International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 13, Issue 1, 2021

Review Article

THE COSMETIC EFFECTS OF VARIOUS NATURAL BIOFUNCTIONAL INGREDIENTS AGAINST SKIN AGING: A REVIEW

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Received: 20 Sep 2020, Revised and Accepted: 20 Oct 2020

ABSTRACT

Nutricosmetics have emerged to indicate the health benefits of the products that create beauty from inside to outside. Nutricosmetic is the latest trend in the beauty industry. Cosmeceuticals are commonly used in skincare regimens to maintain healthy skin and improve visible signs of aging. Natural products that target skin have gained great attention due to the general belief that they are harmless. A review of the biomedical literature was conducted using peer-reviewed journal articles to identify laboratory, animal, and clinical studies that have evaluated recent breakthroughs in the biological properties and potential dermatologic uses of the different natural bioactive ingredients used in nutricosmetics and Cosmeceuticals. Bioactive ingredients used in Nutri-cosmeceutical products are derived from collagen, peptides, proteins, vitamins, carotenes, minerals, omega-3 fatty acids and plant extracts. These ingredients have been shown to provide dermatologic benefits with potential applications for skin regeneration, photoprotection, wound healing, and more. The information provided by this article is valuable to get the picture of the latest trends. In addition, it might be helpful for clinicians and related manufacturing companies. Despite several developments in this field, extensive research is required for performing successful and precise clinical trials in the future. Further improvements would enable the researchers to develop new products in this field.

Keywords: Nutricosmetics, Cosmeceuticals, Biofunctional ingredients, Anti-aging

DOI: http://dx.doi.org/10.22159/ijap.2021v13i1.39806. Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Natural ingredients such as functional food, Nutraceuticals, and Cosmeceuticals are becoming more attractive for the industries like the cosmetic manufacturing industries because people are starting to believe that naturally occurring compounds are safer to humans than artificial compounds [1]. Cosmeceuticals are cosmetic products that have therapeutic benefits against.

Degenerative skin conditions. The combination of cosmetic and pharmaceutical functionality makes them significant in enhancing skin health. They have possible formulations, such as creams, lotions, and ointments [2]. These substances can promote healthy skin, hair, and nails at cellular levels [3].

Nutricosmetics are considered as the latest trend in the beauty industry; they are emerging from a combination of Cosmeceuticals and Nutraceuticals. Nutricosmetics are nutritional supplements that support the biological function of the skin [4]. The skin is composed of a network of components, like collagen, elastin, glycoproteins and hyaluronic acid. These components protect against skin damages, keeping the skin in its proper condition. It acts as a barrier against external environmental factors. When the skin is exposed to UV radiation, there are many micronutrients and natural phenolic compounds that possess antioxidant properties and could reduce the production of free radicals [5]. Melanin is a natural pigment in the skin that absorbs ultraviolet (UV) light [6]. Reactive oxygen species (ROS) along with key enzymes such as tyrosine, elastase, collagenase, and hyaluronidase are involved in skin-damaging [1]. (ROS) are a major precipitating factor in both intrinsic and extrinsic aging process that can cause damage to the different cellular components [7, 8]. With aging, the level of collagen, elastin and hyaluronic acid decreases, leading to a loss of strength and flexibility in the skin, which results in visible wrinkles [9, 10]. Therefore, elastase, hyaluronidase, and tyrosinase inhibitors are of great importance in the formulation of cosmetic products specialized in the treatment of skin aging, which can restore skin elasticity, increase moisture content, stimulate collagen synthesis, and have skin lightening effects [1, 4].

Skin aging causes skin collagen to lose its physical appearance in many ways, such as dry skin, texture loss, age spots, and loose skin. Aging causes skin thinning, and the end result is the formation of wrinkles [11, 12]. It is as a result of the combination of both intrinsic and extrinsic effects [13]. Intrinsic aging involves inherent age factors [14], while extrinsic aging is the result of external factors such as ultraviolet A (UVA) and ultraviolet B (UVB) radiation exposure [15-18]. Photoaging by UV includes an oxidative activity during the metabolism of body tissues; this oxidative process results in the generation of free radicals and the production of ROS [19]. The production of ROS destroys skin antioxidants, initiates a lipid peroxidation reaction, oxidizes DNA and proteins [20], and induces cleavage of collagen and abnormal crosslinking and elastin chain. Hence, UV-induced photoaging causes skin diseases, such as loss of elasticity, pigmentation, and wrinkle formation. The intrinsic enzymatic antioxidants, such as glutathione peroxidase (GP) and catalase are insufficient to neutralize free radicals. Synthetic antioxidants are used in functional foods, cosmetics, and pharmaceuticals to inhibit ROS; know that the use of these antioxidants for a long term is known to exert toxic effects. Therefore, a lot of studies have been directed toward the discovery of more effective and safer natural antioxidants, which are able to counteract the high level of free radical generation in the body [21]. Accordingly, the use of extracts and their bioactive metabolites has proven to be effective against UV radiation [22]. Antioxidants, which are incorporated in cosmetic formulations to reduce aging effects act as ROS scavengers, and lipid peroxidation inhibitors. They can be effective as anti-wrinkle and depigmentation ingredients, thus preventing damage from UV radiation. When UV radiation is absorbed by the skin, it leads to increased ROS generation and induction of oxidative stress, increasing the expression of matrix metalloproteinase 1 (MMP-1) and tyrosinase, both enzymes responsible for collagen breakdown and hyperpigmentation, respectively [23]. Tyrosinase is a rate-limiting step in the biosynthesis of melanin. Several bioactive compounds containing extracts are capable of preventing this pathway; thus reducing melanin synthesis [24].

I have searched the literature in Scopus, PubMed, Google Scholar using the keywords “Antiaging” and “Biofunctional”. There was no year based restriction on selecting the publications. The present study compiled the reported the antiaging effects of various biofunctional ingredients with their possible use as natural Cosmeceuticals.

Collagen hydrolysates

Collagen in its hydrolyzed form is considered to be an antioxidant, the use of antioxidants as a functional ingredient in the diet of people

increased significantly. It is a protein that is highly needed in biomedical and cosmetic industries due to its benefits to the skin. HC has been used as a cosmetic ingredient due to its good moisturizing properties at the stratum corneum (SC) layer of the skin. Collagen Hydrolysates (HC) is obtained by denaturation of collagen followed by an enzymatic process that result in the production of small peptides [25-27]. The use of collagen hydrolyzates has been widely utilized due to their biocompatibility, biodegradability, and weak antigenicity [28].

The lower the molecular weight of peptides, the greater the ability to donate an electron or hydrogen to stabilize radicals [29]. After HC oral ingestion, the levels of collagen-derived peptides in the blood stream increased significantly [30, 31]. The low molecular weight peptides were soluble in water and able to be digested, absorbed, and transported to the systemic circulation system as peptides in the small intestine [32, 33]. Collagen Hydrolysates (HC) have different marine sources such as jumbo squid, oyster, blue mussel, tuna, cod, capelin, mackerel, yellow stripe trevally [34, 35]. These marine bioactive ingredients have the ability to scavenge free radicals, also they can prevent oxidative damage by blocking the radical chain reaction of lipid peroxidation [36, 37]. The antioxidant potency of HC is mostly due to the presence of hydrophobic amino acids in the peptide [38]. Oral ingestion of collagen hydrolyzates promotes the growth of fibroblasts and stimulates the production of new collagen type I in the dermis. It makes the skin smoother, softer and provides enhanced textural properties. Daily intakes of HC decrease the expression levels of matrix metalloproteinase, which is responsible for collagen breakdown [39].

Brown algae-derived compounds

Polyphenols are among the most abundant antioxidants in the human diet; they have food sources such as (fruits, vegetables, cereals, olive oil, chocolate), and beverages (coffee, tea). Brown seaweed accumulates a variety of phloroglucinol-based polyphenols (phlorotannins). They have characteristic antioxidant, antibacterial, anti-inflammatory, and anti-allergic bioactivities [40]. Regarding phloroglucinol, it is well known in cosmetics [41]. Phlorotannins have anti-wrinkle and skin antiaging activities of interest in the cosmetic industry.

Many types of biologically active polysaccharides are present in seaweeds. These compounds are used as ingredients in Cosmeceuticals, with moisturizing and antioxidant capacities. Fucoidans are minor polysaccharides found in the cell wall of brown seaweeds. Fucoidan is useful as an inhibitor of tyrosinase, reducing skin pigmentation and used in skin whitening agents [42]. It has a preventive action against photoaging based on the inhibition of metalloproteinase, which is induced by UVB radiation; this polysaccharide has the ability to eliminate free radicals it aids in the reduction of inflammation, wrinkles, allergies, and sensitive skin reaction. Fucoidan is also able to increase the proliferation of fibroblast and collagen and causes the deposition of other matrix factors [43].

Carotenes and their early precursors such as phytoene and phytofluene are compounds present in all photosynthetic organisms and highly abundant in our diet. Since carotenes accumulate in the skin, they play a role in skin protection against UV light and are therefore involved in skin aging and health [44]. They are used in pharmaceuticals and Nutraceuticals. Carotenoids enhance skin elasticity and can improve its hydration [45]. Fucosterol, as a terpenoid extracted from *Ecklonia stolonifera*, shows a pronounced antioxidant activity [46]. Fucoxanthin may be an effective ultraviolet protector, able to be used in sunscreens to prevent photoaging [47]. The tocopherol content of seaweed is a skin protective compound [48], and is believed to play a major role in the prevention of light-induced pathologies of skin [49]. Pseudopterosins are diterpene glycosides isolated from the Caribbean gorgonian coral *Pseudopterogorgia Elizabeth* is effective in preventing sun damage to the skin and nourishing the skin [50, 51].

Hydroxycinnamic acids

Hydroxycinnamic acids are Phenolic compounds produced by fungi and plants [52, 53]. They exhibit different physiological functions, such as antioxidant, anti-inflammatory, anti-collagenase and anti-melanogenic activity; these properties enable hydroxycinnamic acids themselves and their derivatives in skincare cosmetic formulations. The pharmacological potential displayed by these phenolic acids and derivatives has been largely attributed to the presence of multiple hydroxyl groups in their chemical structure, making them suitable free radical scavengers [54].

p-Coumaric acid is phenolic acid. It is widely distributed in fruits, vegetables, cereals and mushrooms [55, 56]. Studies of p-coumaric acid and its conjugated forms revealed properties, such as antioxidant, anti-inflammatory, as well as other interesting health benefits [57]. Among the above-mentioned properties, their depigmenting potential, antioxidant, anti-collagenase, and anti-inflammatory activities seem to be the most important for cosmeceutical use [58].

Caffeic acid is one of the phenolic acids found in fruits, vegetables, mushrooms and herbs. It is biosynthesized by hydroxylation of p-coumaric acid. It has pronounced antioxidant, UV-absorbing and anti-inflammatory activities, and the attention is now directed toward its incorporation into cosmetic applications [59]. Rosmarinic acid is found in *Rosmarinus officinalis L., Mentha piperita L. Salvia officinalis L., and Thymus vulgaris L*. It has a high radical-scavenging activity, so it is attracting interest from the cosmetic industry [60].

Chlorogenic acid is widely distributed in coffee, apples and pears and is one of the most important hydroxycinnamic acid derivatives in plants. There are numerous publications that support the potential of this compound as an anti-inflammatory, antioxidant and anti-tyrosinase agent [61, 62]. Sinapic acid, with reported antioxidant and anti-inflammatory properties, is also present in fruits and vegetables. It is formed from caffeic acid. Sinapic acid has high radical-scavenging activity [63].

***Monascus*-fermented soybean extracts**

Monascus is a filamentous fungus genus that has been used to produce several bioactive metabolites such as isoflavones, monacolins, and γ-aminobutyric acid [64]. The aglycone isoflavones and coenzyme Q10 (CoQ10) levels in soybeans fermented with *Monascus pilosus* increased about 33.4 and 3.0-fold relative to unfermented samples, respectively (65). These antioxidant compounds are used in many health care products for anti-metabolic syndrome or anti-aging purposes [66, 67]. The inhibitory activity against skin aging-related enzymes and antioxidant activity of *Monascus*-fermented soybean extracts (MFSEs) obtained by using different solvents were examined. The methanol and 80% ethanol extracts showed an effective inhibition against tyrosinase, hyaluronidase, and elastase compared with those of acetone and hot water extracts ($P<0.05$). The antioxidant capacities increased with increasing concentration. According to the inhibitory activities against skin aging-related enzymes and antioxidant properties, these results support the evidence for the nutricosmetic potentials of *Monascus*-fermented soybeans [68].

Mushroom extracts

Mushrooms are recognized as nutritionally important foods as having medicinal benefits [69]. Mushroom has many bioactive compounds such as L-ergothioneine and lentinan, known to exert strong antioxidant [70, 71] and anti-inflammatory [72] activities, respectively. *Agaricus bisporus*, *Lentinula edodes*, and *Pleurotus* species are the most cultivated mushrooms worldwide [73]. *P. Ostreatus* showed the highest content in phenolic acids and cinnamic acid, followed by *L. Edodes* and, finally, *A. bisporus*. [74].

The anti-inflammatory potential of different mushroom extracts has been described and related to its capacity to inhibit specific steps in the pathway leading to nuclear factor-kappa B release [75]. The *Ostreatus* ethanolic extract had better anti-inflammatory activity than *A. bisporus* [76].

Tyrosinase is the rate-limiting enzyme in the melanin biosynthesis pathway [77]. Exposure to UV radiation trigger over-secretion of melanin from melanocytes causes hyperpigmentation [78]. *A. bisporus* displayed the highest anti-tyrosinase activity and *P.*

Ostreatus and *L. Edodes* exhibited very similar activities. Phenolic compounds have been reported to be responsible for the anti-tyrosinase activity of mushroom extracts [79]. Two steroidal triterpenes (betulin and trametenolic acid) from *Inonotus obliquus* were isolated and described for their anti-tyrosinase activity. The activity displayed by the studied mushroom extracts were related with the identified phenolic acids and ergosterol [76].

Bioactive metabolites that display antioxidant activity are able to inhibit tyrosinase and matrix metalloproteinase enzymes responsible for hyperpigmentation and collagen degradation, respectively [80]. *A. bisporus* and *P. Ostreatus* showed the highest radical scavenging activity and reducing power Where *A. bisporus* methanolic extracts gave the highest radical scavenging activity.

Coenzyme Q10

Coenzyme Q10 has three redox states, which are ubiquinone, semiquinone, and Ubiquinol, it is found in many cellular/organelle membranes in every cell in the human body [81, 82]. Coenzyme Q10 (Ubiquinone) is the most abundant form in humans and in most mammals. It has been found in plants and microorganisms. All animals, including humans, can synthesize ubiquinones. The distribution and content of ubiquinones in various foods such as meat, poultry, eggs, cereals, dairy products, and fruits and vegetables have been reported. Coenzyme Q10 is a very popular dietary supplement that is readily available via commercial nutritional sources. Coenzyme Q10 is an endogenous lipid-soluble antioxidant.

The mechanism of action of coenzyme Q10 as an antioxidant has been shown to reduce the production of free radicals; it is involved in the regeneration of vitamin E [81]. It can reduce UVA-induced MMP production in fibroblasts [83]. It also enhances collagen and elastin expression, and inhibit melanin synthesis [84]. Coenzyme Q10 had the efficacy to prevent many of the detrimental effects of photo-aging. Coenzyme Q10 supports and maintain cellular energy levels in human keratinocytes [85, 86], accelerating the regeneration of ATP levels after irradiation in human fibroblasts [86, 87]. Coenzyme Q10 significantly reduces wrinkles and micro-relief lines and improved skin smoothness [88]. High dose of coenzyme Q10 showed additional improvement of wrinkles in the nasolabial folds, corner of the mouth lines, and upper radial lip lines [88].

Collagen peptide

Oral administration of Collagen peptide (CP) increased skin hydration and decreased wrinkles formation in UVB irradiated hairless mice compared to the UVB-irradiated group. The oral effects of CP were examined by measuring the transepidermal water loss (TEWL), skin hydration, wrinkle formation, and hyaluronic acid expression in the dorsal mice skin. The protein expression of skin-hydrating factors, filaggrin and involucrin, was upregulated through oral administration of Collagen peptide. Treatment of CP increased the protein expression of hyaluronic acid synthases accompanied with increased hyaluronic acid production in skin. These results show that oral administration of CP increases hyaluronic acid levels, which are reduced during UVB photoaging [89].

***Hydrangea serrata* leaves**

Hydrangea plants have bioactive compounds such as dihydroisocoumarins, secoiridoids, and stilbenes (hydrangenol, phyllodulcin, macrophylloside) [90]. Hydrangenol, a dihydroisocoumarin, possesses positive effects on skin wrinkles and moisturization. It has a protective effect on the production of procollagen type I, MMP-1, and pro-inflammatory cytokines [90]. A hot water extract of Hydrangea serrata leaves (WHS) has the ability to protect ultraviolet B (UVB)-induced cell viability and production of pro-collagen type I and hyaluronic acid (HA). The administration of WHS lead to a reduction in the increased skin thickness observed upon UVB exposure. In addition, WHS administration has increased the collagen fiber density and pro-collagen type I production [91]. After 12 w of oral WHS (600 mg) administration, a significant reduction in skin wrinkles and a pronounced enhancement in skin elasticity and hydration was observed. WHS has no adverse effects. Therefore, WHS could be used as a health supplement for skin anti-aging [92].

Walnut protein hydrolysate (WPH)

Based on the food-derived bioactive peptides, the walnut protein hydrolysate (WPH, rich in peptides) prepared by enzymatic hydrolyzing proved that their functional ingredients are used for developing anti-photo aging foods. WPH enhanced the elasticity of photoaged skin and stimulated the biosynthesis of extracellular matrix (ECM) components in the dermal layer. WPH inhibited the matrix metalloproteinase-1 (MMP-1) activity, and alleviated epidermal hyperplasia, and repaired the damaged skin mechanical structure in a dose-dependent manner. The elasticity improvement of WPH against the skin photoaging process can be attributed to regulating the component's metabolism and repairing the damaged mechanical structure of ECM [93].

***Oryza sativa L.* extract**

Black rice (*Oryza sativa L.*) has been widely consumed since ancient times in Thailand. The most predominant flavonoids in *O. Sativa L.* are the anthocyanins (ANT), which are coloring agents in plants that account for the colored hues of many types of fruit, vegetables [94]. *O. Sativa* L. is considered as a health-supporting food due to the presence of ANT [95]. ANT has anti-inflammatory properties, which occur via effects on collagen synthesis [96, 97]. Anthocyanin polyphenols present in black rice (*Oryza sativa L.*) have strong antioxidant and anti-inflammatory activities associated with collagen production in rat primary dermal fibroblasts. ANT extracted from black rice ANT increased the mRNA expression of collagen type I alpha 2 (COL1A2) and upregulated type I collagen protein levels in H2O2-stimulated rat dermal fibroblasts (RDFs) without cytotoxicity. In the presence of H_2O_2 treatment of RDFs with ANT led to the activation of signaling pathways, including the extracellular signal-regulated protein kinases1 and 2 (ERK1/2) and Akt, whereas it significantly (p<0 001) inhibited the phosphorylation of IκBα and suppressed the activation of the nuclear factor-kappa B (NF-κB) subunits, p50 and p65, which are transcription factors responsible for inflammation. These results suggest that ANT from *Oryza sativa L.* has anti-inflammatory properties and antiaging potential by modulating type I collagen gene expression and suppressing H_2O_2-induced NF-κB activation in skin fibroblasts [98].

***Cecropia pachystachya* leaves**

Cecropia pachystachya species have shown relevant potential to be used in many pharmaceutical formulations. This study was done to assess the antiaging potential of *C. pachystachya* extract through experimenting its antioxidant, antiglycant, and its ability to inhibit enzymes involved in skin aging like elastin and collagen. Due to the lack of toxicity, ethanol and a mixture of ethanol-water were used as solvents because of their applicability to dermal application in human skin. Flavonoids orientin and iso-orientin present in the hydroethanolic (HE) and the ethanolic (EE) obtained from the leaves of *C. pachystachya* have the ability to prevent the production of advanced glycation end products (AGEs). The extracts stimulated the fibroblast proliferation *in vitro.* HE also exhibited the ability to inhibit the collagenase (metalloproteinaseMMP-2) and elastase activities. Cytotoxicity of the extracts was not observed. The results suggested that the extracts of *C. pachystachya* leave present the potential to be used in dermocosmetic formulations to prevent the skin aging process [99].

Potato peel extract

The potato (*Solanum tuberosum L.*) is among the five most significant food crops of the world. The edible portion of the plant, the tuber, contains many nutritional ingredients, including ascorbic acid, folic acid and potassium. Some biofunctional ingredients, including phenolic compounds such as chlorogenic acid, and flavonoids such as catechin, have been identified in potato peels [100].

Some phenolic compounds and flavonoids influence the synthesis of type I collagen in the dermis. Ascorbic acid stimulates collagen synthesis by promoting the hydroxylation of proline and lysine in procollagen. On the other hand, phenolic compounds and flavonoids have the ability to suppress the synthesis of matrix metalloproteinases (MMPs) through their antioxidant activities, suggesting that a PPE is capable of improving skin aging through effects on collagen [101].

***Aloe barbadensis* leaf extract**

Aloe barbadensis (Aloe Vera) has anti-inflammatory, antioxidant properties, which indicates excellent potential in antiaging cosmetic products. *Aloe barbadensis* contains carbohydrate polymers, uronic acid, tannic acid acids, vitamins, amino acids, and triterpenoids (lupeol, β-sitosterol) that exert protective or disease-preventing effects [102].

The efficacy of a cream containing 10% *A. barbadensis* leaf extract as anti-aging was studied using advanced biophysical techniques to determine hydration of the epidermis and skin elasticity. Therefore, this study showed that the *A. barbadensis* cream improves skin barrier function, increases its moisture content, and enhances skin firmness and elasticity more than a placebo cream. The *in vivo* results has shown that the topical application of *A. barbadensis* cream is a promising preparation in terms of preventing skin aging [103].

***Salvia officinalis* extract**

Phytochemical analysis of *Salvia officinalis* showed the presence of glycosides, alkaloids flavonoids, and Triterpenoids. Rutin, a polyphenolic bioflavonoid, possesses an antioxidant potential [104], so it can act as a skin protective. Rutin enhances vitamin C production, which has a major role in the generation of collagen that is a very important element regarding the health of the skin. The antiaging properties of the extract were studied by investigating the inhibitory enzymatic assays on early aging human skin fibroblasts. The anti-wrinkle potential of *Salvia officinalis* was done by using a UV light-induced photoaging model. MeOH extract of *Salvia officinalis* can inhibit 50% of the activity of aging-related enzymes Col-I, Ela-I and Hya-I. This study showed that MeOH extract of *Salvia officinalis* has confirmed *in vitro* and *in vivo* inhibitory potential of antiaging enzymes assessed possessing a high antioxidant potential. They can be used for developing several cosmetic products and nutricosmetics [105].

***Pourthiaea villosa* (Thunb.) decne extract (PVDE)**

The antioxidant activity, ROS scavenging activity, and beta-galactosidase (SA-b-gal) activity of *Pourthiaea villosa* (Thunb.) Decne extract (PVDE) against the oxidative stress induced by H_2O_2 in human dermal fibroblasts (HDFs) was determined. PVDE contains the following identified compounds: phenolics (p-coumaric acid, caffeic acid, and chlorogenic acid), polyols (quinic acid, and citric acid), and flavonoids such as patuletin, catechin, epicatechin. The antioxidant and anti-aging activities of (PVDE) were evaluated by treating Human dermal fibroblast (HDF) cells with PVDE. The identified compounds from PVDE exhibited significant antioxidant effects. Furthermore, PVDE treatment significantly increased antioxidant enzyme expressions and effectively blocked H2O2-induced matrix metalloproteinase activity through mitogen-activated protein kinase (MAPK) signaling pathways in HDFs. Therefore, these results showed that PVDE affords the advantage of being a functional natural material with antioxidant and anti-aging effects for the skin [106].

Omega polyunsaturated fatty acids

Omega polyunsaturated fatty acids (PUFAs) possess anti-oxidative, anti-inflammatory effects. PUFAs can defend a wide range of diseases characterized by increased MMPs activity [107]. They can also suppress the UV-induced expression of pro-inflammatory cytokines and MMPs in skin cells *in vitro* or skin tissues *in vivo* [108]. It has been shown that palmitoleic acid (omega-7) and gamma-linolenic acid (omega-6) can affect skin regeneration and repair [109]. It has been reported that omega-3 and omega-7 act as inhibitors of MMPs [107].

MEGATM 500 can show the effects of anti-oxidant and anti-inflammatory *in vitro* [110]. It contains more than 50% of palmitoleic acid containing fish oil, and omega-7. The effect of orally administered 7-MEGATM 500 was studied for its effect on the improvement of skin aging in a UVB-induced photo-aging model of hairless mice.

Skin thickness, skin barrier function, and wrinkles were improved by treatment with 7-MEGATM 500. Both gene and protein expression levels of MMP-3 and c-Jun in the skin were significantly reduced by 7-MEGATM 500. So, 7-MEGATM 500 has an effectiveness in the treatment of photo-aging by induced by UVB [111].

***Panax ginseng L.* extract**

A study revealed that red ginseng extracts improved type-I procollagen gene expression, prevent MMP-9 gene induction, thereby reduces facial wrinkles. Bioactive constituents, ginsenoside believed to have anti-skin aging activities. Red ginseng extract also inhibited the increases of epidermal thickness and skin TGF-beta1 content induced by UVB irradiation. These results support the beneficial effects of red ginseng on photoaging, considering it as an effective beauty food [112].

***Curcuma longa* extract**

Curcumin isolated from *C. longa* extract has the potential to produce changes in skin thickness, increased elasticity, decreased pigmentation and wrinkling upon exposure to long-term, low-dose UV-B irradiation in melanin-possessing hairless mice. It prevents the formation of wrinkles and melanin and decrease the expression of matrix metalloproteinase-2 [113].

***Piper betel L.* extract**

Allylpyrocatechol and chavibetol isolated from *P. betel* have been well established to protect photosensitization-mediated lipid peroxidation of rat liver mitochondria. Allylpyrocatechol also prevented the unfavorable effects of the type-II photosensitization-induced toxicity to mouse fibroblastL929 cells. The results suggested that allylpyrocatechol has an important role in protecting biological systems against damage by eliminating free radicals generated from particular endogenous photosensitizers [114].

***Citrus sinensis* extract**

Phenolic compounds such as anthocyanins, flavanones, hydroxycinnamic acids and ascorbic acid are responsible for the anti-photoaging activity *C. sinensis* in modulating cellular responses such as NF-$_k$B and AP-1 translocation and procaspase-3 cleavage to UV-B in human keratinocytes (HaCaT). Therefore, *C. sinensis* has been proposed as a useful natural extract in skin photoprotection with promising applications in the field of dermatology [115].

Peumus boldus Molina

Peumus boldus rich in several aporphine-like alkaloids, among them, boldine. It has been proved that boldine has a UV light-filtering property. It has been shown that boldine is photo-unstable when irradiated at wavelengths up to 300 nm and to display a photo-protector effect against UV-B, both *in vitro* and *in vivo* in mice [116]. Photo-protection was evidenced by the prevention of UV-induced increase in the skin temperature of rodents. It was found that the application of boldine (25 mmol) onto a 12 cm^2 area of the back of human volunteers protected their skin against erythema formation to an extent slightly lower than that of a commercial sun cream [Nivea sun spray LSF-5], which has a UV-protection factor of 5 [117].

Emblica officinalis

Emblica officinalis commonly known as amla. The water extract from dried *Emblica officinalis* powder contains 2 % ascorbic acid and 29.4 % polyphenols, including Gallic acid and elaeocarpusin. *Emblica officinalis* extract is known to provide protection for human dermal fibroblasts against oxidative stress. It elevates the mitochondrial activity of human skin fibroblasts and promotes the production of procollagen. Therefore, it is assumed to be useful for natural dermal care [118].

***Ginkgo biloba* extract**

Ginkgo biloba has an antioxidant and anti-inflammatory agent. The *G. biloba* extract EGb 761, is a natural mixture containing flavone glycosides (33%), mostly quercetin and kaempferol derivatives, and terpenes (6%), which has exhibited the capacity to reduce the number of ultraviolet B (UVB)-induced sunburn cells in mice [119]

Magnolia ovovata Thunb

M. ovovata extract containing magnolol has been found to inhibit NF-$_{k}$B-mediated gene expression and protects against photoaging process through keratinocyte hyperproliferation and decrease degradation of collagen fibers in mouse skin. External topical application of magnolol inhibited matrix metalloprotease-1 from the cells overexpressing p65. These findings suggest that magnolol has a potential photoprotective effect via inhibiting NF-$_{k}$B [120].

***Polypodium leucotomos* extract**

Polypodium leucotomos contains polyphenolic compounds (benzoic acid, cinnamic acid, caffeic acid, and ferulic acid), coumaric acid, quinic acid, malic acid, glucuronic, and vanillic acid. *Polypodium leucotomos* extracts decrease UV-induced inflammatory responses and UV-mediated oxidative DNA damage. Oral intake of the extracts accelerates removal of UV-induced photoproducts and could significantly prevent skin cancer [121].

***Vitis vinifera* extract**

Grape (*Vitis vinifera*) has a health-promoting effect of against age-related diseases. This is due to the high content of phenolic compounds present in this plant. Grape seeds and peels constitute a rich source of polyphenols, including quercetin, catechin, epicatechin, gallic acid, and oligomeric proanthocyanidins. It has been found that grape extracts from the stems, a part of the grape tree rich in phenolic compounds, are able to reduce UVB-induced oxidative damage. Indeed, the topical application of stem's grape extracts on mouse skin before UVB treatment was able to prevent epidermal thickness, erythema, pigmentation, mast cell and inflammatory neutrophil infiltrations, collagen degradation, and the expression of COX-2, Nrf-2, and HO-1 genes [122].

***Solanum lycopersicum* extracts**

The antioxidant activity of ascorbic acid, which is found in fruits such as orange, lemon, tangerine, and tomato, makes it a good candidate as a protective compound against UV irradiation [123, 124]. Ascorbic acid prevents lipid peroxidation and protects keratinocyte exposed to UV radiation from apoptosis [124]. In humans, it has been found that ascorbic acid stimulates collagen synthesis [124]. Tomato (*Solanum lycopersicum*) fruits are a good source of ascorbic acid. The ability of an ascorbic acid-enriched tomato genotype to fight the oxidative stress induced by UVA in normal human keratinocytes has been demonstrated [125]. In particular, pretreatment of cells with tomato extracts before UVA exposure was able to maintain ROS, GSH, and lipid peroxidation levels at the basal levels and there was no evidence of apoptosis or inflammation [125].

***Hamamelis virginiana* extract**

H. virginiana is also known as Witch-hazel is a well-known plant has long been used as cosmetics. The skin antiaging activity of Witch-hazel on a murine dermal fibroblast culture system using both ESR spin-trapping and malondialdehyde generation methods have been evaluated. Polymeric proanthocyanidins and polysaccharides have been isolated from the bark. Anti-inflammatory effect of *Hamamelis* lotion has been evaluated in 30 healthy volunteers using a modified UVB erythema test model. It was found that erythema was suppressed within the range of 20-27% within 48 h compared to another formulation significantly [126]. 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 [127].

Astragalus membranaceus

The active constituents of *A. membranaceus* consist of polysaccharides and flavonoids [128]. *A. membranaceus* has been found to increase the hyaluronan synthase-3 and hyaluronan synthase-2 mRNA expressions resulting in the elevation of hyaluronic acid content in cultures of keratinocytes and fibroblasts. Hyaluronic acid is a constituent of the skin extracellular matrix, it promotes skin elasticity and reduces skin roughness and the depths of wrinkles [129]. Therefore, it is a promising candidate for preventing the age-dependent loss of hyaluronic acid content [130].

Terminalia chebula retz

T. chebula extract has been evaluated for its cell protective activity through anti-oxidative and tyrosinase inhibition activity as well as the anti-proliferative and MMP-2 inhibition activity on early aged human skin fibroblasts [131]. The extract showed 1.37 times more potent MMP-2 inhibition than ascorbic acid on fibroblasts. Isolated compound 1,2,3,4,6-penta-O-galloyl-$_{ß}$-$_{D}$-glucose from this plant extract showed inhibitory activities against elastase and hyaluronidase with significant induction of type II collagen expression in rabbit articular chondrocytes [132].

***Camellia sinensis* extract**

A sunscreen formulation composed of 2–5% green tea extract has been reported to protect UV irradiation-induced photoaging, cutaneous erythema, thickening of the epidermis [133]. Green tea polyphenols catechin, epiglactocatechin, and epiglactocatechin-3-gallate 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 [134]. It has been found that patients treated with a combination regimen of 10% green tea cream and 300 mg twice-daily green tea oral supplementation showed histological improvement in elastic tissue content [135].

Licorice root extracts

Licorice (*Glycyrrhiza glabra L.*) contains a wide variety of bioactive natural products such as Glycyrrhizin, which is a triterpene-type saponin that displays anti-inflammatory properties. Besides glycyrrhizin, certain phenolic components like chalcone isoliquiritigenin and isoflavonoid glabridin are also important for the observed biological activity of licorice root.

Licorice root extracts protect the skin against oxidative stress injuries. Glabridin has many beneficial properties in cosmeceutical products. It acts as antioxidant, anti-inflammatory, and skin-whitening agent that is incorporated in topical products intended specifically for that purpose [42, 43]. The observed notable tyrosinase and elastase inhibitory activity indicates the anti-aging properties of the investigated licorice extracts [136, 137].

Red grapes extract

Resveratrol (RV) is a polyphenolic compound naturally produced by several plants such as red grapes. RV can ameliorate the aging of human skin by significantly stimulating SIRT1, extracellular matrix (ECM) proteins, such as collagens and elastin, while significantly inhibiting inflammatory and dermal-aging biomarkers. Therefore, resveratrol has potential use in topical applications to improve the skin-related aging conditions [138, 139].

The brown seaweed-*turbinaria conoides*

Secondary metabolites produced by seaweeds have broad spectrum of biological activities. ZnO-NP's have been synthesized using *Turbinaria conoides* to investigate their antioxidant and antityrosinase activities. Zinc Oxide nanoparticles were synthesized from the hydroethanolic extract of *Turbinaria conoides.* Anti tyrosinase activity was assessed to validate the skin whitening ability of the ZnO-NPs. The antioxidant activity of the formulated zinc oxide nanoparticles was investigated by total antioxidant capacity, reducing power assay and ferric reducing antioxidant power assay (FRAP). The antioxidant activity of ZnO-NPs synthesized from hydroethanolic extract of *Turbinaria conoides* was maximum relative to that of the hydroethanolic algal extract.

The antityrosinase activity of ZnO-NPs was found to 75% tyrosinase inhibition when compared to hydroethanolic algal extract, which had 56% inhibition at 250µg/ml concentration. These results support the antityrosinase and antioxidant activities manifested by ZnO-NPs synthesized from hydroethanolic extract of *Turbinaria conoides* and it might be used as an antioxidant and as a source of skin whitening agent in cosmetics [140].

CONCLUSION

The biologic activity of various biofunctional skin anti-aging compounds has been elucidated, providing mechanisms for how these compounds may protect against skin aging. Nutricosmetics and Cosmeceuticals show much promise for the treatment of both aging and photoaged skin. Further randomized, placebo-controlled, double-blind studies are needed to substantiate many of the claims made about these naturally-derived bioactive cosmetic compounds. There is a need to study combinations of several classes of natural biofunctional active ingredients that reveal synergistic effects on reversing the signs of aging.

ACKNOWLEDGEMENT

This work was supported by Al-Zaytoonah University of Jordan in 2020.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICTS OF INTERESTS

Declared none

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