Review Article

Interprof. J. Health Sci. 2025, 23(1): IJHS-0685

Molecular Mechanisms of Skin Photoaging and the Therapeutic Applications of Plant-Derived Bioactive Compounds

Abhiruj Navabhatra[1, *], Chonnipha Yangchaiya[2], Apinut Yangchaiya[2], Nirawit Sermsutjarit[1], and Taku Sakanoue[3]

[1]College of Pharmacy, Rangsit University, Pathum Thani 12000, Thailand
[2]Suankularb Wittayalai Thonburi School, Bangkok 10500, Thailand
[3]Section of Host Defences, Institute of Natural Medicine, The University of Toyama, Toyama 9300194, Japan
*Corresponding author: E-mail: Abhiruj.c@rsu.ac.th
Received 11 March 2025; Revised 28 May 2025; Accepted 30 May 2025

Abstract: Chronic exposure to ultraviolet (UV) radiation accelerates skin aging, leading to structural and functional deterioration characterized by dryness, irregular pigmentation, lentigines, hyperpigmentation, wrinkles, and reduced elasticity. Increasing attention has been given to plant-derived natural compounds for their potential therapeutic applications in mitigating UV-induced skin photoaging. This review critically examines the cellular and molecular mechanisms underlying photoaging and explores the therapeutic potential of plant-based natural ingredients. UV radiation induces photoaging through direct damage to cellular macromolecules and indirect oxidative stress mediated by reactive oxygen species (ROS). ROS-driven signaling cascades contribute to key pathological processes, including inflammation, extracellular matrix degradation, apoptosis, mitochondrial dysfunction, and immune suppression. Additionally, recent evidence suggests that UV exposure affects adipose tissue homeostasis and modulates transient receptor potential cation channel V, further exacerbating photoaging. Over the past few decades, mechanistic studies have identified multiple therapeutic targets, paving the way for novel interventions. This review highlights promising plant-derived bioactive compounds that counteract UV-induced skin damage through antioxidant, anti-inflammatory, and photoprotective mechanisms. By elucidating the molecular pathways involved in photoaging and evaluating the efficacy of natural product-based interventions, this work provides insights into potential strategies for preventing and managing UV-induced skin deterioration.

Keywords: Photoaging; ultraviolet (UV) radiation; reactive oxygen species (ROS); plant-derived bioactive compounds; therapeutic interventions

INTRODUCTION

Prolonged exposure to ultraviolet (UV) radiation is a primary cause of photoaging, a skin condition marked by various physical, biochemical, and cellular changes (1). The term "photoaging" was first coined by Kligman and Kligman in 1986 and is often used interchangeably with "dermatoheliosis" (2). The process begins when UV radiation is absorbed by chromophores in the skin, which triggers a series of chemical reactions. These reactions ultimately lead to visible signs of photoaging and can contribute to skin cancer development (3). There are three types of UV radiation: UVA (320–400 nm), UVB (280–320 nm), and UVC (100–280 nm). Although UVC radiation is highly energetic and harmful, it is absorbed by the atmosphere, protecting the Earth's surface from its effects. In contrast, UVA and UVB radiation can penetrate the ozone layer and reach the skin. While these types of radiation have less energy and do not

ionize matter, they can still cause significant damage to skin molecules (4). UV radiation causes skin damage, which leads to alterations in the dermal extracellular matrix (ECM). These changes include wrinkles, skin sagging, rough texture, uneven pigmentation, and histological modifications, including thickened epidermis and altered connective tissue. Disruption of the balance between ECM components—such as collagen, proteoglycans, and glycoproteins—contributes to photoaging, particularly in dermal fibroblasts. While the skin has antioxidant defenses to neutralize reactive oxygen species (ROS) and free radicals, these defenses can be overwhelmed by excessive UV exposure (5). This leads to oxidative damage to key cellular components, such as proteins, lipids, and DNA. The ROS generated by oxidative stress can result in cell death through apoptosis or necrosis. The accumulation of ROS plays a major role in both intrinsic aging and photoaging of the skin, contributing to the onset of skin cancers and other inflammatory skin conditions (6). Research has shown that in photoaged skin, collagen degradation occurs through the inhibition of collagen production by matrix metalloproteinases (MMPs), a group of zinc-dependent enzymes that breakdown ECM components. MMPs are classified into various subgroups on the basis of their structure and substrate specificity, such as collagenases, gelatinases, stromelysins, matrilysins, and membrane-type MMPs (MT-MMPs) (7). ROS influence MMP gene expression through signaling pathways. MMP production is typically triggered by extracellular factors such as growth factors, cytokines, tumor promoters, and UV radiation. Excessive MMP expression has been linked to tissue remodeling, repair, and ECM degradation, with MMP-2 and MMP-9 playing key roles in wrinkle formation and skin thinning (7). Photoprotection refers to the mechanisms developed by organisms to minimize UV damage. These mechanisms are supported by both organic and inorganic substances, such as melanin, produced by various terrestrial and aquatic organisms (8). Several photoprotective compounds have been identified, including scytonemins (found in cyanobacteria), mycosporine-like amino acids (MAAs, found in cyanobacteria, algae, and animals), phenylpropanoids, flavonoids (in higher plants), melanins (in humans, animals, and some bacteria), and other UV-absorbing substances from different organisms. Current treatments, such as topical retinoids and chemical peels, often cause adverse effects, prompting interest in plant-based natural products. These natural compounds, rich in polyphenols, flavonoids, and antioxidants, demonstrate potent UV-protective properties by targeting mechanisms such as ROS generation, inflammation, DNA damage, and apoptosis. Notable examples include fucoidan, luteolin, β-carotene, parthenolide, ginsenosides, and epigallocatechin gallate, all of which modulate signaling pathways like MAPK and NF-κB. Studies using *in vitro* and *in vivo* models show that these agents reduce oxidative stress, inhibit MMPs, and protect against photoaging (2). There is also increasing interest in the use of botanicals for skin protection (9). Research suggests that natural products, especially UV filters, could play a significant role in the future of cosmetics. Many natural compounds show promise as sunscreen additives in the cosmetics industry. This review aims to provide a comprehensive summary of the latest advancements in understanding skin photoaging and its associated pathologies (9, 10). By elucidating the underlying signaling pathways involved, we hope to assist researchers in identifying potential therapeutic targets for managing photoaging. Furthermore, we highlight the potential of plant-based natural ingredients as effective treatments for UV-induced premature skin aging. The growing demand for incorporating natural products into sunscreen formulations is driven by their photoprotective and antioxidant properties, as well as their favorable safety profiles, making them ideal candidates for preventing UV-induced skin damage and skin cancers (11).

PATHOLOGICAL MECHANISMS OF SKIN PHOTOAGING

Photoaging in human dermal fibroblasts is triggered by UV, infrared, and blue light, leading to DNA damage and oxidative stress. This results in the oxidation of biomolecules, disrupting cellular functions and degrading proteins, lipids, and DNA (12). Antioxidants help maintain homeostasis by neutralizing ROS, whereas protein degradation mechanisms such as the ubiquitin–proteasome system and autophagy mitigate oxidative damage. Additionally, epigenetic modifications and genomic instability exacerbate the progression of photoaging (13).

Interaction of UV Radiation with the Skin

The dermal extracellular matrix is composed of a complex network of macromolecules, including collagen, elastic fibers, glycoproteins, and glycosaminoglycans, which collectively confer structural integrity, strength, and flexibility to the skin. Chronic exposure to UV radiation induces the degradation of type I and type III collagens—the predominant collagen types in the dermis—which play pivotal roles in the formation of wrinkles and other characteristic signs of photoaging. Upon absorption by the skin, UV radiation precipitates a cascade of pathological changes in both the epidermis and dermis, driven by both direct and indirect interactions with cellular biomolecules (14). Unlike other forms of radiation, UV radiation is not absorbed by molecular oxygen in the atmosphere, thereby posing no inhalation risk. UVB radiation, which primarily affects the superficial layers of the skin, induces damage to various cellular components, including DNA, aromatic amino acids in proteins, NADH, NADPH, flavins, quinones, porphyrins, carotenoids, urocanic acid, and melanin (2). Notably, UVB radiation is the principal cause of sunburn. In contrast, UVA radiation, although approximately 1,000 times less effective than UVB at causing erythema, plays a significant role in the pathogenesis of skin photodamage and photoaging. This is due to its deeper penetration into the epidermis and dermis, where it contributes to the degradation of the extracellular matrix—a crucial determinant of skin structural integrity (4). Melanin, a vital chromophore in the skin, serves as a protective mechanism by absorbing UV radiation and converting its energy into heat. The degree of photoprotection provided by melanin is contingent upon its distribution and density within the skin, which are factors that vary among individuals. Epidemiological studies suggest that individuals with darker skin phenotypes are up to 500 times less likely to develop UV-induced nonmelanoma skin cancers than are those with fairer skin types (15).

Effects of UV Radiation on DNA, RNA, and Proteins

Ultraviolet radiation (UVR), particularly UVB, causes cellular damage through direct and indirect mechanisms, accelerating skin photoaging. UVB radiation penetrates the epidermis, leading to DNA damage through the formation of cyclobutane–pyrimidine dimers (CPDs) and pyrimidine–pyrimidone (6-4) photoproducts, particularly at methylated cytosine sites. These mutations, known as the "solar-UV signature," can cause premutagenic lesions and, if unrepaired, result in UV-specific mutations (16). CPDs are particularly oncogenic, and their accumulation can lead to apoptosis or uncontrolled keratinocyte growth, contributing to tumor formation (17). UV radiation also damages mRNAs and RNAs, resulting in the production of dysfunctional proteins. Proteins rich in aromatic amino acids, such as tryptophan (Trp) and tyrosine (Tyr), undergo photoionization, generating free radicals and inducing oxidative stress, which leads to cellular damage (2). Additionally, UV-excited photosensitizers produce singlet oxygen, further modifying proteins. Modified proteins can aggregate, leading to diseases such as skin aging. To counteract this, cells activate antioxidant systems and protein degradation pathways, including the ubiquitin–proteasome system (12).

UV Radiation, ROS, and Skin Photoaging

UV radiation causes direct and indirect skin damage by generating ROS through endogenous photosensitizers. ROS, including superoxide anions, hydroxyl radicals, peroxyl radicals, and hydrogen peroxide, are byproducts of cellular metabolism. Excessive ROS accumulation leads to oxidative stress, damaging cellular components such as DNA, proteins, and lipids and contributing to diseases such as cancer and aging (18). Antioxidant enzymes, including superoxide dismutase and catalase, regulate ROS levels, but UV radiation disrupts this balance, increasing ROS in the epidermis and dermis. Photosensitizers such as DNA, aromatic amino acids, and melanin absorb UVB radiation, with melanin offering partial protection. However, excessive UV absorption photoisomerizes urocanic acid, triggering ROS production. UV exposure also activates NADPH oxidase, generating superoxide anions, and stimulates melanin production, further increasing ROS levels. These ROS contribute to photoaging by inducing inflammation, activating cell proliferation pathways, and damaging the extracellular matrix, impairing connective tissue integrity (19).

UVA Radiation and Mitochondrial Dysfunction: Mechanisms of Skin Damage and photoaging

UVA radiation penetrates deeply into the skin, affecting both the epidermis and dermis. The primary harmful effect of UVA exposure is the generation of ROS, which cause oxidative stress and lead to cellular changes such as lipid peroxidation, DNA damage, and protein carbonylation. These alterations can result in mutations, cell death, dermal remodeling, inflammation, and impaired immune function. External factors such as pollutants and visible light may enhance the damaging effects of UVA radiation. Gene expression studies indicate that UVA exposure alters genes, making dermal fibroblasts particularly vulnerable. Additionally, UVA causes pigmentary changes in the skin, a key sign of photoaging, especially in individuals of Asian descent. Mitochondrial dysfunction, which is induced by UV radiation, plays a critical role in skin photoaging (2). UV exposure causes mutations in mitochondrial DNA, disrupting the electron transport chain and reducing ATP production in dermal fibroblasts. This decline in energy production activates processes that impair cellular functions, including caspase activation, membrane depolarization, and cytochrome C release. Disruption increases mitochondrial oxidative stress by increasing ROS levels. Mitochondria have antioxidant defense systems, but UV radiation targets Nrf2, a key regulator of these defenses, impairing their effectiveness. As a result, mitochondria are becoming a primary therapeutic target in efforts to combat skin photoaging (20).

MAPK Signaling Pathway in UVB-Induced Inflammation, Collagen Degradation, and Apoptosis

The MAPK signaling pathway, involving ERK, p38 MAPK, and JNK, is activated by various stimuli. The ERK pathway responds to mitogenic signals, whereas p38 and JNK are triggered by stressors such as UV-B radiation. Oxidative stress plays a key role in MAPK activation, as shown by the inhibition of MAPK sub-pathways with antioxidants (21). ROS initiate the phosphorylation of cytokine receptors such as EGFR and Ras, activating upstream proteins. MAPK activation leads to the translocation of MAPK proteins to the nucleus, where they activate transcription factors such as AP-1, NF-κB, COX-2, and c-Myc, contributing to photodamage (22). UVB-induced reactive oxygen species (ROS) activate the mitogen-activated protein kinase (MAPK) pathway, which promotes inflammation by enhancing the infiltration of inflammatory mediators and inducing epidermal hyperplasia. In response, keratinocytes secrete proinflammatory cytokines such as interleukin-1 (IL-1), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6), as well as inflammatory mediators including intercellular adhesion molecule-1 (ICAM-1) and cyclooxygenase-2 (COX-2). Notably, IL-6 levels typically peak within 12 hours following severe sunburn.

Cytokines also promote fibroblast production of MMPs, which degrade the ECM and collagen. UVB radiation reduces the ECM content by decreasing collagen synthesis or increasing collagen degradation (23). TGF-β stimulates collagen synthesis, but UVB activates Smad7, which inhibits this process. UVB also activates MMPs via the MAPK pathway, leading to collagen breakdown. The transcription factor AP-1, which is activated by UVB, plays a key role in MMP production, further contributing to collagen degradation and loss of skin integrity. NF-κB transcription factors regulate UVB-induced inflammation, immune responses, and cell proliferation. Normally inactive in the cytoplasm and bound to IκB, NF-κB is activated by UVB-induced ROS, which activate IKK, leading to IκB degradation. This allows NF-κB to translocate to the nucleus and initiate transcription. UVB irradiation induces the formation of sunburn cells (SCs), which are keratinocytes that undergo apoptosis. This is driven by UVB-induced DNA damage, TNF-α, Fas activation, and ROS. ROS activate the mitochondrial apoptotic pathway, triggering cytochrome C release, apoptosome formation, and caspase-mediated apoptosis. This process is regulated by the Bcl-2 family of proteins, and p38 MAPK activation promotes the redistribution of proapoptotic proteins such as Bax to the mitochondria, facilitating apoptosis (24).

Immunosuppression in Skin Photoaging

UV radiation weakens the immune response in skin cells, increasing tumor susceptibility in individuals with compromised immune systems. UV exposure disrupts both cellular and humoral immune functions by reducing the number of epidermal Langerhans cells (LCs) and impairing their migration and antigen-presenting abilities. UV radiation also induces the conversion of urocanic acid from its trans to cis form, further hindering LC function (25). Additionally, UV radiation decreases the costimulatory molecule B7 and triggers the release of IL-10, an immunosuppressive cytokine, from keratinocytes. This depletion of LCs and the release of proinflammatory cytokines activate regulatory T cells (TREGs), shifting the Th1/Th2 balance toward Th2 dominance and enhancing the production of IL-12, thereby sustaining an immunosuppressive environment (26).

UV Irradiation and Skin Adipose Tissue

Skin adipose tissue, consisting of dermal white adipose tissue (DWAT) and subcutaneous white adipose tissue (SWAT), plays a crucial role in skin photoaging. Chronic UV exposure leads to DWAT thinning and fibrosis, which contributes to rough skin texture and wrinkles. UV radiation also affects SWAT metabolism, reducing lipid accumulation and altering metabolic processes, possibly through soluble factors such as IL-6, IL-8, and monocyte chemotactic protein-3. The resulting reduction in lipid content leads to skin atrophy and wrinkle formation (2).

Role of MicroRNAs (miRNAs) and Advanced Glycation End Products (AGEs) in Skin Photoaging

DNA methyltransferase 1 (DNMT1) is critical for maintaining DNA methylation, and aging alters global DNA methylation patterns in skin cells. MicroRNAs, such as miR-217 and miR-23a-3p, regulate fibroblast senescence by targeting DNMT1 and enzymes involved in hyaluronic acid synthesis, highlighting their role in photoaging. UVB radiation also disrupts collagen regulation through miR-34, leading to skin weakness and reduced elasticity. Additionally, glycation results in the formation of AGEs, which stiffen dermal matrix proteins, contributing to skin aging. Glycated elastin fibers in solar elastosis aggregate abnormally and further promote photoaging (13).

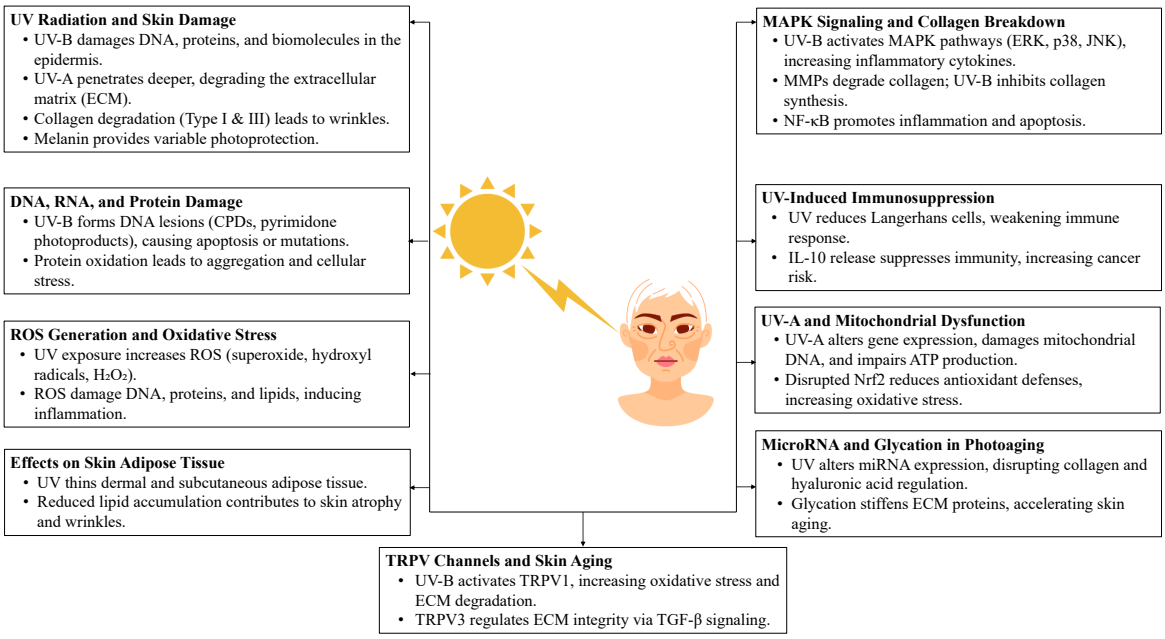

Figure 1. Illustrates the pathomechanisms of UV-induced photoaging.

Role of Transient Receptor Potential Cation Channel V (TRPV) in Skin Photoaging

TRP ion channels, including those in the TRPV subfamily, are involved in sensory processes and play a key role in skin photoaging. UV-B exposure increases the calcium ion concentration via TRPV1, leading to Nrf2 degradation and oxidative stress, which accelerates photoaging. In HaCaT cells, UV radiation activates Src kinase, causing TRPV1 trafficking to the membrane and increasing MMP-1 levels. TRPV3, which is regulated by the TGF-β pathway, maintains skin health by modulating extracellular matrix production. Further research, particularly animal studies, is needed to assess the therapeutic potential of TRP channels in photoaging (2). A range of interconnected factors and underlying mechanisms have been implicated in the pathogenesis of photoaging. These contributing elements are comprehensively summarized in Figure 1.

PLANT-BASED NATURAL PRODUCTS: A POTENTIAL THERAPY FOR UV-INDUCED PHOTOAGING

The use of natural ingredients in cosmetics has a long history, dating back to ancient civilizations. Today, the focus is on bioactive natural substances that protect the skin from external factors, particularly UV radiation and free radicals, both of which contribute to premature aging—a major concern for many (27). Plant-derived antioxidant compounds are especially appealing because they neutralize free radicals (28). One enzyme responsible for skin aging is elastase, which breaks down elastin in the dermis, reducing skin elasticity and causing wrinkles. To counteract this, antiaging cosmetics containing natural elastase inhibitors are essential. As we age, collagen loss also contributes to skin sagging and wrinkling. UV exposure increases MMP-1 expression, leading to collagen breakdown and accelerating wrinkle formation. Therefore, natural agents that inhibit AP-1 and MMPs are key to effective cosmeceuticals. Furthermore, hyaluronidases breakdown hyaluronic acid (HA) and its binding ligands, crucial components of the ECM. As we age, HA levels decrease, leading to skin dehydration and a loss of firmness, both of which contribute to wrinkles. Inhibiting HA degradation helps maintain healthy skin and its connective tissue (7).

Plant-based Natural Products and Their Bioactive Compounds

The incorporation of natural compounds into cosmetic formulations has significantly increased, primarily because of their potential to enhance their cosmeceutical efficacy (29). A wide array of natural products, particularly those rich in phenolic compounds, flavonoids, and antioxidants, are crucial for mitigating the detrimental effects of UV radiation by neutralizing UV-induced free radicals. Plant secondary metabolites are commonly classified into distinct categories on the basis of their molecular structure and biosynthetic pathways, offering a diverse range of bioactive properties that contribute to skin health and protection (30, 31) (Table 1).

Phenolic Compounds (PCs)

Phenolic compounds (PCs) constitute a large and diverse class of plant secondary metabolites that are classified into three primary categories: phenolic acids, flavonoids, and high-molecular-weight polyphenols. To date, more than 8,000 distinct phenolic structures have been identified (32). PCs confer a wide array of skin health benefits, including photoprotection, anti-inflammatory properties, antiaging effects, and photochemoprevention. These therapeutic effects are largely attributed to the chemical structure of PCs, wherein the phenolic rings and hydroxyl groups contribute to their potent antioxidant and free radical scavenging capabilities (33). The antioxidant mechanisms of PCs include the inhibition of ROS biosynthesis, the trapping of ROS, and the reduction of metal ions that catalyze ROS production. While the exact anti-inflammatory mechanisms of PCs remain under investigation, it is widely suggested that they exert their effects by neutralizing free radicals, inhibiting immune cell activity, and modulating proinflammatory mediators such as IL-6 and prostaglandin E2 (PGE2). Additionally, PCs are believed to modulate transcription factors, such as NF-κB and Nrf2, and influence eicosanoid synthesis (34). In terms of their antiaging properties, PCs regulate gene expression related to skin health, enhance oxidative stress protection, and promote skin cell renewal. Furthermore, they contribute to the maintenance of skin structure by stimulating the synthesis of elastin

and collagen, inhibiting MMPs, and suppressing the activity of collagenases and elastases. Certain plant-derived PCs also play a role in activating DNA repair mechanisms to address damage within skin cells. Nonflavonoid PCs, including vanillic acid, caffeic acid, ferulic acid, and resveratrol, have been demonstrated to be able to protect the skin from UV-induced damage. In particular, caffeic and ferulic acids protect phospholipid membranes from UV-induced peroxidation and regulate antioxidant defenses, including glutathione (GSH) and catalase. Additionally, these compounds provide protection against UVA-induced melanogenesis through indirect modulation of the Nrf2 pathway in melanoma cells. Flavonoids, another prominent subclass of PCs, are especially recognized for their UV-protective properties. These compounds absorb UV radiation and mitigate ROS-induced oxidative damage. Flavonoids protect skin cells from UV damage via UV absorption, antioxidant activity, and the modulation of various cellular signaling pathways. Furthermore, flavonoids reduce the activity of MMPs in skin cells through both direct inhibition and induction by MMP inhibitors. Epigallocatechin-3-gallate (EGCG), a flavonoid present in green tea, is particularly notable for its protective effects against UV-induced skin damage. EGCG scavenges various ROS, including superoxide and hydroxyl radicals, and has been shown to protect against UV-induced inflammation, wrinkling, and aging through the modulation of the NF-κB and MAPK pathways. It also inhibits MMP-2, MMP-9, and neutrophil elastase. Moreover, EGCG has been reported to protect against photocancerogenesis by reducing tumor incidence and growth in UVB-exposed mouse models (35).

Resveratrol

Resveratrol, a polyphenol found in grape skins, seeds, and red wine, is known for its strong antioxidant properties and potential to promote longevity by activating sirtuin 1 (SIRT1) and other sirtuins, enzymes that regulate metabolism and gene expression. SIRT1 has been linked to improved mitochondrial function, cancer suppression, and lifespan regulation in various species, including humans. Research has shown that resveratrol prevents cell death, enhances cell proliferation, and reduces oxidative damage. It is naturally produced by plants such as grapes and berries to protect against UV radiation and pathogens. Preclinical studies indicate that resveratrol extends lifespan in yeast, nematodes, and fruit flies while also improving age-related markers such as inflammation and vascular function in mice. Resveratrol has shown potential in preventing Alzheimer's disease by blocking NF-kB proteins and protecting neurons (36). It also enhances physical performance, bone health, and mental well-being, acting similarly to phytoestrogens to support bone density and prevent osteoporosis (37). Additionally, it offers cardiovascular protection, improves kidney function, and helps delay cellular aging by activating beneficial genes and inhibiting others. In oncology, clinical trials have shown that resveratrol promotes the apoptosis of malignant cells in colorectal cancer patients. It also regulates cysteine levels and enzymes such as MnSOD, providing neuroprotection. The anti-inflammatory effects of resveratrol may benefit conditions such as diabetes, improving insulin sensitivity and protecting against photoaging (38). Despite its many benefits, the use of resveratrol is limited by its low solubility, bioavailability, and stability. While it shows promise in extending lifespan in certain organisms, further research is needed to confirm these effects in humans (39).

Curcumin

Curcumin has shown promise in slowing the aging process by reducing age-related inflammation. Studies in model organisms such as Drosophila, mice, and nematodes indicate that curcumin, along with its metabolite tetrahydro-curcumin, can extend lifespan. In nematodes, curcumin increased longevity by reducing reactive oxygen species production through specific genes. In Drosophila, curcumin supplementation prolonged lifespan by decreasing malondialdehyde and lipofuscin levels while increasing superoxide dismutase (SOD) activity. Additionally, curcumin improves endothelial function and reduces arterial stiffness, highlighting its potential for treating age-related vascular changes. It is widely used to manage inflammatory conditions and exhibits strong anticancer activity, particularly against cancer stem cells (40, 41).

Table 1. Plant-derived natural compounds have been shown to mitigate signs of aging by increasing skin elasticity and reducing the formation of wrinkles.

Plant/compound	Mechanism	References
Alchemilla mollis	Inhibits AP-1 activation, reduces the levels of c-Jun and c-Fos, and enhances the Nrf2 signaling pathway in NHDF cells.	(61)
Allium sativum	Inhibits UV-induced increases in SA-β-gal levels and the UV-induced reduction of SIRT1 activity in HaCaT cells.	(62)
Andrographis paniculata	Stimulates VEGF production and upregulates integrin β1 expression in human epidermal stem cells.	(59)
Azadirachta indica	Downregulates c-Jun and c-Fos proteins and upregulates TGF-β expression in NHDF cells.	(63)
Camelia sinensis	*C. sinensis* reduces UVB-induced ROS production in fibroblasts and boosts antioxidant enzyme expression (SOD, CAT, and GPX) to combat oxidative stress. It also activates the Nrf2 pathway by enhancing its transcription and nuclear translocation, strengthening antioxidant defenses.	(64)
Kochia scoparia	Activation of PPAR α/γ inhibits UV-induced MMP and ROS increases. *K. scoparia* and *Rosa multiflora* extracts (KR), acting as PPAR α/γ agonists, improved dermal thickness and fibroblast recovery by increasing TGF-β and procollagen 1 while reducing MMP-13. With minimal epidermal effects, except for reduced IL-1α expression, KR shows promise as a safe treatment for photoaging.	(65)
Polysaccharides from *Panax ginseng*	Attenuates UV-induced MMP-1 expression via AP-1 transactivation in HaCaT cells.	(66)
Spatholobus suberectus	It inhibited elastase activity, suppressed ROS, and reduced cellular damage in UVB-exposed HaCaT cells. SSE regulated the expression of MMPs, TIMP-1, COL1A1, elastin, and HAS2, while also inhibiting UVB-induced phosphorylation of MAPK, NF-κB, and c-Jun.	(67)
Essential oil from *Zingiber montanum*	*Z. montanum* oil exhibited a time- and concentration-dependent ability to scavenge ROS radicals and demonstrated potential wound-healing properties. Additionally, it reduced MMP expression, promoted type I procollagen synthesis, and inhibited elastase activity.	(68)

Terpenoids

Terpenoids contribute to the antiaging effects of essential oils, which have been shown to treat anxiety, dementia, and other neurological disorders through *in vitro*, *in vivo*, and clinical studies. The therapeutic efficacy of these oils is due to their diverse bioactive compounds. Aromatherapy has been found to improve cognitive function in Alzheimer's patients and offers significant health benefits, particularly for cognitive performance. The effects of aromatherapy are enhanced by various application methods, including topical use, inhalation, and ingestion. Terpenoid molecules, which are small and lipophilic, can pass through the nasal mucosa, enter the bloodstream, cross the blood–brain barrier, or penetrate the skin. Ursolic acid, a triterpenoid found in fruits and herbs such as apples, cranberries, peppermint, and rosemary, is known for its hepatoprotective effects and role in modulating antiaging biomarkers (42, 43).

Carotenoids

Carotenoids are a diverse class of tetraterpenoids characterized by a central carbon chain with alternating single and double bonds, complemented by various cyclic or acyclic end groups. This conjugated system of double bonds endows carotenoids with several bioactive properties, including photoprotective effects (44). Carotenoids are capable of absorbing UVR, acting as antioxidants by scavenging reactive species such as peroxides and singlet molecular oxygen generated during photooxidation and inhibiting lipid peroxidation. Furthermore, carotenoids can induce cellular protective responses through the activation of phase 2 cytoprotective genes. Lycopene, one of the most extensively investigated carotenoids, is particularly efficacious in neutralizing singlet oxygen radicals, which are among the most deleterious ROS generated in the skin upon exposure to sunlight. The topical application of lycopene has been shown to mitigate UVB-induced skin damage by inhibiting the enzymatic activities of ornithine decarboxylase and myeloperoxidase, both of which contribute to the pathophysiology of UVB-induced damage. In addition to its antioxidant effects, lycopene also has anti-inflammatory properties and prevents the activation of caspase-3, a key mediator in the apoptotic pathway. Notably, a lycopene-rich tomato extract has been successfully developed and formulated into a sunscreen lotion, demonstrating its potential for topical photoprotection. Oral administration of lycopene also offers photoprotective benefits. In a clinical study, daily consumption of 16 mg of lycopene for 10 weeks resulted in a 40% reduction in skin erythema induced by solar radiation (45). Furthermore, supplementation with 24 mg of β-carotene per day or a carotenoid mixture comprising β-carotene, lutein, and lycopene (8 mg each per day) for 12 weeks was found to provide significant protection against UV-induced erythema (46).

Alkaloids

Alkaloids represent a diverse class of naturally occurring compounds distinguished by the presence of a nitrogen atom within a heterocyclic ring. Among the alkaloids investigated for their photoprotective and antioxidant properties are caffeine, theophylline, and theobromine. Notably, caffeine has been the subject of extensive research in the context of photoprotection (47). Both topical and oral administration of caffeine have demonstrated significant anticancer effects. In addition, caffeine has been shown to mitigate skin carcinogenesis in murine models exposed to UVR (48). Furthermore, the oral consumption of caffeine has been associated with reductions in tumor incidence, multiplicity, and volume while selectively inducing apoptosis in UVB-induced skin tumors. Epidemiological studies suggest a correlation between increased caffeine intake and a reduced risk of skin cancer, particularly basal cell carcinoma (49, 50). This protective effect is hypothesized to be mediated by enhanced apoptosis in damaged cells while sparing normal epidermal cells. In recent investigations, the efficacy and safety of sunscreen formulations containing caffeine have been evaluated. *In vitro* analyses revealed that these formulations presented increased sun protection factor (SPF) values, with subsequent *in vivo* studies confirming these results. Caffeine was found to act synergistically with traditional UV filters, such as ethylhexyl methoxycinnamate, avobenzone, and titanium dioxide, functioning both as a photoprotector and a photostabilizer (51).

Consequently, caffeine has emerged as a promising bioactive compound in the formulation of sunscreen products.

Thymus vulgaris

Thymus vulgaris L., or thyme, a member of the Lamiaceae family, has been evaluated in a double-blind, placebo-controlled clinical trial for its potential to slow skin aging (31). This study revealed that a phytocosmetic formulation containing *T. vulgaris* significantly reduced facial wrinkles and expression lines and promoted facial shape remodeling in female volunteers without causing skin reactions or discomfort. These effects are linked to increased adiponectin production and peroxisome proliferator-activated receptor gamma (PPAR-γ) expression, resulting in soft tissue enhancement similar to that of soft tissue fillers. This action is attributed to the presence of carvacrol and thymol, isomers known to increase PPAR-γ expression. Thymol, a phenolic compound found in various plants, has antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. It has potential in treating metabolic disorders, atherosclerosis, cardiovascular diseases, and conditions affecting the kidneys, lungs, liver, immune system, gastrointestinal tract, and nervous system. Thymol works by modulating molecular targets such as PPAR-γ, pAMPK, PPAR-α, and protein kinase A (PKA). Topical thymol alleviates atopic dermatitis, reduces inflammation, and improves wound healing in psoriasis models. Lipid nanoparticles containing thymol enhance drug delivery, reduce toxicity, and exhibit anti-inflammatory effects. Carvacrol, which shares similar sources and pharmacological effects with thymol, also modulates PPAR-γ. It inhibits tyrosinase, increases skin thickness, and promotes human keratinocyte proliferation, potentially benefiting skin aging. Studies suggest that combining thymol and carvacrol yields superior results compared with using them individually, supporting their potential in the development of effective antiaging cosmetic products from *T. vulgaris* (10).

Panax ginseng

Panax ginseng, a member of the Araliaceae family, has been used in traditional medicine for over 2,000 years in countries such as Korea, China, and Japan. Its pharmacological effects are attributed to ginsenosides, which, along with other compounds such as polysaccharides, peptides, and phytosterols, influence lipid and carbohydrate metabolism, angiogenesis, and various physiological systems, including the neuroendocrine, cardiovascular, immune, and neurodegenerative systems. In dermatology, ginseng has been shown to inhibit melanogenesis, protect against UV radiation, promote wound healing, reduce wrinkling, improve skin hydration, and alleviate atopic dermatitis, making it a promising ingredient for antiaging skincare. Clinical studies have demonstrated the photoprotective effects of an enzyme-modified ginseng extract, which significantly improved skin health by reducing UVB-induced aging, as shown by decreased photodamage and roughness and increased smoothness. These effects are attributed to ginsenosides Rg1, F2, Rb1, and K, which prevent UV-induced DNA damage, activate repair mechanisms, and modulate the MMP and MAPK pathways. Additionally, ginsenoside Rg3 enhances skin health by regulating key signaling pathways, whereas ginseng extracts activate the protein kinase B pathway to further protect against UV damage. Ginseng also inhibits melanogenesis, contributing to skin whitening through the suppression of key molecules involved in melanin production, such as tyrosinase and α-melanocyte-stimulating hormone. This effect is attributed to ginsenosides Rb1, F1, and Rh23 and certain acids, such as p-coumaric and salicylic acids. Furthermore, ginseng and its active compounds show potential in treating conditions such as atopic dermatitis, hair loss, acne, and skin wound healing and improving hydration, supporting its use in the development of advanced skincare products that target aging, pigmentation, and skin elasticity (52, 53).

Triticum aestivum L.

Triticum aestivum L., or common wheat, is one of the oldest cultivated crops in the Poaceae family and is traditionally used for malt and beer production. It has long been used to treat conditions such as oxidative stress, cardiovascular diseases, diabetes, and inflammation and is commonly consumed as a food, drink, or supplement (54). Recent studies on a

polar lipid extract from its endosperm revealed that wheat oil improved crow feet wrinkles and skin hydration in a 12-week clinical trial, whereas *ex vivo* tests demonstrated increased collagen production in UV-exposed skin, suggesting its antiaging potential (55, 56). In addition to its antiwrinkle effects, wheatgrass has shown promise in the management of atopic dermatitis. A study of 2,4-dinitrochlorobenzene-induced atopic dermatitis in mouse and human keratinocytes revealed that wheatgrass extract reduced symptoms by lowering IgE and inflammatory marker levels. In HaCat cells, wheat extract inhibited STAT1 activation and increased SOCS1 gene expression. Furthermore, wheat oil reduces UVB-induced photoaging, promotes collagen synthesis, reduces transepidermal water loss (TEWL), and maintains key skin barrier components (57). Wheat extract oil also enhances hyaluronic acid and collagen synthesis by inhibiting MMP-1 and has shown potential in promoting skin wound healing by stimulating cell proliferation. Its mechanisms include modulating fibronectin synthesis, increasing HA synthase activity, and increasing collagen expression in dermal fibroblasts while influencing the secretome to regulate key cellular processes, highlighting its potential in skin regeneration and wound healing (56).

Andrographis paniculata

Andrographis paniculata (Burm.f.) Ness., an herbaceous plant from the Acanthaceae family, is widely distributed across India, China, and Southeast Asia. Known for its traditional medicinal uses, it contains a variety of bioactive compounds, including diterpenoid lactones, flavonoids, terpenoids, phenolic acids, chalcones, xanthones, and volatile compounds. This chemical diversity contributes to its broad range of therapeutic effects, such as anti-inflammatory, analgesic, antioxidant, antihyperglycemic, hepatoprotective, antibacterial, and cardiovascular protective effects (58). Clinical and ex vivo trials with a 50% hydroethanolic extract revealed that eight weeks after topical application, the extract significantly reduced wrinkles, sagged, and increased dermal density in 32 female participants. These effects were linked to the ability of the extract to stimulate epidermal cell renewal, promote epidermal stem cell proliferation, and upregulate integrin β1. The extract also elevated the levels of vascular endothelial growth factor (VEGF) (59). Additionally, recent studies suggest that the extract provides photoprotection against UVA and UVB radiation, likely due to its flavonoid content and associated sun protection factor (60).

MECHANISMS BY WHICH PLANT-BASED NATURAL PRODUCTS PREVENT PHOTOAGING

Plant-derived natural ingredients have been the subject of extensive research and are increasingly incorporated into cosmetic formulations because of their potential to enhance aesthetic appearance. These compounds have been shown to offer significant benefits in mitigating photoaging through a variety of mechanisms, including:

Antioxidants

The treatment of photoaging traditionally involves two approaches: (1) preventing UVR effects through sunscreens, protective clothing, and limiting sun exposure and (2) repairing UVR-induced damage via FDA-approved retinoids such as tretinoin and tazarotene (69). Recent research has highlighted the potential of antioxidants from nutritional supplements and medicinal plants as promising treatments for photoaging. Vitamin C, a widely studied antioxidant, counteracts lipid peroxidation, mitigates ROS-induced damage, inhibits NF-κB activation, and stimulates collagen production. While oral vitamin C supplementation has shown mixed results, topical application is highly effective in reducing wrinkles and improving skin health. Combining vitamin C with vitamin E has synergistic effects, reducing DNA damage from UVB radiation. Polyphenols from plants such as *Opuntia ficus-indica*, *Zuccagnia punctata*, and rosemary protect against UVR by reducing ROS production and promoting collagen synthesis (70, 71). Resveratrol activates antiaging proteins such as SIRT1, reduces MMP expression, and enhances collagen and elastin production (36). Green tea polyphenols, citrus flavonoids, and cocoa flavonoids improve skin elasticity, protect against UV-induced damage, and reduce erythema (72). Other compounds, such as cinnamaldehyde and carotenoids, also provide UVR

protection by stabilizing ROS and enhancing collagen integrity. Nutraceutical supplements, including polyphenols and marine-derived antioxidants such as MAAs, offer photoprotection, reduce proinflammatory cytokines, and protect against UV-induced skin damage. In conclusion, plant-based antioxidants, including vitamin C, polyphenols, and carotenoids, show promise in preventing and treating photoaging. These compounds, whether applied topically or taken orally, protect the skin from UVR, reduce oxidative stress, and promote cellular repair, potentially playing a significant role in photoaging management as research progresses (73).

Anti-Inflammatory Activity

Bioactive compounds possess potent anti-inflammatory properties, offering significant benefits for skin protection and antiaging. For example, resveratrol counteracts UVB-induced inflammation by reducing the expression of proinflammatory markers such as p65 and Bax while promoting the expression of antiapoptotic proteins such as Bcl-2 (74). Similarly, EGCG, a polyphenol found in green tea, mitigates UVB-induced leukocyte infiltration and suppresses inflammatory mediators, including nitric oxide (NO) and prostaglandins (PGE2, PGF2α, PGD2), thus preventing inflammation-related skin damage (75). Genistein, an isoflavone derived from soy, downregulates proinflammatory cytokines (CXCL1, IL-1, and MIF) and inhibits COX-2 expression, reinforcing its anti-inflammatory and photoprotective effects (76). Luteolin exerts anti-inflammatory effects by suppressing IL-20 production and disrupting the p38 MAPK pathway, reducing MMP-1 and IL-6 expression in fibroblasts (77). Chrysin, known for its strong antiphotoaging properties, prevents collagen degradation, oxidative damage, and inflammation in human dermal fibroblasts (78). Naringenin inhibits UVB-induced inflammation by modulating MMPs (MMP-1, MMP-3, and MMP-13) and balancing pro- and anti-inflammatory cytokine levels (79). Quercetin protects the skin from UV-induced damage and aging by interacting with key signaling molecules, such as PKCδ and JAK2, which play critical roles in anti-inflammatory responses (80). Chlorogenic acid (CGA) further reduces ROS accumulation and promotes DNA repair, mitigating UVA-induced inflammation and apoptosis in human dermal fibroblasts (81). Additionally, gallic acid has been shown to have anti-inflammatory effects in dermatitis and psoriasis models by modulating immune responses; downregulating TNF-α, IL-4, and IL-17; and upregulating IL-10 and TGF-β. It also improves skin health by regulating keratin expression through Nrf2 suppression (82, 83).

Anti-photoaging and DNA Repair Mechanisms

By mitigating the detrimental effects of UV radiation, oxidative stress, and inflammation, natural compounds derived from plants play a vital role in safeguarding skin health. Various bioactive plant-derived compounds exhibit strong protective and reparative properties against photoaging. For example, resveratrol, a polyphenol found in red grapes, peanuts, and berries, has antiphotoaging effects by regulating MMPs and promoting VEGF-B expression, enhancing tissue vascularization (84). It also modulates apoptotic pathways, upregulating heat shock protein 27 (HSP27) and the antiapoptotic protein Bcl-2 while downregulating proapoptotic markers such as p65, Bax, and cleaved caspase-3, preserving cellular integrity under UV stress (36). EGCG, a catechin in green tea, prevents UVA-induced aging by preventing telomere shortening, restoring TGF-β1 secretion, and reducing the levels of oxidative stress markers such as malondialdehyde (MDA). EGCG further inhibits MMPs and inflammatory mediators such as nitric oxide (NO) and prostaglandins while enhancing DNA repair through the Keap1–Nrf2 pathway (85). Genistein, an isoflavone from soybeans, offers antiphotoaging benefits by inhibiting UVB-induced inflammation, reducing wrinkle formation, and activating DNA repair mechanisms via the upregulation of Gadd45 gene expression. Additionally, it mitigates oxidative damage and preserves mitochondrial integrity through modulation of the p66Shc signaling pathway (76, 86). Luteolin, a flavonoid in carrots, broccoli, and celery, protects against photoaging by inhibiting UVB-induced erythema, oxidative stress, and MMP activation. It enhances collagen synthesis and regulates SIRT3 activity, reinforcing its role in preserving collagen (87). Naringenin, a citrus flavanone, inhibits MMP-13 expression and

modulates cytokine levels, preventing UVB-induced wrinkles and maintaining skin hydration (88). Quercetin, a polyphenol from fruits and vegetables, binds to PKCδ and JAK2, triggering protective responses against UV-induced aging, reducing ROS accumulation, and preserving mitochondrial integrity (88). Chlorogenic acid (CGA), which is abundant in coffee beans, counteracts UVA-induced oxidative stress by reducing ROS and facilitating DNA repair in dermal fibroblasts (81). Clinical studies have demonstrated the photoprotective effects of enzyme-modified ginseng extract, which improves skin health by reducing UVB-induced aging, roughness, and photodamage while activating DNA repair mechanisms and modulating the MMP and MAPK pathways. Ginsenosides Rg1, F2, and Rb1 and compound K from ginseng further protect against UV damage by enhancing DNA repair and regulating key signaling pathways, including the protein kinase B pathway (52, 89).

Collagen preservation and skin elasticity

Collagen preservation and skin elasticity are crucial for maintaining youthful and healthy skin, and several bioactive compounds have demonstrated potential mechanisms to support these processes. For example, resveratrol regulates matrix metalloproteinases (MMPs), which breakdown collagen, thereby mitigating the damage caused by UV exposure. It also upregulates VEGF-B, promoting tissue vascularization and supporting overall skin health (84). Similarly, compounds such as α-mangostin from *Garcinia mangostana* and limonoids from *Carapa guianensis* contribute to collagen biosynthesis, whereas ursolic and pomolic acids from *Eriobotrya japonica* stimulate collagen and hyaluronic acid production (31). Jasmonate, a plant hormone, inhibits UV-induced MMP-1 activity and helps recover proteoglycan expression, further supporting its antiaging properties (13). Clinical studies have also demonstrated the benefits of ferulic acid, which enhances skin elasticity and serves as a potent moisturizer while also acting as a natural skin lightener (90). Resveratrol's ability to inhibit apoptosis and reduce oxidative stress strengthens collagen preservation and elasticity, making it a promising antiaging agent (36). Similarly, EGCG from green tea counters UVA-induced collagen degradation, preserves collagen fibers, and promotes DNA repair (35, 85). Genistein, an isoflavone from soybeans, supports skin elasticity by inhibiting inflammatory cytokines, reducing MMP expression, and increasing collagen synthesis (76). Other compounds, such as luteolin and chrysin, also promote collagen synthesis and prevent its degradation, with luteolin regulating SIRT3 activity and chrysin enhancing collagen secretion (77, 87). Thyme (*T. vulgaris*) has been shown in clinical trials to reduce facial wrinkles and expression lines, with effects attributed to increased adiponectin production and PPAR-γ expression (10). Wheat (*Triticum aestivum*) extract has demonstrated antiaging potential by improving skin hydration, reducing wrinkles, and promoting collagen synthesis in clinical and *ex vivo* studies. Wheat oil also helps reduce UVB-induced photoaging, supports skin hydration, and enhances collagen production, contributing to improved skin regeneration and wound healing (54, 57). These compounds collectively offer promising options for preserving collagen, supporting skin elasticity, and preventing signs of skin aging.

Skin Lightening Effects

Melanogenesis inhibition refers to the reduction or prevention of melanin production, the pigment responsible for skin coloration, and several bioactive compounds have been identified for their potential to mitigate skin pigmentation (91). Resveratrol, a well-known polyphenol, inhibits melanogenesis by suppressing tyrosinase, a key enzyme in melanin synthesis, and modulating related proteins. Its antioxidant properties further contribute to skin lightening by alleviating oxidative stress, a factor that enhances melanogenesis (92). Similarly, EGCG from green tea reduces melanogenesis by downregulating melanogenic enzymes, including tyrosinase, and promoting the degradation of melanin in melanocytes. Its anti-inflammatory and antioxidant effects also counteract factors that enhance pigmentation, such as UV-induced inflammation (35, 93). Genistein, an isoflavone from soy, reduces melanogenesis by inhibiting tyrosinase activity and modulating signaling pathways linked to oxidative stress and skin inflammation (76, 94). Chrysin, a flavonoid found in passionflower, suppresses tyrosinase activity and

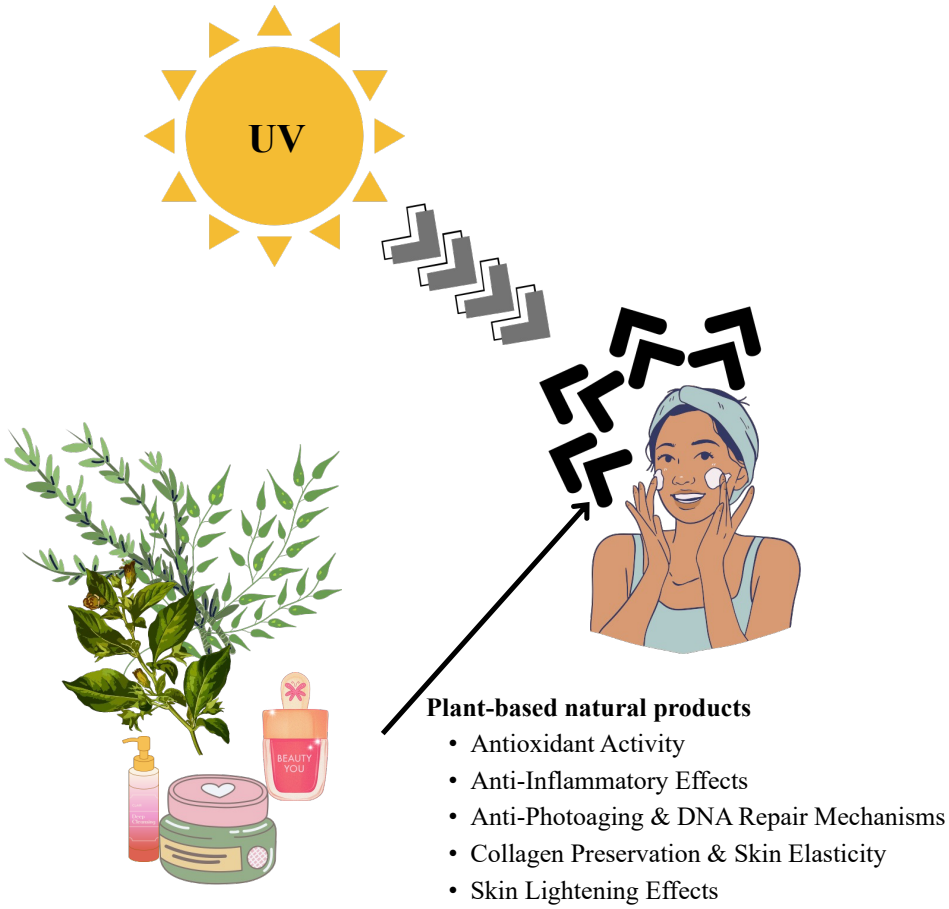

Figure 2. Delineates the potential mechanisms through which plant-based natural products mitigate the effects of photoaging.

reduces melanin levels, with its antioxidant properties further enhancing its skin-lightening effects (95). Other compounds, including luteolin, naringenin, quercetin, and rutin, also inhibit melanogenesis by targeting enzymes involved in melanin synthesis and modulating oxidative stress pathways (96). Additionally, studies suggest that cationic noisome-loaded gallic acid, compared with its free form, enhances melanin suppression, tyrosinase inhibition, and antioxidant effects (97). Like thymol, carvacrol inhibits tyrosinase, increases skin thickness, and promotes keratinocyte proliferation, with combined thymol and carvacrol resulting in superior results (31). Ginseng and its active compounds, including ginsenosides and certain acids, inhibit melanogenesis and contribute to skin whitening while also offering benefits for skin conditions such as atopic dermatitis, acne, and skin aging (98). These compounds collectively offer promising solutions for skin lightening and pigmentation regulation, supporting the development of advanced skincare products. An expanding body of scientific literature has elucidated the underlying mechanisms by which plant-derived natural products exert antiphotoaging effects. These mechanistic pathways are comprehensively illustrated in Figure 2.

CONCLUSIONS AND FUTURE PERSPECTIVES

The skin is a vital organ with cosmetic and physiological functions, is highly vulnerable to photoaging, which can significantly impact its appearance and health. This vulnerability underscores the need for effective preventive and therapeutic strategies against UV-induced damage. In response to this growing concern, considerable research efforts have focused on understanding the mechanisms underlying skin photoaging to enhance

its management in both clinical and aesthetic contexts. Current research has revealed several critical pathways involved in photoaging, including UV-induced alterations in cellular macromolecules, oxidative stress, and the activation of associated signaling cascades. Studies have also explored mechanisms such as UV-induced inflammation, apoptosis, immune suppression, mitochondrial dysfunction, adipose tissue depletion, the accumulation of AGEs, and the activation of transient receptor potential vanilloid ion channels. Given the intricate interplay among these mechanisms, a more comprehensive understanding of their interactions is essential. Since UV-induced signaling pathways are highly interconnected, a holistic, integrative approach is needed to fully delineate their roles and uncover novel therapeutic targets for mitigating skin photoaging. Despite these mechanistic insights, substantial efforts have been made to develop preventive interventions. Among the most promising alternatives to synthetic agents are plant-based natural products, particularly polyphenolic compounds. These bioactive compounds have gained attention because of their favorable safety profiles, broad availability, and potential therapeutic efficacy. As a result, plant-derived polyphenols are increasingly incorporated into pharmaceutical and cosmeceutical formulations, serving as natural sunscreens, anticarcinogenic agents, cell proliferation modulators, and antiphotoaging compounds. Despite their promise, significant gaps remain in the understanding of how these compounds exert their effects. While existing research suggests their potential, much remains unknown about the specific cellular and molecular mechanisms through which polyphenols modulate UV-induced skin aging. This lack of understanding limits their full therapeutic potential. Additionally, incorporating polyphenols into sunscreen formulations presents several challenges. Despite strong evidence supporting polyphenols for photoprotection, several challenges hinder their commercial application. Key issues include insufficient data on optimal concentrations and the need for stable, effective formulations. Interactions with other sunscreen ingredients must also be evaluated for safety and efficacy. Although animal studies offer useful insights, translating these results to human use remains difficult. Clinical trials are essential to assess long-term safety in diverse populations. High-throughput screening may help identify the most effective bioactive compounds. Additionally, standardizing plant extracts is critical to ensure consistency, reproducibility, and reliable assessment of therapeutic outcomes, given the variability in phytochemical composition. In conclusion, while plant-based polyphenolic compounds represent promising defenses against UV-induced skin aging, significant research is still needed to fully elucidate their potential. A more comprehensive understanding of their mechanisms, optimal formulations, and real-world effectiveness will be essential in translating these compounds from laboratory studies to effective clinical interventions.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the support of Rangsit University for granting access to comprehensive research databases and electronic resources, which significantly facilitated the development of this literature review.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Salminen A, Kaarniranta K, Kauppinen A. Photoaging: UV radiation-induced inflammation and immunosuppression accelerate the aging process in the skin. Inflamm Res. 2022;71(7-8):817-31. https://doi.org/10.1007/s00011-022-01598-8
2. Tanveer MA, Rashid H, Tasduq SA. Molecular basis of skin photoaging and therapeutic interventions by plant-derived natural product ingredients: A comprehensive review. Heliyon. 2023;9(3):e13580. https://doi.org/10.1016/j.heliyon.2023.e13580
3. Yu ZW, Zheng M, Fan HY, Liang XH, Tang YL. Ultraviolet (UV) radiation: a double-edged sword in cancer development and therapy. Mol Biomed. 2024;5(1):49. https://doi.org/10.1186/s43556-024-00209-8
4. Verma A, Zanoletti A, Kareem KY, Adelodun B, Kumar P, Ajibade FO, et al. Skin protection from solar ultraviolet radiation using natural compounds: a review. Environ Chem Lett.

2023;22(1):273-95. https://doi.org/10.1007/s10311-023-01649-4
5. Zorina A, Zorin V, Kudlay D, Kopnin P. Molecular Mechanisms of Changes in Homeostasis of the Dermal Extracellular Matrix: Both Involutional and Mediated by Ultraviolet Radiation. Int J Mol Sci. 2022;23(12). https://doi.org/10.3390/ijms23126655
6. Jin SG, Padron F, Pfeifer GP. UVA Radiation, DNA Damage, and Melanoma. ACS Omega. 2022;7(37):32936-48. https://doi.org/10.1021/acsomega.2c04424
7. Feng C, Chen X, Yin X, Jiang Y, Zhao C. Matrix Metalloproteinases on Skin Photoaging. J Cosmet Dermatol. 2024;23(12):3847-62. https://doi.org/10.1111/jocd.16558
8. Schneider G, Figueroa FL, Vega J, Chaves P, Álvarez-Gómez F, Korbee N, et al. Photoprotection properties of marine photosynthetic organisms grown in high ultraviolet exposure areas: Cosmeceutical applications. Algal Research. 2020;49. https://doi.org/10.1016/j.algal.2020.101956
9. Parisi M, Verrillo M, Luciano MA, Caiazzo G, Quaranta M, Scognamiglio F, et al. Use of Natural Agents and Agrifood Wastes for the Treatment of Skin Photoaging. Plants (Basel). 2023;12(4). https://doi.org/10.3390/plants12040840
10. Torres-Contreras AM, Garcia-Baeza A, Vidal-Limon HR, Balderas-Renteria I, Ramirez-Cabrera MA, Ramirez-Estrada K. Plant Secondary Metabolites against Skin Photodamage: Mexican Plants, a Potential Source of UV-Radiation Protectant Molecules. Plants (Basel). 2022;11(2). https://doi.org/10.3390/plants11020220
11. Resende D, Jesus A, Sousa Lobo JM, Sousa E, Cruz MT, Cidade H, et al. Up-to-Date Overview of the Use of Natural Ingredients in Sunscreens. Pharmaceuticals (Basel). 2022;15(3). https://doi.org/10.3390/ph15030372
12. Gromkowska-Kepka KJ, Puscion-Jakubik A, Markiewicz-Zukowska R, Socha K. The impact of ultraviolet radiation on skin photoaging - review of in vitro studies. J Cosmet Dermatol. 2021;20(11):3427-31. https://doi.org/10.1111/jocd.14033
13. Lee L-Y, Liu S-X. Pathogenesis of Photoaging in Human Dermal Fibroblasts. Int J Dermatol Venereol. 2020;3(1):37-42. https://doi.org/10.1097/JD9.0000000000000068
14. Machalinski B, Oszutowska-Mazurek D, Mazurek P, Parafiniuk M, Szumilas P, Zawislak A, et al. Assessment of Extracellular Matrix Fibrous Elements in Male Dermal Aging: A Ten-Year Follow-Up Preliminary Case Study. Biology (Basel). 2024;13(8). https://doi.org/10.3390/biology13080636
15. Solano F. Photoprotection and Skin Pigmentation: Melanin-Related Molecules and Some Other New Agents Obtained from Natural Sources. Molecules. 2020;25(7). https://doi.org/10.3390/molecules25071537
16. Vechtomova YL, Telegina TA, Buglak AA, Kritsky MS. UV Radiation in DNA Damage and Repair Involving DNA-Photolyases and Cryptochromes. Biomedicines. 2021;9(11). https://doi.org/10.3390/biomedicines9111564
17. Fraikin GY. Role of Various UV-Induced DNA Lesions in Human Skin Carcinogenesis. J Biomed Res Environ Sci. 2024;5(5):466-73. https://doi.org/10.37871/jbres1916
18. Allegra A, Pioggia G, Tonacci A, Musolino C, Gangemi S. Oxidative Stress and Photodynamic Therapy of Skin Cancers: Mechanisms, Challenges and Promising Developments. Antioxidants (Basel). 2020;9(5). https://doi.org/10.3390/antiox9050448
19. Pourzand C, Albieri-Borges A, Raczek NN. Shedding a New Light on Skin Aging, Iron- and Redox-Homeostasis and Emerging Natural Antioxidants. Antioxidants (Basel). 2022;11(3). https://doi.org/10.3390/antiox11030471
20. He H, Xiong L, Jian L, Li L, Wu Y, Qiao S. Role of mitochondria on UV-induced skin damage and molecular mechanisms of active chemical compounds targeting mitochondria. J Photochem Photobiol B. 2022;232:112464. https://doi.org/10.1016/j.jphotobiol.2022.112464
21. Prasanth MI, Gayathri S, Bhaskar JP, Krishnan V, Balamurugan K. Understanding the role of p38 and JNK mediated MAPK pathway in response to UV-A induced photoaging in Caenorhabditis elegans. J Photochem Photobiol B. 2020;205:111844. https://doi.org/10.1016/j.jphotobiol.2020.111844
22. Bachelor MA, Bowden GT. UVA-mediated activation of signaling pathways involved in skin tumor promotion and progression. Semin Cancer Biol. 2004;14(2):131-8. https://doi.org/10.1016/j.semcancer.2003.09.017
23. Pillai S, Oresajo C, Hayward J. Ultraviolet radiation and skin aging: roles of reactive oxygen species, inflammation and protease activation, and strategies for prevention of inflammation-induced matrix degradation - a review. Int J Cosmet Sci. 2005;27(1):17-34. https://doi.org/10.1111/j.1467-2494.2004.00241.x

24. Van Laethem A, Nys K, Van Kelst S, Claerhout S, Ichijo H, Vandenheede JR, et al. Apoptosis signal regulating kinase-1 connects reactive oxygen species to p38 MAPK-induced mitochondrial apoptosis in UVB-irradiated human keratinocytes. Free Radic Biol Med. 2006;41(9):1361-71. https://doi.org/10.1016/j.freeradbiomed.2006.07.007
25. Bocheva GS, Slominski RM, Slominski AT. Immunological Aspects of Skin Aging in Atopic Dermatitis. Int J Mol Sci. 2021;22(11). https://doi.org/10.3390/ijms22115729.
26. Agrawal R, Hu A, Bollag WB. The Skin and Inflamm-Aging. Biology (Basel). 2023;12(11). https://doi.org/10.3390/biology12111396.
27. Xie M, Jiang Z, Lin X, Wei X. Application of plant extracts cosmetics in the field of anti-aging. JDSCT. 2024;1(2). https://doi.org/10.1016/j.jdsct.2024.100014
28. Michalak M. Plant-Derived Antioxidants: Significance in Skin Health and the Aging Process. Int J Mol Sci. 2022;23(2). https://doi.org/10.3390/ijms23020585.
29. Liu JK. Natural products in cosmetics. Nat Prod Bioprospect. 2022;12(1):40. https://doi.org/10.1007/s13659-022-00363-y
30. Chan LKW, Lee KWA, Lee CH, Lam KWP, Lee KFV, Wu R, et al. Cosmeceuticals in photoaging: A review. Skin Res Technol. 2024;30(9):e13730. https://doi.org/10.1111/srt.13730
31. Costa EF, Magalhaes WV, Di Stasi LC. Recent Advances in Herbal-Derived Products with Skin Anti-Aging Properties and Cosmetic Applications. Molecules. 2022;27(21). https://doi.org/10.3390/molecules27217518
32. Zhang Y, Cai P, Cheng G, Zhang Y. A Brief Review of Phenolic Compounds Identified from Plants: Their Extraction, Analysis, and Biological Activity. Nat Prod Commun. 2022;17(1). https://doi.org/10.1177/1934578X211069
33. Sun W, Shahrajabian MH. Therapeutic Potential of Phenolic Compounds in Medicinal Plants-Natural Health Products for Human Health. Molecules. 2023;28(4). https://doi.org/10.3390/molecules28041845
34. Al-Khayri JM, Sahana GR, Nagella P, Joseph BV, Alessa FM, Al-Mssallem MQ. Flavonoids as Potential Anti-Inflammatory Molecules: A Review. Molecules. 2022;27(9). https://doi.org/10.3390/molecules27092901
35. Nisa RU, Nisa AU, Tantray AY, Shah AH, Jan AT, Shah AA, et al. Plant phenolics with promising therapeutic applications against skin disorders: A mechanistic review. J Agric Food Res. 2024;16. https://doi.org/10.1016/j.jafr.2024.101090
36. Hecker A, Schellnegger M, Hofmann E, Luze H, Nischwitz SP, Kamolz LP, et al. The impact of resveratrol on skin wound healing, scarring, and aging. Int Wound J. 2022;19(1):9-28. https://doi.org/10.1111/iwj.13601
37. Wada-Hiraike O. Benefits of the Phytoestrogen Resveratrol for Perimenopausal Women. Endocrines. 2021;2(4):457-71. https://doi.org/10.3390/endocrines2040041
38. Podgrajsek R, Ban Frangez H, Stimpfel M. Molecular Mechanism of Resveratrol and Its Therapeutic Potential on Female Infertility. Int J Mol Sci. 2024;25(7). https://doi.org/10.3390/ijms25073613
39. Vesely O, Baldovska S, Kolesarova A. Enhancing Bioavailability of Nutraceutically Used Resveratrol and Other Stilbenoids. Nutrients. 2021;13(9). https://doi.org/10.3390/nu13093095
40. Hur GH, Ryu AR, Kim YW, Lee MY. The Potential Anti-Photoaging Effect of Photodynamic Therapy Using Chlorin e6-Curcumin Conjugate in UVB-Irradiated Fibroblasts and Hairless Mice. Pharmaceutics. 2022;14(5). https://doi.org/10.3390/pharmaceutics14050968
41. Mao X, Zhang X, Zheng X, Chen Y, Xuan Z, Huang P. Curcumin suppresses LGR5(+) colorectal cancer stem cells by inducing autophagy and by repressing TFAP2A-mediated ECM pathway. J Nat Med. 2021;75(3):590-601. https://doi.org/10.1007/s11418-021-01505-1
42. Bjorklund G, Shanaida M, Lysiuk R, Butnariu M, Peana M, Sarac I, et al. Natural Compounds and Products from an Anti-Aging Perspective. Molecules. 2022;27(20). https://doi.org/10.3390/molecules27207084
43. Yang W, Chen X, Li Y, Guo S, Wang Z, Yu X. Advances in Pharmacological Activities of Terpenoids. Nat Prod Commun. 2020;15(3). https://doi.org/10.1177/1934578X20903
44. Zerres S, Stahl W. Carotenoids in human skin. Biochim Biophys Acta Mol Cell Biol Lipids. 2020;1865(11):158588. https://doi.org/10.1016/j.bbalip.2019.158588
45. Balic A, Mokos M. Do We Utilize Our Knowledge of the Skin Protective Effects of Carotenoids Enough? Antioxidants (Basel). 2019;8(8). https://doi.org/10.3390/antiox8080259
46. Stahl W, Sies H. beta-Carotene and other carotenoids in protection from sunlight. Am J Clin Nutr. 2012;96(5):1179S-84S. https://doi.org/10.3945/ajcn.112.034819
47. Osz BE, Jitca G, Stefanescu RE, Puscas A, Tero-Vescan A, Vari CE. Caffeine and Its Antioxidant Properties-It Is All about Dose and Source. Int J

Mol Sci. 2022;23(21). https://doi.org/10.3390/ijms232113074
48. Conney AH, Lu YP, Lou YR, Kawasumi M, Nghiem P. Mechanisms of Caffeine-Induced Inhibition of UVB Carcinogenesis. Front Oncol. 2013;3:144. https://doi.org/10.3389/fonc.2013.00144
49. Ferrucci LM, Cartmel B, Molinaro AM, Leffell DJ, Bale AE, Mayne ST. Tea, coffee, and caffeine and early-onset basal cell carcinoma in a case–control study. Eur J Cancer Prev. 2014;23(4):296-302. https://doi.org/10.1097/CEJ.0000000000000037
50. Pauwels EKJ, Volterrani D. Coffee Consumption and Cancer Risk: An Assessment of the Health Implications Based on Recent Knowledge. Med Princ Pract. 2021;30(5):401-11. https://doi.org/10.1159/000516067
51. Elias ML, Israeli AF, Madan R. Caffeine in Skincare: Its Role in Skin Cancer, Sun Protection, and Cosmetics. Indian J Dermatol. 2023;68(5):546-50. https://doi.org/10.4103/ijd.ijd_166_22
52. Choi W, Cho JH, Park SH, Kim DS, Lee HP, Kim D, et al. Ginseng root-derived exosome-like nanoparticles protect skin from UV irradiation and oxidative stress by suppressing activator protein-1 signaling and limiting the generation of reactive oxygen species. J Ginseng Res. 2024;48(2):211-9. https://doi.org/10.1016/j.jgr.2024.01.001
53. Jiang R, Xu X, Sun Z, Wang F, Ma R, Feng K, et al. Protective Effects of Ginseng Proteins on Photoaging of Mouse Fibroblasts Induced by UVA. Photochem Photobiol. 2020;96(1):113-23. https://doi.org/10.1111/php.13156
54. Mishra N, Tripathi R, Pandey D, Shah K, Chauhan NS. Wheatgrass (Triticum aestivum): a miraculous microgreen: an overview. J Future Foods. 2025;5(3):239-47. https://doi.org/10.1016/j.jfutfo.2024.07.003
55. Boisnic S, Keophiphath M, Serandour AL, Branchet MC, Stéphanie Le Breton SL, Lamour I, et al. Polar lipids from wheat extract oil improve skin damages induced by aging: Evidence from a randomized, placebo-controlled clinical trial in women and an ex vivo study on human skin explant. J Cosmet Dermatol. 2019;18(1). https://doi.org/10.1111/jocd.12967
56. Son DJ, Jung JC, Choi YM, Ryu HY, Lee S, Davis BA. Wheat Extract Oil (WEO) Attenuates UVB-Induced Photoaging via Collagen Synthesis in Human Keratinocytes and Hairless Mice. Nutrients. 2020;12(2). https://doi.org/10.3390/nu12020300
57. Lee JH, Ki HH, Kim DK, Lee YM. Triticum aestivum sprout extract attenuates 2,4-dinitrochlorobenzene-induced atopic dermatitis-like skin lesions in mice and the expression of chemokines in human keratinocytes. Mol Med Rep. 2018;18(3):3461-8. https://doi.org/10.3892/mmr.2018.9339
58. Kumar S, Singh B, Bajpai V. Andrographis paniculata (Burm.f.) Nees: Traditional uses, phytochemistry, pharmacological properties and quality control/quality assurance. J Ethnopharmacol. 2021;275:114054. https://doi.org/10.1016/j.jep.2021.114054
59. You J, Roh KB, Li Z, Liu G, Tang J, Shin S, et al. The Antiaging Properties of Andrographis paniculata by Activation Epidermal Cell Stemness. Molecules. 2015;20(9):17557-69. https://doi.org/10.3390/molecules200917557
60. Fardiyah Q, Ersam T, Suyanta, Slamet A, Suprapto, Kurniawan F. New potential and characterization of Andrographis paniculata L. Ness plant extracts as photoprotective agent. Arab J Chem. 2020;13(12):8888-97. https://doi.org/10.1016/j.arabjc.2020.10.015
61. Hwang E, Ngo HTT, Seo SA, Park B, Zhang M, Yi TH. Protective effect of dietary Alchemilla mollis on UVB-irradiated premature skin aging through regulation of transcription factor NFATc1 and Nrf2/ARE pathways. Phytomedicine. 2018;39:125-36. https://doi.org/10.1016/j.phymed.2017.12.025
62. Kim HK. Protective Effect of Garlic on Cellular Senescence in UVB-Exposed HaCaT Human Keratinocytes. Nutrients. 2016;8(8). https://doi.org/10.3390/nu8080464
63. Ngo HT, Hwang E, Seo SA, Park B, Sun ZW, Zhang M, et al. Topical application of neem leaves prevents wrinkles formation in UVB-exposed hairless mice. J Photochem Photobiol B. 2017;169:161-70. https://doi.org/10.1016/j.jphotobiol.2017.03.010
64. Zhao P, Alam MB, Lee SH. Protection of UVB-Induced Photoaging by Fuzhuan-Brick Tea Aqueous Extract via MAPKs/Nrf2-Mediated Down-Regulation of MMP-1. Nutrients. 2018;11(1). https://doi.org/10.3390/nu11010060
65. Jeon H, Kim DH, Nho YH, Park JE, Kim SN, Choi EH. A Mixture of Extracts of Kochia scoparia and Rosa multiflora with PPAR alpha/gamma Dual Agonistic Effects Prevents Photoaging in Hairless Mice. Int J Mol Sci. 2016;17(11). https://doi.org/10.3390/ijms17111919
66. Kim JE, Jang SG, Lee CH, Lee JY, Park H, Kim JH, et al. Beneficial effects on skin health using polysaccharides from red ginseng by-product. J

Food Biochem. 2019;43(8):e12961. https://doi.org/10.1111/jfbc.12961
67. Kwon KR, Alam MB, Park JH, Kim TH, Lee SH. Attenuation of UVB-Induced Photo-Aging by Polyphenolic-Rich Spatholobus Suberectus Stem Extract Via Modulation of MAPK/AP-1/MMPs Signaling in Human Keratinocytes. Nutrients. 2019;11(6). https://doi.org/10.3390/nu11061341
68. Navabhatra A, Maniratanachote R, Yingngam B. Antiphotoaging properties of Zingiber montanum essential oil isolated by solvent-free microwave extraction against ultraviolet B-irradiated human dermal fibroblasts. Toxicol Res. 2022;38(2):235-48. https://doi.org/10.1007/s43188-021-00107-z
69. Poon F, Kang S, Chien AL. Mechanisms and treatments of photoaging. Photodermatol Photoimmunol Photomed. 2015;31(2):65-74. https://doi.org/10.1111/phpp.12145
70. Auh JH, Madhavan J. Protective effect of a mixture of marigold and rosemary extracts on UV-induced photoaging in mice. Biomed Pharmacother. 2021;135:111178. https://doi.org/10.1016/j.biopha.2020.111178
71. Petruk G, Del Giudice R, Rigano MM, Monti DM. Antioxidants from Plants Protect against Skin Photoaging. Oxid Med Cell Longev. 2018;2018:1454936. https://doi.org/10.1155/2018/1454936
72. Skarupova D, Vostalova J, Rajnochova Svobodova A. Ultraviolet A protective potential of plant extracts and phytochemicals. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2020;164(1):1-22. https://doi.org/0.5507/bp.2020.010
73. Gao L, Liu X, Luo X, Lou X, Li P, Li X, et al. Antiaging effects of dietary supplements and natural products. Front Pharmacol. 2023;14:1192714. https://doi.org/10.3389/fphar.2023.1192714.
74. Zhou F, Huang X, Pan Y, Cao D, Liu C, Liu Y, et al. Resveratrol protects HaCaT cells from ultraviolet B-induced photoaging via upregulation of HSP27 and modulation of mitochondrial caspase-dependent apoptotic pathway. Biochem Biophys Res Commun. 2018;499(3):662-8. https://doi.org/10.1016/j.bbrc.2018.03.207
75. Farhan M. The Promising Role of Polyphenols in Skin Disorders. Molecules. 2024;29(4). https://doi.org/10.3390/molecules29040865
76. Tang SC, Hsiao YP, Ko JL. Genistein protects against ultraviolet B-induced wrinkling and photoinflammation in in vitro and in vivo models. Genes Nutr. 2022;17(1):4. https://doi.org/10.1186/s12263-022-00706-x
77. Gendrisch F, Esser PR, Schempp CM, Wolfle U. Luteolin as a modulator of skin aging and inflammation. Biofactors. 2021;47(2):170-80. https://doi.org/10.1002/biof.1699
78. Zhu L, Lu Y, Yu WG, Zhao X, Lu YH. Anti-photoageing and anti-melanogenesis activities of chrysin. Pharm Biol. 2016;54(11):2692-700. https://doi.org/10.1080/13880209.2016.1179334
79. Österlund C, Hrapovic N, Lafon-Kolb V, Amini N, Smiljanic S, Visdal-Johnsen L. Protective Effects of Naringenin against UVB Irradiation and Air Pollution-Induced Skin Aging and Pigmentation. Cosmetics. 2023;10(3). https://doi.org/10.3390/cosmetics10030088
80. Shin EJ, Lee JS, Hong S, Lim TG, Byun S. Quercetin Directly Targets JAK2 and PKCdelta and Prevents UV-Induced Photoaging in Human Skin. Int J Mol Sci. 2019;20(21). https://doi.org/10.3390/ijms20215262
81. Xue N, Liu Y, Jin J, Ji M, Chen X. Chlorogenic Acid Prevents UVA-Induced Skin Photoaging through Regulating Collagen Metabolism and Apoptosis in Human Dermal Fibroblasts. Int J Mol Sci. 2022;23(13). https://doi.org/10.3390/ijms23136941
82. Dewi NKDP, Suryadewi KD, Fitriari DM, Andini KL, Laksmiani NPL. Molecular docking of gallic acid as anti-photoaging in silico. Pharmacy Reports. 2021;1(2). https://doi.org/10.51511/pr.18
83. Hu G, Zhou X. Gallic Acid Ameliorates Atopic Dermatitis-Like Skin Inflammation Through Immune Regulation in a Mouse Model. Clin Cosmet Investig Dermatol. 2021;14:1675-83. https://doi.org/10.2147/CCID.S327825
84. Cui B, Wang Y, Jin J, Yang Z, Guo R, Li X, et al. Resveratrol Treats UVB-Induced Photoaging by Anti-MMP Expression, through Anti-Inflammatory, Antioxidant, and Antiapoptotic Properties, and Treats Photoaging by Upregulating VEGF-B Expression. Oxid Med Cell Longev. 2022;2022:6037303. https://doi.org/10.1155/2022/6037303
85. Sun J, Jiang Y, Fu J, He L, Guo X, Ye H, et al. Beneficial Effects of Epigallocatechin Gallate in Preventing Skin Photoaging: A Review. Molecules. 2024;29(22). https://doi.org/10.3390/molecules29225226
86. Wojciak M, Drozdowski P, Skalska-Kaminska A, Zagorska-Dziok M, Ziemlewska A, Niziol-Lukaszewska Z, et al. Protective, Anti-Inflammatory, and Anti-Aging Effects of Soy Isoflavones on Skin Cells: An Overview of In Vitro and In Vivo Studies. Molecules. 2024;29(23). https://doi.org/10.3390/molecules29235790

87. Mu J, Ma H, Chen H, Zhang X, Ye M. Luteolin Prevents UVB-Induced Skin Photoaging Damage by Modulating SIRT3/ROS/MAPK Signaling: An in vitro and in vivo Studies. Front Pharmacol. 2021;12:728261. https://doi.org/10.3389/fphar.2021.728261
88. Gupta A, Jain P, Nagori K, Adnan M, Ajazuddin. Treatment strategies for psoriasis using flavonoids from traditional Chinese medicine. Pharmacol Res - Modern Chin Med. 2024;12. https://doi.org/10.1016/j.prmcm.2024.100463
89. Lee HY, Kim EJ, Cho DY, Jung JG, Kim MJ, Lee JH, et al. Photoprotective Effect of Fermented and Aged Mountain-Cultivated Ginseng Sprout (Panax ginseng) on Ultraviolet Radiation-Induced Skin Aging in a Hairless Mouse Model. Nutrients. 2023;15(7). https://doi.org/10.3390/nu15071715
90. Proietti I, Guida S, Dybala A, Spagnoli A, Potenza C. Effects of CE Ferulic® Combined with Microneedling in the Treatment of Pigmentary Disorders: A Monocentric, Split Face, Comparative Study. Cosmetics. 2024;11(3). https://doi.org/10.3390/cosmetics11030101
91. Manap ASA, Lum YK, Ong LH, Tang Y-Q, Gew LT, Chia AYY. Perspective approaches on melanogenesis inhibition. Dermatol Sin. 2021;39(1):1-12. https://doi.org/10.4103/ds.ds_46_20
92. Boo YC. Human Skin Lightening Efficacy of Resveratrol and Its Analogs: From in Vitro Studies to Cosmetic Applications. Antioxidants (Basel). 2019;8(9). https://doi.org/10.3390/antiox8090332
93. Wang W, Di T, Wang W, Jiang H. EGCG, GCG, TFDG, or TSA Inhibiting Melanin Synthesis by Downregulating MC1R Expression. Int J Mol Sci. 2023;24(13). https://doi.org/10.3390/ijms241311017
94. Ningsih IY, Wardhani LK, Eka Nuryuanda AR, Puspitasari E, Hidayat MA. Genistein Content and Tyrosinase Inhibitory Activity of Edamame (Glycine max) Extracts. J Trop Pharm Chem. 2022;6(2):2407-6090. https://doi.org/10.30872/j.trop.pharm.chem.v6i2.243
95. Lee Y, Song HY, Byun EB. Anti-melanogenic effects of hydroxyethyl chrysin through the inhibition of tyrosinase activity: In vitro and in silico approaches. Heliyon. 2025;11(2):e41718. https://doi.org/10.1016/j.heliyon.2025.e41718
96. Liu-Smith F, Meyskens FL. Molecular mechanisms of flavonoids in melanin synthesis and the potential for the prevention and treatment of melanoma. Mol Nutr Food Res. 2016;60(6):1264-74. https://doi.org/10.1002/mnfr.201500822
97. Chaikul P, Khat-Udomkiri N, Iangthanarat K, Manosroi J, Manosroi A. Characteristics and in vitro anti-skin aging activity of gallic acid loaded in cationic CTAB niosome. Eur J Pharm Sci. 2019;131:39-49. https://doi.org/10.1016/j.ejps.2019.02.008
98. Liu J, Xu X, Zhou J, Sun G, Li Z, Zhai L, et al. Phenolic acids in Panax ginseng inhibit melanin production through bidirectional regulation of melanin synthase transcription via different signaling pathways. J Ginseng Res. 2023;47(6):714-25. https://doi.org/10.1016/j.jgr.2023.05.002