



Exploring Natural Antiaging Agents in Cosmetics: A Systematic Review of Mechanisms and Efficacy

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ABSTRACT

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antioxidant, cosmetic product, cosmetology, environmental chemistry, natural antiaging, plant-based antiaging, sustainable chemistry

The growing consumer demand for sustainable and efficacious antiaging solutions has intensified focus on natural ingredients in cosmetic science. This systematic review synthesizes evidence from 32 studies (Scopus/PubMed, 1900–2024) to evaluate the efficacy and molecular mechanisms of plant-derived antiaging ingredients. Key findings demonstrate that extracts from *Leontopodium alpinum*, *Stenocarpus sinuatus*, *Echinacea purpurea*, and 28 other botanicals combat skin aging through multifaceted biological activities. These agents potentially neutralize reactive oxygen species (ROS) via NRF2 pathway activation, enhance endogenous antioxidants (SOD, catalase), and suppress inflammation by inhibiting NF- κ B/MAPK signaling—reducing pro-inflammatory cytokines (TNF- α , IL-6) and matrix metalloproteinases (MMPs). Critically, they stimulate collagen synthesis by activating TGF- β /Smad pathways (*Centella asiatica*) and inhibit collagenase/elastase enzymes (*Sclerocarya birrea*: 99% collagenase inhibition). Fermentation-derived compounds (*Magnolia officinalis* fermented extract) and nanoparticle formulations (Panax ginseng berry nanoparticles) significantly enhance bioavailability and clinical outcomes, improving skin elasticity, dermal density, and wrinkle depth in human trials. However, challenges in stability and skin delivery remain, suggesting the need for advanced encapsulation methods like liposomes.

1. INTRODUCTION

The skin, as the body's largest organ, plays a crucial role in protecting the body from external threats while also facilitating social interaction [1]. It serves as a barrier against microbial invasions, maintains temperature stability, and enables the sense of touch [2]. The aging process, which begins at birth and becomes more pronounced over time [3], is influenced by a complex interplay of genetic and environmental factors [4]. Skin aging can be categorized into intrinsic aging, driven by internal factors such as chronological changes, and extrinsic aging, caused by external stressors like sun exposure and pollution [5].

Intrinsic aging is an inevitable biological process characterized by a decrease in collagen production, a slowdown in skin cell renewal, and reduced moisture retention. These changes lead to fine lines, wrinkles, and a loss of skin elasticity. Extrinsic aging, on the other hand, is largely influenced by lifestyle choices and environmental factors. UV radiation, poor diet, smoking, pollution, and the use of harsh skincare products can accelerate the degradation of collagen and elastin fibers, resulting in premature aging signs such as wrinkles, age spots, and uneven skin tone [6].

Recent studies have shown that while internal factors contribute to only about 10% of the aging process, lifestyle and environmental factors play a more significant role, with just 3% of skin aging attributed to genetic factors [7]. This highlights the importance of managing external influences to mitigate the effects of aging. Interestingly, research indicates that women tend to experience more chronological aging, while men are more susceptible to photoaging [8].

The growing awareness of aging mechanisms, particularly extrinsic aging, has driven the beauty and skincare industry to adapt to the evolving demands of a dynamic market. The industry faces the challenge of balancing the use of "organic" and "synthetic" ingredients, with a notable shift towards eco-friendly cosmetics. Consumers are increasingly seeking products that are not only effective but also environmentally sustainable, prioritizing natural ingredients over chemically synthesized alternatives [9].

Natural ingredients offer several advantages, including their alignment with the metabolic pathways developed by plants over centuries. These ingredients can modulate multiple molecular pathways involved in skin aging, such as inhibiting the activation of NF- κ B, which triggers inflammation, and inducing Nrf2, which enhances the cellular antioxidant

defense system [10]. Additionally, stimulating the TGF- β pathway and inhibiting MMPs can suppress the aging process by promoting collagen production and reducing collagen degradation [10, 11].

The global cosmetics industry has experienced significant growth, with an estimated annual growth rate of 7.14% from 2017 to 2023. This surge has led to increased interest in developing innovative and effective cosmetic products [12, 13]. Manufacturers are tasked with creating high-quality, cost-effective, and eco-friendly products that minimize potential risks associated with harmful ingredients [14]. Consequently, there is a rising demand for cosmetic products based on herbal ingredients that offer fewer adverse effects [15].

This review evaluates the scientific evidence supporting naturally derived ingredients in skin-rejuvenating formulations and analyzes their mechanisms of action. Exploring the potential of natural antiaging agents provides a comprehensive overview of their efficacy and safety, paving the way for future eco-friendly and effective cosmetic advancements.

2. DATA COLLECTIONS

2.1 Literature research

To achieve a thorough understanding of the mechanisms and efficacy of natural antiaging agents in cosmetics, an extensive literature review was conducted using the Publish or Perish application. Comprehensive searches were performed in databases such as Scopus and PubMed, employing a combination of keywords like 'antiaging*', 'plants', 'extracts', and 'cosmetics'. The asterisk (*) was used as a wildcard character in the search queries to expand the scope and capture variations of the specified keywords. For example, searching for "antiaging" would yield results with terms like "anti-aging," "antiageing," and "anti-ageing."

Studies published in English from 1900 to 2024 that evaluated naturally derived substances in cosmetic antiaging products were included. Articles were excluded if they were not original research, did not focus on cosmetic antiaging, or were not available in full text.

2.2 Study inclusion

Studies that met the inclusion criteria were chosen for the review. The process of including studies was managed using an internet-based platform named Covidence. The method of selecting studies for inclusion is illustrated using a flow diagram based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

2.3 Selected antiaging studies

A comprehensive search across Scopus and PubMed yielded a total of 183 reference titles. Employing Publish or Perish as the database manager, all references underwent an initial screening to eliminate duplicates (n=1). Following this process, 32 full-text reviews remained for evaluation. However, one article was excluded due to the absence of pertinent data related to the study outcomes (Figure 1).

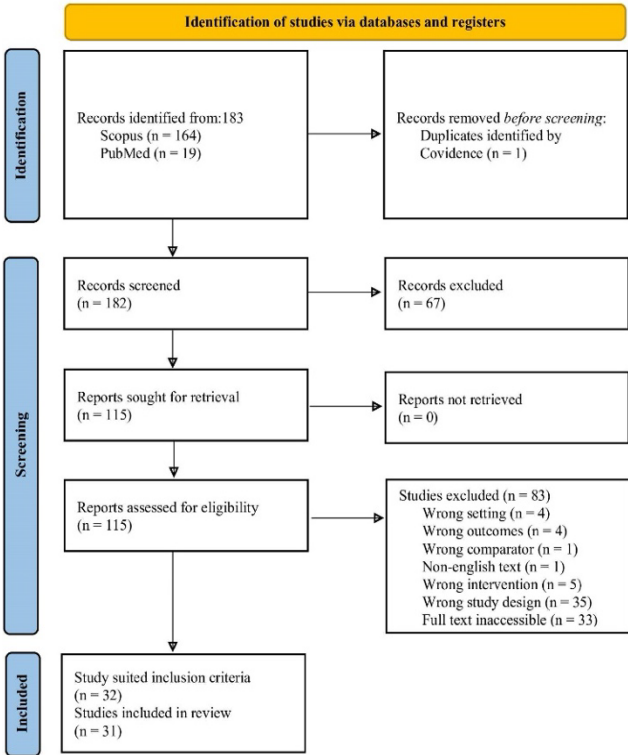


Figure 1. PRISMA flow diagram for the systematic review

2.4 Data extraction

Data extraction was performed using a standardized form in Microsoft Excel, with the extracted data cross-checked for accuracy and completeness. The data included author information, publication year, plant name, extraction method, antiaging measurement, and study outcome.

2.5 Risk of bias assessment

The evaluation of bias risk in the included studies was customized according to the design of each study. For clinical trials, the Jadad scale was used, where scores of 3, 4, and 5 denoted a low risk of bias. For in vitro studies, a qualitative assessment was carried out based on the transparency of the methodology, clarity of treatment protocols, use of positive and negative controls, replication of tests, and completeness in reporting the test results. Risk assessments were conducted independently by the researchers, with any differing opinions resolved through discussion to reach a consensus.

3. RESULTS

The summary of data extracted from all published literature on the natural anti-aging potential is presented in Table 1. Numerous plant-based resources have demonstrated excellent anti-aging properties, as illustrated in Figure 2. The findings show that natural anti-aging ingredients possess diverse and potent biological activities that can be utilized in cosmetic formulations. These ingredients exhibit antioxidant, anti-inflammatory, anti-collagenase, anti-elastase, anti-tyrosinase, and anti-hyaluronidase activities.

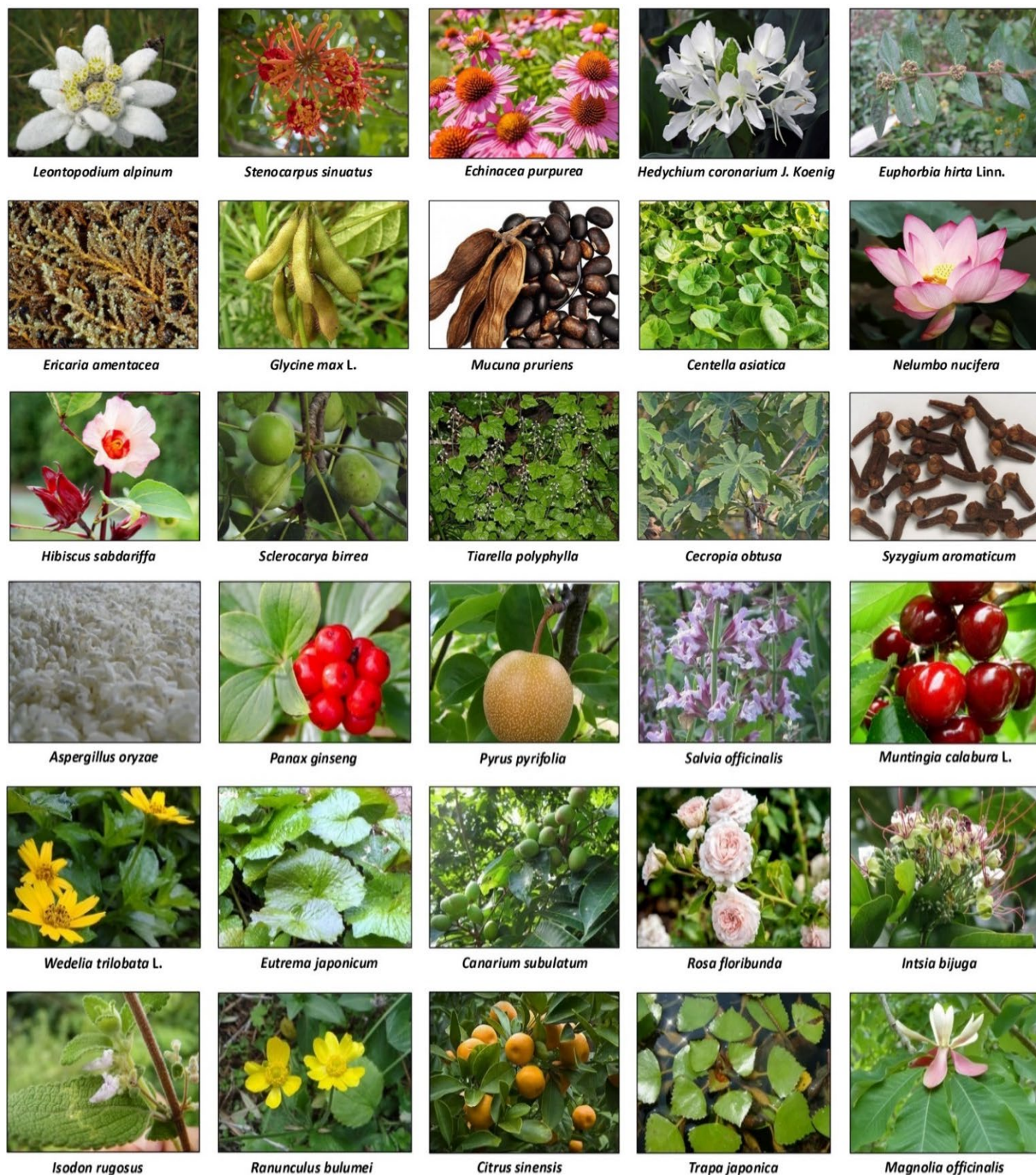


Figure 2. Numerous plant-based resources with potential anti-aging properties

3.1 Overview of included studies and phytochemical resources

A total of 32 studies were included in this review, comprising in vitro, in vivo, and several clinical investigations. Most studies evaluated antioxidant activity (DPPH, ABTS, ROS assays) and antiaging-related enzyme inhibition (collagenase, elastase, hyaluronidase, tyrosinase), while others confirmed their effects on fibroblast proliferation, collagen

synthesis, and UV protection.

Several studies also reported enhanced activity through fermentation (e.g., *Magnolia officinalis*, *Cornus mas* L.) and nanoparticle formulations (e.g., *Panax ginseng* berries), improving compound stability and bioavailability. Collectively, these findings highlight the diversity of phytochemical resources explored for natural antiaging cosmetics.

Table 1. Summary of all data extraction of selected published literature articles on potential natural anti-aging

Plant Name	Part	Antianging Assay	Key Findings	Testing Results	Ref.
<i>Leontopodium alpinum</i> (Edelweiss)	-	Antioxidant	Exhibited strong antioxidant activity in multiple in vitro experiments when exposed to UVB irradiation. Demonstrated anti-inflammatory and anti-wrinkle properties, with enhanced moisturization.	Significant improvement in dermal density, skin elasticity, periorbital wrinkle reduction, and skin thickness compared to the placebo.	[16]
<i>Stenocarpus sinuatus</i> (Firewheel tree)	Leaves	Anti-collagenase, anti-elastase, anti-tyrosinase, anti-hyaluronidase	Evaluated the effectiveness in inhibiting enzymes responsible for skin aging.	The SSHF methanol extract significantly inhibited collagenase, elastase, tyrosinase, and hyaluronidase, with IC ₅₀ values of 60.03, 177.5, 67.5, and 38.8 µg/mL. Glycerol extraction showed substantial suppression of collagenase, elastase, and tyrosinase. Enhanced scratch closure in HaCaT keratinocyte monolayers.	[17]
<i>Echinacea purpurea</i> (Purple coneflower)	Leaves, stalks, and flowers	Radical scavenging, anti-collagenase, anti-elastase, anti-tyrosinase, anti-hyaluronidase, wound healing	Glycol extract provides a quick and efficient way to make extracts that are powerful antioxidants.	The absolute extracted from the rhizome exhibited the most potent inhibition of collagenase. Both the rhizome and leaf sheath concretes had encouraging activity against hyaluronidase.	[18]
<i>Hedychium coronarium</i> J. Koenig (butterfly ginger family)	Rhizomes, leaf sheaths, and leaves	Antioxidant, anti-collagenase, anti-elastase, anti-tyrosinase, anti-hyaluronidase	The absolutes generated from rhizomes showed the highest antioxidant activity.	Oil-in-water (o/w) cream formulated with the extract exhibited notable antioxidant activity when applied topically. Reduce UV-induced oxidative stress and inflammation in skin cells, inhibit skin-related enzymes like tyrosinase, collagenase, and hyaluronidase.	[19]
<i>Euphorbia hirta</i> Linn.	Herb	Antioxidant	The extract of <i>E. hirta</i> L. demonstrates 80% DPPH free radical scavenging at 100 µg/mL.	BSE and daidzein demonstrated complementary anti-aging mechanisms.	[20]
<i>Ericaria amentacea</i> (Mediterranean Seaweed)	Frond	Antioxidant, anti-tyrosinase, anti-collagenase, anti-hyaluronidase, photoprotective	Extracts from lyophilized apices or thalli exhibited strong biological activity.	Demonstrated strong antioxidant activity and inhibited key skin-aging enzymes - hyaluronidase, collagenase, and elastase.	[21]
<i>Glycine max</i> (L.) (Black Soybean)	Bean	H ₂ O ₂ scavenging, anti-hyaluronidase	BSE showed stronger H ₂ O ₂ scavenging, while daidzein was more effective at inhibiting hyaluronidase.	<i>C. asiatica</i> extract significantly inhibited elastase activity.	[22]
<i>Mucuna pruriens</i> var. <i>pruriens</i> and <i>Mucuna pruriens</i> var. <i>utilis</i> (cowhage)	Seed	Anti-aging, antioxidant, and moisturizing properties	<i>M. pruriens</i> var. <i>utilis</i> showed higher levels of flavonoids and phenolics.	Ethanol stem extract exhibited exceptional anti-collagenase activity (up to 99%).	[23]
<i>Centella asiatica</i> , <i>Nelumbo nucifera</i> Gaertn, and <i>Hibiscus sabdariffa</i>	<i>C. Asiatica</i> aerial part, <i>H. sabdariffa</i> flower, and <i>N. nucifera</i> petal	Antioxidant, anti-collagenase, and anti-elastase assays	The extracts showed strong DPPH radical scavenging and collagenase inhibition.	Reduced caspase-3 enzyme activity, decreased MMP-1 expression, and increased type I procollagen production.	[24]
<i>Sclerocarya birrea</i> (A. Rich.) Hochst (Marula)	Stems, leaves, and fruits	Anti-elastase and anti-collagenase	Stem extracts showed the most potent inhibitory effects.	Significantly reduced MMP-1 and protein carbonyl concentrations.	[25]
<i>Tiarella polyphylla</i> D. Don	Herb	Anti-photoaging (evaluated against UVB-induced damage in human foreskin fibroblast (HS68))	Mitigated UVB-induced cellular damage and improved cell survival rates.	DPPH radical scavenging and superoxide dismutase-like activity.	[26]
<i>Cecropia obtusa</i>	Leaf	Anti-photoaging (assess the antiaging Impact on human fibroblasts and keratinocytes when exposed to ultraviolet radiation)	Enhanced collagen and hyaluronic acid levels.		[27]
<i>Syzygium aromaticum</i> L.	-	Antioxidant and anti-wrinkling	Boosted elastase inhibition and reduced MMP-1 content.		[28]

<i>Aspergillus oryzae</i> (rice)	Seed	Anti-photoaging	Reduced MMP-1 and skin fibroblast elastase (SFE) gene expressions.	Enhanced elastase-inhibitory activity in UVA-treated fibroblasts.	[29]
<i>Panax ginseng</i> Meyer berries	Fruit	Antioxidant, anti-tyrosinase	GBAuNPs and GBAgNPs exhibited remarkable antioxidant and anti-tyrosinase properties.	GBAuNPs showed cytotoxic effects on melanoma cell lines, while GBAuNPs were non-toxic to fibroblast cell lines.	[30]
<i>Pyrus pyrifolia</i>	Callus from young leaves	Antioxidant, cell proliferation, procollagen synthesis (skin rejuvenators)	Exhibited free radical scavenging activity and increased procollagen type I C-peptide.	Enhanced keratinocyte wound repair rates and fibroblast wound recovery rates.	[31]
<i>Salvia officinalis</i>	Leaves	Antioxidant, anti-hyaluronidase, anti-collagenase, anti-elastase	Methanol extract showed strong antioxidant activity and inhibited aging-related enzymes.	Significantly reduced wrinkle scores in UV-induced photoaging models.	[32]
<i>Muntingia calabura</i> L. (Kersen)	Fruit	Antioxidant, anti-collagenase, anti-elastase	Ethanol extract displayed significant antioxidant properties.	The ethyl acetate fraction showed the highest effectiveness in suppressing elastase and collagenase enzymes.	[33]
<i>Wedelia trilobata</i> L.	Flower	Antioxidant	Extracts demonstrated robust scavenging capabilities.	IC ₅₀ value of 7.98 ± 0.40 µg/mL for pure WT floral extracts, comparable to ascorbic acid.	[34]
<i>Eutrema japonicum</i> (Miq.) Koidz. (wasabi or Japanese horseradish)	Flowers, roots, and leaves	Antioxidant, anti-elastase, anti-collagenase, anti-hyaluronidase	Floral extract showed the strongest DPPH scavenging activity.	Floral extract exhibited higher inhibitory effects on collagenase, elastase, and hyaluronidase than others.	[35]
<i>Canarium subulatum</i>	Fruit	Photoprotective and skin-barrier-strengthening	Cs-ME prevented UV-induced cell death and reduced age-related gene expression.	Increased expression of epidermal barrier components through ERK/p38-AP-1 signaling.	[36]
<i>Rosa floribunda</i>	Flower petal	Antioxidant, anti-collagenase, anti-elastase, anti-hyaluronidase, anti-tyrosinase	ReNPs demonstrated significant radical scavenging activity.	Showed strong anti-aging effects through dose-dependent inhibition of aging-related enzymes.	[37]
<i>Intsia bijuga</i>	Heartwood	Anti-tyrosinase, antioxidant, and sun protector	The 50% ethanol extract showed significant antioxidant and antityrosinase properties.	Phytosome F3 exhibited exceptional antioxidant, antityrosinase, and SPF values.	[38]
<i>Isodon rugosus</i> (Wall. ex Benth.) Codd	Callus from the stem and leaf	Antioxidant, anti-collagenase, anti-elastase, anti-hyaluronidase, anti-tyrosinase	Rosmarinic acid was the primary contributor to antioxidant and anti-aging effects.	Pentacyclic triterpenoids were associated with inhibiting elastase, collagenase, and tyrosinase.	[39]
<i>Ranunculus bulumei</i>	Aerial part	Photoaging protective	Rb-ME showed lower expression of the MMP9 and COX-2 genes.	Elevated levels of SIRT1 and type-1 collagen in HaCaT cells.	[40]
<i>Citrus sinensis</i> (Sweet orange)	Peel	Antioxidant, anti-elastase, anti-collagenase (in vitro), and anti-wrinkle (in vivo)	CSPE demonstrated strong antioxidant activity.	Topical administration of CSPE-NLC cream significantly improved UV-induced photoaging symptoms in mice.	[41]
<i>Trapa japonica</i>	Fruit	Cell proliferation, collagen synthesis, and anti-wrinkle	PEP exhibited notable enhancements in cell proliferation and collagen synthesis.	Demonstrated antiaging properties in clinical trials.	[42]
<i>Magnolia officinalis</i>	Bark	Tyrosinase inhibitory, antioxidant, antimicrobial, and antiaging	Fermented methanol extract showed the highest antioxidant and anti-tyrosinase activities.	Fermented extracts exhibited enhanced antibacterial effects.	[43]
<i>Nephelium lappaceum</i> Linn.	Leaves, branches, seeds, and peels	Antioxidant, anti-melanogenesis, tyrosinase inhibition	Evaluated the anti-aging activities of different parts of the plant.	Extracts showed potential for skin applications.	[44]
<i>Rubus fraxinifolius</i> Poir.	Leaves	Antioxidant and anti-elastase	Older leaves yielded extracts with higher antioxidant and elastase enzyme inhibitory activities.	Distilled water extract showed significant potential as an active ingredient in antiaging cosmetics.	[45]

<i>Cornus mas</i> L. (dogwood)	Fruit	Antioxidant, inhibition of collagenase and elastase activity	<i>Cornus mas</i> L. ferment exhibited higher antioxidant activity.	DPPH and ABTS assays showed higher antioxidant activity in the fermented extract compared to the non- fermented extract.	[46]
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3.2 In vitro antioxidant capacity: The first line of defense against aging

Antioxidant activity represents the primary defense mechanism against oxidative stress, a major contributor to skin aging. Numerous included studies demonstrated the potent ability of natural extracts to neutralize reactive oxygen species (ROS) and prevent lipid peroxidation as well as DNA damage in skin cells.

Leontopodium alpinum (Edelweiss) callus culture extract (LACCE) revealed strong antioxidant activity in vitro, showing a significant ability to scavenge free radicals and protect against UVB-induced oxidative stress [16]. *Echinacea purpurea* extracts exhibited pronounced antioxidant properties, evidenced by their potent radical scavenging and Fe²⁺-chelating activities [18]. Similarly, rhizomes of *H. coronarium* exhibited the highest antioxidant activity among the tested extracts, demonstrating strong free radical scavenging and ferric-reducing abilities [19].

Euphorbia hirta extract achieved over 80% DPPH inhibition at a concentration of 100 µg/mL. When formulated into an oil-in-water (O/W) cream using stearic acid as an emulsifier, the extract-loaded cream retained notable antioxidant capacity, with 87.89% scavenging activity at the same concentration. The formulation also showed favorable physicochemical stability, maintaining a pH of 4.4-5.1, suitable viscosity, and no phase separation after centrifugation at 3,000 rpm for 30 minutes. These findings indicate that *E. hirta* Linn. extract possesses significant potential as an anti-aging agent in cosmetic formulations [20].

Extracts of *Centella asiatica*, *Nelumbo nucifera*, and *Hibiscus sabdariffa* also demonstrated significant DPPH and ABTS radical scavenging activity [24]. *Wedelia trilobata* flower extract showed an IC₅₀ value comparable to ascorbic acid, confirming its strong antioxidant potency [34]. The floral extract of *Eutrema japonicum* (Miq.) Koidz displayed the highest DPPH scavenging activity among the tested parts of the plant [35].

Furthermore, extracts from the older leaves of *Rubus fraxinifolius* exhibited an IC₅₀ value of 14.02 ± 0.148 µg/mL using the DPPH assay and 5.02 ± 0.217 µg/mL using the ABTS method, along with the highest FRAP value, indicating strong reducing capacity [45]. Both the extract and the ferment of *Cornus mas* L. demonstrated notable antioxidant and anti-aging properties, with the fermented form showing higher activity as confirmed by DPPH and ABTS assays [46]. In addition, nanoparticle formulations derived from *Panax ginseng* berries significantly enhanced antioxidant and anti-tyrosinase activity, suggesting improved bioavailability and efficacy of the active compounds [30].

3.3 Inhibition of skin-aging related enzymes

3.3.1 Protection of extracellular matrix: Anti-collagenase and anti-elastase activities

Several natural extracts included in this review exhibited strong anti-collagenase and anti-elastase activities. The methanol extract of *Stenocarpus sinuatus* leaves showed significant inhibitory effects on both collagenase and elastase,

with IC₅₀ values comparable to positive controls [17]. Similarly, *Echinacea purpurea* extracts demonstrated substantial inhibition of collagenase and elastase, complementing their antioxidant properties and contributing to improved dermal structure [18].

Hedychium coronarium rhizome, *Ericaria amentacea*, *Centella asiatica*, *Nelumbo nucifera* Gaertn, and *Hibiscus sabdariffa* extract exhibited notable inhibitory effects on skin-related enzymes like collagenase, which are implicated in skin aging processes such as wrinkle formation [19, 21, 24]. Among all evaluated plants, *Sclerocarya birrea* stem extract exhibited the most potent anti-collagenase activity, reaching up to 99% inhibition, positioning it as one of the most promising natural anti-aging agents [25].

Other extracts, such as *Salvia officinalis*, *Muntingia calabura* (particularly the ethyl acetate fraction), *Eutrema japonicum* (Miq) Koidz, *Rosa floribunda*, and *Isodon rugosus*, also demonstrated enzyme inhibitory effects on skin-related enzymes like collagenase and elastase [32, 33, 35, 37, 39].

3.3.2 Regulation of pigmentation and hydration: Anti-tyrosinase and anti-hyaluronidase activities

The inhibition of tyrosinase and hyaluronidase enzymes plays an essential role in maintaining even skin tone and optimal hydration. Therefore, regulating the activities of these enzymes is a crucial strategy in both anti-aging and skin-brightening approaches. Several studies reported that natural extracts effectively suppress tyrosinase and hyaluronidase activities.

S. sinuatus methanol extract, *Echinea pupurea*, *Hedychium coronarium* J. Koenig, *Ericaria amentacea*, synthesized magnesium nanoparticles (RcNps) from *Rosa floribunda* petals, and *Isodon rugosus* (Wall. ex Benth.) Codd exhibited significant inhibitory effects on tyrosinase and hyaluronidase, which are beneficial for maintaining skin hydration and could potentially delay the visible signs of aging, such as uneven pigmentation [17-19, 21, 37, 39]. The pentacyclic triterpenoids found in *Isodon rugosus* (Wall. ex Benth.) Codd was specifically associated with tyrosinase inhibition [39].

Glycine max L. (black soybean) extract and its major isoflavone, daidzein, also demonstrated notable anti-hyaluronidase activity. While the black soybean extract demonstrated stronger hydrogen peroxide scavenging ability, daidzein showed superior inhibition of hyaluronidase, with an IC₅₀ value of 95.80 ± 3.98 µg/mL versus BSE's IC₅₀ of 152.56 ± 13.98 µg/mL. This suggests that daidzein contributes significantly to maintaining skin hydration and elasticity by preventing the enzymatic degradation of hyaluronic acid [22].

M. pruriens var. *utilis* showed higher levels of flavonoids and phenolics compared to var. *pruriens* and demonstrated strong antioxidant activity and inhibition of key skin-aging enzymes, including hyaluronidase [23]. *Eutrema japonicum* (Miq.) Koidz and *Salvia officinalis* also exhibited a notable inhibitory effect on hyaluronidase and help prevent wrinkle formation [32, 35].

Pérez et al. [30] investigated the potential of ginseng berry extract (GBE) in producing gold and silver nanoparticles. The nanoparticles exhibited remarkable antioxidant, anti-tyrosinase, and antibacterial properties, with GBAuNPs

proving non-toxic to fibroblast cell lines. Sari et al. [38] evaluated the anti-aging potential of *Intsia bijuga* extracts, where the 50% ethanol extract demonstrated significant antioxidant and anti-tyrosinase activities, while the Phytosome F3 formulation exhibited exceptional antioxidant, anti-tyrosinase, and SPF-enhancing effects.

Wu et al. [43] found that the methanol extract of *Magnolia officinalis* bark fermented with *Aspergillus niger* demonstrated the highest antioxidant and anti-tyrosinase activities. The fermented extracts exhibited enhanced antibacterial effects and inhibitory activity against enzymes linked to skin aging. Likewise, Boonpisuttinant et al. [44] investigated the in vitro anti-ageing activities of ethanolic extracts from different parts of Pink rambutan (*Nephelium lappaceum* L.), including leaves, branches, seeds, and peels from ripe and young fruits. The extraction yields ranged from 10.62% to 30.63%, with flavonoids being the main phytochemicals in most extracts. The PR-Y-M and PR-Y-Sox extracts had the highest total phenolic and flavonoid contents, respectively. The PR-L-M extract showed the highest antioxidant activities. All PR extracts at 0.01 and 0.1 mg/mL showed no cytotoxicity on B16F10 cells and human skin fibroblasts. The PR-R-Sox extract exhibited the highest anti-melanogenesis and mushroom tyrosinase inhibition activities, comparable to kojic acid. The PR-Y-Sox extract showed collagen biosynthesis and stimulation of anti-ageing genes (Sirt1 and Foxo1) similar to standards L-ascorbic acid and resveratrol.

3.4 Cell-based assays: Anti-photoaging, wound healing, and collagen synthesis

Beyond enzyme inhibition and antioxidant defense, several natural extracts demonstrated protective effects on skin structure and function through various biological pathways. Kim et al. [26] reported that *Tiarella polyphylla* extract effectively mitigated UVB-induced cellular damage by improving cell survival rates, reducing caspase-3 enzyme activity, decreasing MMP-1 expression, and increasing type I procollagen production. These findings indicate its potential role in maintaining collagen integrity under photooxidative stress.

Alves et al. [27] examined the effects of *Cecropia obtusa* extract on UV-exposed keratinocytes and fibroblasts. The extract enhanced collagen and hyaluronic acid levels, reduced MMP-1 and protein carbonyl concentrations, and exhibited antioxidant and anti-aging effects by inhibiting the UV-triggered elevation of pro-inflammatory cytokines.

Hwang et al. [28] assessed the anti-wrinkle benefits of *Syzygium aromaticum* L. extract on human skin fibroblasts. The extract reduced MMP-1, MMP-2, MMP-3, and MMP-9 gene expression. Jamaluddin et al. [29] evaluated the anti-photoaging properties of *Aspergillus oryzae* fermentation extracts. The extracts significantly reduced MMP-1 and skin fibroblast elastase (SFE) gene expression and suppressed MMP-1 secretion, particularly in UVB-exposed co-cultures.

Park et al. [31] analyzed the anti-aging potential of *Pyrus pyrifolia* callus extract. The extract showed increased procollagen type I C-peptide levels in fibroblasts. It also enhanced keratinocyte and fibroblast wound recovery rates. Likewise, Hwang et al. [36] demonstrated that *Canarium subulatum* methanol extract (Cs-ME) protected against UV-induced cell death and ROS generation. Cs-ME increased the expression of epidermal barrier components and showed

cytoprotective, anti-aging, and skin barrier-strengthening actions.

Hong et al. [40] found that *Ranunculus bulumei* methanol extract (Rb-ME) showed lower expression of MMP9 and COX-2 genes and higher levels of SIRT1 and type-1 collagen in HaCaT cells subjected to UVB irradiation. Amer et al. [41] demonstrated that *Citrus sinensis* peel extract (CSPE) possessed strong antioxidant activity. Topical administration of CSPE-NLC cream significantly ameliorated UV-induced photoaging symptoms in mice. Jang et al. [42] identified a newly synthesized peptide (PEP) from *Trapa japonica* fermentation extract (FTJ), which markedly enhanced cell proliferation and collagen synthesis, providing further evidence of the regenerative potential of fermented natural compounds.

3.5 Clinical and in vivo evidence

In addition to in vitro investigations, several studies have provided in vivo and clinical evidence supporting the anti-aging efficacy of natural extracts. A clinical study on *Leontopodium alpinum* extract demonstrated significant improvements in skin elasticity and dermal density, and reduced periocular wrinkles compared to a placebo [16]. Similarly, *Trapa japonica* extract, evaluated through a clinical trial, showed notable increases in collagen synthesis and cell proliferation [42].

In an in vivo study, *Citrus sinensis* peel extract significantly ameliorated UV-induced photoaging symptoms in mice, improving skin texture and reducing wrinkle formation through antioxidant and anti-inflammatory mechanisms [41]. These findings collectively provide strong translational evidence that natural bioactive compounds exert measurable benefits in maintaining youthful skin appearance and function under real biological conditions.

4. DISCUSSION

4.1 General trends of natural ingredients

This systematic review highlights a significant and growing shift toward the use of natural ingredients in the formulation of anti-aging cosmetic products. This trend is fueled by increasing consumer preference for sustainable, environmentally friendly, and efficacious skincare solutions that reflect a broader commitment to natural and holistic wellness. The reviewed studies collectively emphasize the diverse bioactivities of natural anti-aging agents, demonstrating their potential not only as powerful functional ingredients but also as safer and more sustainable alternatives to synthetic compounds.

One of the most salient trends observed is the marked preference for plant-based extracts, which are replete with bioactive compounds such as antioxidants, flavonoids, and polyphenols. These compounds are instrumental in combating skin aging by neutralizing free radicals, inhibiting the activity of enzymes responsible for collagen and elastin degradation, and modulating inflammatory pathways. For instance, the study by Cho et al. [16] on *Leontopodium alpinum* (Edelweiss) callus culture extract (LACCE) revealed its strong antioxidant activities in vitro. LACCE exhibited a significant ability to scavenge free radicals and protect against UVB-induced oxidative stress. In vivo clinical trials further demonstrated

that LACCE significantly improved skin elasticity and dermal density, and reduced periorcular wrinkles compared to a placebo. These results highlight LACCE's potential as an effective antiaging agent in cosmetics.

Similarly, the potent inhibitory effects of *Stenocarpus sinuatus* (Firewheel tree) extract on collagenase, elastase, tyrosinase, and hyaluronidase, as reported by Younis et al. [17], underscore the efficacy of natural extracts in addressing various aspects of skin aging. The methanol extract of *S. sinuatus* exhibited significant inhibitory effects on these enzymes, with IC₅₀ values comparable to positive controls. These findings suggest that *S. sinuatus* extract could be a valuable addition to antiaging cosmetic formulations.

Another significant trend is the increasing interest in the use of fermented extracts and nanoparticles derived from natural sources. Fermentation processes enhance the bioavailability and efficacy of natural compounds, making them more effective in cosmetic formulations. For example, the study by Wu et al. [43] on *Magnolia officinalis* bark fermented with *Aspergillus niger* demonstrated higher antioxidant and anti-tyrosinase activities compared to non-fermented extracts. The fermented methanol extract showed the highest antioxidant and anti-tyrosinase activities, suggesting that fermentation can significantly enhance the efficacy of natural ingredients.

Similarly, the use of nanoparticles, such as those synthesized from *Panax ginseng* Meyer berries by Pérez et al. [30], offers enhanced delivery and penetration of active ingredients into the skin, thereby improving their antiaging effects. The nanoparticles exhibited remarkable antioxidant, anti-tyrosinase, and antibacterial properties, with gold nanoparticles (GBAuNPs) proving non-toxic to fibroblast cell lines. This highlights the potential of nanoparticles in enhancing the therapeutic potential of natural ingredients.

4.2 Bioactive compounds mediating antiaging effects

The remarkable anti-aging effects of botanical and marine-derived compounds are attributed to their complex blend of bioactive constituents that work through various molecular pathways to support skin regeneration. Polyphenols, particularly flavonoids like quercetin (from *Hedychium coronarium*) and rutin (*Echinacea purpurea*), act as potent antioxidants. They neutralize reactive oxygen species (ROS), inhibit collagenase and elastase via zinc ion chelation at enzyme active sites, and preserve extracellular matrix integrity [47]. Phenolic acids, such as rosmarinic acid (abundant in *Isodon rugosus* callus cultures), excel in scavenging free radicals and amplifying endogenous antioxidant defenses through Nrf2-ARE pathway activation.

Triterpenoids, exemplified by asiaticoside in *Centella asiatica* and ursolic acid in *Nephelium lappaceum*, boost collagen production by stimulating TGF- β /Smad signaling while curbing MMP expression through AP-1 transcription factor modulation [48]. Alkaloids like mucunaine in *Mucuna pruriens* seeds exhibit dual efficacy: they inhibit hyaluronidase-mediated hyaluronic acid breakdown, enhance moisture retention, and suppress melanogenesis via competitive tyrosinase inhibition.

Marine ecosystems yield sulfated polysaccharides such as fucoidan from *Ericaria amentacea* seaweed, which form protective barriers against UV-induced DNA damage and

promote fibroblast proliferation via integrin signaling. Peptidic innovations, like the novel peptide from *Trapa japonica* fermentation extract (FTJ), boost type I procollagen synthesis by 140% compared to controls and prevent elastin fragmentation through elastase allosteric modulation [42]. Fermentation-derived metabolites—such as *Aspergillus oryzae*-processed rice extracts—unlock bioactive aglycones (e.g., genistein) with 20x higher antioxidant capacity than glycosidic forms. Volatile terpenes, including linalool (*Rosa floribunda*) and limonene (*Citrus sinensis* peels), synergistically penetrate the stratum corneum to quench singlet oxygen radicals and enhance macromolecule delivery [49].

Molecular structure critically dictates function: ortho-dihydroxy configurations in catechol-containing flavonoids enable superior metal chelation, as seen in *Sclerocarya birrea* ellagitannins. These compounds synergize within phytocomplexes, where minor constituents enhance primary effects—e.g., chlorogenic acid in *Cecropia obtusa* stabilizes flavonoid quinones to bolster photoprotection. Modern extraction methods, such as supercritical CO₂ processing of *Magnolia officinalis* bark, unveil novel bis-obovato derivatives that suppress MMP-1 at nanomolar concentrations.

The varied structural frameworks of these compounds provide a comprehensive array of anti-aging functions, spanning from epigenetic modulation (e.g., resveratrol-like stilbenes in *Pyrus pyrifolia* that activate SIRT1) to strengthening intercellular junctions (e.g., Glycine max isoflavones promoting claudin-4 expression). Advances in computational docking are now enabling the targeted identification and combination of these natural compounds, supporting the development of precision anti-aging cosmeceuticals that leverage the intricate biochemistry found in nature.

4.3 Molecular mechanism of polyphenols as antiaging

The skin is constantly exposed to various environmental stimuli, such as ultraviolet (UV) radiation, air pollution, or smoking, which accelerate the aging process (Figure 3). Skin aging is characterized by loss of elasticity, wrinkle formation, a reduced dermal-epidermal junction, and delayed wound healing. Therefore, many studies have shown that natural polyphenol compounds can delay the aging process by regulating age-related signaling pathways in aged dermal fibroblasts [50].

Polyphenols, diverse plant-derived compounds classified into flavonoids, stilbenes, phenolic acids, and lignans, counteract these processes through multifaceted mechanisms [51]. Firstly, they potently scavenge ROS and enhance endogenous antioxidant defenses (e.g., via activating the NRF2 pathway, increasing HO-1, SOD, catalase), thereby mitigating oxidative stress induced by UV or pollutants like PM 2.5. This reduction in oxidative stress subsequently dampens pro-inflammatory signaling; polyphenols like curcumin, fisetin, myricetin, and syringaresinol inhibit the activation of NF- κ B and MAPK pathways (ERK, JNK, p38), reducing the expression and secretion of inflammatory cytokines (TNF- α , IL-6, IL-1 β , COX-2, PGE2) and matrix-degrading enzymes (MMP-1, MMP-3, MMP-9), thus preventing collagen and elastin breakdown.

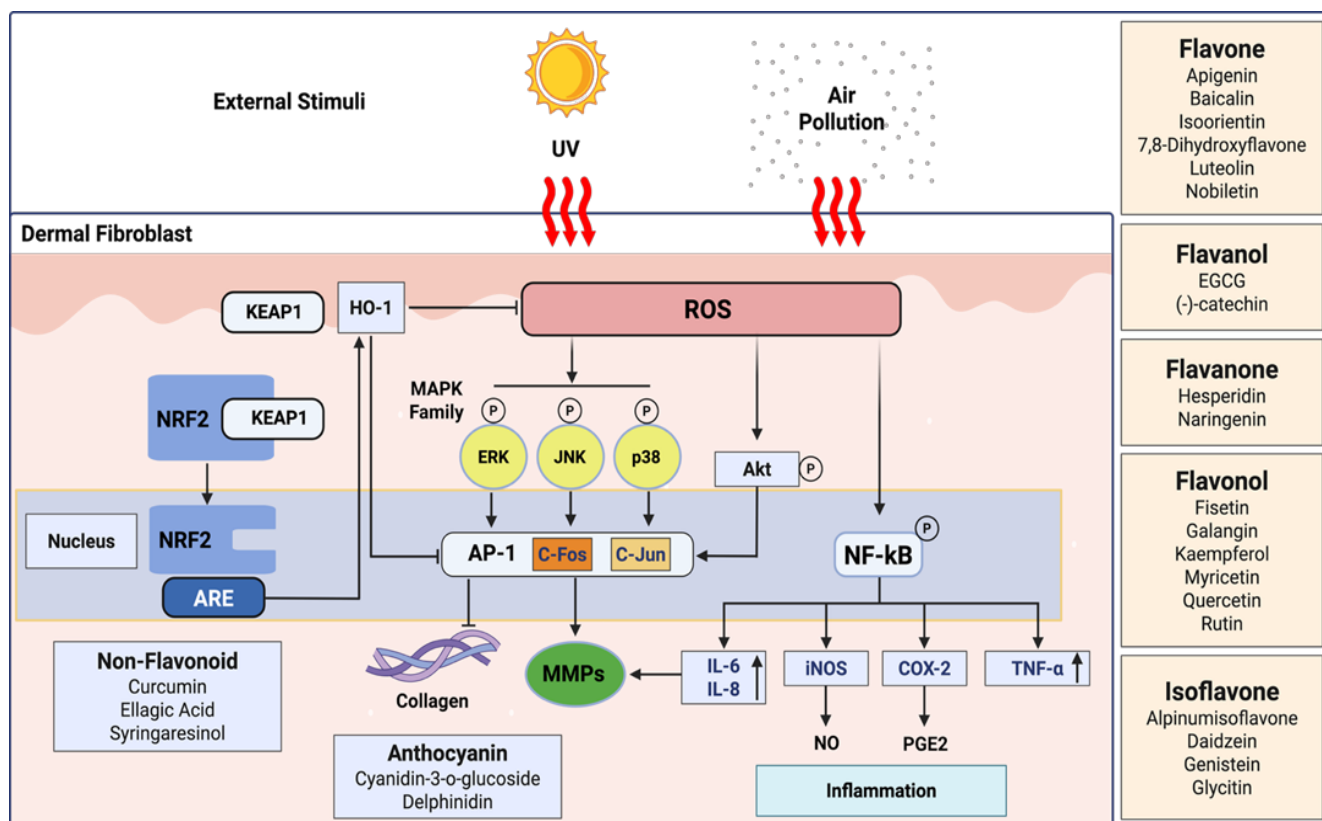


Figure 3. Molecular mechanism of polyphenols with anti-aging activity

Secondly, polyphenols positively regulate the TGF- β /Smad signaling pathway, crucial for collagen biosynthesis. UV irradiation suppresses this pathway, leading to reduced collagen production [52]. Polyphenols such as apigenin, glycitin, daidzein, fisetin, and galangin enhance the expression of TGF- β and promote the phosphorylation of Smad2/3, facilitating the formation of Smad complexes that translocate to the nucleus to upregulate procollagen gene transcription. Galangin additionally modulates microRNAs (e.g., suppresses hsa-miR-4535 targeting Smad4), further promoting collagen synthesis. Thirdly, polyphenols combat cellular senescence, characterized by markers like SA- β -gal activity and elevated p16, p21, and p53. They act as senolytics (e.g., fisetin) or suppress the senescence-associated secretory phenotype (SASP), which secretes pro-inflammatory factors, exacerbating tissue damage. Fisetin, kaempferol, baicalin, and naringenin reduce senescent cell burden and SASP secretion, partly by inhibiting NF- κ B and PI3K/AKT/mTOR pathways. Fourthly, they restore impaired autophagy, a cellular clearance mechanism vital for removing damaged components. Polyphenols like cyanidin-3-o-glucoside (C3G) and isoorientin enhance autophagy flux by increasing levels of key proteins (Atg5, LC3-II), counteracting UV-induced lysosomal dysfunction, and promoting cell survival. Lastly, certain polyphenols aid DNA repair mechanisms. Apigenin and silibinin enhance nucleotide excision repair (NER) by upregulating proteins like XPA, XPB, XPC, XPG, and p53, reducing UV-induced DNA damage (e.g., cyclobutane pyrimidine dimers) [53].

While demonstrating significant efficacy *in vitro* and in animal models (e.g., improving skin elasticity, reducing wrinkles, increasing collagen density), challenges remain regarding the bioavailability, stability, and skin delivery of polyphenols due to their sensitivity to light/heat and low

solubility. Encapsulation strategies like liposomes are being explored to overcome these limitations. Future research should focus on elucidating polyphenol effects on autophagy and senescence in dermal fibroblasts, identifying novel aging biomarkers, optimizing topical formulations for enhanced delivery, and conducting clinical trials, potentially exploring synergistic combinations of polyphenols for maximal anti-aging benefits in functional cosmetics and dermatological applications.

4.4 Implications for the cosmetic industry

Natural cosmetic ingredients offer a multitude of advantages over their synthetic counterparts, including fewer side effects, less irritation, quicker skin absorption, and superior biodegradability [51]. As a result, current research is focused on discovering antiaging cosmetic ingredients from a variety of natural sources. Amid increasing consumer worries about the safety and sustainability of ingredients, the shift towards "clean beauty" is clear, with a preference for products composed of natural elements free from harmful chemicals. Examples of commercially available antiaging products made from natural ingredients can be found in Table 2.

The increasing use of natural ingredients in antiaging products mirrors consumers' inclination towards environmentally friendly options and underscores the cosmetics industry's efforts to mitigate the environmental impact of synthetic compounds [54]. Natural ingredients generally break down more easily in the environment, which helps to reduce the ecological footprint of cosmetic products. The market for antiaging products now features a diverse array of natural ingredients, such as Patchouli Oil, Avocado Oil, *Rosa Damascena* Flower Extract, *Calendula Officinalis* Flower Extract, and Rosemary Leaf Extract.

Table 2. Commercial product from natural ingredients

Product	Natural Ingredient	Benefit
 Kiehl's Creamy Eye Treatment with Avocado	Avocado oil, hydrogenated castor oil, hydrogenated jojoba oil, sunflower seed oil	Antioxidant, emollient
 Dr. Hauschka Rose Day Cream	Avocado oil, <i>Rosa damascena</i> flower wax	Antioxidant, emollient
 REN Clean Skincare Evercalm Global Protection Day Cream	Kudzu extract, calendula officinalis flower extract, rosemary leaf extract	Antioxidant
 Origins Plantscription Antiaging Power Serum	<i>Rosa damascena</i> flower oil, safflower seed oil, rosemary leaf, cucumber fruit extract	Antioxidant, soothing
 Tata Harper Retinoic Nutrient Face Oil	<i>Rosa rubiginosa</i> seed oil, olive oil, calendula flower extract, borage leaf extract, jojoba seed oil, apricot kernel oil	Antioxidant, soothing, emollient
 REN Bio Retinoid Anti-Wrinkle Concentrate Oil	Bakuchiol, <i>Hippophae rhamnoides</i> oil, rosemary leaf extract, <i>rosa canina</i> fruit oil, soybean oil, palm oil, <i>Hippophae rhamnoides</i> oil, linseed seed oil, sunflower seed oil, <i>Bidens pilosa</i> extract	Antioxidant, antimicrobial/antibacterial, soothing, emollient, moisturizer/humectant



Pai Skincare Rosehip BioRegenerate Oil

Rosa canina seed & fruit extract, Rosmarinus officinalis leaf extract

Antioxidant, antimicrobial/antibacterial, emollient, moisturizer/humectant



Herbivore Botanicals Bakuchiol Retinol Alternative Smoothing Serum

Bakuchiol, *Tremella fuciformis* sporocarp extract, turmeric root extract, blueberry fruit extract

Antioxidant, skin brightening, soothing

These natural ingredients offer a range of benefits for the skin, including antioxidant properties [55], moisturizing effects, protection from environmental stressors, and soothing characteristics, among other benefits [56]. Some natural ingredients can serve multiple functions, providing flexibility in skincare formulations. It is crucial for consumers to understand the relationship between specific natural ingredients and their skin benefits in order to make informed choices. For example, bakuchiol, a natural alternative to synthetic retinol, provides similar antiaging benefits to retinol but with a lower risk of skin irritation. By choosing products that are tailored to their skin's specific needs, consumers can enhance their skincare routines, selecting antioxidant-rich formulations to protect against environmental damage or soothing products for sensitive skin.

5. CONCLUSIONS

This systematic review concluded by exploring prospective natural anti-aging ingredients in cosmetics. The evaluation identified photoprotective chemicals, antioxidants, anti-inflammatory compounds, anti-hyaluronidase agents, anti-tyrosinase agents, anti-collagenase agents, and anti-elastase agents. The aggregation of data from multiple trials has provided deeper insights into the potential benefits of these natural compounds in treating skin aging, shedding light on their safety profiles and mechanisms of action. Despite the encouraging findings, further research is needed to refine their compositions, dosages, and administration methods. More thorough clinical investigations, randomized controlled trials, and observational studies could strengthen the evidence for using these natural anti-aging substances in cosmetics. This systematic review is a valuable resource for researchers, cosmetic formulators, and consumers seeking safe and effective ways to combat aging. It paves the way for future advancements in all-natural anti-aging cosmetics. The review highlights the potential of natural compounds in combating aging through biological and enzymatic pathways, offering a foundational reference for future development of natural

ingredient-based cosmetic products and encouraging further research to explore formulations, in vivo efficacy, and the potential synergy of active compounds.

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