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RECENT STUDIES REGARDING THE USE OF MEDICINAL PLANT EXTRACTS AS SKINCARE PHOTOPROTECTIVE COSMECEUTICALS: A REVIEW

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Abstract

Cosmeceuticals are commonly used in skincare regimens to maintain healthy skin and improve visible signs of aging. Natural products that target the skin have gained a great attention due to the general belief that they are harmless. Recently, the therapeutic potential of medical plants used in dermatology has been explored, and some of them have been developed as drugs for the treatment of various skin disorders. A review of the literature was conducted using a peer-reviewed journal articles to identify laboratory, animal, and clinical studies that have studied recent breakthroughs in the biological properties and potential dermatologic uses of the different bioactive medicinal plants that could be potentially used in formulation of various cosmeceuticals that could attack the photoaged skin. The information provided by this article is valuable to get the picture of the latest trends and it might be helpful for dermatologists and cosmeceutical manufacturing companies. Despite the several developments in this area, further improvements would enable the researchers to develop new products in this field.

Keywords: medicinal plants; cosmeceuticals; Photoprotection; ultraviolet radiations; reactive oxygen species.

Introduction

Plant-derived bioactive compounds have been used in cosmeceuticals for a wide variety of beauty treatments for the skin, face, lips, hair, and nail care with beneficial actions against photoaging, inflammation, hair loss, lip care, and ultraviolet (UV) toxicity [1]. Further, UV radiation causes skin tanning and endothelial cell necrosis and suppresses immunological functions. Some natural phytobioactive compounds can prevent these deleterious effects with skin care [2, 3]. Cosmeceuticals are beauty products derived from natural sources, such as plants purported to have high, almost pharmaceutical, efficacy, sensorial advantages, and safety that could be applied on the human skin, making it appear younger and healthier. They have numerous beneficial effects on human skin [4].

Human skin is the largest body organ. Skin is exposed to the outside and protects the human body from external stimulation. Skin aging can be classified as intrinsic aging and photo-aging. Intrinsic aging is represented by internal factors accompanied by genetic events, while the extrinsic is related to external factors such as stress, radiation, pollution, and smoking [5]. Chronic UV exposure is the primary cause of photoaging [6]. Aging skin characterized by changes in skin thickness, appearance of wrinkles, irregular hyperpigmentation and degeneration of dermal elastic fibers [7, 8]. Light absorbed into the skin transmits its energy to various plastids, such as nucleic acids, amino acids, and melanin. Then, the plastid produces free radicals; these radicals are subjected to chain reactions to create a harmful reactive oxygen species (ROS) [5]. ROS cause tissue damage in skin through destroying the antioxidant enzymes such as glutathione reductase (GR), superoxide dismutase (SOD), glutathione peroxidase (GPX), and catalase (CAT) [9]. Photo-oxidative stress can also disturb cell signaling, pro-inflammatory processes, and promotes photo ageing through Lipid peroxidation (LPO) [10]. Skin photoaging is associated with the up-regulation of metalloproteinases (MMPs) in skin dermal fibroblasts upon UV exposure. MMPs play a crucial role in the degradation of extracellular matrix (ECM) in connective tissues [11]. High production of ROS results in overexpression of MMP-1 causing collagen and elastin degradation, which is considered as a major factor causing skin aging. Furthermore, Keratinocytes release inflammatory cytokines including interleukins and tumor necrosis factor (TNF)-α upon exposure to UV [12]. Therefore, the way of protecting the skin from UV and preventing aging is by inhibiting the oxidative stress caused by ROS. Thus, the study of natural resources with antioxidant properties to remove ROS is being actively pursued [13].

Melanin is responsible for skin color; it protects the skin from absorbing ultraviolet (UV) radiation and scavenges reactive oxygen species (ROS) [14]. Tyrosinase is a key enzyme that catalyzes melanin synthesis within melanocytes. However, overproduction of melanin in the skin may cause hyperpigmentation, melanoma [15]. Therefore; tyrosinase inhibitors are important in cosmetics and pharmaceuticals as whitening agents and for the treatment of pigmentory disorders [16]. Elastin is a highly elastic protein found in skin and other connective tissues; it helps in maintaining tissue configuration [17]. Overexposure to UV irradiation up regulate the expression of elastase, which hydrolyzes the dermal elastin fibers [18]. This may to lead to reduced skin elasticity, which induces wrinkling and sagging [19].

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. Synthetic antioxidants are used in cosmetics, and pharmaceuticals to inhibit ROS; However, the long term use of these antioxidants is known to exert toxic effects. Therefore, lot of studies have been directed toward the discovery of more effective and much safer natural antioxidants [20]. Accordingly, the use of plant extracts and their bioactive metabolites has proven to be effective against UV radiation [21].

Akebia quinata fruit extract

Akebia quinata (Thunb.) Decne. (*A. quinata*) is widely distributed in East Asia. The *A. quinata* extract has been shown to have antioxidant activity and free radical scavenging capability [22]. *Akebia quinata* extract contained chlorogenic acid, isochlorogenic

acid A, isochlorogenic acid C, triterpenoid saponins [23, 24]. The accumulation of free radicals and advanced glycation end products (AGEs) in the skin plays an important role in skin aging. *Akebia quinata* fruit extract (AQFE) possess antioxidant and a dose dependent antiglycation activity. AQFE protects human dermal fibroblasts (HDFs) from oxidative stress and inhibits cellular damage induced by oxidative stress. The overall results suggest that AQFE may work as an anti-skin aging agent by preventing oxidative stress and other complications associated with AGEs formation [25].

Corn silk extract

Corn silk (CS, Zea mays L.) has been consumed as a herbal medicine in Korea [26], China, United States, and France for millennia [27]. CS contains an abundance of phenolic compounds, such as flavonoids (maysin, apigmaysin, luteolin) [28, 29], anthocyanins (cyanidin, peonidin) [30], chlorogenic acid, and other biologically active substances, such saponins and allantoin [31]. The potential photoprotective effects of dietary corn silk on UVB-induced skin damage in mice and the mechanisms behind these effects on human skin cells were investigated. Corn silk contains flavonoids and other bioactive compounds and antioxidants, which may prevent skin photoaging through antioxidant and anti-inflammatory effects. Oral administration of corn silk water extract decreased epidermal thickness, wrinkle formation. The pro-inflammatory NF-$_k$B target genes (IL-1beta, iNOS, and COX-2) and MMP-9 expressions were reduced. CS has Lowered skin lipid peroxidation and blood DNA oxidation levels and higher blood glutathione levels were detected. Antioxidant transcription factor Nrf2-related catalase and SOD1 proteins and glutaredoxin mRNA levels increased. The CS extract contained potential antioxidants, which might have contributed to its anti-photoaging effects in tissues and cells. CS extract may reduce UVB-induced skin damage through antioxidant and anti-inflammatory mechanisms [32].

Erjingwan extract

Erjingwan (EJW) decoction is composed of *Lycium barbarum* and *Polygonatum sibiricum*.

EJW is a tonic formula that can maintain youth. It has been investigated that *Lycium barbarum* polysaccharide can decrease DNA damage through reducing oxidative stress [33]. Moreover, it can inhibit cell aging through the p53-mediated pathway [34]. *Polygonatum sibiricum* has been validated to have antioxidant effects, and it can enhance telomerase activity [35, 36]. Therefore, the compatibility of these two medicinal herbs contributes to the antiaging process. EJW extracts significantly improved skin elasticity without affecting. EJW extracts could downregulate the MMP1 expression and upregulate the COL1A2 expression. In addition, it promoted the Nrf2 pathway while it inhibited the NF-κB pathway. With the application of cream containing EJW extracts, the skin aging state was significantly improved. Furthermore, in vitro studies showed that EJW extracts contributed to the repair of skin after injury. The antiaging effects of EJW extracts were related to its antioxidant and anti inflammatory abilities [37].

Licorice root extracts

Licorice (*Glycyrrhiza glabra* L., Fabaceae) contains a wide variety of bioactive natural products such as Glycyrrhizin, which is a triterpene-type saponin that displays anti-inflammatory properties [38]. 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 [39, 40], accelerate wound epithelization [41], and efficiently reduce the symptoms of atopic dermatitis (AD). 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]. Extraction of licorice (*Glycyrrhiza glabra*) bioactive constituents such as glabridin (Gla) and isoliquiritigenin (Iso) have been done using a green ultrasound-assisted extraction (UAE) method with the aid of a cosmetically active solvent, glycerol. It is a fast and efficient method for preparation of extracts with excellent radical scavenging, Fe2+ chelating and antioxidant activity. Furthermore, the observed notable tyrosinase and elastase inhibitory activity of the extracts, as well as their anti-inflammatory activity, indicate the anti-

aging properties of the investigated extracts. The fact that the extracts were prepared using a safe and a cosmetically active solvent makes them suitable for direct use in specialized cosmeceutical formulations [44].

***Helichrysum teretifolium* extract**

Helichrysum teretifolium (L.) is widely distributed along the coast of South Africa [45]. The genus *Helichrysum* in general is a rich source of phenolic compounds like flavonoids, chalcones, and phloroglucinol phenolics, which are reported to be used as anti-inflammatory agents and for skin conditions [46, 47].Ten flavonoid-related structures were isolated from a *H. teretifolium* methanolic extract and identified. Most of the *H. teretifolium* constituents display efficient hydroxyl and peroxyl radical absorbance capacities, inhibiting lipid peroxidation, as well as serving as good sources with anti-tyrosinase activity and anti-elastase activities in in vitro systems. The total extract of *H. teretifolium* showed potent antioxidant activity. *H. teretifolium* total extract represents a rich source of bioactive constituents that can help to prevent accumulation of free radicals in the body. Therefore, they could be good candidates for the prevention and/or treatment of skin-related aging conditions [48].

***Magnolia officinalis* extract**

Magnolia officinalis is a member of the Magnoliaceae family. Pharmacological studies have indicated that *M. officinalis* has antioxidative properties [49]. Fermented *M. officinalis* extracts enhance antioxidant activity [50]. However, the choice of an appropriate species is necessary to obtain a high physiological activity. For example, *A. oryzae*-fermented *M. officinalis* extract was reported to exhibit negligible antioxidant activity [50]. The physiological characteristics of *Magnolia officinalis* bark (MOB) extracts was improved by *Aspergillus niger* fermentation. The physiological characteristics of the fermented extracts, such as, tyrosinase inhibitory activity, antioxidant activity, antibacterial activity, and anti-skin-aging activity, were evaluated. Cytotoxicity of the fermented extracts was analyzed to determine their safety. The fermented methanol extract exhibited the highest anti tyrosinase activity, total phenolic content, and antioxidant activity. The fermented methanol extracts inhibited skin aging-related enzymes such as collagenase, elastase, MMP-1, andMMP-2. These results could be attributed to an increase in the concentration of original active compounds and the biosynthesis of new compounds during fermentation. In cytotoxicity assays, the *A. niger*-fermented extracts were nontoxic. In general, methanol-extracted *M. officinalis* fermented by *A. niger* for 72 h has the most active antioxidant, skincare, or antiaging compounds for healthy food or cosmetics applications [51].

Melon concentrate

Oral supplementation with a specific melon concentrate increased endogenous antioxidant defenses and reduced oxidative stress in several targeted organs [52-54]. It is important to know if a topical application will induce the same antioxidant effects as oral supplementation.

Therefore, a topical administration of a melon concentrate alone or in combination has been studied to evaluate the potential skin photoprotective effects of a food supplementation. Dried melon juice concentrate particularly rich in superoxide dismutase (SOD) has been used. Melon concentrate application and/or supplementation increased MED. The endogenous antioxidant enzymes are also increased. In addition, melon concentrate has reduced the sunburn cells and melanin level on irradiated skin. Due to its antioxidant properties, it is suggested that administration of melon concentrate (oral and/or topical) could be a useful tool for skin photoprotection [55].

Red grapes extract

Resveratrol is a polyphenolic compound naturally produced by several plants such as red grapes [56, 57]. RV can ameliorate the aging of human skin by significantly stimulating SIRT1, extracellular matrix (ECM) proteins, such as collagens and elastin (ELN), and antioxidants while significantly inhibiting inflammatory and dermal-aging biomarkers [58]. However, as an effective compound in several commercial products RV suffers from rapid metabolism, especially through the oral route and possibly in cosmetics [57, 59]. Butyrate and isobutyrate analogs are more biologically active

compared to resveratrol, they can ameliorate the aging of human skin by altering the gene expression of SIRT1, collagens, extra cellular matrix proteins (like elastin, fibrillin and laminin). At the same time, butyrate and isobutyrate analogs of resveratrol significantly inhibited the inflammatory and aging biomarkers. Therefore, they have a potential use in topical applications to improve the skin related aging conditions [60].

Lotus seed embryos extract

Skin care products use lotus plant extract as an antiaging compound [61-63]. Lotus seed embryos are commonly used in traditional Chinese medicine and consumed as tea ingredient or eaten raw which is believed to have antiaging properties. Neferine is an alkaloid extract from the seed embryos of lotus (*Nelumbo nucifera* Gaertn). Neferine is one of the major bisbenzylisoquinoline extract derived from seed embryos of lotus along with liensinine and isoliensinine [64]. The antioxidant and anti-inflammatory properties of neferine have been shown [65]. HDFs subjected to UV-A irradiation showed increased production of ROS and malondialdehyde (MDA). Neferine has a protective effect against UV-A induced oxidative stress and photoaging in human dermal fibroblasts (HDFs). However, HDFs treated with neferine followed by UV-A irradiation reduced the ROS and lipid peroxidation and restored the cellular enzymatic and non enzymatic antioxidants pool. Moreover, neferine treatment inhibited UV-A induced matrix metalloproteinase-1 (MMP-1) expression in HDFs. After neferine treatment, there was a reduction in morphological alterations observed in HDFs upon UV-A irradiation. All of these results suggest that neferine has strong antioxidative and photoprotective properties, so it may be a potential agent for the prevention and treatment of UV-A mediated skin photoaging [66].

***Salvia officinalis* extract**

Salvia officinalis extract includes phytochemical compounds such as glycosides, alkaloids flavonoids, and Triterpenoids. Rutin, a polyphenolic bioflavonoid possesses antioxidant properties, so it can act as a skin protective. Rutin enhances vitamin C production, which has a major role in the generation of collagen, which is a very important element regarding the health of the skin. The antiaging properties of the extract was studied by investigating the inhibitory enzymatic assays on early aging human skin fibroblasts. The antiwrinkle 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 [67].

***Anemarrhena asphodeloides* rhizomes extract**

The rhizomes of *Anemarrhena asphodeloides* Bunge (*Liliaceae*) have been used in traditional medicine [68, 69]. Timosaponin A-III (TA-III) is one of the major chemical components that are known to exist in the medicinal herb of *Anemarrhena asphodeloides*. The photoprotective properties of TA-III on UVB-exposed HaCaT cells were studied on the antiwrinkle effects and skin safety in terms of clinical trial. There is an increase in MMP-1 expression and pro-inflammatory cytokines upon UVB irradiation. These increases were alleviated by TA-III pretreatment of UVB-exposed HaCaT cells, therefore TA-III ameliorated skin wrinkling. On the other hand, TA-III showed no dermatological toxicity in participants. As a result, TA-III could provide protection against photoaging and daily application of TA-III for 12 weeks significantly reduced signs of facial aging by limiting wrinkle formation. So, it has been confirmed for use as a cosmeceutical for prevention of skin wrinkles [70].

***Ulmus macrocarpa* Hance extract**

Ulmus macrocarpa Hance has been used as an oriental medicine in the treatment of severe metabolic diseases in South Korea [71]. The antioxidant and anti-aging effects of *Ulmus macrocarpa* Hance (UMH) extracts on the H_2O_2-induced ROS in human dermal fibroblasts (HDFs) and UVB-exposed hairless mice was investigated. The anti-aging activity of UMH extracts was estimated in vivo using the SKH-1 hairless mice. The UMH extracts reduced the H_2O_2-induced intracellular ROS production and the cell damages in

human dermal fibroblasts (HDFs) by activating antioxidant enzymes and inhibiting MAPK pathways. These results suggest that UMH extracts can reduce the expression of MMPs and the reduced MMPs lead to the inhibition of collagen degradation. In addition, oral administration of the UMH extracts decreased the depth, thickness, and length of wrinkles on UVB exposed hairless mice. Therefore, UMH extracts play an advantage of the functional materials in antioxidant and anti-aging of skin [72].

***Aloe vera* extract**

Aloe vera (also known as *Aloe barbadensis* Mill.) is a flowering plant of the family *Asphodelaceae* currently naturalized in many tropical countries. In traditional medicine, it has been widely used for centuries to treat skin disorders [73]. Today, this species is used worldwide as a valuable ingredient for cosmetics (including creams, lotions, soaps, and shampoos), and drugs (such as tablets and capsules) [74]. The bioactive features of *Aloe vera* leaf (fillet, mucilage, and rind) and flower have been characterized, and the phenolic composition and antioxidant, anti-inflammatory, antimicrobial, tyrosinase inhibition, and cytotoxic activities were also studied. The fillet consisted of alpha-tocopherol, a powerful fat-soluble antioxidant . Also, there are predominance of chromones and anthrones in the leaf samples, and the highest contents were found in mucilage and rind extracts, which revealed very interesting antioxidant properties. On the other hand, the flower extract was rich in apigenin glycoside derivatives that are capable of inhibiting the tyrosinase activity (IC50 = 4.85 mg/mL). Thus, the studied *Aloe vera* samples displayed high potential to be exploited by cosmeceutical industries [75].

***Amorphophallus konjac* extract**

Amorphophallus konjac (Family: Araceae) is a perennial plant commonly known as konjak. Konjac is a traditional food ingredient and medicine used in China, Japan and South East Asia. *A. konjac* is a rich source of glycosyl ceramides and glucomannan. Konjac derived glycosylceramides have been used as dietary supplements for dry skin [76]. Ceramides are a variety of sphingolipids, present in the skin keeping it moist and healthy [77]. Loss of ceramides causes dry skin and dermatitis that subsequently leads to the appearance of wrinkle in the skin [78]. Plant derived ceramides are chemically identical to those found in our skin. The skin health benefits of oral supplementation of a hydroalcoholic extract from *Amorphophallus konjac* tubers standardized to 5% glycosylceramides have been assessed. The oral intake of *A. konjac* extract significantly decreased in a time-dependent manner the skin dryness, hyperpigmentation, redness, itching ($p < 0.05$). Further, *A. konjac* extract was well-tolerated and no adverse events were recorded. These results demonstrates that konjac tubers have skincare properties when glycosyl ceramides are orally ingested [79].

***Bergenia pacumbis* extract**

The *Bergenia* species are herbs native to central Asia, and one of the most promising medicinal plants of the family *Saxifragaceae*. Antioxidant, anti-inflammatory properties have been reported in different species of *Bergenia* [80-82]. The major bioactive phenolics compounds ; bergenin, arbutin, and gallic acid, are principal contributor of the therapeutic properties of *Bergenia* species [83] that are responsible for their medicinal activities. The antioxidant, tyrosinase, and elastase inhibition potential of *Bergenia pacumbis* of Nepali origin has been evaluated. Crude methanol extract followed by water and ethyl acetate extract of *B. pacumbis* has tyrosinase inhibitory potential compared to standard drug Kojic acid. On the other hand, methanol and ethyl acetate extracts of *B. pacumbis* showed the elastase inhibition compared to standard Quercetin. The presence of arbutin might be the defined source of tyrosinase inhibition from *B. pacumbis* [84]. Purification of the extracts might enhance the inhibitory potential of *B. pacumbis* on the tyrosinase and elastase. Major compounds have been identified during this study such as Bergenin, Catechin, Arbutin, Gallic acid, Quercetin, and Diosmetin, in methanol extract which has reported beneficial bioactivities. According to the results, there is a scientific evidence that the crude extracts of B. pacumbis from Nepalese origin in different extracting solvents have shown significant potential on inhibiting free radicals as well as skin related problems [85].

***Salvia aramiensis* Rech. f. Extract**

Salvia aramiensis Rech. f. grown in Turkey [86]. Its flowers and leafy branches are used as herbal tea. *S. aramiensis* essential oil is a potent antimicrobial and antioxidant agent [87]. It has been learned that *S. aramiensis* species are rich in flavonoids, phenolic compounds, as well as diterpenes and triterpenes [88]. These compounds show a natural antioxidant property by stopping or inhibiting the reactions caused by free radicals [89]. Encapsulation drug delivery systems have been used to increase the effectiveness of the active compounds where water solubility is low and to improve their stability [90]. Rosmarinic acid is the main phenolic compound of the extract that has been identified. Furthermore 70% methanol extract showed more than 50% inhibition on collagenase and elastase enzymes at all the concentrations. The extract and its formulation was found to be nontoxic on the L929 fibroblast cell line. Accordingly, a successfully developed and a long-term antioxidant and enzyme inhibitory formulation containing *S. aramiensis* was developed during this study [91].

***Adenostemma lavenia* (L.) O. Kuntze**

Adenostemma lavenia (L.) O. Kuntze belongs to the *Asteraceae* family and grows in the tropical regions of Asia. It has been shown that *A. lavenia* extract had anti-inflammatory anti melanogenic activities [92-94]. Obviously, *A. lavenia* leaf extract contains a higher amount of the diterpenoid ent-11alpha - hydroxy-15-oxo-kaur-16-en-19-oic acid (11alpha OH-KA), which may be responsible for 50% of the antimelanogenic activity in the extracts [94]. 11alphaOH-KA exhibits various pharmaceutical potentials such as skin whitening. 11alphaOH-KA activated the antioxidative transcription factor which was accompanied by enhanced hemeoxygenase expression levels. Accordingly, these results suggest that 11alphaOH-KA and its source, *A. lavenia*, can be attractive materials for antiaging and related diseases [95].

Brown black wolfberry extract

Wolfberry is an important medicinal plant with high nutritional value. Modern medical researches show that wolfberry possesses diverse pharmacological effects, such as anti-aging, and immunomodulatory activities [96]. Melanoidins are the main biologically active substance in BBW along with phenols and flavonoids. Phenolic, flavonoids, and melanoidins possess potent of ROS scavenging ability. In this study, the anti-aging potential of brown black wolfberry (BBW) was explored using the Drosophila melanogaster and D-gal induced aging mice as the animal model. In vivo study results indicated that BBW significantly increased the survival time and alleviated the oxidative stress caused by H_2O_2 of Drosophila melanogaster. At the same time, BBW significantly decreased oxidative damage and D-gal-induced aging in mice and inhibited lipid peroxidation by enhancing the anti-oxidant enzyme activities and up-regulating the expressions of the endogenous stress defense genes of Drosophila melanogaster [97].

***Curcuma longa* L. essential oil**

The rhizome of *Curcuma longa* L., a popular Chinese herb contains curcuminoids, which are extensively used in various industries [98 -99]. The essential oil of *C. longa* (CL-EO) shows anti-inflammatory, antioxidant, antimicrobial, anticancer, and antiviral effects [100]. The major components in CL-EO were ar-turmerone, curlone, β-turmerone, 8,9-dehydro-9-formyl-cycloisolongifolene, β-sesquiphellandrene, germacrone, ar-curcumene, α-himachalene, and ledane. CL-EO can reduce skin photoaging in a UVB-irradiated nude mouse model. It is believed that ar-turmerone, curlone, and β-turmerone were the major contributors to the anti-skin aging effect of CL-EO. Therefore, CL-EO could be used in the formulation of functional cosmetic products [101].

***Leontopodium alpinum* Callus Culture Extract (LACCE)**

Edelweiss (*Leontopodium Alpinum*) in the family *Asteraceae* is a wildflower that grows in rocky limestone places [102]. Recently, several studies have shown the efficacy of edelweiss extracts for anti-inflammation in mice and rats and human keratinocytes and endothelial cells [103]. In addition, the root extracts of edelweiss contain antioxidants, such as leontopodic acid A and 3,5-dicaffeoylquinic acid, which can be used as anti-aging agents [104]. The efficacy of *Leontopodium Alpinum* callus culture extract (LACCE); using multiple assays from in vitro to in vivo as well as transcriptome profiling was

investigated. There is a strong antioxidant activity of LACCE in response to UVB treatment as shown through several in vitro assay results. Moreover, LACCE suppressed inflammation and wrinkling; while, the moisturizing activity was increased by LACCE. In vivo testing demonstrated that constant application of LACCE on the face and skin tissues improved antiperiorbital wrinkles, skin elasticity, dermal density, and skin thickness. LACCE up-regulated genes that were involved in the positive regulation of the programmed cell death, developmental process, and cornification process that is forming the skin barriers, which provide many advantages in the human skin. While, down-regulated genes were stress-responsive genes, suggesting LACCE did not cause any harmful stress on the skin. This study demonstrated LACCE is a promising agent for antiaging cosmetics [105].

Pomegranate derived anthocyanins cream

Punica granatum L. (pomegranate); is a kind of small tree native to Asia and Africa. Secondary active metabolites such as alkaloids, tannins, polyphenolic compounds in addition to vitamins and minerals were identified in pomegranate [106]. Anthocyanins of pomegranate seeds arils have been extracted and evaluated [107]. These anthocyanins play a major role in the activity of pomegranate as antioxidant and cancer protective especially skin cancers [108]. Anthocyanins as an antioxidant are improving the mitochondrial activity and useful in preventing oxidative damage of the skin [109]. Also, anthocyanins have been reported for their protective effect against UV-induced skin erythema [110]. This work aimed to study the applicability of the anti-oxidant properties of semi-purified anthocyanins isolated from fresh pomegranate arils extract as an effective anti-aging, through preparing a topical cold cream loaded with pomegranate anthocyanins followed by being evaluated for its stability, irritation, encapsulation efficiency, and release characteristics, as well as ex vivo permeation study and application into human volunteers. According to the results, there is an absence of any interaction between anthocyanins and the used polymers. The formulated cream potentially reduced skin aging when applied to human volunteers' skin. Furthermore, the skin permeation displayed a good permeation of 43.16% after 210 min. Therefore, pomegranate anthocyanins could be used as a safe, stable, homogeneous, nonirritant and effective topical anti-aging drug formulation for aged people [111].

***Santalum Album* extract**

Santalum album L. contains an essential oil (sandalwood oil) that is broadly used in the cosmetic, perfumery, and aromatherapy industries. The seed oil of the *Santalum album* is
containing santalbic acid (or ximenynic acid) and stearolic acid (9-octadecenoic acid). In universal, ximenynic acid exhibits many biological activities and pharmacological effects, including antibacterial, antifungal, anti-inflammatory activities. Novel acetylenic fatty acids named Ximenynic acid (XMA) were successfully isolated from the seeds of Santalum album L by N-Hexane extraction. Ximenynic acid (or Santalbic acid) is one of the few acetylenic fatty acids occurring at higher levels in plant seed oils. The antiaging activities were assessed by anti-collagenase enzyme assay. The antiaging assay showed that XMA exhibited significant collagenase inhibition activity as compared with Catechin. These findings suggested that the acetylenic fatty acids XMA could be served as a novel antiaging in pharmaceutical as well as the cosmetic industry [112].

Conclusion

The greater demand of the plant-based bioactive compounds usage leads many researchers in search of novel plants in the development of cosmeceuticals for skincare anti-photoaging therapy. The biologic activity of various medicinal plant extracts based skin anti-photoaging aging compounds has been elucidated, providing mechanisms for how these compounds may protect against skin photoaging. Further randomized, placebo controlled, double-blind studies are needed to substantiate many of the claims made about these plant-derived bioactive cosmetic compounds. There is a need to study combinations of several classes of plant biofunctional active ingredients that reveal synergistic effects on reversing signs of photoaging.

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