides (Triterpenoid saponin), oleanolic acid	Type - I procollagen gene and protein expression, prevent MMp-9 gene induction, and elongated the fibrillin -1 fiber length. Increase of expression of procollagen Type - I and decrease MMP-1	[146-148]
Pterocarpus santalinus	Fabaceae	Bark	Terpenoids, pigments-santalin, erthyrodiol	Inhibits the activity and expression of collagenase (MMP-1) and gelatinase (MMP-2) and inhibits tyrosinase	[89,149]
Persicaria dissitiflora	Polygonaceae	Entire plant	Terpenoid, cineol	Inhibits elastase and free radical scavenging activity	[87]

(Contd...)

Table 1: *(Continued)*

Botanical name	Family	Part used	Active constituents	Possible mechanism of action	References
Psidium guajava	Myrtaceae	Leaves	Phenolic com pounds caffeic acid, ferulic acid, rutin trihydrate, quercetin dehydrate	Inhibits elastase	[150]
Persicaria hydropiper	Polygonaceae	Whole plant	Flavonoids (Isoquercitrin and isorhamnetin), flavonoid glycosides and phenylpropanoid glycosides	Free radical scavenging activity, inhibition of elastase activity and MMP-1 expression	[149]
Platycarya strobilacea	Juglandaceae	Fruits	Ellagic acid	Free radical scavenging activity, elastase inhibition and expression of MMp-1 and type-I collagen synthesis	[151]
Peucedanum graveolens (Dill)	Apiaceae	Seeds	Carvone, limonene, phellandrene, cineole, myrcene, paramyrcene, isomyristicin, myristicin, myristin, apiol and dillapiol, furanocoumarin, oxypeucedanin, oxypeucedanin hydrate and falcarindiol	Improves skin elasticity	[72]
Portulaca oleracea	Portulacaceae	Whole plant	Kaempferol, myricetin, luteolin, apigenin, quercetin, genistein, and genistin, monoterpenes such as portulosides A and B, diterpenes such as portulene, and β-amyrin, ascorbic acid, α-tocopherol, β-carotene, glutathione, melatonin, portulacerebroside A, catechol, and bergapten	Antioxidant and free radical scavenging activity	[152-154]
Pinus densiflora	Pinaceae	Bark	Catechin	Antioxidant and free radical scavenging activity	[155]
Prunus dulcis Mill.	Rosaceae	Nuts	Chlorogenic acid, cryptochlorogenic acid, neochlorogenic acid	Free radical scavenging activity and antioxidant	[156]
Rosmarinus officinalis L.	Lamiaceae/ Labiatae	Leaves	Carnosic acid and rosmarinic acid, caffeic acid, ursolic acid, betulinic acid, rosmaridiphenol and rosmanol	Protection from free radicals	[157,158]
Terminalia chebula	Combretaceae	Fruits	Hydrolysable tannins such as chebulinic acid, gallotannins, casuarinin, chebulanin, corilagin, neochebulinic acid, terchebulin, and gallic acid phenolics such as ellagic acid, chebulic acid	Tyrosinase and MMP-2 inhibition, elastase, hyaluronidase inhibition and collagen synthesis, antioxidative	[151,159,160]

(Contd...)

Table 1: *(Continued)*

Botanical name	Family	Part used	Active constituents	Possible mechanism of action	References
Tamarindus indica	Fabaceae	Seed coat	Tartaric acid, carotene, vitamin C, tannins	Radical scavenging and lipid peroxidation reducing activity	[161]
Triticum aestivum	Poaceae	Grains	Phenolic compounds, phytochemicals, carbohydrates	Inhibition of MMP-1 expression	[162]
Tagetes erecta	Asteraceae	Flowers	Provitamin A "-carotene," b-amyrin and syringic acids	Inhibits elastase, hyaluronidase, and MMP-1	[5]
Viola hondoensis	Violaceae	Whole plant	Flavonol glycosides	Inhibition of MMP-1 expression at both mRNA and protein levels	[163]
Vitis vinifera	Vitaceae	Seed, shoot	Proanthocyanidins and resveratrol, Phenolic acids, flavonols, tannins, procyanidins, anthocyanins, carotenoids, terpenes	Free radical scavenging activity and inhibit matrix metalloproteinase in human skin fibroblasts	[5,68,164-166]
Vaccinium Uliginosum L.	Ericaceae	Berries	Anthocyanins like cyaniding-3-glucoside, petunidin-3-glucoside, malvidin-3-glucoside and delphinidin-3- glucoside	Removal of reactive oxygen species, diminished UV-B augmented - release of inflammatory interleukin (IL)-6 and IL-8	[78]
Vetiveria zizconoides	Poaceae	Root	Vetivone [α and β] and vetiverol	Antioxidant	[167]
Zingiber officinale	Zingiberaceae	Rhizome	Β- sitosterol palmitate, isovanillin, glycol monopalmitate, hexacosanoic acid2,3 dihydroxypropyl ester, maleimide-5-oxime, p-hydroxybenzaldehyde, adenine, 6-gingerol	Inhibits elastase	[5,150]
Zanthoxylum bungeanum	Rutaceae	Fruit husk	Chlorogenic acid, hyperoside, and quercitrin	Anti-elastase activity	[73]

substantially nowadays. This may be attributed to the fact that the ingredients used in synthetic anti-aging formulations are associated with the harmful adverse side effects.[168] On the other hand, the natural skin care products are safe, quickly absorbed by the skin and are hypoallergenic in nature.[169] Plant extracts are considered safe,[170] because of the simple fact that they come from nature.[171] In addition, the natural herbs have despicable mammalian toxicity and can be handled safely. This makes the use of herbal formulations as skin care products more attractive and common.[168] The bioactive components such as flavonoids, polyphenols, tannins, and quercetin present in various plants may be combined together to give the synergistic effect in reducing wrinkles, photoaging, depigmentation, diminish redness and improves other signs of skin aging by increasing the free radical scavenging activity, antagonizing the UV signaling pathway, inhibiting various enzymes such as elastases, HYAL, and MMP. Still, the scientific validation on the use of herbal products as anti-aging and anti-wrinkle agents should be further explored on the basis of different evaluation procedures and scientific models. This review facilitates the scientists working in this area for the development of new anti-aging and anti-wrinkle formulations with better efficiency and safety.[169]

ACKNOWLEDGMENTS

The authors are thankful to the University Grants Commission for the financial assistance provided to carry out the research under the PDFW scheme.

REFERENCES

1. Papakonstantinou E, Roth M, Karakiulakis G. Hyaluronic acid: A key molecule in skin aging. Dermatoendocrinol 2002;4:253-8.
2. Makrantonaki E, Adjaye J, Herwig R, Brink TC, Groth D, Hultschig C, *et al.* Age-specific hormonal decline is accompanied by transcriptional changes in human sebocytes *in vitro*. Aging Cell 2006;5:331-44.
3. Brincat MP. Hormone replacement therapy and the skin. Maturitas 2000;35:107-17.
4. Fisher GJ, Kang S, Varani J, Bata-Csorgo Z, Wan Y, Datta S, *et al.* Mechanisms of photoaging and chronological skin aging. Arch Dermatol 2002;138:1462-70.
5. Maity N, Nema NK, Abedy MK, Sarkar BK, Mukherjee PK. Exploring *Tagetes erecta* Linn flower for the elastase, hyaluronidase and MMP-1 inhibitory activity. J Ethnopharmacol 2011;137:1300-5.
6. Fulop T, Khalil A, Larbi A. The role of elastin peptides in modulating the immune response in aging and age-related diseases. Pathol Biol (Paris) 2012;60:28-33.
7. Wary KK, Thakker GD, Humtsoe JO, Yang J. Analysis of VEGF-responsive genes involved in the activation of endothelial cells. Mol Cancer 2003;2:25.
8. Losso JN, Munene CN, Bansode RR, Bawadi HA. Inhibition of matrix metalloproteinase-1 activity by the soybean Bowman-Birk inhibitor. Biotechnol Lett 2004;26:901-5.
9. Mukherjee PK, Maity N, Nema NK, Sarkar BK. Bioactive compounds from natural resources against skin aging. Phytomedicine 2011;19:64-73.
10. Rittié L, Fisher GJ. UV-light-induced signal cascades and skin aging. Ageing Res Rev 2002;1:705-20.
11. Labat-Robert J, Fourtanier A, Boyer-Lafargue B, Robert L. Age dependent increase of elastase type protease activity in mouse skin. Effect of UV-irradiation. J Photochem Photobiol B 2000;57:113-8.
12. Han A, Chien AL, Kang S. Photoaging. Dermatol Clin 2014;32:291-9, vii.
13. Gilchrest BA. Skin aging and photoaging. Dermatol Nurs 1990;2:79-82.
14. Sharma V, Sharma S, Pracheta J, Paliwal R. Withania somnifera: A rejuvenating ayurvedic medicinal herb for the treatment of various human ailments. Int J Pharmtech Res 2011;3:187-92.
15. Vioux-Chagnoleau C, Lejeune F, Sok J, Pierrard C, Marionnet C, Bernerd F. Reconstructed human skin: From photodamage to sunscreen photoprotection and anti-aging molecules. J Dermatol Sci 2006;2:S1-12.
16. Philips N. Counteraction of skin inflammation and aging or cancerbypolyphenols. In: Epifano F, editor. Anti-Inflammatory and Anti-Allergy Agents in Medicinal Chemistry. Netherlands: Bentham Science; 2010.
17. Philips N. Experimental physiology in anti-skin aging. In: Columbus F, editor. Skin Anatomy and Physiology Research Development. Hauppauge, NY, USA: Nova Science; 2009.
18. Lee CW, Choi HJ, Kim HS, Kim DH, Chang IS, Moon HT, *et al.* Biflavonoids isolated from *Selaginella tamariscina* regulate the expression of matrix metalloproteinase in human skin fibroblasts. Bioorg Med Chem 2008;16:732-8.
19. Khorramizadeh MR, Tredget EE, Telasky C, Shen Q, Ghahary A. Aging differentially modulates the expression of collagen and collagenase in dermal fibroblasts. Mol Cell Biochem 1999;194:99-108.
20. Millis AJ, Hoyle M, McCue HM, Martini H. Differential expression of metalloproteinase and tissue inhibitor of metalloproteinase genes in aged human fibroblasts. Exp Cell Res 1992;201:373-9.
21. Berton A, Godeau G, Emonard H, Baba K, Bellon P, Hornebeck W, *et al.* Analysis of the *ex vivo* specificity of human gelatinases A and B towards skin collagen and elastic fibers by computerized morphometry. Matrix Biol 2000;19:139-48.
22. Brennan M, Bhatti H, Nerusu KC, Bhagavathula N, Kang S, Fisher GJ, *et al.* Matrix metalloproteinase-1 is the major collagenolytic enzyme responsible for collagen damage in UV-irradiated human skin. Photochem Photobiol 2003;78:43-8.
23. Tsuji N, Moriwaki S, Suzuki Y, Takema Y, Imokawa G. The role of elastases secreted by fibroblasts in wrinkle formation: Implication through selective inhibition of elastase activity. Photochem Photobiol 2001;74:283-90.
24. Rijken F, Kiekens RC, van den Worm E, Lee PL, van Weelden H, Bruijnzeel PL. Pathophysiology of photoaging of human skin: Focus on neutrophils. Photochem Photobiol Sci 2006;5:184-9.
25. Rijken F, Kiekens RC, Bruijnzeel PL. Skin-infiltrating neutrophils following exposure to solar-simulated radiation could play an important role in photoageing of human skin. Br J Dermatol 2005;152:321-8.
26. Fisher GJ, Datta SC, Talwar HS, Wang ZQ, Varani J, Kang S, *et al.* Molecular basis of sun-induced premature skin ageing and retinoid antagonism. Nature 1996;379:335-9.
27. Fisher GJ, Talwar HS, Lin J, Lin P, McPhillips F, Wang Z, *et al.* Retinoic acid inhibits induction of c-Jun protein by ultraviolet radiation that occurs subsequent to activation of mitogen-activated protein kinase pathways in human skin *in vivo*. J Clin Invest 1998;101:1432-40.
28. Fligiel SE, Varani J, Datta SC, Kang S, Fisher GJ, Voorhees JJ. Collagen degradation in aged/photodamaged skin *in vivo* and after exposure to matrix metalloproteinase-1 *in vitro*. J Invest Dermatol 2003;120:842-8.
29. Quan T, Qin Z, Xia W, Shao Y, Voorhees JJ, Fisher GJ. Matrix-degrading metalloproteinases in photoaging. J Investig Dermatol Symp Proc 2009;14:20-4.
30. Sternlicht MD, Werb Z. How matrix metalloproteinases regulate cell behavior. Annu Rev Cell Dev Biol 2001;17:463-516.
31. Baumann L. Skin ageing and its treatment. J Pathol 2007;211:241-51.

32. Juhlin L. Hyaluronan in skin. J Intern Med 1997;242:61-6.
33. Tammi R, Ripellino JA, Margolis RU, Tammi M. Localization of epidermal hyaluronic acid using the hyaluronate binding region of cartilage proteoglycan as a specific probe. J Invest Dermatol 1988;90:412-4.
34. Armstrong SE, Bell DR. Relationship between lymph and tissue hyaluronan in skin and skeletal muscle. Am J Physiol Heart Circ Physiol 2002;283:H2485-94.
35. Tzellos TG, Sinopidis X, Kyrgidis A, Vahtsevanos K, Triaridis S, Printza A, *et al.* Differential hyaluronan homeostasis and expression of proteoglycans in juvenile and adult human skin. J Dermatol Sci 2011;61:69-72.
36. Tzellos TG, Klagas I, Vahtsevanos K, Triaridis S, Printza A, Kyrgidis A, *et al.* Extrinsic ageing in the human skin is associated with alterations in the expression of hyaluronic acid and its metabolizing enzymes. Exp Dermatol 2009;18:1028-35.
37. Reed RK, Lilja K, Laurent TC. Hyaluronan in the rat with special reference to the skin. Acta Physiol Scand 1988;134:405-11.
38. Toole BP. Hyaluronan: From extracellular glue to pericellular cue. Nat Rev Cancer 2004;4:528-39.
39. Papakonstantinou E, Karakiulakis G, Roth M, Block LH. Platelet-derived growth factor stimulates the secretion of hyaluronic acid by proliferating human vascular smooth muscle cells. Proc Natl Acad Sci U S A 1995;92:9881-5.
40. Papakonstantinou E, Roth M, Tamm M, Eickelberg O, Perruchoud AP, Karakiulakis G. Hypoxia differentially enhances the effects of transforming growth factor-beta isoforms on the synthesis and secretion of glycosaminoglycans by human lung fibroblasts. J Pharmacol Exp Ther 2002;301:830-7.
41. Papakonstantinou E, Kouri FM, Karakiulakis G, Klagas I, Eickelberg O. Increased hyaluronic acid content in idiopathic pulmonary arterial hypertension. Eur Respir J 2008;32:1504-12.
42. Klagas I, Goulet S, Karakiulakis G, Zhong J, Baraket M, Black JL, *et al.* Decreased hyaluronan in airway smooth muscle cells from patients with asthma and COPD. Eur Respir J 2009;34:616-28.
43. Lee JY, Spicer AP. Hyaluronan: A multifunctional, megadalton, stealth molecule. Curr Opin Cell Biol 2000;12:581-6.
44. Girish KS, Kemparaju K. The magic glue hyaluronan and its eraser hyaluronidase: A biological overview. Life Sci 2007;80:1921-43.
45. Oikarinen A. Connective tissue and aging. Int J Cosmet Sci 2004;26:107-8.
46. Antonicelli F, Bellon G, Debelle L, Hornebeck W. Elastin-elastases and inflamm-aging. Curr Top Dev Biol 2007;79:99-155.
47. Nishimori Y, Kenjoh Y, Matsumoto K, Kawai M. UVB-induced ultrastructural changes of collagen bundles in hairless mouse skin. J Dermatol Sci 1997;15:125.
48. Silva AR, Menezes PF, Martinello T, Novakovich GF, Praes CE, Feferman IH. Antioxidant kinetics of plant-derived substances and extracts. Int J Cosmet Sci 2010;32:73-80.
49. Stadtman ER. Protein oxidation and aging. Free Radic Res 2006;40:1250-8.
50. Chidambaram U, Pachamuthu V, Natarajan S, Elango B, Suriyanarayanan, Ramkumar KM. *In vitro* evaluation of free radical scavenging activity of *Codariocalyx motorius* root extract. Asian Pac J Trop Med 2013;6:188-94.
51. Kohen R. Skin antioxidants: Their role in aging and in oxidative stress - New approaches for their evaluation. Biomed Pharmacother 1999;53:181-92.
52. Fisher GJ, Quan T, Purohit T, Shao Y, Cho MK, He T, *et al.* Collagen fragmentation promotes oxidative stress and elevates matrix metalloproteinase-1 in fibroblasts in aged human skin. Am J Pathol 2009;174:101-14.
53. Gasca CA, Cabezas FA, Torras L, Bastida J, Codina C. Chemical composition and antioxidant activity of the ethanol extract and purified fractions of cadillo (*Pavonia sepioides*). Free Radic Antioxid 2013;3:55-61.
54. Kohen R, Gati I. Skin low molecular weight antioxidants and their role in aging and in oxidative stress. Toxicology 2000;148:149-57.
55. Hunt KJ, Hung SK, Ernst E. Botanical extracts as anti-aging preparations for the skin: A systematic review. Drugs Aging 2010;27:973-85.
56. Ng TB, Liu F, Wang ZT. Antioxidative activity of natural products from plants. Life Sci 2000;66:709-23.
57. Barrantes E, Guinea M. Inhibition of collagenase and metalloproteinases by aloins and aloe gel. Life Sci 2003;72:843-50.
58. Oh HI, Shim JS, Gwon SH, Kwon HJ, Hwang JK. The effect of xanthorrhizol on the expression of matrix metalloproteinase-1 and Type-I procollagen in ultraviolet-irradiated human skin fibroblasts. Phytother Res 2009;23:1299-302.
59. Burlando B, Verotta L, Cornara L, Bottini-Massa E. Herbal Principals in Cosmetics: Properties and Mechanisms of Action. New York, NY, USA: CRC Press Taylor & Francis Group; 2010.
60. Tada Y, Kanda N, Haratake A, Tobiishi M, Uchiwa H, Watanabe S. Novel effects of diosgenin on skin aging. Steroids 2009;74:504-11.
61. Jung E, Lee J, Baek J, Jung K, Lee J, Huh S, *et al.* Effect of *Camellia japonica* oil on human Type I procollagen production and skin barrier function. J Ethnopharmacol 2007;112:127-31.
62. Lee J, Jung E, Lee J, Huh S, Kim J, Park M, *et al.* Panax ginseng induces human Type I collagen synthesis through activation of Smad signaling. J Ethnopharmacol 2007;109:29-34.
63. Fujii T, Wakaizumi M, Ikami T, Saito M. Amla (*Emblica officinalis* Gaertn.) extract promotes procollagen production and inhibits matrix metalloproteinase-1 in human skin fibroblasts. J Ethnopharmacol 2008;119:53-7.
64. Girish KS, Kemparaju K. Inhibition of *Naja naja* venom hyaluronidase by plant-derived bioactive components and polysaccharides. Biochemistry (Mosc)

2005;70:948-52.
65. Rahman S, Sultana S. Glycyrrhizin exhibits potential chemopreventive activity on 12-O-tetradecanoyl phorbol-13-acetate-induced cutaneous oxidative stress and tumor promotion in Swiss albino mice. J Enzyme Inhib Med Chem 2007;22:363-9.
66. Visavadiya NP, Soni B, Dalwadi N. Evaluation of antioxidant and anti-atherogenic properties of *Glycyrrhiza glabra* root using *in vitro* models. Int J Food Sci Nutr 2009;60 Suppl 2:135-49.
67. Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: A component of tumeric (*Curcuma longa*). J Altern Complement Med 2003;9:161-8.
68. Maffei Facino R, Carini M, Aldini G, Bombardelli E, Morazzoni P, Morelli R. Free radicals scavenging action and anti-enzyme activities of procyanidines from *Vitis vinifera.* A mechanism for their capillary protective action. Arzneimittelforschung 1994;44:592-601.
69. Hrenn A, Steinbrecher T, Labahn A, Schwager J, Schempp CM, Merfort I. Plant phenolics inhibit neutrophil elastase. Planta Med 2006;72:1127-31.
70. Kanashiro A, Souza JG, Kabeya LM, Azzolini AE, Lucisano-Valim YM. Elastase release by stimulated neutrophils inhibited by flavonoids: Importance of the catechol group. Z Naturforsch C 2007;62:357-61.
71. Isenburg JC, Simionescu DT, Starcher BC, Vyavahare NR. Elastin stabilization for treatment of abdominal aortic aneurysms. Circulation 2007;115:1729-37.
72. Sohm B, Cenizo V, André V, Zahouani H, Pailler-Mattei C, Vogelgesang B. Evaluation of the efficacy of a dill extract *in vitro* and *in vivo*. Int J Cosmet Sci 2011;33:157-63.
73. Artaria C, Maramaldi G, Bonfigli A, Rigano L, Appendino G. Lifting properties of the alkamide fraction from the fruit husks of *Zanthoxylum bungeanum*. Int J Cosmet Sci 2011;33:328-33.
74. Lee SH, Choi SY, Kim H, Hwang JS, Lee BG, Gao JJ, *et al.* Mulberroside F isolated from the leaves of *Morus alba* inhibits melanin biosynthesis. Biol Pharm Bull 2002;25:1045-8.
75. Katsube T, Imawaka N, Kawano Y, Yamazaki Y, Shiwaku K, Yamane Y. Antioxidant favonol glycosides in mulberry (*Morus alba* L.) Leaves isolated based on LDL antioxidant activity. Food Chem 2006;97:25-31.
76. Bozin B, Mimica-Dukic N, Simin N, Anackov G. Characterization of the volatile composition of essential oils of some *Lamiaceae* spices and the antimicrobial and antioxidant activities of the entire oils. J Agric Food Chem 2006;54:1822-8.
77. Asbaghian S, Shafaghat A, Zarea K, Kasimov F, Salimi F. Comparison of volatile constituents, and antioxidant and antibacterial activities of the essential oils of *Thymus caucasicus*, T. *Kotschyanus* and T. Vulgaris. Nat Prod Commun 2011;6:137-40.
78. Bae JY, Lim SS, Kim SJ, Choi JS, Park J, Ju SM, *et al.* Bog blueberry anthocyanins alleviate photoaging in ultraviolet-B irradiation-induced human dermal fibroblasts. Mol Nutr Food Res 2009;53:726-38.
79. Jones K, Hughes J, Hong M, Jia Q, Orndorff S. Modulation of melanogenesis by aloesin: A competitive inhibitor of tyrosinase. Pigment Cell Res 2002;15:335-40.
80. Cho S, Lee S, Lee MJ, Lee DH, Won CH, Kim SM, *et al.* Dietary *Aloe vera* supplementation improves facial wrinkles and elasticity and it increases the Type I procollagen gene expression in human skin *in vivo*. Ann Dermatol 2009;21:6-11.
81. Thring TS, Hili P, Naughton DP. Anti-collagenase, anti-elastase and anti-oxidant activities of extracts from 21 plants. BMC Complement Altern Med 2009;9:27.
82. Hsu MF, Chiang BH. Stimulating effects of *Bacillus subtilis* natto-fermented Radix astragali on hyaluronic acid production in human skin cells. J Ethnopharmacol 2009;125:474-81.
83. Ma XQ, Shi Q, Duan JA, Dong TT, Tsim KW. Chemical analysis of radix astragali (*Huang qi*) in China: A comparison with its adulterants and seasonal variations. J Agric Food Chem 2002;50:4861-6.
84. Lee KK, Kim JH, Cho JJ, Choi JD. Inhibitory effects of 150 plant extracts on elastase activity, and their anti-inflammatory effects. Int J Cosmet Sci 1999;21:71-82.
85. Lee KK, Choi J. The effects of *Areca catechu* L extracts on anti ageing. Int J Cosmet Sci 1999;21:285-95.
86. Choi J, Byun D. Studies of anti-aging action of Garlic. *Allium sativum* L. Comparative study of garlic and ginseng compounds on antiaging action. Korean Biochem J 1986;19:140-6.
87. Kim JY, Yang HJ, Lee KH, Jeon SM, Ahn YJ, Won BR, *et al*. Antioxidative and antiaging effects of Jeju native plant extracts [II]. J Soc Cosmet Sci Korean 2007;33:165-73.
88. Apak R, Güçlü K, Demirata B, Ozyürek M, Celik SE, Bektasoglu B, *et al.* Comparative evaluation of various total antioxidant capacity assays applied to phenolic compounds with the CUPRAC assay. Molecules 2007;12:1496-547.
89. Reddy PM, Gobinath M, Rao MK, Venugopalaiah P, Reena N. A review on importance of herbal drugs in cosmetics. Int J Adv Pharm Nanotechnol 2011;1:121-39.
90. Kim S, Chung JH. Berberine prevents UV-induced MMP-1 and reduction of Type I procollagen expression in human dermal fibroblasts. Phytomedicine 2008;15:749-53.
91. Kim S, Kim Y, Kim JE, Cho KH, Chung JH. Berberine inhibits TPA-induced MMP-9 and IL-6 expression in normal human keratinocytes. Phytomedicine 2008;15:340-7.
92. Gangadharan A, Jacob E, Jose D. Phytochemical analysis, antibacterial and anti hyaluronidase activity of three indigenous medicinal plants. World J Pharm Pharm Sci 2014;3:751-61.
93. Melzig MF, Löser B, Ciesielski S. Inhibition of neutrophil elastase activity by phenolic compounds from plants. Pharmazie 2001;56:967-70.
94. Koksal E, Gulcin I. Antioxidant activity of cauliflower

(*Brassica oleracea* L.). Turk J Agric Forestry 2008;32:65-78.
95. Fonseca YM, Catini CD, Vicentini FT, Nomizo A, Gerlach RF, Fonseca MJ. Protective effect of *Calendula officinalis* extract against UVB-induced oxidative stress in skin: Evaluation of reduced glutathione levels and matrix metalloproteinase secretion. J Ethnopharmacol 2010;127:596-601.
96. Li YH, Wu Y, Wei HC, Xu YY, Jia LL, Chen J, *et al.* Protective effects of green tea extracts on photoaging and photommunosuppression. Skin Res Technol 2009;15:338-45.
97. Sharangi AB. Medicinal and therapeutic potentialities of tea (*Camellia sinensis* L.) - A review. Food Res Int 2009;42:529-35.
98. Katiyar SK, Ahmad N, Mukhtar H. Green tea and skin. Arch Dermatol 2000;136:989-94.
99. Kim DS, Park SH, Kwon SB, Li K, Youn SW, Park KC. (-)-Epigallocatechin-3-gallate and hinokitiol reduce melanin synthesis via decreased MITF production. Arch Pharm Res 2004;27:334-9.
100. Yoshimura M, Watanabe Y, Kasai K, Yamakoshi J, Koga T. Inhibitory effect of an ellagic acid-rich pomegranate extract on tyrosinase activity and ultraviolet-induced pigmentation. Biosci Biotechnol Biochem 2005;69:2368-73.
101. Kumar S, Singh N, Archana S. Green tea polyphenols: Versatile cosmetic ingredient. Int J Adv Res Pharm Biosci 2012;1:348-62.
102. Shimogaki H, Tanaka Y, Tamai H, Masuda M. *In vitro* and *in vivo* evaluation of ellagic acid on melanogenesis inhibition. Int J Cosmet Sci 2000;22:291-303.
103. Lee SY, Kim MR, Choi HS, Moon HI, Chung JH, Lee DG, *et al.* The effect of curculigoside on the expression of matrix metalloproteinase-1 in cultured human skin fibroblasts. Arch Pharm Res 2009;32:1433-9.
104. Sumiyoshi M, Kimura Y. Effects of a turmeric extract (*Curcuma longa*) on chronic ultraviolet B irradiation-induced skin damage in melanin-possessing hairless mice. Phytomedicine 2009;16:1137-43.
105. Cronin H, Draelos ZD. Top 10 botanical ingredients in 2010 anti-aging creams. J Cosmet Dermatol 2010;9:218-25.
106. Ruslay S, Abas F, Shaari K, Zainal Z, Hasnah M, Daud S, *et al*. Characterization of the components present in the active fractions of health gingers (*Curcumaxanthorrhiza* and *Zinziber zerumbet*) by HPLKC-DAD-ESIMS. Food Chem 2007;104:1183-91.
107. Ermertcan AT, Inan S, Ozturkcan S, Bilac C, Cilaker S. Comparison of the effects of collagenase and extract of *Centella asiatica* in an experimental model of wound healing: An immunohistochemical and histopathological study. Wound Repair Regen 2008;16:674-81.
108. Haftek M, Mac-Mary S, Le Bitoux MA, Creidi P, Seité S, Rougier A, *et al.* Clinical, biometric and structural evaluation of the long-term effects of a topical treatment with ascorbic acid and madecassoside in photoaged human skin. Exp Dermatol 2008;17:946-52.
109. Bonte F, Dumas M, Chaudagne C, Meybeck A. Influence of asiatic acid, madecassic acid, and asiaticoside on human collagen I synthesis. Planta Med 1994;60:133-5.
110. Nema NK, Maity N, Sarkar B, Mukherjee PK. Cucumis sativus fruit-potential antioxidant, anti-hyaluronidase, and anti-elastase agent. Arch Dermatol Res 2011;303:247-52.
111. Cimino F, Cristani M, Saija A, Bonina FP, Virgili F. Protective effects of a red orange extract on UVB-induced damage in human keratinocytes. Biofactors 2007;30:129-38.
112. Kim JH, Byun JC, Bandi AK, Hyun CG, Lee NH. Compounds with elastase inhibition and free radical scavenging activities from *Callistemon lanceolatus*. J Med Plant Res 2009;3:914-20.
113. Fonseca AM, Bizerra AM, Souza JS, Monte FJ, Oliveira MC, Mattos MC, *et al*. Constituents and antioxidant activity of two varieties of coconut water (*Cocos nucifera* L.). Braz J Pharmacogn 2012;19:193-8.
114. Calabrese V, Randazzo SD, Catalano C, Rizza V. Biochemical studies on a novel antioxidant from lemon oil and its biotechnological application in cosmetic dermatology. Drugs Exp Clin Res 1999;25:219-25.
115. Samee W, Vorarat S. Simultaneous determination of gallic acid, catechin, rutin, ellagic acid and quercetin in flower extracts of *Michelia alba*, *Caesalpinia pulcherrima* and *Nelumbo nucifera* by HPLC. Thai Pharm Health Sci J 2007;2:131-7.
116. Aharafzadeh S. Medicinal plants as anti-ageing materials: A review. Glob J Med Plant Res 2013;1:234-6.
117. An BJ, Kwak JH, Park JM, Lee JY, Park TS, Lee JT, *et al.* Inhibition of enzyme activities and the antiwrinkle effect of polyphenol isolated from the persimmon leaf (*Diospyros kaki* folium) on human skin. Dermatol Surg 2005;31:848-54.
118. Lee YL, Lee MH, Chang HJ, Huang PY, Huang IJ, Cheng KT, *et al.* Taiwanese native plants inhibit matrix metalloproteinase-9 activity after ultraviolet B irradiation. Molecules 2009;14:1062-71.
119. Ko RK, Kim GO, Hyun CG, Jung DS, Lee NH. Compounds with tyrosinase inhibition, elastase inhibition and DPPH radical scavenging activities from the branches of *Distylium racemosum* Sieb. Et Zucc. Phytother Res 2011;25:1451-6.
120. Shalaby NM, Maghraby AS, el-Hagrassy AM. Effect of *Daucus carota* var. *Boissieri* extracts on immune response of *Schistosoma mansoni* infected mice. Folia Microbiol (Praha) 1999;44:441-8.
121. Adil MD, Kaiser P, Satti NK, Zargar AM, Vishwakarma RA, Tasduq SA. Effect of *Emblica officinalis* (fruit) against UVB-induced photo-aging in human skin fibroblasts. J Ethnopharmacol 2010;132:109-14.
122. Scartezzini P, Antognoni F, Raggi MA, Poli F, Sabbioni C. Vitamin C content and antioxidant activity of the fruit and of the Ayurvedic preparation of *Emblica*

officinalis Gaertn. J Ethnopharmacol 2006;104:113-8.
123. Ho JN, Lee YH, Lee YD, Jun WJ, Kim HK, Hong BS, *et al*. Inhibitory effect of aucubin isolated from *Eucommia ulmoides* against UVB - Induced matrix metalloproteinase-1 production in human skin fibroblasts. Biosci Biotechnol Biochem 2005;11:2227-31.
124. Lee BC, Lee SY, Lee HJ, Sim GS, Kim JH, Kim JH, *et al.* Anti-oxidative and photo-protective effects of coumarins isolated from *Fraxinus chinensis*. Arch Pharm Res 2007;30:1293-301.
125. Cho YH, Kim JH, Lee BC, Pyo HB. Cosmetic Composition Comprising Extract of *Fraxinus chinensis* having Skin Damage Inhibition Effect. Korea Patent 1020050076942; 2007. Available from: http://www.patent.ipexl.com/KR/1020050076942.html. [Last accessed on 14 Oct 2016].
126. Fujimura T, Tsukahara K, Moriwaki S, Kitahara T, Sano T, Takema Y. Treatment of human skin with an extract of *Fucus vesiculosus* changes its thickness and mechanical properties. J Cosmet Sci 2002;53:1-9.
127. Sahasrabudhe A, Deodhar M. Anti - Hyaluronidase, anti - Elastase activity of *Garcinia indica.* Int J Bot 2010;6:299-303.
128. Damle M. *Glycyrrhiza glabra* (*Liquorice*)-A potent medicinal herb. Int J Herb Med 2014;2:132-6.
129. Tsoyi K, Park HB, Kim YM, Chung JI, Shin SC, Shim HJ, *et al.* Protective effect of anthocyanins from black soybean seed coats on UVB-induced apoptotic cell death *in vitro* and *in vivo*. J Agric Food Chem 2008;56:10600-5.
130. Hori M. Inhibition of advanced glycation end product formation by herbal teas and its relation to antiaging. J Antiaging Med 2012;9:135-45.
131. Jain A, Dubey S, Gupta A, Kannojia P, Tomar V. Potential of herbs as cosmaceuticals. Int J Res Ayurveda Pharm 2010;1:71-7.
132. Seiberg M. Non-denatured soybean extracts in skin care: Multiple anti-aging effects. In: Ng TB, editor. Soybean-Biochemistry, Chemistry and Physiology. New York, USA: InTech Publishers; 2011. p. 119-36.
133. Mahadevan S, Park Y. Multifaceted therapeutic benefits of *Ginkgo biloba* L.: Chemistry, efficacy, safety, and uses. J Food Sci 2008;73:R14-9.
134. Tiedtke J, Marks OA. Multi-functional botanical active based on ginko for anti-aging. Cosmetic Sci Technol 2005;2005:18-25.
135. Grabowska K, Podolak I, Galanty A, Zaluski D, Makowska-Was J, Sobolewska D, *et al. In vitro* anti-denaturation and anti-hyaluronidase activities of extracts and galactolipids from leaves of *Impatiens parviflora* DC. Nat Prod Res 2016;30:1219-23.
136. Prajapati MS, Patel JB, Modi K, Shah MB. *Leucas aspera*: A review. Pharmacogn Rev 2010;4:85-7.
137. Kim YH, Kim KS, Han CS, Yang HC, Park SH, Ko KI, *et al.* Inhibitory effects of natural plants of Jeju Island on elastase and MMP-1 expression. J Cosmet Sci 2007;58:19-33.
138. Satyavati GV, Raina MK, Sharma M. Indian Medicinal Plants. New Delhi: ICMR; 1976. p. 178.
139. Gupta VK, Sharma SK. Plants as natural antioxidants - A review. Nat Prod Radiance 2006;5:326-34.
140. Moon H, Jung JC. Effect of meso-dihydroguaiaretic acid from *Machilus thunbergii* Sieb and Zucc on MMP-1 expression in heat shock-induced cultured primary human fibroblasts. Phytother Res 2006;20:714-6.
141. Cho YH, Kim JH, Sim GS, Lee BC, Pyo HB, Park HD. Inhibitory effects of antioxidant constituents from *Melothria heterophylla* on matrix metalloproteinase-1 expression in UVA-irradiated human dermal fibroblasts. J Cosmet Sci 2006;57:279-89.
142. Cardozo KH, Guaratini T, Barros MP, Falcão VR, Tonon AP, Lopes NP, *et al.* Metabolites from algae with economical impact. Comp Biochem Physiol C Toxicol Pharmacol 2007;146:60-78.
143. Carillon S, López E, Casas MM, Avila E, Castillo RM, Carranco ME, *et al*. Potential use of seaweeds in the laying hen ration to improve the quality of n-3 fatty acid enriched eggs. J Appl Phycol 2008;20:721-8.
144. Mirshafiey A, Khodadadi A, Rehm BH, Khorramizadeh MR, Eslami MB, Razavi A, *et al.* Sodium alginate as a novel therapeutic option in experimental colitis. Scand J Immunol 2005;61:316-21.
145. Mishra AP. Formulation and evaluation of herbal antioxidant for cream of *Nardostachys jatamansi* collected from Indian himalayan region. Asian Pac J Trop Med 2014;4:679-85.
146. Cho S, Won CH, Lee DH, Lee MJ, Lee S, So SH, *et al.* Red ginseng root extract mixed with torilus fructus and *Corni fructus* improves facial wrinkles and increases Type I procollagen synthesis in human skin: A randomized, double-blind, placebo-controlled study. J Med Food 2009;12:1252-9.
147. Lee HJ, Kim JS, Song MS, Seo HS, Moon C, Kim JC, *et al.* Photoprotective effect of red ginseng against ultraviolet radiation-induced chronic skin damage in the hairless mouse. Phytother Res 2009;23:399-403.
148. Kang TH, Park HM, Kim YB, Kim H, Kim N, Do JH, *et al.* Effects of red ginseng extract on UVB irradiation-induced skin aging in hairless mice. J Ethnopharmacol 2009;123:446-51.
149. Kim JH, Cho YH, Lee BC, Pyo HB. Cosmetic Composition Comprising Extracts of Pterocarpus Santalinus Capable of Inhibiting Activity. Korea Patent; 2007. Available from: http://www.patent.ipexl.com/KR/1020050076940.html. [Last accessed on 14 Oct 2016].
150. Tsukahara K, Nakagawa H, Moriwaki S, Takema Y, Fujimura T, Imokawa G. Inhibition of ultraviolet-B-induced wrinkle formation by an elastase-inhibiting herbal extract: Implication for the mechanism underlying elastase-associated wrinkles. Int J Dermatol 2006;45:460-8.
151. Kim SJ, Sancheti SA, Sancheti SS, Um BH, Yu SM, Seo SY. Effect of 1,2,3,4,6-penta-O-galloyl-beta-D-glucose on elastase and hyaluronidase activities

and its Type II collagen expression. Acta Pol Pharm 2010;67:145-50.
152. Boulos L. Medicinal Plants of North Africa. UK: Reference Publications; 1983. p. 70.
153. Nadkarni KM, Nadkarni AK. Indian Materia Medica. Delhi: Popular Prakashan; 1999. p. 106.
154. Sanja SD, Sheth NR, Patel NK, Patel D, Patel B. Characterization and evaluation of antioxidant activity of *Portulaca oleracea*. Int J Pharm Pharm Sci 2009;1:5-10.
155. Choi MJ, Choi BT, Shin HK, Shin BC, Han YK, Baek JU. Establishment of a comprehensive list of candidate antiaging medicinal herb used in korean medicine by text mining of the classical korean medical literature, 'dongeuibogam,' and preliminary evaluation of the antiaging effects of these herbs. Evid Based Complement Alternat Med 2015;2015:873185.
156. Sultana Y, Kohli K, Athar M, Khar RK, Aqil M. Effect of pre-treatment of almond oil on ultraviolet B-induced cutaneous photoaging in mice. J Cosmet Dermatol 2007;6:14-9.
157. Baylac S, Racine P. Inhibition of human leukocyte elastase by natural fragrant extacts of aromatic plants. Int J Aromather 2004;14:179-82.
158. Calabrese V, Scapagnini G, Catalano C, Dinotta F, Geraci D, Morganti P. Biochemical studies of a natural antioxidant isolated from rosemary and its application in cosmetic dermatology. Int J Tissue React 2000;22:5-13.
159. Manosroi A, Jantrawut P, Akihisa T, Manosroi W, Manosroi J. *In vitro* anti-aging activities of *Terminalia chebula* gall extract. Pharm Biol 2010;48:469-81.
160. Satardekar KV, Deodhar MA. Anti-ageing ability of *Terminalia* species with special reference to hyaluronidase, elastase inhibition and collagen synthesis *in vitro*. Int J Pharmacogn Phytochem Res 2010;2:30-4.
161. Radhakrishnan NS, Ismail IS. Cosmetic potential of Southeast Asian herbs: An overview. J Phytochem Rev 2015;14:5-12.
162. Korac RR, Khambholja KM. Potential of herbs in skin protection from ultraviolet radiation. Pharmacogn Rev 2011;5:164-73.
163. Moon HI, Lee J, Zee OP, Chung JH. The effect of flavonol glycoside on the expressions of matrix metalloproteinase-1 in ultraviolet-irradiated cultured human skin fibroblasts. J Ethnopharmacol 2005;101:176-9.
164. Cornacchione S, Sadick NS, Neveu M, Talbourdet S, Lazou K, Viron C, *et al. In vivo* skin antioxidant effect of a new combination based on a specific *Vitis vinifera* shoot extract and a biotechnological extract. J Drugs Dermatol 2007;6 6 Suppl: S8-13.
165. Hou WC, Lin RD, Cheng KT, Hung YT, Cho CH, Chen CH, *et al.* Free radical-scavenging activity of Taiwanese native plants. Phytomedicine 2003;10:170-5.
166. Baxter RA. Anti-aging properties of resveratrol: Review and report of a potent new antioxidant skin care formulation. J Cosmet Dermatol 2008;7:2-7.
167. Sharma PV. Dravyaguna Vijnana. Vol. 2. Varanasi: Chauklambha Bharathi Academy; 1993. p. 537.
168. Farooqi AH, Sharma S, Kumar S. Herbal Skin Care Formulation and a Process for the Preparation there of U.S. Patent 6368639; 2002. Available from: http://www.patent.ipexl.com/US/6368639.html. [Last accessed on 14 Oct 2016].
169. Sahu RK, Roy A, Matlam M, Deshmukh VK, Dwivedi J, Jha AK. Review on skin aging and compilation of scientific validated medicinal plants, prominence to flourish a better research reconnoiters in herbal cosmetics. Res J Med Plant 2013;7:1-22.
170. Matsui MS, Hsia A, Miller JD, Hanneman K, Scull H, Cooper KD, *et al*. Non-sunscreen photoprotection: Antioxidants add value to a sunscreen. J Investig Dermatol Symp Proc 2009;14:56-9.
171. Ernst E. 'First, do no harm' with complementary and alternative medicine. Trends Pharmacol Sci 2007;28:48-50.

Source of Support: Nil. **Conflict of Interest:** None declared.