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Bioactive compounds from natural resources against skin aging

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ABSTRACT

Skin aging involves degradation of extracellular matrix (ECM) in both the epidermal and dermal layers, it leaves visible signs on the surface of skin and the physical properties of the skin are modified. Chronological aging is due to passage of time, whereas premature aging occurred due to some environmental factors on skin produces visible signs such as irregular dryness, dark/light pigmentation, sallowness, severe atrophy, telangiectases, premalignant lesions, laxity, leathery appearance and deep wrinkling. There are several synthetic skincare cosmetics existing in the market to treat premature aging and the most common adverse reactions of those include allergic contact dermatitis, irritant contact dermatitis, phototoxic and photo-allergic reactions. Recent trends in anti-aging research projected the use of natural products derived from ancient era after scientific validation. Ample varieties of phytomolecules such as aloin, ginsenoside, curcumin, epicatechin, asiaticoside, ziyuglycoside I, magnolol, gallic acid, hydroxychavicol, hydroxycinnamic acids, hydroxybenzoic acids, etc. scavenges free radicals from skin cells, prevent trans-epidermal water loss, include a sun protection factor (SPF) of 15 or higher contribute to protect skin from wrinkles, leading to glowing and healthy younger skin. Present era of treating aging skin has become technologically more invasive; but herbal products including botanicals are still relevant and combining them with molecular techniques outlined throughout this review will help to maximize the results and maintain the desired anti-skin aging benefits.

Introduction

One of the most frequent dermatologic concerns is skin aging, it is a complex evitable process of human life and scientific researches are revealing many of the possibilities that cause physiological aging as the time passes. The detailed mechanisms involved some interesting alleyway in age-dependent decline of cell tissue function to produce harmful effects during proteolytic degradation of fiber network that leaves visible signs on the surface of the skin. There are two types of skin aging, one is chronological aging which is due to the passage of time and another is premature aging or photoaging due to environmental aggressors. The term "photoaging" was first coined in 1986. It describes the clinical signs including irregular dryness, dark/light pigmentation, sallowness, deep furrows or severe atrophy, telangiectases, premalignant lesions, laxity, and a leathery appearance. Other signs include elastosis (a coarse, yellow, cobblestoned effect of the skin) and actinic purpura (easy bruising related to vascular wall fragility in the dermis) (Gilchrest 1990).

Microscopic differences for photoaged skin, in contrast can be associated with either increased epidermal thickness or pronounced epidermal atrophy with histological changes like accumulation of elastin-containing material just below the dermal-epidermal junction or disorganization of collagen, etc. Collagen is one of the main building blocks of human skin. It is synthesized from its precursor molecules called procollagen which is derived from dermal fibroblasts regulated by transforming growth factor-β (TGF-β), a cytokine that promotes collagen production and activator protein-1 (AP-1), a transcription factor promotes collagen breakdown by up regulating enzymes called matrix metalloproteinases (MMPs) (Fig. 1). UV radiation is absorbed by skin molecules and generates reactive oxygen species (ROS) causes "oxidative damage" to cellular components like cell walls, lipid membranes, mitochondria, and DNA. Each UV exposure induces a wound response with subsequent imperfect repair, leaving an invisible "*solar scar*," repetitive UV exposure eventually lead to development of a visible "*solar scar*," manifesting as a visible wrinkle over a lifetime (Lavker 1995).

Abbreviations: AP-1, activator protein-1; CREB, cyclic-AMP responsive element-binding protein; ESR, electron spin resonance; ECM, extracellular matrix; ERK, extracellular signal-regulated kinases; HDF, human dermal fibroblast; IL, interleukin; JNK, Jun N-terminal kinase; MMPs, matrix metalloproteinases; MAPK, mitogen-activated protein kinase; NF-κB, neuclear factor-kB; ROS, reactive oxygen species; SPF, sun protection factor; TIMP, tissue inhibitors of matrix-metalloproteinase; TNF-α, tissue necrosis factor-α; TEWL, trans-epidermal water loss; TGF-β, transforming growth factor-β; UV, ultraviolet.

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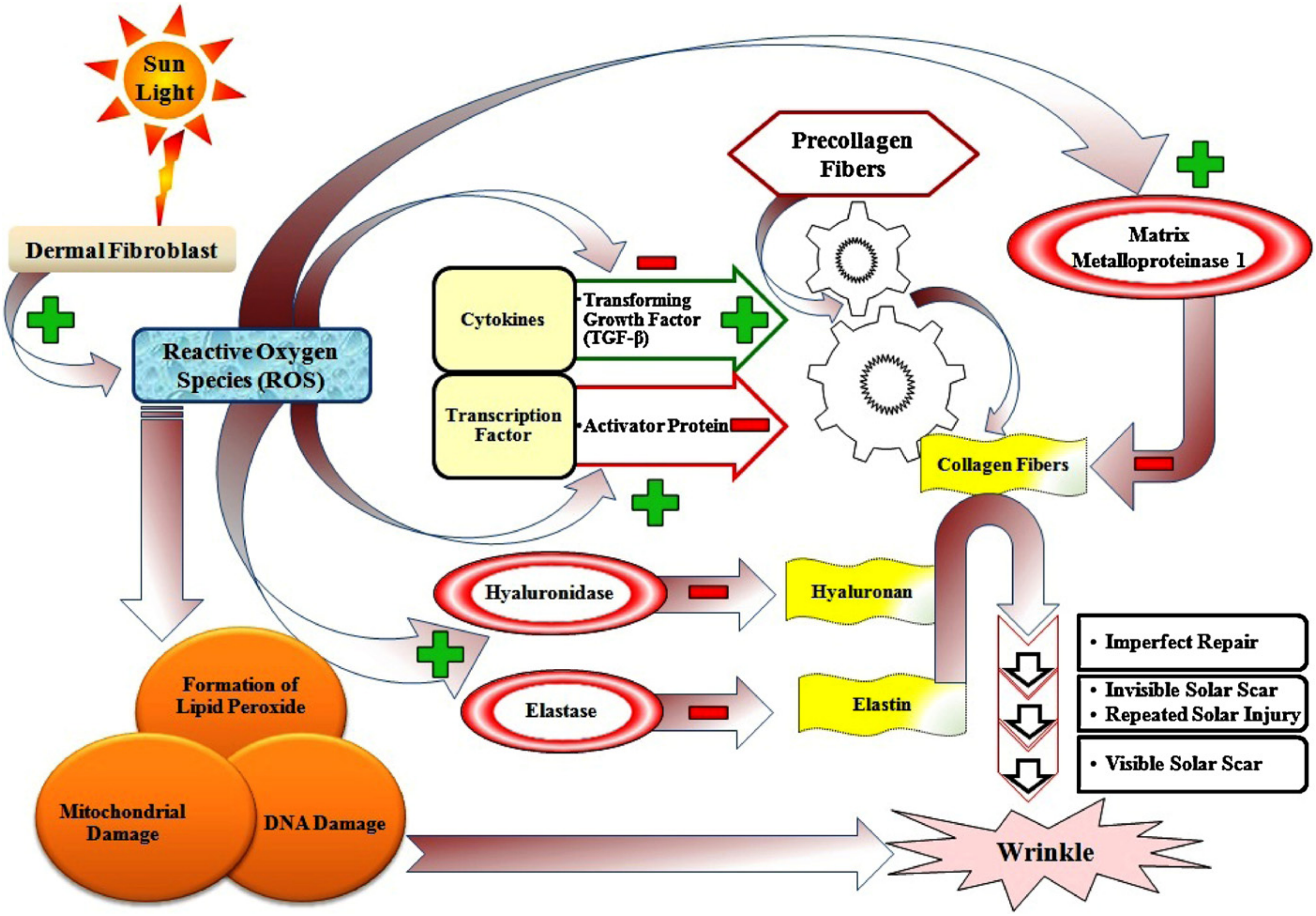

Fig. 1. Pathway of premature skin aging [+, induction; −, inhibition].

It has been found that a wide variety of new cosmeceuticals and formulas can facilitate the skin to repair wrinkles, leading to a younger healthy looking face, glowing skin and fight against skin aging, accelerate the synthesis of collagen (Kim et al. 2007). Botulinum toxin from *Clostridium botulinum* has the stretching effects over wrinkle skin. It works by blocking neurotransmission that can paralyze the muscles, which results in non-constriction of the muscle for a period of 3–4 months. This inability prevents the skin to fold, thus eliminating possibility of wrinkling (Ramos-e-Silva and da Silva Carneiro 2007). But, the major risks of using botulinum toxin over skin are; allergic reaction, muscle weakness, double vision, hoarseness of voice, blurred vision, drowsiness, headache, dry mouth, fatigue, and flu-like symptoms (Baizabal-Carvallo et al. 2011). However, the "modern" botulinum treatment for skin stretching has great risks. The most promising topical treatments incorporate antioxidants, estrogen, vitamins and minerals. They scavenge free radicals and are known to contribute to the physiological aging by permanently damaging cell structure and function. In addition, it is generally documented that physiological improvement has a philosophical effect on skin health: a healthy diet, supplemented with a vitamins and minerals have anti-aging as well as anti-wrinkle effect.

Medicinal plants preventing skin aging (see Table 1, main constituents, Fig. 2)

There are several synthetic skincare products containing active ingredients including monoethanolamine, diethanolamine, sodium laureth sulfate, triethanolamine, etc. have adverse reactions such as allergic contact dermatitis, irritant contact dermatitis, phototoxic and photo-allergic reactions. Ayurveda is one of the most ancient systems of traditional medicine and has over 200 herbs, minerals and several formulations for management of aging and enhances the health and beauty of the skin. The whole range of cosmetic usage and its practice as conceived by the ancient Indians was based on natural resources and there has been great upsurge in recent years (Mukherjee et al. 2010). Ayurveda is one of the ancient systems of medicine in India, where the concept of skin aging have been discussed in several aspects. In this age old Indian medicine system several concerns about aging has been discussed in Sanskrit like *Vayasthapana* (age defying), *Varnya* (brighten skin glow), *Sandhaniya* (cell regeneration), *Vranaropana* (healing), *Tvachya* (nurturing), *Shothahara* (anti-inflammatory), *Tavachahnivardhani* (strengthening skin metabolism) and *Tvagrasayana* (retarding aging) (Datta and Paramesh 2010). Natural skin care products are quickly absorbed by the superficial layers of the skin and are usually hypo-allergenic in nature. Many herbs, particularly fruits, vegetables, and whole grains contain antioxidants, polyphenols scavenging free radicals and eliminates byproducts of metabolism. They are also being used as diet that is both healthy for the body in general and helpful for avoiding the typical signs of aging, while a few are astonishingly high in these beneficial antioxidant food molecules (Mukherjee et al. 2007). Today, herbal cosmetics are growing popular not only in Asian countries but also in other countries due to its significant impact on skin aging. This article is aimed at reviewing the possible medicinal plants and their constituents, which have been reported to have skin aging prevention

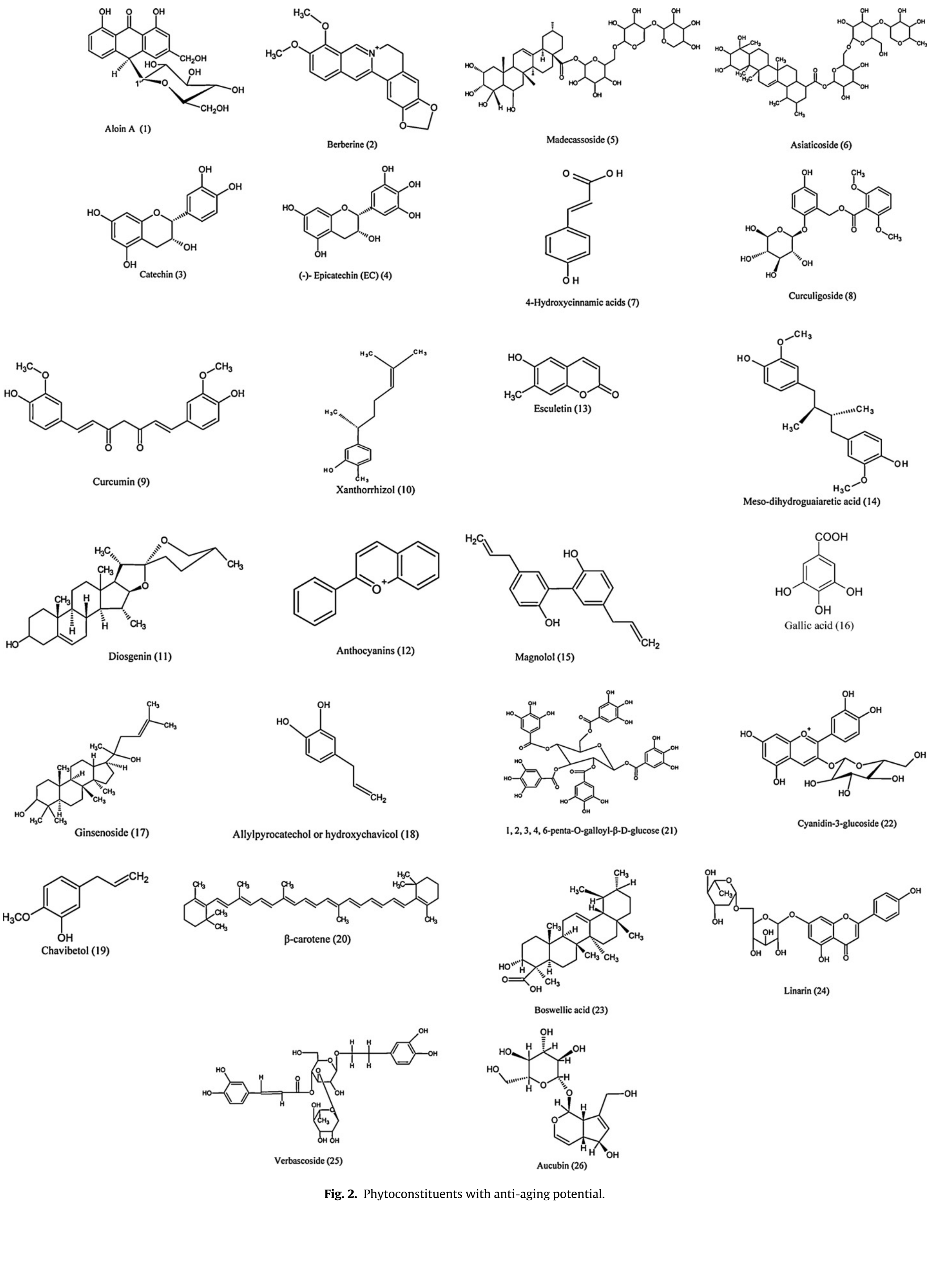

Fig. 2. Phytoconstituents with anti-aging potential.

Table 1
List of anti-aging plants and their mechanism of action.

S. no.	Name of the plants and family	Part used	Possible mechanism of action	References
1.	*Aesculus hippocastanum* L. (Hippocastanaceae)	Leaves	Generate contraction forces	Fujimura et al. (2006)
2.	*Aloe vera* (Liliaceae)	Gel	Inhibit stimulated granulocyte MMPs Inhibit tyrosine hydroxylase and 3,4-dihydroxyphenylalanine oxidase	Barrantes and Guinea (2003) Jones et al. (2002)
3.	*Astragalus membranaceus* (Fisch.) Bunge (Fabaceae)	Leaves	Increase the content of hyaluronic acid Increase the cellular expression of telomerase reverse transcriptase	Xia et al. (2002) Hsu and Chiang (2009)
4.	*Berberis aristata* DC. (Berberidaceae)	Berries	Inhibited expression of MMP-9 and suppressed TPA-induced IL-6 expression Type-I procollagen expression increased	Kim et al. (2008b) Kim and Chung (2008a)
5.	*Calendula officinalis* L. (Asteraceae)	Flower	Control the activity/secretion of MMP-2 and MMP-9	Yris et al. (2010)
6.	*Camellia japonica* L. (Theaceae)	Oil	Induce type-1 procollagen synthesis and inhibit MMP-1 activity	Jung et al. (2007)
7.	*Camellia sinensis* L. (Theaceae)	Leaves	Suppress UV irradiation induced cutaneous erythema, thickening of the epidermis, overexpression of CK5/6, CK16, MMP-2, MMP-9	Li et al. (2009)
8.	*Centella asiatica* L. Urban. (Umbelliferae)	Whole plant	Improvement of the clinical score for deep and superficial wrinkles, suppleness, firmness, roughness and skin hydration Induce type-I collagen synthesis	Haftek et al. (2008) Lee et al. (2006)
9.	*Citrus sinensis* L. (Rutaceae)	Fruit	NF-κB and AP-1 translocation and procaspase-3 cleavage	Cimino et al. (2007)
10.	*Curculigo orchioides* G. (Hypoxidaceae)	Rhizome	Inhibited MMP-1 expression	Lee et al. (2009b)
11.	*Curcuma longa* L. (Zingiberacease)	Rhizome	Inhibited MMP-2 expression	Sumiyoshi and Kimura (2009)
12.	*Curcuma xanthorrhiza* Roxb. (Zingiberaceae)	Rhizome	Inhibited MMP-1 expression	Oh et al. (2009)
13.	*Dioscorea composita* or *Dioscorea villosa* L. (Dioscoreaceae)		Increased bromodeoxyuridine uptake and intracellular cAMP level in keratinocytes	Tada et al. (2009)
14.	*Emblica officinalis* L. (Euphorbiaceae)	Fruit	Inhibited type-I collagen collagenase, increase TIMP-1 level	Takashi et al. (2008)
15.	*Fraxinus chinensis* Roxb. (Oleaceae)		Decreased the MMP-1 mRNA expression	Lee et al. (2007)
16.	*Glycine max* L. Merr. (Fabaceae)	Seeds	Inhibit melanosome phagocytosis Prevented the activation of caspase-3 pathway	Tsoyi et al. (2008)
17.	*Kaempferia pandurata* Roxb. (Zingiberaceae)	Rhizomes	Inhibition of UV induced phosphorylations of mitogen activated protein kinases	Shim et al. (2009)
18.	*Labisia pumila* (Blume) (Myrsinaceae)	Root	Inhibition of TNF-α, COX-2, MMP-1 and MMP-9 expression	Choi et al. (2010)
19.	*Machilus thunbergii* Sieb and Zucc (Lauraceae)	Stem bark	Strong inhibition of MMP-1	Moon and Jung (2006)
20.	*Magnolia ovovata* Thunb. (Magnoliaceae)		Inhibit the NF-κB-mediated gene expression	Tanaka et al. (2007)
21.	*Melothria heterophylla* (Lour.) Cogn. (Cucurbitaceae)		Inhibited MMP-1 activity	Cho et al. (2006)
22.	*Panax ginseng* L. (Araliaceae)	Roots	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	Cho et al. (2009) Lee et al. (2009a)
23.	*Piper betel* L. (Piperaceae)	Leaves	Protect photosensitization-mediated lipid peroxidation (LPO)	Mula et al. (2008)
24.	*Prunus dulcis* Mill. (Rosaceae)	Nut	Antioxidant and free radical scavenging potential	Sultana et al. (2007)
25.	*Tagetes erecta* L. (Asteraceae)	Flowers	Photoprotection	Del et al. (2010)
26.	*Terminalia chebula* Retz. (Combretaceae)	Fruits	Tyrosinase and MMP-2 inhibition Elastase, hyaluronidase, MMP-2 enzyme inhibition	Manosroi et al. (2010) Kim et al. (2010)
27.	*Theobroma cacao* L. (Sterculiaceae)	Bean	Down regulation of hydroxyproline and pepsin-resistant hydroxyproline content	Mitani et al. (2007)
28.	*Vaccinium uliginosum* L. (Ericaceae)	Berries	Removal of reactive oxygen species, diminished UV-B augmented-release of inflammatory interleukin (IL)-6 and IL-8	Bae et al. (2009)
29.	*Viola hondoensis* W. Becker and H. Boissieu (Violaceae)	Whole plant	Inhibition of MMP-1 expression, at the both mRNA and protein levels	Moon et al. (2005)
30.	*Vitis vinifera* L. (Vitaceae)	Shoot	Antioxidant and free radical scavenging capacity	Cornacchione et al. (2007)
31.	*Zingiber officinale* L. (Zingiberaceae)	Rhizomes	Inhibits fibroblast derived elastase	Tsukahara et al. (2006)

potential. Review on these plants and their constituents are being described in later section to highlight the potentials of medicinal plants useful in skin aging from natural resources.

Aesculus hippocastanum L. (Family: Hippocastanaceae)

A. hippocastanum is able to generate contraction forces by non-muscle (fibroblast) cells using fibroblast populated collagen gels. It plays an important role in determining cell morphology, vasoconstriction, and wound healing (Fujimura et al. 2006).

Aloe vera L. (Family: Liliaceae)

Aloin A (1) and B have been shown to inhibit *Clostridium histolyticum* collagenase reversibly and non-competitively. Both aloe gel and aloin are also effective inhibitors of stimulated granulocyte MMPs (Barrantes and Guinea 2003). Aloesin [2-acetonyl-8-beta-d-glucopyranosyl-7-hydroxy-5-methylchromone] isolated from the *A. vera* have been reported to modulate melanogenesis via competitive inhibition of tyrosinase. Tyrosine hydroxylase and 3,4-dihydroxyphenylalanine oxidase activities of tyrosinase from normal human melanocyte cell lysates were inhibited by aloesin in a dose dependent manner (Jones et al. 2002).

Astragalus membranaceus (Fisch.) Bunge (Family: Fabaceae)

It is perennial herb, indigenous to China, Republic of Korea, Mongolia, and Siberia. Primarily, the active constituents of *A. membranaceus* consist of polysaccharides and flavonoids (Xia et al. 2002). *A. membranaceus* have been found to increase the content of hyaluronic acid in cultures of keratinocytes and fibroblasts by elevating the hyaluronan synthase-3 and hyaluronan synthase-2 mRNA expressions (Hsu and Chiang 2009). Therefore, it is a promising candidate for preventing the age-dependent loss of hyaluronic acid content.

Berberis aristata DC. (Family: Berberidaceae)

B. aristata has a prominent role in Ayurveda for the treatment of liver and gallbladder ailments. Russian healers used it for inflammations, high blood pressure, and abnormal uterine bleeding (Kirtikar and Basu 1984). Decoction of roots of *B. aristata* has been claimed for skin troubles and in blood purification. *B. aristata* mixed with honey is useful in the treatment of aphthous sores abrasions and ulcerations of the skin (Nadkarni 1976). Topical formulation containing *B. aristata* has been reported to prevent acne vulgaris with the patients suffering skin disorders (Mamgain 2000). The plant is native to India and also found throughout South East Asia. Berberine (2) isolated from *B. aristata* have been reported to inhibit basal and TPA-induced expression and activity of MMP-9, and also suppressed TPA-induced IL-6 expression, ERK activation and AP-1 DNA binding activity in UV-induced skin inflammation, aging process and degradation of extracellular matrix proteins (Kim et al. 2008b). The MMP-1 and type I procollagen expression in human dermal fibroblasts regulated by berberine has been reported by Kim and Chung (2008a).

Calendula officinalis L. (Family: Asteraceae)

C. officinalis flowers have long been employed in folk therapy. The main uses are as remedies for burns (including sunburns), bruises, cutaneous and internal inflammatory diseases of several origins. Oral treatment of hairless mice maintained glutathione levels close to non-irradiated control mice and affects the activity/secretion of MMP-2 and MMP-9 stimulated by exposure to UVB irradiation (Yris et al. 2010).

Camellia japonica L. (Family: Theaceae)

Anti-skin aging property of *C. japonica* oil has been reported by Jung et al. (2007), in human dermal fibroblast cells by human COL1A2 promoter luciferase assay in a concentration dependent manner. It has been found that human type-I procollagen synthesis is induced by *C. japonica* oil while MMP-1activity has been inhibited. *C. japonica* oil also can hold trans-epidermal water loss (TEWL) without interrupting any adverse reactions.

Camellia sinensis L. (Family: Theaceae)

Originally cultivated in East Asia, this plant grows as large as a shrub. Sunscreen formulated with 2–5% green tea extract has been reported to protect UV irradiation induced photoaging, photoimmunosuppression, cutaneous erythema, thickening of the epidermis, overexpression of CK5/6, CK16, MMP-2, MMP-9, etc. (Li et al. 2009). A double-blind, placebo-controlled trial have been executed with moderate photoaging treated with either a combination regimen of 10% green tea cream and 300 mg twice-daily green tea oral supplementation or a placebo regimen for 8 weeks to monitor the clinical and histologic appearance of photoaging skin (Chiu et al. 2005). It has been found that patients treated with a combination regimen of topical as well as oral showed histological improvement in tissue elastic content, but clinically significant changes have not been observed and it may require longer supplementation for clinically observable improvements. Nichols and Katiyar (2010) reported that green tea polyphenols catechin (3), epiglactocatechin (4), epiglactocatechin-3-gallate, etc. favorably sunscreens supplement to protect the skin from the adverse effects of UV radiation-induced inflammation, oxidative stress and DNA damage including the risk of skin cancers.

Centella asiatica L. Urban. (Family: Umbelliferae)

C. asiatica is a perennial herb found in India, Sri Lanka, Madagascar, South Africa, Australia, China, and Japan. It contains several active triterpenoids, saponins, including madecassoside (5), asiaticoside (6), centelloside, and asiatic acid, which has been reported to increase cellular hyperplasia, collagen production, granulation tissue levels of DNA, protein, total collagen, hexosamine, rapid maturation and cross-linking of collagen, etc. (Suguna et al. 1996; Shetty et al. 2006). Madecassoside isolated from *C. asiatica*, known to induce collagen expression and modulate inflammatory mediators. To justify this statement Haftek et al. (2008) have performed a randomized double-blind clinical trial and found significant improvement of the clinical score for wrinkles, suppleness, firmness, roughness and skin hydration. Asiaticoside is another active saponin, which induced type I collagen synthesis in human dermal fibroblast cells. The molecular mechanism behind this has been partially assumed that SB431542, an inhibitor of the TGFβ receptor I (TβRI) kinase, which is known to be an activator of the Smad pathway (Lee et al. 2006). Topical formulation of aqueous extract of *C. asiatica* showed increased cellular proliferation and collagen synthesis on the skin wound of rats, which is an evidence of increasing collagen content and tensile strength. The treated wounds epithelialised faster and the rate of wound contraction was higher (Kumar et al. 1998). Triterpines including asiatic acid, madecassic acid and asiaticoside extracted from *C. asiatica* were screened on human foreskin fibroblast monolayer cultures and observed that collagen synthesis was increased in a dose-dependent manner whereas the specific activity of neosynthesized collagen was decreased (Maquart et al. 1990). Tenni et al. (1988) has reported that triterpinoid fraction can influence the biosynthesis of collagen, fibronectin and proteoglycans in human skin fibroblast cultures.

Citrus sinensis L. (Family: Rutaceae)

Cimino et al. (2007) have accounted that phenolic compounds such as anthocyanins, flavanones, hydroxycinnamic acids (7) and ascorbic acid is responsible for the anti-photoaging activity of three different varities of *C. sinensis* in modulating cellular responses such as NF-κB and AP-1 translocation and procaspase-3 cleavage to UV-B in human keratinocytes (HaCaT). Thus, *C. sinensis* has been proposed as a useful natural standardised extract in skin photoprotection with promising applications in the field of dermatology.

Curculigo orchioides Gaetrn. (Family: Hypoxidaceae)

Curculigoside (8) isolated from rhizomes of *C. orchioides* have been reported to possess strong inhibitory activity against MMP-1in cultured human skin fibroblasts suggest its skin improvement property (Lee et al. 2009b).

Curcuma longa L. (Family: Zingiberacease)

The effect of a *C. longa* extract have been found to do potential changes in skin thickness, increased elasticity, decreased pigmentation and wrinkling caused by long-term, low-dose UV-B irradiation in melanin-possessing hairless mice (Sumiyoshi and Kimura 2009). It prevents the formation of wrinkles and melanin as well as increases in the diameter and length of skin blood vessels and decrease expression of matrix metalloproteinase-2 (MMP-2). Therefore, skin wrinkling can be minimized by curcumin (9).

Curcuma xanthorrhiza Roxb. (Family: Zingiberaceae)

Xanthorrhizol (10) isolated from *C. xanthorrhiza* was investigated on the expression of MMP-1 and type-I procollagen in UV-irradiated human skin fibroblasts (Oh et al. 2009). Xanthorrhizol and *C. xanthorrhiza* extract (0.01–0.5 μg/ml) induced a significant, dose-dependent decrease in the expression of MMP-1 protein and increased the expression of type-1 procollagen.

Dioscorea composita or Dioscorea villosa L. (Family: Dioscoreaceae)

Extracts of *D. composita* or *D. villosa* are consumed as supplemental health foods containing large amounts of the plant steroid, diosgenin, etc. Efficacy of diosgenin (11) against skin aging has been established with *in vitro* human 3D skin equivalent model. It showed enhanced DNA synthesis and increased bromodeoxyuridine uptake and intracellular cAMP level in adult human keratinocytes (Tada et al. 2009). These results suggest that for restoration of keratinocyte proliferation in aged skin, diosgenin have a potential effect.

Emblica officinalis L. (Family: Euphorbiaceae)

E. officinalis shows significant type I collagen promotion and anti-collagenase effects on primary mouse fibroblast cells at a concentration of 0.1 mg/ml, determined by immunocytochemistry and Western blot analysis (Chanvorachote et al. 2009). Fruit extract has been reported to stimulate the proliferation of fibroblasts and induced production of procollagen in a concentration and time dependent manner. On the contrary, MMP-1 production from fibroblasts was dramatically decreased whereas TIMP-1 was significantly increased (Takashi et al. 2008).

Fraxinus chinensis Roxb. (Family: Oleaceae)

Study reveals that five major compounds have been isolated from *F. chinensis* extract; among them esculetin (12) has been found to have potent free radical scavenging activity with dose-dependently decreases the expression levels of MMP-1 mRNA and protein in UVB-irradiated human dermal fibroblasts (HDFs) (Lee et al. 2007).

Glycine max L. Merr (Family: Fabaceae)

Anthocyanin (13) isolated from black soybean [*G. max* (L.) Merr] seed responsible for down regulation of *in vitro* and *in vivo* UVB induced reactive oxygen species levels and apoptotic cell death through the prevention of caspase-3 pathway activation and reduction of proapoptotic Bax protein levels (Tsoyi et al. 2008). This finding highlights that anthocyanin from the seed coat of black soybean is useful compounds to modulate UVB-induced photoaging.

Hamamelis virginiana L. (Family: Hamamelidaceae)

H. virginiana is also known as *Witch-hazel* is a well known plant has long been used as cosmetics. The oil isolated from fresh leaves and twigs by steam distillation is used as mild astringent, and has also been recommended for certain skin conditions, such as boils, ulcers, itching eczema, bruises, etc. (Harry 1963). Decoction from the twigs is accounted for its use to treat swellings, inflammations and tumours. Both bark and leaves contain volatile oil, hamamelitannin, catechins, gallic acid, etc. (Engel et al. 1998; Wang et al. 2003). Its astringent action may be attributed for it relatively high tannin content, which has great value in the treatment of varicose veins due to haemostatic property. It's soothing and anticouperose effects are useful for mucosa, skin and minor capillary problems. It has also been used in treating atopic dermatitis with Hamamelis ointment, sun protection, facial toning lotion for oily skin, control minor pimple formation, and reduces the pain of sprains or athletic injuries (Swoboda and Meurer 1992). Masaki et al. (1995) have evaluated the anti-skin aging activity of *Witch-hazel* on a murine dermal fibroblast culture system using both ESR spin-trapping and malondialdehyde generation methods. Polymeric proanthocyanidins and polysaccharides have been isolated from the bark. It showed increased the proliferation of the cells and reduced the transepidermal water loss and erythema formation, while screened on cultured human keratinocytes (Deters et al. 2001). Anti-inflammatory effect of hamamelis lotion has been evaluated on 30 healthy volunteers using a modified UVB erythema test model. It was found that erythema was suppressed with in the range of 20–27% within 48 h compared to other formulation significantly (Hughes-Formella et al. 1998). Anti-inflammatory efficacy of the topical preparations with 10% hamamelis distillate was screened on 40 human volunteers in a modified UV erythema test with three UV dosages. Even though the effect was less, but the UV erythema was reduced significantly (Hughes-Formellam et al. 2002).

Kaempferia pandurata Roxb. (Family: Zingiberaceae)

In a dose-dependent manner (0.01–0.5 μg/ml) *K. pandurata* extract have been reported significantly to reduce the expression of MMP-1 and increased the expression of type-1 procollagen at the protein and mRNA levels through the inhibition of UV induced phosphorylations of MAPKs such as ERK (extracellular-regulated kinase), JNK (Jun N-terminal kinase) and p38 kinase, respectively.

It also led to the inhibition of AP-1 DNA binding activity in human skin fibroblasts (Shim et al. 2009).

Labisia pumila Blume. (Family: Myrsinaceae)

L. pumila also known as "*Kacip Fatimah*," showed free radical scavenging activity. Its extract markedly inhibited the TNF-α production. Extract of *L. pumila* down regulated the enhanced MMP-1 and MMP-9 expression in keratinocytes dose-dependently (Choi et al. 2010) which suggest potential of its extract as an anti-photoaging cosmetic ingredient.

Machilus thunbergii Sieb and Zucc (Family: Lauraceae)

Meso-dihydroguaiaretic acid (14) obtained from the stem bark of *M. thunbergii* have been reported for its strong inhibitory effect on MMP-1 in primary human fibroblasts by heat shock induced premature skin aging (Moon and Jung 2006).

Magnolia ovovata Thunb. (Family: Magnoliaceae)

M. ovovata extract has been found to inhibit NF-κB-mediated gene expression and prevents photoaging processes through keratinocyte hyperproliferation and diminish degradation of collagen fibers in mice skin. Magnolol (15) is the compound responsible for the protective activity without hampering other inducible transcription factors such as AP-1 and cyclic-AMP responsive element-binding protein (CREB) (Tanaka et al. 2007). Magnolol inhibited matrix metalloprotease-1 (MMP-1) from the cells overexpressing p65. These findings suggest that magnolol has potential effect against photoaging via inhibiting NF-κB by external topical application.

Melothria heterophylla (Lour.) Cogn. (Family: Cucurbitaceae)

1,2,4,6-Tetra-O-galloyl-β-glucopyranose and gallic acid (16) isolated from *M. heterophylla* known to play an important role over MMPs expression in photoaging by mediating the degradation of extracellular matrix proteins, but no inhibition of MMP-1 mRNA expression (Cho et al. 2006). Both these compounds significantly inhibited MMP-1 expression at the protein level and have a potent antioxidant activity suggesting the usefulness as an anti-photoaging agent.

Panax ginseng L. (Family: Araliaceae)

Bioactive constituents, ginsenoside (17) believed to have anti-skin aging activities. A randomized, double-blind, placebo-controlled study revealed that red ginseng extract improved type-I procollagen gene and protein expression, prevent MMP-9 gene induction and elongated the fibrillin-1 fiber length, thereby reduces facial wrinkles (Cho et al. 2009). Red Ginseng extract inhibited the increases of epidermal thickness and skin TGF-β1 content induced by UVB irradiation, which may be due to partial inhibition of the increase of skin TGF-β1 (Lee et al. 2009a). These results substantiate the alleged beneficial effects of red ginseng on photoaging and support its use as an effective "beauty food."

Piper betel L. (Family: Piperaceae)

Allylpyrocatechol (18) and chavibetol (19) isolated from *P. betel* have been established to protect photosensitization-mediated lipid peroxidation of rat liver mitochondria effectively. Allylpyrocatechol has been found to be significantly more potent (Mula et al. 2008). Allylpyrocatechol also prevented the unfavorable effects of the type-II photosensitization-induced toxicity to mouse fibroblast L929 cells. The results suggested that allylpyrocatechol have an important role in protecting biological systems against damage, by eliminating $^1O_2$ generated from certain endogenous photosensitizers.

Prunus dulcis Mill. (Family: Rosaceae)

The role of almond oil in reducing the degradative changes induced in skin upon exposure to UV radiation has been proposed by Sultana et al. (2007) illustrated that biochemical parameters, glutathione, and lipid peroxidation have been ameliorated by almond oil.

Tagetes erecta L. (Family: Asteraceous)

Small bushy plants widely cultivated in India, Mexico and Central America. The flowers are popularly known as *Marigold* contains provitamin A 'β-carotene' (20) responsible for photoprotection (Del et al. 2010). Methanol extract of flower has been found to possess *in vitro* inhibition of hyaluronidase and elastase and MMP-1, which suggested the potential of this plant as anti-wrinkle (Maity et al. 2011).

Terminalia chebula Retz. (Family: Combretaceae)

In vitro skin cell protective activity of *T. chebula* have been evaluated through antioxidative and tyrosinase inhibition activity as well as the antiproliferative and MMP-2 inhibition activity on early aged human skin fibroblasts (Manosroi et al. 2010). The plant showed 1.37 times more potent MMP-2 inhibition than ascorbic acid on fibroblasts determined by zymography. Isolated compound 1,2,3,4,6-penta-O-galloyl-β-D-glucose (21) from this plant showed antielastase and antihyaluronidase inhibitory activity with significant induction of type II collagen expression in rabbit articular chondrocytes (Kim et al. 2010).

Theobroma cacao L. and Cola acuminate Schott and Endl. (Family: Sterculiaceae)

Cacao bean and cola nut are popular edible plants that contain polyphenols and xanthine derivatives, which protective effects against UV-induced erythema when topically applied to the dorsal skin of hairless mice. The desired mechanism behind this has been highlited by Mitani et al. (2007) which suggested that the total hydroxyproline and pepsin-resistant hydroxyproline content down regulated markedly increased after UV irradiation.

Vaccinium uliginosum L. (Family: Ericaceae)

Fruits of bog blueberry (*V. uliginosum*) are rich in anthocyanins like cyanidin-3-glucoside (22), petunidin-3-glucoside, malvidin-3-glucoside, and delphinidin-3-glucoside which have been documented for pigmentation and attenuation of photoaging through removal of reactive oxygen species (ROS) production and the resultant DNA damage responsible for activation of p53 and Bad in UV-B-irradiated human dermal fibroblasts (Bae et al. 2009).

Viola hondoensis W. Becker and H. Boissieu (Family: Violaceae)

Moon et al. (2005) isolated quercetin-3-O-β-D-(6″-feruloyl)-galactopyranoside an isoflavonoid from the stems of *V. hondoensis* which reduced UV-irradiated human skin fibroblasts MMP-1 expression at the protein levels in dose-dependent manner.

Vitis vinifera L. (Family: Vitaceae)

V. vinifera shoot extract has stronger *in vitro* antioxidant capacity than vitamin C or vitamin E on cultured normal human keratinocytes and also *in vivo* photoaging activity of a serum based formulation of this extract in combination with a biotechnological extract (Ronacare Hydroine) (Cornacchione et al. 2007). The dermatologic evaluation showed that a 4-week twice daily application of a serum containing the combination improved the main clinical signs of photoaged skin.

Zingiber officinale L. (Family: Zingiberaceae)

Topical application of *Z. officinale* extract to hairless mouse skin significantly inhibited the wrinkle formation induced by chronic UV-B irradiation at a suberythemal dose accompanied by a significant prevention of the decrease in skin elasticity (Tsukahara et al. 2006).

Miscellaneous

Tamsyn et al. (2009) have screened 21 plants for their anti-collagenase, anti-elastase and antioxidant activity. Triterpenoids known as boswellic acids (23) isolated from frankincense (*Boswellia* spp.) (Family: Burseraceae) resin showed anti-elastase activity (Melzig et al. 2001). Rosemary extracts from *Rosmarinus officinalis* L. (Family: Lamiaceae) have also been reported to have good anti-elastase activity (Baylac and Racine 2004). Acevedo et al. (2005) isolated two compounds known as linarin (24) and verbascoside (25) from *Buddleja scordioides* H.B.K. (Family: Buddlejaceae) to determine the photoprotective properties and verbascoside showed the largest SPF measurement. A quinazolinedione alkaloid isolated from the fruits of *Evodia officinalis* (Dode) Huang (Family: Rutaceae) have been reported to have MMP-1 inhibitory activity (Jin et al. 2008). Aucubin (26) isolated from *Eucommia ulmoides* Oliv. (Family: Eucommiaceae) has been found to inhibit MMP-1 and also decrease the senescence associated β-galactosidase activity, which indicates it as an antiphoto-induced aging compound (Jin et al. 2005). Recently, *Cucumis sativus* L. (Family: Cucurbitaceae) fruit has been found to possess *in vitro* inhibition of hyaluronidase and elastase and MMP-1, which suggested the potential of this plant as anti-wrinkle (Nema et al. 2011).

Discussion

Skin aging is a major symptom in modern days involving the process of photo-aging due to the industrialization, pollution and global warming in the world. It has been reported that repetitive exposure to UV radiation accelerates skin aging leading to the formation of peroxyl free radicals which break down to form malondialdehyde (MDA) subsequently cross-links and polymerizes collagen, leading to loss of skin elasticity and decreasing the capacity of the skin to hold water, which are implicated in formation of the most obvious symptom of aging skin wrinkling (Kim et al. 2007). Most promising topical treatments of skin aging includes herbal extracts, vitamins and antioxidants food supplement, which have been accepted widely to scavenge free radicals from skin cells and to restore skin elasticity. Indeed, herbal anti-wrinkle or anti-aging formulations slow down or reverse the effects of skin aging and help people to live longer, healthier, happier lives. Preliminary experiments have revealed that topically used antioxidants such as vitamins A and E, squalene, co-enzyme Q10, ferulic acid, idebenone, pycnogenol and silymarin ameliorate long-term damage from environmental influences and also promote self-repair, are being used into topical skin care formulations (Pinnell 2003).

However, phyto-pharmaceuticals, which have become popular over the last few years, require significantly more researches to formulate any positive conclusions for their topical application. Many botanical antioxidants are available and they are generally classified into carotenoids, flavonoids, and polyphenols which are divided into several classes of chemicals: anthocyanins, bioflavonoids, proanthocyanidins, catechins, hydroxycinnamic acids, and hydroxybenzoic acids. They are accountable to provide UV protection and metal chelation in addition to antioxidant properties (Mukherjee and Wahile 2006).

Topical herbal therapy an important treatment and preventative step in the photoaging process of skin aging. Cosmetic formulations based on botanical ingredients have been used since ancient times play a major role in contemporary cosmetics. Present era of treating aging skin has become technologically more invasive; but herbal products including botanicals are still relevant and can be highly efficacious. Scientific researches continue to corroborate traditional uses of many plants for skin benefits to elucidate biochemical mechanisms of action for a growing number of phytochemicals. Additional clinical trials is mandatory to optimize the application of natural ingredients for cosmetics, but scientific validation for the safety and efficacy of botanical extracts and compounds for treating aging skin is utmost necessary (Mukherjee and Ponnusankar 2010). According to Global Cosmetic Industry Business Magazine, the global market for natural beauty products from India were 1.3 million US$ in 1963–1964, 25.7 million US$ in 1979–80, 336 million US$ during 2004–2005 and touched US$14.7 billion in 2006 with growth of the ingredients expected to be around 5% per year through 2011. The herbal cosmetics products are set for a significant growth depending on their capability to renew cells, minimize pores, and restore hydration and have created an US$83 billion worldwide market. Furthermore, overall growth is expected to show a steady development of the prior decade, with stable gains projected over herbal extracts through clinically supported anti-aging benefits and proven safety.

Conclusion

The scientific validity on the use of herbs as anti-wrinkle activity should be explored further based on different models. The plants from traditional and other resources need to be evaluated based on the combined approaches of exploitation and exploration to find effective leads from natural resources useful in the treatment of skin wrinkling.

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