

Review

Natural Antioxidants from Plant Extracts in Skincare Cosmetics: Recent Applications, Challenges and Perspectives

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Abstract: In recent years, interest in the health effects of natural antioxidants has increased due to their safety and applicability in cosmetic formulation. Nevertheless, efficacy of natural antioxidants in vivo is less documented than their prooxidant properties in vivo. Plant extracts rich in vitamins, flavonoids, and phenolic compounds can induce oxidative damage by reacting with various biomolecules while also providing antioxidant properties. Because the biological activities of natural antioxidants differ, their effectiveness for slowing the aging process remains unclear. This review article focuses on the use of natural antioxidants in skincare and the possible mechanisms underlying their desired effect, along with recent applications in skincare formulation and their limitations.

Keywords: natural antioxidants; vitamins; flavonoids; polyphenols; plant extracts



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1. Introduction

The skin is the body's largest living organ, and it protects the body from the outside environment by maintaining homeostasis, keeping harmful microbes and chemicals out, and blocking sunlight [1]. The stratum corneum, the outermost layer of the skin, is a selectively permeable, heterogeneous epidermal layer that provides protection against dryness and environmental damage while retaining sufficient moisture to function. [2]. Impairment in skin barrier function frequently manifests as altered stratum corneum integrity, which leads to an increase in transepidermal water loss and a decrease in skin hydration [3]. The term "cosmeceutical" refers to cosmetics that contain active chemicals having drug-like properties. Cosmeceuticals with medicinal properties have beneficial local effects and prevent degenerative skin diseases. [4]. They enhance appearance by supplying nutrients required for healthy skin. They can improve skin tone, texture, and radiance while reducing wrinkles. Cosmeceuticals are a rapidly expanding subset of the natural personal care industry. Although natural ingredients have been used for centuries in skincare, they are becoming increasingly prevalent in modern formulations [5]. The phrase "natural" refers to a substance that is derived directly from plants or animal products and is generated or found in nature [6]. Herbs, fruits, flowers, leaves, minerals, water, and land can be sources of natural ingredients. Natural ingredients' efficacy in skincare products is determined by their in vitro and in vivo efficacy as well as the type of dermatological base into which they are incorporated. Plants have long been used for medicinal purposes, and it is likely that new products containing natural oils and herbs will continue to emerge on the market in the coming years. Before the use of synthetic substances with similar properties, plants were the primary sources of all cosmetics [7]. Natural plant molecules continue to pique the interest of researchers. However, using extracts necessitates paying close attention to extraction methods, plant-to-solvent ratios, and active-ingredient content. The

use of plant extracts in skincare products is demanded by consumers, who are becoming increasingly concerned with purchasing ecofriendly products [8]. However, consumers, are frequently unaware that natural products are complex mixtures of many chemical compounds that can cause adverse reactions. To avoid this issue, researchers should chemically characterize their extracts with regard to composition [9]. Furthermore, the *in vitro* cytotoxic potential of extracts should be tested in several human cell lines prior to human use, and the irritant potential of cosmetic formulations can be screened. These procedures can help to ensure the safety of natural products and thus their acceptability on the market [10,11]. Bioactive extracts and phytochemicals from various botanicals are used for two purposes: (1) body care and (2) as ingredients to influence the biological functions of the skin, providing nutrients for healthy skin [12]. Vitamins, antioxidants, essential oils and oils, hydrocolloids, proteins, terpenoids, and other bioactive substances are all abundant in botanical products [13]. These extracts can have a variety of properties depending on their compositions. Modern skincare cosmetics are distinguished by their multiactivity, which enables multidirectional complex effects even in relatively simple formulations. The biologic impacts of the most widely used cosmetic surgery, which involves coating the epidermis with a hydrolipid occlusion layer or various forms of antiradical protection, are a good example. The meaning of cosmetic multi-activity is encoded in a legal definition of cosmetic product use: “keeping (the skin) in good condition” [14–16]. A comprehensive search was performed to find reports of the use of natural antioxidants in skincare in PubMed, Science Direct, and Scopus, and the articles satisfying the search criteria were screened and filtered. In this review article, we summarize the use of natural antioxidants and their possible mechanisms in skincare applications.

2. Antioxidants

Antioxidants are molecules that can oxidize themselves before or instead of other molecules. They are compounds or systems that can interact with free radicals and stop a chain reaction before vital molecules are harmed [17]. Antioxidants are used in food, cosmetics, beverages, pharmaceuticals, and even the feed industry. They can be used as health supplements and active ingredients as well as stabilizers [18]. Antioxidants can be synthetic or natural, and both are used in cosmetic products [19]. Synthetic antioxidants (e.g., butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), and propyl gallate) are widely used because they are inexpensive to produce [20]. However, research suggests that excessive consumption of synthetic antioxidants may pose health risks. Despite the fact that synthetic antioxidants dominate the market, demand for natural antioxidants has increased in recent years and is expected to continue [21]. This pattern can be explained by a growing consumer preference for organic and natural products that contain fewer additives and may have fewer side effects than synthetic ingredients.

3. Natural Antioxidants in Cosmetics

Natural antioxidants used in the cosmetic industry include various substances and extracts derived from a wide range of plants, grains, and fruits, and are capable of reducing oxidative stress on the skin or protecting products from oxidative degradation [22]. One of the major causes of oxidative stress that accelerates skin aging is reactive oxygen species (ROS) [23]. Intrinsic aging is associated with the natural process of aging, whereas extrinsic aging is associated with external factors that affect the aging process (e.g., air pollution, UV radiation, and pathogenic microorganisms). Photoaging is most likely the primary cause of ROS production [24–28]. Factors that drive the process of skin aging are presented in Figure 1. Several potential skin targets have been discovered to interact with ROS (e.g., lipids, DNA, and proteins) [29]. Antioxidant molecules can be enzymes or low-molecular-weight antioxidants that donate an electron to reactive species, preventing the radical chain reaction, which prevents the formation of reactive oxidants, or behave as metal chelators, oxidative enzyme inhibitors, or enzyme cofactors [30]. Antioxidants can also be used as stabilizers, preventing lipid rancidity. Lipid oxidation occurs not only in cosmetics but

also in the human body [31]. Thus, when antioxidants are present in a product, they may serve multiple functions. The number of radicals increases during the initiation phase of lipid oxidation. Molecular oxygen and fatty acid radicals react during the propagation phase, resulting in the formation of hydroperoxide products. Hydroperoxides are unstable and can degrade to produce radicals, which can accelerate the propagation reaction. The termination phase is dominated by radical reactions. Antioxidants can inhibit lipid oxidation by reacting with lipid and peroxy radicals and converting them to more stable, non-radical products [32–35]. Additionally, antioxidants can deplete molecular oxygen, inactivate singlet oxygen, eliminate peroxidative metal ions, convert hydrogen into other antioxidants, and dissipate UV light [36]. Antioxidants can be used in cancer treatments, because the production of ROS is altered during tumorigenesis, with anti-inflammatory and antimicrobial effects. Plants are well known for producing natural antioxidant compounds that can reduce the amount of oxidative stress caused by sunlight and oxygen [37]. Plant extracts are used in a variety of patents and commercial cosmetic products. Green tea, rosemary, grape seed, basil grape, blueberry, tomato, acerola seed, pine bark, and milk thistle are some of the plant extracts commonly found in cosmetic formulations. Polyphenols, flavonoids, flavanols, stilbenes, and terpenes are natural antioxidants found in plant extracts (including carotenoids and essential oils) [38]. Antioxidants are classified as primary or natural antioxidants and as secondary or synthetic antioxidants according to their function. Mineral antioxidants (such as selenium, copper, iron, zinc, and manganese), vitamins (C and E), and phyto-antioxidants are examples of primary antioxidants. Generally, a mineral antioxidant is a cofactor of enzymatic antioxidants [39–43]. Secondary or synthetic antioxidants capture free radicals and stop the chain reaction. BHA, BHT, propyl gallate, metal chelating agents, tertiary butylhydroquinone, and nordihydroguaiaretic acid are examples of secondary antioxidants [44,45]. The use of plant antioxidants is increasing and may eventually replace the use of synthetic antioxidants. A natural antioxidant can be a single pure compound/isolate, a combination of compounds, or plant extracts; these antioxidants are widely used in cosmetic products. Table 1 presents a summary of natural antioxidants commonly used in cosmetic preparations. Innate antioxidants act as oxygen free radical scavengers (singlet and triplet), ROS, peroxide decomposers, and enzyme inhibitors [46–48]. Polyphenols and terpenes are the most common phyto-antioxidants; this distinction is based on their molecular weight, polarity, and solubility. Polyphenols have benzene rings with -OH groups attached. The number and position of -OH groups on the benzene ring determine their antioxidant activity. Phenolic groups influence protein phosphorylation by inhibiting lipid peroxidation. The most abundant polyphenols are flavonoids and stilbenes, and the most abundant terpenes are carotenoids, which act as singlet oxygen quenchers [49].



Figure 1. Driving factors of skin aging.

Table 1. Natural antioxidants.

S. No	Source	Antioxidant	Potential Activity	Reference
1.	Apple	Phenolic compounds	Inhibitors of sulfotransferases, influence epigenetic processes and heritable changes not encoded in the DNA sequence, DNA protection against UV radiation	[50,51]
2.	Baccharis species	Phenolic compounds	Inhibit reactive oxygen and nitrogen species (RONS), inhibit carrageenan induced edema	[52]
3.	Basil leaves	Phenolic compounds	Antiacne, antiaging, remove dead skin cells	[53,54]
4.	Blueberry pomace	Phenolic compounds	Enhance polyphenol oxidase activity, potent antioxidant	[55,56]
5.	Cape gooseberry	Phenolic compounds and carotenoids	Anticoagulant, antispasmodic	[57,58]
6.	Carrot	Carotenoids, anthocyanins	Protection from UV-induced lipid peroxidation, in treatment of erythropoietic protoporphyria	[59,60]
7.	Chest nut	Polyphenols	Moisturizer, in treatment of oxidative stress-mediated diseases and photoaging	[61,62]

Table 1. *Cont.*

S. No	Source	Antioxidant	Potential Activity	Reference
8.	Coffee leaves	Chlorophylls and carotenoids	Antioxidant, antimicrobial, antiaging	[63,64]
9.	Feijoa	Phenolic compounds	Antioxidant, antimicrobial	[65,66]
10.	Ginkgo biloba leaves	Flavonoids	Prevent UVB-induced photoaging, anti-inflammatory, antioxidant, blood microcirculation	[67,68]
11.	Goji berry	Phenolic compounds	Antioxidant, prevent skin aging, immunomodulatory	[69,70]
12.	Goldenberry	Polyphenols	Anti-inflammatory, antiallergic	[71]
13.	Grape	Anthocyanins and phenolic compounds	Protection from UV radiation, antioxidant and antiaging, depigmenting, anti-inflammatory, wound healing	[72,73]
14.	Green algae	Carotenoids and phenolic compounds	Prevention of skin aging, protection from UVR, inhibition of melanogenesis, anti-inflammatory, antioxidant	[74,75]
15.	Green propolis	Phenolic compounds	Anti-inflammatory, antimicrobial, wound healing	[76,77]
16.	Jussara fruit	Phenolic compounds	Antioxidant, natural coolant	[78,79]
17.	Kumquat peel	Phenols and flavonoids	Antioxidant, anti-inflammatory, skin lightening, suppression of lipid accumulation	[80,81]
18.	Mango	Carotenoids	Wound healing, prevent skin aging, antioxidant	[82,83]
19.	Myrtle	Phenolic compounds, flavonoids, and anthocyanins	Treatment of burn injury, anti-inflammatory, antifungal	[84,85]
20.	Olive	Phenolic compounds	Antioxidant, anticancer, antiallergic, antiatherogenic, antimutagenic effects	[86,87]
21.	Papaya seeds	Phenolic compounds	Antioxidant, insecticidal and repellent, antibacterial, wound healing, anti-inflammatory and immunomodulatory	[88,89]
22.	Peach fruit	Flavonoids and phenolic compounds	Anticancer, antioxidant	[90,91]
23.	Peel of egg plant	Phenolic compounds, flavonoids, tannins, and anthocyanins	Antioxidant, anti-inflammatory, antiviral and antimicrobial	[92]

Table 1. *Cont.*

S. No	Source	Antioxidant	Potential Activity	Reference
24.	Peppermint	Phenolic compound and essential oils	Antioxidant, antiaging	[93]
25.	Pineapple	Polyphenols	Antimalarial, antinociceptive, and anti-inflammatory activities, improve skin barrier function	[94,95]
26.	Pomegranate	Phenolic compounds	Anti-inflammatory, antioxidant, antimicrobial, promote hair follicles	[96,97]
27.	Propolis	Phenolic compounds	Wound healing, immunomodulatory, anti-inflammatory	[98,99]
28.	Red Macroalgae	Proteins, polyphenols and polysaccharides	Prevent skin-aging processes, promote transepidermal water loss, simulate sebum content, and increase erythema and melanin production	[100,101]
29.	Bananas	Phenolic compounds and flavonoids	Provide UV protection, antimicrobial, wound healing	[102,103]
30.	Spent grain	Phenolic compounds	Antioxidant, skin lightening, anti-inflammatory	[104,105]
31.	Turmeric	Phenolic compounds	Anti-inflammatory, antioxidant, treatment of psoriasis	[106,107]
32.	Strawberry	Anthocyanins and phenolic compounds	Antimicrobial, antioxidant, antiaging	[108,109]
33.	Sweet potato	Polyphenols and anthocyanins	Antioxidant, wound healing, serve as natural, safe and effective colorants, antimicrobial, antifungal	[110,111]
34.	Tomato	Flavonoids and lycopene	Antioxidant, protection from cell damage, provide protection against UV rays, wound repair	[112,113]
35.	Horse radish	Phenolic compounds and flavonoids	Antimicrobial, antioxidants	[114]
36.	Withania somnifera	Phenolic compounds	Antioxidant, skin whitening	[115,116]

4. Vitamins

The consumption and absorption of vitamins and antioxidants, primarily through diet and, essentially, through the use of manufactured supplements, is critical to human health [117]. The skin is our largest organ, and as our external environmental barrier, it is at the forefront of the fight against damaging free radicals from external sources. ROS are formed by ultraviolet light and environmental pollutants [118]. Free radicals are highly reactive molecules with an unpaired electron that cause damage to the molecules and tissues around them. Free radicals cause the most significant damage to biomembranes and DNA [119]. It is believed that using vitamins and antioxidants in cosmetics on a topical basis can help to protect from and possibly repair the damage caused by free radicals. Furthermore, some vitamins may be beneficial to the skin due to their effects, such as

reduction in pigmentation and bruising, activation of collagen production, keratinization refinement, and anti-inflammatory effects [120].

5. Vitamin A

Vitamin A was the first vitamin to be approved by the Food and Drug Administration as an anti-wrinkle agent that improves the appearance of the skin's surface and has antiaging properties. Vitamin A is a fat-soluble substance that belongs to the retinoid family [121]. Aside from retinol, that group includes structurally related substances with retinol-like biological properties. Because the biological activities of the substances vary, it is given in retinol equivalents for standardization [122]. Vitamin A and its derivatives are among the most effective antiaging agents. Cell apoptosis, differentiation, and proliferation are all regulated by retinoids. Retinoids' anti-wrinkle properties promote keratinocyte proliferation, strengthen the protective function of the epidermis, limit transepidermal water loss, prevent collagen degradation, and inhibit metalloproteinase activity [123,124]. Retinoid activity is associated with a high affinity for nuclear receptors, specifically retinoid acid receptors and retinoid X receptors. For many years, vitamin A, its derivatives, and beta-carotene (pro vitamin A) have been popular cosmetic additives. Carrots, tomatoes, and other yellow vegetables are good sources of beta-carotene [125]. Vitamin A is primarily found in animal foods such as egg yolk and liver. As a precursor to vitamin A, beta-carotene is a powerful lipid-soluble antioxidant capable of quenching singlet oxygen—a highly reactive free radical [126]. Singlet oxygen can cause DNA damage and is mutagenic. Beta-carotene has been shown to have photoprotective effects on the skin. It provided protection against UVA radiation effects in studies on mouse and guinea-pig skin. Furthermore, both beta-carotene and vitamin A were discovered to be photoprotective, as they reduced the amount of lipid peroxyl radicals in UV-exposed murine skin [127,128]. However, because beta-carotene is unstable, other forms of vitamin A are commonly used in cosmetic formulations. Vitamin A and its derivatives, particularly retinol, are among the most effective antiaging agents [129]. Fat-soluble retinol enters the stratum corneum and (to a lesser extent) the dermis. It is critical to increase retinol penetration, thereby broadening its spectrum of activity, and to control a potential action in laboratory tests before improving procedure effectiveness. After entering the keratinocyte, retinol penetrates its interior and binds to an appropriate receptor [130,131]. Retinol-binding protein receptors in the cytosol have a high affinity for retinol. Retinoids may influence transcription and growth factor secretion in the epidermis. They are responsible for the proliferation of the epidermis' living layer, the strengthening of the epidermis' protective role, and the reduction in excessive transepidermal water loss. Furthermore, retinoids protect against collagen degradation, reduce the activity of metalloproteinase, and promote angiogenesis in the dermal papillary layer. Retinol loosens the connections between epidermal cells, allowing keratinization to occur [132,133]. Furthermore, it promotes epidermis turnover and the proliferation of epidermal cells in the basal layer and stratum corneum. The proliferation AP-1 transcription factor, which is activated by various stimuli, growth factors, and cytokines, plays an important role in keratinocytes. The AP-1 complex, which includes the c-Jun/c-fos and c-Jun transcription factor, was increased in retinol-treated aged human skin. Because retinoids have anticomedogenic properties, they regulate the shedding process within sebaceous gland ducts [134]. Most importantly, retinoids inhibit the activity of enzymes involved in lipogenesis as well as sebocyte differentiation and cellular division [135]. Furthermore, they reduce skin discoloration, reduce pigmentation by approximately 60%, and contribute to the proper distribution of melanin in the skin. Topically applied retinoids also influence melanocyte function, resulting in a regular melanin distribution in the epidermis [136]. They are widely used in various cosmetic formulations. Examples of vitamin A and derivatives in cosmetics are presented in Table 2.

Table 2. Vitamin A uses in cosmetics and skincare.

S. No.	Vitamin A and Its Derivatives	Functions	Application	References
1.	Retinol	Inhibits collagenase and the expression of MMP, stimulates GAGS synthesis and collagen type 1	Used in dyspigmentation, dryness, anti-wrinkle treatment	[137]
2.	Retinoic acid	Reduces inflammation in sebaceous glands, inhibits keratosis, stimulates epidermal cell proliferation	Used in treatment of psoriasis, chronic inflammation of hair	[138]
3.	Retinyl acetate and palmitate	Stimulates epidermal cell proliferation, regulation of sebum, converts into retinoid acid	Stabilizes properties in wrinkle treatment, acts as antioxidant	[139]
4.	Retinaldehyde	Stimulates epidermal cell proliferation, oxidizes into retinoic acid	Works as stabilizer in treatment of wrinkle	[140]
5.	Naphthalenecarboxylic acid	Acts as a strong modulator for keratinization in hair follicles, increases proliferation, changes expression of genes and synthesis of mRNA	Reduces inflammation, acne, excessive keratosis	[141]
6.	Tazarotene	Regulates keratinocyte differentiation, proliferation, and inflammation	Used in treatment of psoriasis and acne, works as photoprotection from sunlight	[142]

6. Vitamin B

Vitamin B is a water-soluble nutrient found in a variety of foods, particularly whole grains and green leafy vegetables. Panthenol is the alcohol version of pantothenic acid, which is known as vitamin B5. It has been used in hair care products for many years because it acts as a humectant, increasing the water content and improving the elasticity of hair [117]. Panthenol is an effective moisturizer in cosmetics because of its ability to attract water into the stratum corneum and soften the skin. Niacinamide belongs to the vitamin B family [143]. It is produced in the body by the conversion of nicotinic acid, which has the same vitamin activity as its amide. Because niacinamide is involved in cellular energy metabolism, DNA synthesis regulation, and transcription processes, various biological effects can be observed after in vitro and in vivo substitution [144]. Niacinamide is a potent inhibitor of the nuclear poly (ADP-ribose) polymerase-1 (PARP-1) that regulates NF-B-mediated transcription and is thus critical for the expression of adhesion molecules and pro-inflammatory mediators [145]. The anti-inflammatory effects of niacinamide are primarily based on the inhibition of leucocyte chemotaxis, the release of lysosomal enzymes, and

the transformation of lymphocytes, rather than on direct vasogenic effects. By inhibiting keratinocyte factors, niacinamide prevents the reversible transfer of melanosomes from melanocytes to keratinocytes. This distinguishes niacinamide from other “lightening” substances that directly inhibit tyrosinase (e.g., arbutin and kojic acid). By inhibiting keratinocyte factors, niacinamide prevents the reversible transfer of melanosomes from melanocytes to keratinocytes. This distinguishes niacinamide from other “lightening” substances that directly inhibit tyrosinase (e.g., arbutin and kojic acid). Niacinamide’s photoprotective effect is based on both photocarcinogenesis inhibition and protection against UV-induced immunosuppression [146,147].

7. Vitamin C

Vitamin C, i.e., ascorbic acid (AA), is a hydrophilic molecule that can be found in its reduced form (ascorbic acid or ascorbate) or in its oxidized form dehydroascorbic acid, which is a byproduct of two-electron oxidation of AA [148]. Vitamin C is a powerful antioxidant that can neutralize oxidative stress via an electron donation/transfer process. In addition to regenerating other antioxidants in the body, such as alpha-tocopherol, vitamin C can reduce the amounts of unstable species of oxygen, nitrogen, and sulfur radicals (vitamin E) [149,150]. Furthermore, research with human plasma has shown that vitamin C is effective for preventing lipid peroxidation caused by peroxide radicals. Additionally, vitamin C promotes iron, calcium, and folic acid absorption, which prevents allergic reactions, and a decrease in the intracellular vitamin C content can lead to immunosuppression [151]. Vitamin C is required for the synthesis of immunoglobulins, the production of interferons, and the suppression of interleukin-18, (a regulating factor in malignant tumors) production. When applied topically, vitamin C can neutralize ROS caused by solar radiation and environmental factors such as smoke and pollution [152]. Vitamin C has proven to be effective for the treatment of hyperpigmentation, melasma, and sunspots. This appears to be related to its ability to obstruct the active site of tyrosinase—the enzyme that limits melanogenesis. Tyrosinase catalyzes the hydroxylation of tyrosine in 3,4-dihydroxyphenylalanine, resulting in the formation of a precursor molecule of melanin [153]. Furthermore, vitamin C promotes keratinocyte cell differentiation and improves dermal–epidermal cohesion [154,155].

8. Vitamins E and K

Vitamin E is a lipid-soluble vitamin found in various foods, particularly soy, nuts, whole-wheat flour, and oils. Because of its ability to reduce lipid peroxidation, it has numerous health benefits for the eyes and cardiovascular system [156]. Numerous cutaneous benefits have been demonstrated when vitamin E is applied topically. The most important property of vitamin E is its strong antioxidant capacity. The term “protector” has been used to describe the actions of vitamin E and its derivatives because of their ability to quench free radicals, particularly lipid peroxyl radicals [157,158]. Several studies have indicated that they can reduce UV-induced erythema and edema. Clinical improvement in the visible signs of skin aging has been linked to reductions in both skin wrinkling and skin tumor formation [159]. Tocopherol and its acetyl ester derivative, tocopherol acetate, have been studied extensively. While tocopherol is the most active form of vitamin E, topically applied vitamin E esters have also been shown to penetrate the epidermis [156,160].

Phytonadione (vitamin K) is required for the hepatic production of several clotting factors. Vitamin K is primarily obtained from green leafy vegetables as well as from intestinal bacteria [161]. In clinical practice, it is used to reverse prothrombin deficiency states caused by coumadin use. Because parental vitamin K improves bleeding time, there is a rationale for using topical vitamin K to correct and prevent some of the vascular manifestations of aging [162]. Topical 1% vitamin K applied twice daily was found to be effective for both accelerating the resolution of bruising and reducing future bruising. This was attributed to the ability of vitamin K to prevent and remove extravasated blood in the skin as well as the ability of retinol to correct certain aspects of photoaging [163].

9. Polyphenols

Botanical compounds from a variety of chemical classes, including polyphenols, monoterpenes, flavonoids, organosulfides, and indoles, have been shown in mouse models to have antimutagenic and anticarcinogenic properties when administered topically or orally [164]. These compounds' mechanisms of action include anti-inflammatory and immune response stimulation, detoxification, antioxidant modulation, and gene expression alteration [165]. Research has revealed that these compounds act via multiple pathways and thus maintain tissue homeostasis via multiple mechanisms [166]. Polyphenols have been extensively studied and are reported to have antioxidant and anti-inflammatory properties. Polyphenolic compounds are found in various plants, including tea leaves, grape seeds, blueberries, almond seeds, and pomegranate extract [167]. The beneficial properties of polyphenols have been supported by several studies on skin cells and on human skin; thus, these compounds are increasingly being incorporated into cosmetic and medicinal products [168]. The main polyphenols in green tea are catechins gallic acid, epigallocatechin, epigallocatechin, and epigallocatechin-3-gallate (EGCG). Research indicates that EGCG inhibits UVB-induced hydrogen peroxide release from cultured normal epidermal keratinocytes and suppresses MAPK phosphorylation. Furthermore, EGCG reduces inflammation by activating NFκB. Other phenolic acids found in green tea include gallic acids and theanine, as well as the alkaloids caffeine, theophylline, and theobromine. Theaflavins, which are found in black tea, have been shown to inhibit UVB-induced AP-1 induction by suppressing the action of extracellular-regulated kinase (ERK) and c-jun N-terminal kinase (JNK). Tea polyphenols can also prevent UVB-induced phosphatidylinositol 3-kinase activation (IP3K) [169,170]. On a molecular level, oral green tea administration to SKH-1 mice increased the number of UV-induced p53- and p21-positive cells, as well as the number of apoptotic sunburn cells [171]. In addition to reducing the amount of ROS in the skin, tea polyphenols provide photoprotection by counteracting UVB-induced local and systemic immunosuppression. UVR-induced changes in the IL-10/IL-12 cytokines are inhibited by EGCG. This is achieved by inhibiting the infiltration of IL-10 secreting CD11b+ macrophages into the irradiated site via antigen-presenting cells in the skin and draining lymph nodes [172].

The polyphenolic phytoalexin component resveratrol is responsible for many of the beneficial effects of grape seeds, including the antioxidant, anti-inflammatory, and antiproliferative activity. The most extensively studied polyphenol is resveratrol (3,5,4'-trihydroxy-trans-stilbene) [164]. Resveratrol's protective benefits were demonstrated in *in vivo* studies, with topical application to SKH-1 hairless mice prior to UVB exposure resulting in significant inhibition of UV-mediated edema and inflammation. Resveratrol's protective effects were discovered at the molecular level through inhibition of the inflammation mediator COX-2, inhibition of ornithine decarboxylase, reduction in hydrogen peroxide, and decreased lipid peroxidation. The antioxidant property of resveratrol is critical to its protective effect [173]. Resveratrol reduces UVA-induced oxidative stress in human keratinocytes by downregulating the Keap1-a protein that binds to Nrf2 and marks it for degradation. Furthermore, SIRT1 protects against UVB and ROS-induced cell death by modulating p53 and c N-terminal kinase of c-Jun (JNK) [174].

Sulforaphane, a natural antioxidant found in broccoli, has anticarcinogenic, antidiabetic, and antimicrobial properties. Topical application of sulforaphane extracts to mouse skin protected against UVR-induced inflammation and edema by activating Nrf2 and consequently upregulating phase 2 antioxidant enzymes. According to research, the activity of Nrf2 decreases as we age [175]. The reasons for Nrf2's reduced activity are unknown, but there is evidence that Nrf2 loses its ability to bind to the antioxidant response element sequence in antioxidant genes [176]. Importantly, Nrf2 agonists, such as lipoic acid and sulforaphane, appear to be able to reverse the ability of Nrf2 to bind to the cis-element. Sulforaphane has been shown to restore Nrf2 transactivation and provide cytoprotection against UVB-induced injury of human lens epithelial cells not only by increasing the expression of phase 2 enzymes but also by increasing the amount of the antioxidant enzyme

catalase. The restoration of Nrf2 activity in aging cells as well as cells exposed to UVB indicates that sulforaphane is a natural compound with important preventative and therapeutic effects [177].

Turmeric is a popular spice with anti-inflammatory properties. Its active ingredients are bisdemethoxycurcumin, demethoxycurcumin, and curcumin [178]. Curcumins reduce inflammation by inhibiting the NF κ B and MAPK signaling pathways and reducing the expression of inducible nitric oxide and COX2. Additionally, curcumins inhibit UVB-induced TNF mRNA expression and reduce matrix metalloproteinase-1 (MMP-1) expression in keratinocytes and fibroblasts [179]. A recent study found that tobacco smoke—a major risk factor for skin cancer—induced epithelial–mesenchymal transition via the Wnt/b-catenin signaling pathway, and that curcumin reversed the effect. Curcumin anticancer activity appears to occur via the inhibition of the Sonic hedgehog and Wnt/b-catenin pathways, which reduces the expression of cancer stem cell markers such as CD44 and ALDH1A1 [180].

In recent years, the photoprotective effects of various groups of multicellular algae have been demonstrated. Mycosporine-like amino acids are UV-absorbing compounds that are abundantly produced by many algae species and have long been used in commercial sunscreens [181]. In addition to their UV-absorbing properties, algae extract can protect against UVR-induced ROS. *Corallina pilulifera* methanol extract exhibited potent antioxidant activity, protecting against UVA radiation-induced oxidative stress [182]. Many brown-algae species have exhibited photoprotective properties. *Ecklonia cava* is high in polyphenols, which protect against photo-oxidative stress. Similarly, extracts from *Unidaria crenata* had significant free radical scavenging abilities and reduced UVB-induced apoptosis and lipid and protein oxidation in keratinocytes [183]. Fucoxanthin, a carotenoid isolated from the brown algae *Sargassum siliquastrum*, has been shown to reduce fibroblast apoptosis caused by UVB exposure. Fucoxanthin is found in many other brown algae species, including *Undaria*, *Hijikia*, and *Sargassum*; it has been shown to reduce UVB-induced photoaging in mice by reducing VEGF and MMP-13 expression [184]. Other components of the brown algae *sargassum sagamianum*, such as plastoquinones, sargaquinoic acid, and sargachromenol, have been shown to provide UVB protection, indicating the abundance of photoprotective compounds in algae extract [185].

Proteins, minerals, carbohydrates, polyphenols and vitamins are among the active components found in aloe vera leaf extracts. Aloe vera has various beneficial properties, including antioxidant, antibacterial, anti-inflammatory, and immunity-regulating properties [186]. Because of its antibacterial properties, aloe vera gel can be used to treat skin conditions such as acne vulgaris. Aloe vera was shown to reduce UVA-induced redox imbalance, reduce UVA-associated lipid membrane oxidation, and increase overall cell survival in HaCaT keratinocytes. In a mouse model, oral aloe vera supplementation reduced UVB-induced apoptosis of epithelial cells as well as MMP-2 and MMP-13 formation and the depth of UV-associated wrinkling [187]. Furthermore, research into the effects of combining natural antioxidants for skin topical application has yielded promising results. Topical delivery of aloe vera and curcumin resulted in enhanced antioxidant protection. The benefits of various combinations of phytoproducts have only recently been studied, and they represent a vast area that needs to be explored further [188].

Flavonoids are the most abundant group of active plant compounds; over 5000 flavonoids have been extracted and identified. Many papers have been written about flavonoids and their activities [189]. Flavonoids are derivatives of 1,3-diphenylpropan-1-one (chalcone); the best known groups are the cyclic compounds containing the phenylchromone system (benzopyrone). Flavonoids are found in nature in the form of glycosides (sometimes called bioflavonoids). Flavonoid glycosides are composed of an actual flavonoid (aglycon) and a hydrocarbon. The most common flavonoid glycosides are disaccharide rutinose (D-glucose bound to L-rhamnose) and monosaccharide rhamnose. The pairs quercetin/rutin and diosmetin/diosmin are two examples of aglycons and their corresponding glycosides [190]. The most well-known activity of flavonoids on the skin is associated with their antioxidant

properties. Most phenol-containing flavonoids have a relatively high reduction potential and are forms of resonance-stabilized anion radicals. Flavonoids' scavenging activity is heavily influenced by their structural and physicochemical properties (i.e., logP) [191]. There are always mixtures of many compounds from this group in commonly used plant extracts in the form of aglycones and lipophilic glycosides. This enables a broad spectrum of antiradical activity; commonly used natural flavonoid mixtures scavenge nearly all types of free radicals and ROS [192–194]. It is important that these compounds have a high affinity for singlet oxygen and the ability to reduce tocopheryl and tocotrienol anion radicals [195]. Various factors that induce ROS generation are inhibited by flavonoids, preventing further ROS generation and skin aging (Figure 2). Flavonoids derived from green-tea leaves/seeds and wine grape leaves, as well as oligomers of these compounds found in Mediterranean pine bark (Pycnogenol), are considered to be the most effective for protecting the skin from free radicals. The antiradical activity of flavonoids is supported by their ability to absorb ultraviolet radiation in a wide range, with maximum far ultraviolet B (250–280 nm) and A (350–385 nm). Many flavonoids have a strong affinity for protein structures. On the molecular level, these interactions can be divided into two categories: (1) The first category includes Van der Waals interactions between aromatic rings and lipophilic amino acid residues. Such bonds are particularly preferred in the case of isoflavones and flavonols with planar, polarizable structures that exhibit electron delocalization within all three rings. (2) Flavonoids' hydroxyl or ketone groups form hydrogen bonds with protein chains' carbonyl or hydroxyl groups. The bond's strength is determined by the proton acidity, which is particularly high in flavones and flavonols. Compounds with a carbonyl group at position 4 increase the acidity of hydroxyl groups at position 7, resulting in partial dissociation and ionic-bond formation with basic amino acid residues [189].

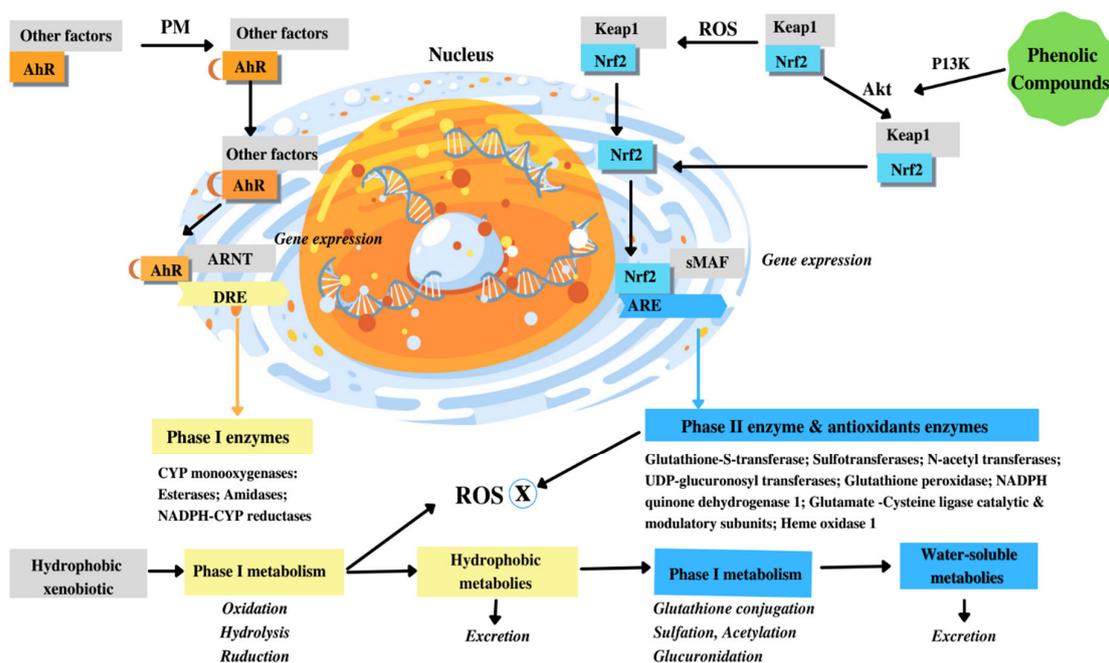


Figure 2. Induction of ROS by various factors and the role of phenolic compounds.

With regard to cosmetic activity, one of the most important properties of flavonoids binding to proteins is their affinity for both types of estrogenic receptors. Isoflavones have a powerful effect. Genistein's affinity for estrogen receptors and 17-estradiol is estimated to be 0.7% and 13.0%, respectively [196]. Binding of genistein or another flavonoid elicits receptor dimerization and appropriate gene induction. Hence, this activity is comparable to typical estrogen activity [197]. A higher plasma concentration of the active property compensates for the relatively low activity (estimated in relation to the activity of estrogenic receptors

and 17-estradiol as 0.025% and 0.8%, respectively) [198]. The anti-inflammatory activity of flavonoids demonstrates their multi-activity. This action is commonly exploited in the field of cosmetology. These compounds' activity stems from their complex interactions with proinflammatory factors and enzymes, which either directly or indirectly participate in the generation or propagation of inflammatory stages. Because of their ability to scavenge free radicals, flavonoids inhibit the oxidative processes of membrane lipids, resulting in arachidonic acid release. Additionally, because of their affinity for proteins and metals, chelation flavonoids (for example, apigenin glycosides found in chamomile) inactivate 5-lipoxygenase and cyclooxygenase, both of which play important roles in the transformation of arachidonic acid into proinflammatory leukotrienes (LTs) and prostaglandins [199]. The effect of flavonoids on blood vessels is important for their anti-inflammatory and anti-irritant properties. Flavonoids reduce tissue congestion and have potent antiedematous properties. Thus, they alleviate inflammatory symptoms [200].

Histamine, which is released during inflammation and allergy, travels through vessels surrounding tissues and basophiles, i.e., blood cells, and significantly increases the vessel permeability [201]. Quercetin, kaempferol, and myricetin all inhibit mast cell histamine release. Additionally, numerous flavonoids influence basophile histamine release [202]; in this case, the inhibition is solely determined by the structure of the flavonoid. Within this scope, only compounds with a ketone group at position 4 and a C2–C3 double-bond in the pyrone ring are active. Hence, this is the same class of compounds that inhibit the TXA2 receptor [203,204]. Glycosides (rutin and naringin) and flavanones (taxifolin and hesperidin) are inactive due to a lack of a C2–C3 bond. Furthermore, cyanidin and catechin, which lack the ketone group, are inactive. Quercetin is considered to be effective for inhibiting histamine release. Morin, which differs from quercetin only in one ring's OH group configuration and does not inhibit histamine release, demonstrates the importance of the position of the OH group for flavonoid activity [205].

Cosmetic Nanoformulation Containing Natural Antioxidants

Treatment with active phytomolecules has recently gained much interest in the field of the pharmaceutical healthcare system. The application of nanotechnology has enhanced the cosmetics field in recent years [206]. Many varieties of nanoparticles, such as polymeric nanoparticles, nanosuspensions, nanoemulsions, liposomes, niosomes, dendrimers, have taken over the field of cosmetic formulations. The use of nanoformulation helped to overcome poor bioavailability; reduced hematological toxic effects; and decrease other side effects, such as alopecia, nausea, vomiting, diarrhea, fatigue, and skin rash [207]. Table 3 lists some of the nanoformulations used in cosmetic applications.

The use of engineered nanomaterials has garnered much attention in cosmetics manufacturers to harvest the potential of nanocosmetics in their formulations [208]. Moreover, great concern regarding their safety has been raised, and much exploration is necessary to determine their efficacy in delivering active ingredients into the skin. The new regulation formed by European Union has passed amendments in its cosmetics directory for safer nanocosmetics to enter into the market, safeguarding the beauty and health of consumers [209].

Table 3. List of nanoformulations in cosmetics.

Plant	Active Compound	System	Application	Reference
<i>White tea</i>	Phenolic compounds	Polymeric nanoparticle	Protect bioactive compounds, enhance subsequent bioactivity and bioavailability	[210]
<i>Centella asiatica</i>	Asiaticoside Madecassoside Asiatic acid Madecassic acid	Nanoencapsulation	Enhance skin protection activity	[211]
<i>Camellia sinensis</i>	Phenolic compounds	Nanoemulsion	Improve emulsion stability	[212]
<i>Hibiscus sabdariffa</i>	Polyphenolic compounds	Liposome	Protect and deliver water-soluble functional compounds	[213]
<i>Curcuma longa</i>	Phenolic compounds (curcumin)	Liposome, ethosome, transferosome	Better skin penetration and protect skin from hydration	[214]
<i>Fraxinus angustifolia</i>	Phenolic compounds	Ethosome	Increase intracellular antioxidant activity	[215]
<i>Aloe vera</i>	Phenolic compounds	Liposomes	Enhance bioavailability and increase the collagen synthesis	[216]
<i>Orthosiphon Stamineus</i>	Phenolic compounds (rosmarinic acid, eupatorin)	Liposome (lecithin)	Improve the extract's solubility and permeability	[217]
<i>Vitis vinifera</i>	Phenolic compounds	Nanoemulsion	Improve solubility and antioxidant efficiency	[218]
<i>Panax quinquefolius</i>	Saponin (Ginsenoside)	Liposome	Increase intracellular antioxidant activities	[219]
<i>Polygonum aviculare</i>	Phenolic compounds (quercetin and myricetin)	Liposome	Improve transdermal drug delivery	[220]
<i>Phyllanthus urinaria</i>	Phenolic flavonoids, saponins compounds	Nanoemulsion	Improve drug delivery to the skin	[221]
<i>Achyrocline satureioides</i>	Flavonoid compound (quercetin)	Nanoemulsion	Increase in drug absorption on skin	[222]

10. Limitations of Natural Antioxidants in Skincare

Topical antioxidants, mostly in the form of cosmetic preparations, have been widely used and are safe. However, the practical relevance of the effects described here cannot be proven explicitly, because there is a scarcity of clinical data, and the available data are of limited relevance. Furthermore, the data and publications available frequently do not indicate what galenic concept the preparations were based on or whether the cutaneous bioavailability of antioxidants in the target compartment was validated. Nonetheless, the data provide interesting points for dermatologists to consider with regard to topical therapy. Topical application of vitamins and other natural ingredients can cause contact dermatitis, erythema multiforme, and xanthomatous reactions in rare cases. However, due

to the lack of separation techniques, many plant extracts are yet to be investigated for their compounds [223]. Although these compounds are safer than synthetic antioxidants, cosmetics containing natural antioxidants are more expensive than those containing synthetic antioxidants. Furthermore, even though preliminary research shows promising effects, validation with clinical results is necessary. Natural antioxidants are prone to degrade, and their bioavailability is limited by low absorption. Polyphenols present in herbs have low stability, and their sensitivity to light and heat limits their use in cosmetics. Cosmetics containing plant extracts in contact with skin causes allergic reactions. Moreover, various forms of adverse effects may occur due to antioxidants, such as acute toxicity, skin and eye irritation, skin sensitization, and photosensitization.

11. Conclusions

Consumers are increasingly turning away from synthetic chemicals in beauty and cosmetic products in favor of natural alternatives. Plant extracts can be used in cosmetic science to beautify and maintain the physiological balance of human skin due to the inherent economic potential in the exploitation of natural resources in ecosystems. Additionally, they are biodegradable and have lower toxicity than synthetic cosmetic ingredients. However, several by-products of plant-processing industries (for example, the food industry) pose a significant disposal problem. Some of these by-products, however, are promising sources of compounds with biological properties suitable for cutaneous application. Thus, natural plant extracts derived from both naturally occurring plants and industrially processed plants can be used to create natural topical antioxidants, lighteners, and preservatives, maximizing the utility of products that are currently underutilized or discarded. As primary ingredients in cosmetics, vitamins and antioxidants are extremely popular. There is substantial scientific evidence, as well as anecdotal experience, of the benefits of these more bioactive cosmetics for consumers. To be beneficial, an ingredient must be stable in production, storage, and use; nontoxic to the consumer; and active at the target site once applied. More research is needed to improve the penetration of these bioactive cosmetics into the skin. Perhaps instrumentation, e.g., iontophoresis, is needed to improve delivery into the skin. Market-driven economics clearly suggest that antioxidant and vitamin formulations are popular and well liked. However, the instability and hydrophilic nature of vitamins limit their use. In recent years, drug delivery systems have been developed, and they appear to overcome these limitations through improved encapsulation and targeted delivery. Furthermore, research has led to a better understanding of these molecules, which has resulted in the development of more stable derivatives with different chemical properties. Typically, vitamins are effective for treating hyperpigmentation, differentiating keratinocytes, preventing skin photodamage, and improving dermal–epidermal junction cohesion. Flavonoids, multi-active ingredients found in many cosmetics, are primarily used for their antioxidant and soothing properties. Despite their multifunctional properties, flavonoids are underutilized. The objective of this study was to discuss the potential applications of flavonoids as the main active ingredients in cosmeceuticals. We discussed major potential antioxidants from plant sources that can be used in cosmetics. Although the use of antioxidants is promising, there are limited clinical trials in humans examining the role of antioxidants in preventing skin aging. Thus, further experimental data can be explored in the future, and synergistic effects are recommended for better efficacy in combination.

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