

Unmet Need and Challenges of Skin Aging by Herbal Anti-aging Cosmeceuticals: An Overview

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Abstract

Skin is the largest organ and acts as the first line of defense of our body. After a certain period of time, our skin loses its skin tone and elasticity that we called aging. Skin aging is the result of programmed senescence and prolonged environmental injury to the skin. Skin aging can be controlled by the use of antioxidants and free radical scavengers. Nowadays, the significance of herbals and herbal products is gaining worldwide. The demand of herbal medicine is increasing rapidly due to their skin friendliness, low cost, and lack of side effects. Plants have potential activities such as anti-aging, anti-wrinkle, antioxidant, anti-inflammatory, and skin whitening activities. The aim of this review article is to provide information regarding the control of skin aging by antioxidant-rich herbal medicines.

Key words: Antioxidants, cosmeceuticals, herbal cosmetics, skin aging

INTRODUCTION

Skin

Skin is the largest organ in a human body, which helps to cover the muscles, bones, and all parts of the body.^[1] Skin performs a wide variety of functions resulting from chemical and physical reactions inside these components.^[2] It serves many important functions, including:

- Protecting the body against trauma.
- Regulating body temperature.
- Sensing painful and pleasant stimuli.^[3]
- Manufactures Vitamin D.
- Absorbs certain drugs.^[4]
- Excretion of metabolic wastes.^[5]
- Maintains homeostasis.^[6]

Skin is the body's protective barrier against a whole battery of environmental aggressors both of natural and anthropogenic origins.^[7] The color, thickness, and texture of skin vary over the body.^[8] There are two main kinds of human skin: Glabrous skin (non-hairy skin) and hair-bearing skin.^[9]

Due to external and internal causes, the collagen fibers and elastic fibers present in the dermal

tissue of the skin are modified or damaged which leads to wrinkles formation and sagging on the skin because the elasticity of the skin is reduced, it is one of the measures causes for the skin aging [Figure 1].^[10]

Skin consists of three main layers - the epidermis, the dermis, and the subcutis each of which is made up of several sub-layers. Skin appendages - such as follicles and sebaceous and sweat glands also play various roles in its overall function [Table 1].^[12]

Skin aging

Skin aging is a complex biological process.^[14] Skin aging is particularly important because of its social impact. It is visible and also represents an ideal model organ for investigating the aging process. The "biological clock" affects both the skin and the internal organs in a similar way, causing irreversible

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degeneration.^[15] The phenomenon of aging in human skin comprises two elements: Intrinsic, or the chronological aging process, and extrinsic aging from environmental stressors, often called photoaging.^[16]

Types of skin aging

Intrinsic aging

The intrinsic process occurs through the passage of time.^[17] Intrinsic aging is also called chronological aging or endogenous aging. It is influenced by your body's many internal processes, including:

- Genetic factors
- Cellular metabolism
- Hormonal changes.^[18]

Within the skin, collagen production slows down and elastin has a bit less spring. Dead skin cells do not shed as quickly and turnover of new skin cells may decrease slightly.^[19] Essentially intrinsic skin aging can only be seen in quite old age and is characterized by unblemished, smooth, pale(r), drier, and less elastic skin with fine wrinkles.^[20]

Extrinsic aging

Extrinsic skin aging is superimposed on intrinsic skin aging process.^[21] Extrinsic aging is often referred to as photoaging. Photodamage implies changes beyond those associated with aging alone, defined as cutaneous damage caused by chronic exposure to solar radiation and is associated with the emergence of neoplastic lesions.^[22] Extrinsic factors are, to varying degrees, controllable and include exposure to sunlight, pollution or nicotine, repetitive muscle movements such as squinting or frowning and miscellaneous lifestyle components such as diet, sleeping position, and overall health.^[23]

Extrinsic signs of aging include dryness, loss of volume, fine lines and deep wrinkles, sagging, coarseness, blotchy or irregular pigmentation or dark spots, and loss of elasticity. At its

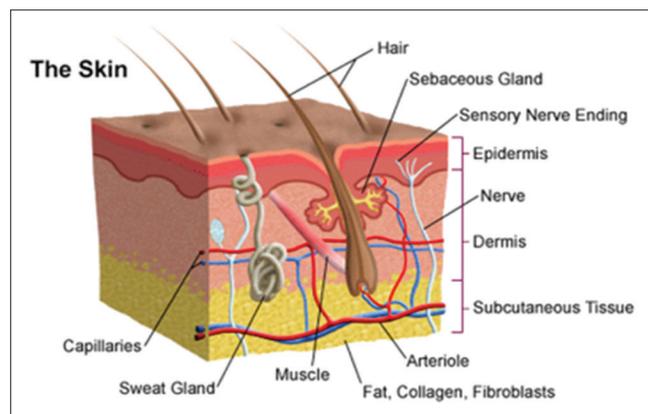


Figure 1: Structure of skin^[11]

worst, extrinsic aging due to overexposure to ultraviolet (UV) light may also result in skin cancer [Figure 2] [Table 2].^[24]

Skin anti-aging approaches

Cosmetological care

“Cosmetic products definition” means any substance or mixture intended to be placed in contact with the external parts of the human body^[28] cosmetic products are used to protect skin against exogenous and endogenous harmful agents and enhance the beauty and attractiveness of skin.^[29] Not only women but also there is an increasing number of males are using cosmetics usually to enhance their own facial features.^[30] Cosmetics are not “over the counter” or prescription drugs or drug additives; their role is merely to improve your appearance.^[31] The efficacy of a cosmetic product depends not only on the active ingredients but also on the delivery system to improve its efficacy.^[32] The federal food, drug, and cosmetic act defines cosmetics by their intended use, as “articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body for altering the appearance,^[33] without affecting the body’s structure or functions.”^[34]

Cosmeceuticals

Cosmeceuticals fulfill an important psycho-social biological need of human beings in feeling good about themselves and in trying to maintain the structural and functional integrity of the body.^[35] Cosmeceuticals

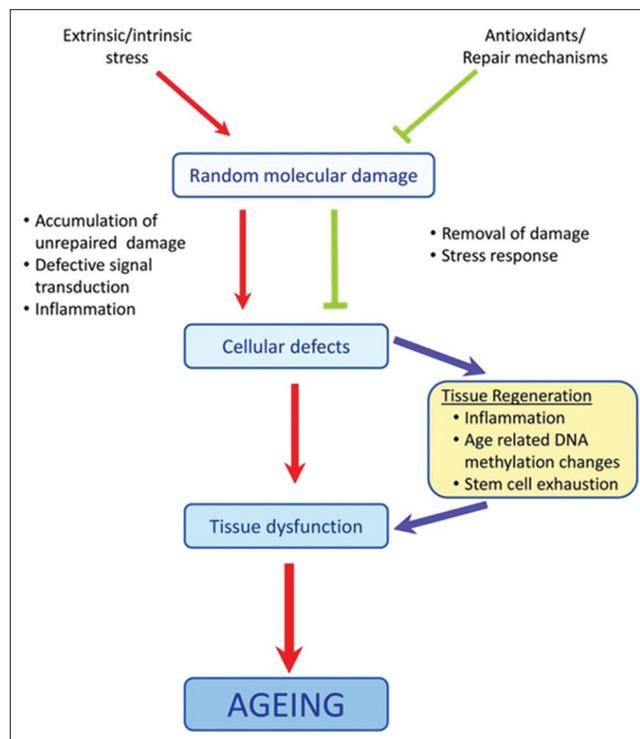


Figure 2: Mechanism of skin aging^[25]

Table 1: Structure and function of skin^[13]

Parameters	Epidermis	Dermis	Subcutaneous
Structure	Superficial part of the skin; stratified squamous epithelium; composed of four of five strata	Deep part of the skin; connective tissue composed of two layers	Not part of the skin; loose connective tissue with abundant deposits of adipose tissue
Functions	Prevents water loss and the entry of chemicals and microorganisms; protects against abrasion and ultraviolet light produces Vitamin D; gives rise to hair, nails, and glands	Is responsible for the structural strength and flexibility of the skin; the epidermis exchanges gases, nutrients, and waste products with blood vessels in the dermis	Attaches the dermis to underlying structures; adipose tissue provides energy storage, insulation, and padding; blood vessels and nerves from the subcutaneous tissue supply the dermis

Table 2: Different parts of skin and effect of aging^[26,27]

Epidermis	Flattening of dermal-epidermal junction, variation in size, shape, thickness, and staining properties of keratinocytes, decreased number of melanocytes
Dermis	Decreased thickness (atrophy), decreased cellularity and vascularity, degeneration of elastin fibers, fewer fibroblasts and mast cells, decreased number, and distorted structure of specialized nerve endings
Subcutaneous fat	Overall decrease, change in distribution
Appendages	Depigmented hair, loss of hair, abnormal nail plates, fewer glands

are the cosmetic products having biologically active ingredients which have medical or drug-like benefits.^[36] Cosmeceuticals active ingredients are constantly being developed by big and small corporations engaged in pharmaceuticals, biotechnology, natural products, and cosmetics, while advances in the field and knowledge of skin biology and pharmacology have facilitated the cosmetic industry's development of novel active compounds more rapidly.^[37] Cosmeceutical formulations now have expanded from skin to body to hair, and a number of topical cosmeceutical treatments for conditions such as photoaging, hyperpigmentation, wrinkles, and hair damage have come into widespread use.^[38] Cosmeceuticals ingredients must be safe, efficacious, novel, stable, and inexpensive to manufacture and can be metabolized within the skin.^[39] Cosmeceuticals are generally presented as lotions or creams and are mostly targeted at dermatological issues.^[40]

Herbal cosmetics

Nowadays, herbal extracts are used in the cosmetic preparations for augmenting beauty and attractiveness.^[41] Therapy with herbal drugs is an old traditional medicine.^[42] Plants have become a potential source for the development

of new drug entities for cosmeceuticals and pharmaceutical applications.^[43] Herbal cosmetics are the preparation, which represents cosmetic associated with active, bioactive ingredients, or pharmaceuticals. The use of phytochemicals from a variety of botanicals has dual function:

- They serve as cosmetics for the care of body and its part and
- The botanical ingredients influence biological function of the skin and provide nutrients necessary for the healthy skin.^[44]

Importance of herbal cosmetics

1. Ingredients used for the making of natural cosmetics are tested dermatologically and are hypo-allergenic. There will be no skin eruption, rashes, or skin irritation of any kind.
2. When compared to chemical-based products, natural products are priced reasonably.^[45]
3. Herbalists today, believe to help people build their good health with the help of natural sources.^[46]
4. Herbal cosmetics and herbal products are not harmful for the body as they do not have any side effects.^[47]

Antioxidants

Antioxidants are natural substances made up of vitamins and minerals.^[48] Antioxidants are molecules that can neutralize free radicals by accepting or donating an electron to eliminate the unpaired condition.^[49] The use of antioxidants can also be considered important for maintaining the stability of the formulations. The fragrance and color of a cosmetic product are decisive factors in the product acceptance by consumers. Thus, the protection of lipid oxidation is important, since many products have limited shelf life due to oxidation of the excipients, which may result in alteration of their fragrance and color.^[50]

Antioxidants neutralize damaging free radicals thus protecting cells from both.

- Endogenous stress by-products of cellular energy.
- Exogenous stressors-UV light, pollution, and cigarette smoke.

Table 3: Role of active ingredients in skin aging

Tocopherol	Vitamin E binds free radicals and prevents their destructive action on lipids, cells, and cell membranes. Vitamin E promotes the biological stability of the cells and smoothes and strengthens the skin. It has also moisturizing properties
Vitamin-A	Vitamin A is responsible for the normal texture and functioning of skin and other tissues. It activates the natural regeneration of dermal tissue and improves its elasticity. It counteracts excessive cornification of the skin. Delays formation of premature wrinkles ^[52]
Vitamin-C	Vitamin C provides many benefits to the skin most significantly, increased synthesis of collagen and photoprotection. Photoprotection allows the skin to correct the previous photodamage, the synthesis of collagen and inhibition of MMP-1 was proven to decrease wrinkles, and the inhibition of tyrosinase and anti-inflammatory activity result in depigmenting solar lentigines ^[53]
Grape seeds extract	Vitis vinifera grape seed extract is reported to function as anti-caries agent, antidandruff, antifungal, antimicrobial, antioxidant, flavoring, light stabilizer, and sunscreen agent. The grape seed hydroethanolic extract is rich in polyphenols (proanthocyanidins). The antioxidant and scavenging activities of proanthocyanidins had been reported ^[54]
Carotenoids	Beta-carotenes are commonly referred to as “sun protectants” that is, his ability in preventing UV radiations damage of the human skin. UV light renders the human skin to photo-oxidative damage because of the formation of ROS such as singlet oxygen, peroxy, and superoxide radicals. ROS have a damage effect on the DNA, proteins, and lipids and are known to be a cause of erythema, skin aging, and cancer ^[55]
Phenolics compounds	The antioxidant activity of phenolics is possible through various mechanisms of action: Inhibition of the ROS formation and the ROS trapping and the extinction of singlet oxygen; and reducing the chelated metal ions interrupting the cascade of free radical reactions in lipid peroxidation and protecting the other compounds with antioxidant activity ^[56]
Niacinamide	A potent antioxidant, this substance is related to Vitamin B-3 (niacin). It helps reduce water loss in the skin and may improve skin elasticity
NAG	It is a simple amino sugar and nutrient that plays a role in forming and maintaining the body's tissues and significant increases in both hyaluronic acid and collagen. Topically applied NAG improves skin moisturization as well as the appearance of fine lines/wrinkles ^[57]
Tea extract	Polyphenols in tea extracts are highly effective at reducing the inflammation and oxidative stress that can destroy the health of your skin cells. Tea contains catechins, a very powerful group of water-soluble polyphenol antioxidants that are easily oxidized. Green tea, which is manufactured from fresh, unfermented tea leaves in which oxidation is minimal, has catechins present in significant quantities ^[58]

MMP-1: Matrix Metalloproteinase-1, UV: Ultraviolet, ROS: Reactive oxygen species, NAG: N-acetyl glucosamine

Antioxidants comprised a group of diverse molecules including (but not limited to).

- Coenzyme Q-10 (Co Q-10).
- Idebenone.
- Polyphenols.
- Alpha lipoic acid (ALA).
- Vitamins (A, B, C, and E) [Table 3].^[51]

Challenging skin aging by herbalism

Piper betel

P. betel, a herb belongs to family Piperaceae rich in antioxidant properties, it also possesses anticancer and neuroprotective properties. It acts as an anti-aging agent by neutralizing free radicals, used in the treatment of wrinkles, aging, diabetes mellitus, kidney problems, and cancer.^[59] The phenolic constituent allylpyrocatechol obtained from the leaves, show action against obligate oral anaerobes responsible for halitosis. The leaf extract also has a stimulatory outcome on pancreatic lipase and antioxidant activity.^[60]

Soybean

The soybean (*glycine max*) is an annual legume of the Fabaceae family.^[61] Soybean contains isoflavones that have been described to have anti-aging effects, when UV radiation is the main cause of the aging process. These molecules inhibit UV-induced metalloproteinases and increase collagen synthesis.^[62]

Brahmi

Brahmi buti, *Bacopa monnieri* (Fam. Scrophulariaceae) is a classic brain and nerve tonic used for the treatment of cognitive disorders of aging.

St. John's wort

St. John's wort is the dried flowering tops or aerial parts of *Hypericum perforatum* (Fam. Hypericaceae) gathered before or during flowering. The preparation contains hypericin its isomer pseudohypericin and hyperforin. St. John's Wort has value in the treatment of depression and anxiety associated with aging.^[63]

Custard apple

Annona squamosa is a medium-sized tree which belongs to the family Annonaceae. It is well-known with many local names such as sugar apple, custard apple, and sweetsop in English, Sirafal in Hindi, and Matomoko in Kenya.^[64] Custard apple is not only a delicious fruit but also is excellent for the skin as well. It contains nutrients such as Vitamin C, Vitamin A, Vitamin B, and antioxidants, which are required for rejuvenating the skin's health.^[65] Custard apple leaves are flooded with antioxidants, it can be used topically to neutralize free radicals that make the skin age much faster.^[66]

Folkloric record reported the use of *A. squamosa* as an insecticidal, an antitumor agent, anti-diabetic, antioxidant, anti-lipidemic, and anti-inflammatory agent which has been characterized due to the presence of the cyclic peptides.^[67]

Turnip green

Turnips are popular, nutritious root vegetables. They are round, tuberous roots grown in many parts of Europe, and Asia as one of the cool-season vegetables. Botanically, they belong to Brassicaceae family, a broad family of greens and vegetables which also includes cabbage, kale, and Brussel sprouts and its biological name is *Brassica rapa*. Although this bulbous root is widely recognized, its fresh green tops indeed are more nutritious, several times richer in vitamins, minerals, and antioxidants.^[68] Turnips are an excellent source of antioxidant Vitamin C. This vitamin fights and eliminates free radicals which are responsible for causing skin aging. Thus, it helps to keep signs of aging such as spots, wrinkles, and fine lines at bay.^[69] Due to the presence of healthy nutrients and minerals, turnips possess bounty of skin, hair, and health benefits.^[70]

Dong Quai root

Angelica sinensis (commonly known as dong quai) is a fragrant, perennial herb found in mainland China, Japan, and Korea. Other common names for dong quai include Chinese Angelica, dang gui (Chinese), toki (Japanese), tanggwui (Korean), and kinesisk kvan (Danish).^[71]

The herb is a powerful natural antioxidant that can help preserve your youthful appearance and prevent many of the body's signs of aging. It is used to diminish the appearance of blemishes, wrinkles, and other nasty marks on the skin.^[72] Dong quai extracts and its constituents include modulation of enzyme activity, cellular proliferation, anxiolytic activity, insecticidal and antifungal activity, and antioxidants activity.^[73]

Garlic

Garlic has anti-oxidant, antiseptic, antibacterial, and antiviral properties. While it is used to help treat intestinal, respiratory and skin infections, its most important use is to help reduce

high blood pressure, lower levels of harmful blood fats, (low-density lipoprotein cholesterol, and triglycerides), reduce blood stickiness, dilate blood vessels, and improve peripheral blood flow.^[74]

Gelatine

It is extracted from protein derived from animal/plant/marine which helps in moisturizing, restructuring and also acts as an anti-wrinkle treatment extract used in cosmetic creams.^[75]

Kalmegh

Andrographis paniculata commonly known as "Kalmegh" belonging to the family Acanthaceae is traditionally used as a medicinal herb to treat different diseases in India, China, and Southeast Asia.^[76]

AP has been reported to have a broad range of pharmacological effects including anticancer, antidiarrheal, anti-hepatitis, anti-HIV, antihyperglycemic, anti-inflammatory, antimicrobial, antimalarial, antioxidant, cardiovascular, cytotoxic, hepatoprotective, immunostimulatory, and sexual dysfunctions.^[77]

Green tea

The green tea is obtained from the tea plant *Camellia sinensis* belongs to the family Theaceae.^[78] Green tea has an antioxidant effect, antibacterial and antiviral activity, cancer chemopreventive properties, contributes to a reduction in the risk of cardiovascular disease, enhances weight loss, and among other effects [Table 4].^[79]

CONCLUSION

Skin aging is a dynamic and multifactorial process. The main cause of skin aging contributes to environmental factors such as sunlight, air pollution, and chemical and mechanical stimulation. On the other hand, internal factors such as malnutrition, obesity, alcohol consumption, and smoking and can also speed up the process of aging with the production of oxygen free radicals and DNA damage. Furthermore, in skin aging, loss of lipid and water content in different skin layers are one of the important damaging factors. The herbal cosmetic products are the best option to reduce skin problems such as hyperpigmentation, skin wrinkling, and skin aging. The demand of herbal cosmetic is rapidly expanding. The advantages of herbal cosmetics are lower cost, side effects free, environmental friendly, safe to use, etc. also have a great future ahead as compared to the synthetic cosmetics. Herbs and herbal preparations have a high potential due to their antioxidant activity, primarily. Antioxidants such as vitamins (Vitamin C and Vitamin E), flavonoids, and phenolic acids play the main role in fighting against free radical.

Table 4: Plant inhibitors with their possible molecular mechanisms as anti-aging agents

Herbs	Biological name	Mechanism
Pomegranate	<i>Punica granatum</i>	Extract protects human immortalized HaCaT keratinocytes against UVB-induced oxidative stress and markers of photoaging, and therefore, might be a useful supplement in skin care products. The Catechin, an active component of <i>Punica granatum</i> , inhibited the UVB-induced skin photoaging
Cabbage palm fern	<i>Polypodium leucotomos</i>	<i>Polypodium leucotomos</i> demonstrates dual protective effects on the extracellular matrix through the inhibition of the proteolytic enzymes and the stimulation of TIMPs, structural collagens (Types I, III, and V) of extracellular matrix, and TGF- β in fibroblasts
Coffea	<i>Coffea arabica</i>	<i>Coffea arabica</i> extract, diminished UVB irritation induced photo-aging by inhibiting MMPs and elevating type I pro-collagen production through ROS scavenging and downregulation of MAPK pathway
Kacip fatimah	<i>Labisia pumila</i>	<i>Labisia pumila</i> extracts clearly showed the photo protective potential and could be used as an agent against extrinsic aging. Apart from that, <i>Labisia pumila</i> could also upregulate the synthesis of collagen in human dermal fibroblast cells ^[80]
Wild carrot	<i>Daucus carota</i>	Free radical scavenging activity
Amla	<i>Emblica officinalis</i>	By promoting procollagen production and inhibiting MMP1 in human skin fibroblasts
Liquorice	<i>Glycirrhiza glabra</i>	Antioxidant inhibits hyaluronidases ^[81]
Aloe	<i>Aloe barbadensis</i> Mill.	Stimulation of the synthesis of essential matrix components, such as collagen, hyaluronic acid, and stimulate collagen synthesis ^[82]
Gotukola	<i>Centella asiatica</i>	Downregulation of hydroxyproline and pepsin-resistant hydroxyproline content
Cocoa	<i>Theobroma cacao</i> L.	Tyrosinase and MMP-2 inhibition Manosroi Elastase, hyaluronidase, MMP-2 enzyme inhibition
Haritaki	<i>Terminalia chebula</i> Retz.	Removal of ROS, diminished UV-B augmented-release of inflammatory IL-6 and IL-8 ^[83]
Western blueberry	<i>Vaccinium uliginosum</i> L.	Black rice crude extracts showed a reduction of ROS such as lipid peroxide and superoxide anion radicals
Black rice	<i>Oryza sativa</i> L. Indica	Leaves extracts of <i>Psidium guajava</i> Linn. exhibited similar trends of scavenging DPPH radical as ascorbic acid ^[84]
Guava	<i>Psidium guajava</i> Linn.	Horse chestnut is the saponins known as "aescin" or "escin." escin has been shown to inhibit the breakdown of hyaluronic acid ^[85]
Horse chestnut	<i>Aesculus hippocastanum</i>	Act as potent free-radical scavengers, immunosuppression and a reduction of the inflammatory sunburn reaction ^[86]
French maritime pine	<i>Pinus pinaster</i>	Cinnamon contains a good amount of phenolic antioxidants. This counteracts the damaging effects of free radicals
Cinnamomum	<i>Cinnamomum zeylanicum</i>	Leaves of <i>Lantana camara</i> contains Lantadenes, shows antioxidant activity and acts as free radical scavenging ^[87]
Lantana	<i>Lantana camara</i>	Flower extract could inhibit the tyrosinase activity that causes hyper-pigmentation, which induces skin aging ^[88,89]
Golden shower tree	<i>Cassia fistula</i> L.	<i>Eucommia ulmoides</i> showed a potent inhibitory effect on the MMP-1 production and increased collagen synthesis ^[90]
Rubber Bark Tree (Du-Zhong)	<i>Eucommia ulmoides</i> (Oliv.)	Act by inhibiting UV-induced metalloproteinases and increasing collagen synthesis ^[91]
Red clover	<i>Trifolium pratense</i> L.	

TGF- β : Transforming growth factor beta, MMP-1: Matrix Metalloproteinase-1, UVB: Ultraviolet B, ROS: Reactive oxygen species, IL: Interleukin, DPPH: 1,1-diphenyl-2-picrylhydrazyl

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