



REVIEW ARTICLE

# Molecular and cellular mechanisms of natural cosmetics and medical treatment in skin-antiaging: A review article

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## Abstract

The aging process is intricate and characterized by the progressive degeneration of skin morphology and physiology. Hereditary factors, lifestyle choices and environmental impacts, including xenobiotic pollutants, pathogenic agents, dietary poisons and ultraviolet radiation, all impact this inevitable process. Natural anti-aging products are categorized and presented based on their familial origin. In recent years, the pharmacological assessment of many plant species, including food, aromatic and medicinal plants, has involved both *in vivo* and *in vitro* biological studies to evaluate the potential use of plant products for skin anti-aging. This review seeks to ascertain the pharmacological effects of these plants on wrinkle formation, oxidative stress, dermal pigmentation, photodamage and cutaneous hydration. In addition, this review emphasizes that lifestyle health factors, including nutrition, sleep quality, physical exercise, alcohol intake and smoking, contribute to enhancing skin health and postponing the effects of skin aging. Also, this review highlights the advantages and disadvantages of the main medical skin-antiaging treatments and the comparison between natural skin anti-aging and medical skin anti-aging treatments. In the future, further research should be conducted on novel processes of skin aging, finding other natural active substances, incorporating biological products and devising safer and more effective administration strategies with improved bioavailability or permeability for pertinent experimental subjects.

**Keywords:** medicinal plants; photodamage; ultraviolet radiation; wrinkle formation; xenobiotic pollutants

## Introduction

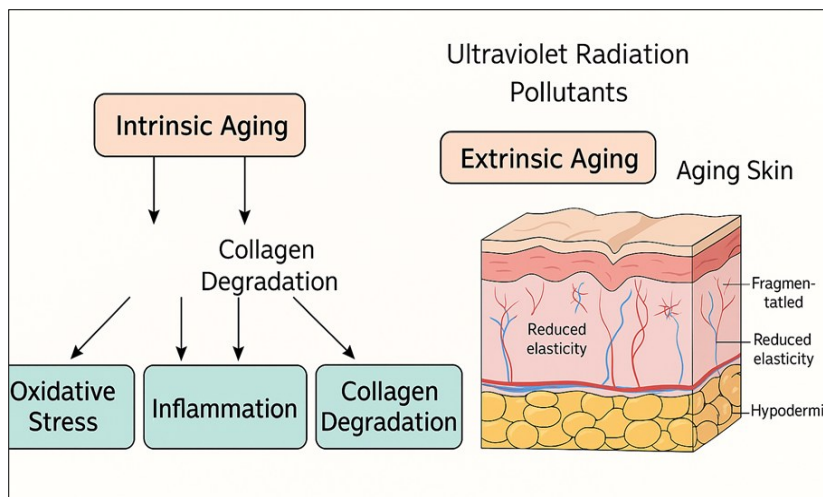
The human body's largest organ is the skin. It protects the body from external influences by harmful microbes and limiting exposure to sunlight and ultraviolet rays. This protection helps to maintain homeostasis. The typical surface area of mature human skin is 1.5 to 2.0 m<sup>2</sup>. Skin thickness differs by anatomical region and sex, with men's skin averaging 1.3 mm and women's 1.26 mm (1). The integument comprises three primary layers: the epidermis, dermis and hypodermis, as shown in Fig. 1.

The stratum corneum, the outermost layer of the skin, possesses a physiological pH ranging from 4.1 to 5.8. Diverse mechanisms facilitate their creation. It is a heterogeneous, selectively permeable epidermal layer that keeps enough moisture for proper operation while guarding against environmental deterioration and desiccation (2).

Its barrier function often compromises stratum corneum integrity, resulting in heightened trans-epidermal water loss and diminished skin hydration. Skin aging is a temporal process that is physiological, natural and biochemical, arising from the interplay of extrinsic and intrinsic causes, leading to cumulative detrimental alterations in the morphology, physiology and appearance of skin layers. Extrinsic factors include things like (UV) radiation, nutrition, air pollution, alcohol and tobacco use, lifestyle and pollutants, while

internal factors include things like genetic and physiological changes (3). Body temperature regulation, fluid balance, electrolyte levels, protein loss, vitamin D synthesis, waste removal, sensory perception, immunological response and skin barrier integrity are all impacted by physiological changes in the skin. The main factors affecting the look of the skin include cosmetic problems such as wrinkles, pigmented spots, decreased suppleness and thinning, which can lead to emotional, mental and psychological difficulties (4).

The increased incidence of skin disorders includes the emergence of dermatoses linked to skin aging, benign and malignant neoplasms, pruritus, chronic lesions, xerosis and skin depigmentation, all of which detrimentally impact skin health and diminish the prospects for healthy aging. Cosmetics, encompassing body and skin care products, are designed for use on various body areas to preserve, cleanse and enhance aesthetics, hence preserving a youthful and healthy appearance through superficial modification without altering physiological functions. Different body care items include perfumes, lipsticks, lip glosses, nail polishes, skin moisturizers, eye and facial cosmetics, shampoos, hair dyes and deodorants (4). A distinction between pharmaceuticals and cosmetics is that the former refers to compounds utilized in medical treatment or as medicinal agents. Moreover, pharmaceuticals are designed for therapeutic purposes or to avert diseases through interaction with the human body. Cosmetics and pharmaceuticals



**Fig. 1.** Mechanism of skin aging.

must undergo premarket screening tests and successfully pass these evaluations to demonstrate safety and efficacy before being launched. Cosmetic formulations contain dangerous compounds; thus, using goods with these substances endangers human health (5).

The term “cosmeceutical” signifies that cosmetics incorporate active compounds with pharmacological properties. Cosmeceuticals possessing therapeutic characteristics are utilized for their advantageous local effects and the prevention of degenerative skin conditions. They provide the essential nutrients necessary for optimal skin health to improve human look. Moreover, they can enhance skin tone, texture and luminosity while reducing wrinkles. Cosmeceuticals are swiftly emerging as a segment of the natural personal care sector. Natural components have gained prominence in contemporary formulas, despite their historical use in skincare for decades. Cosmeceuticals are not categorized as pharmaceuticals since they cannot treat or heal diseases; thus, they are regarded as cosmetics with therapeutic characteristics (6).

Natural denotes a substance obtained directly from botanical or animal sources, existing in the natural environment. Herbs, fruits, flowers, leaves, minerals, water and soil comprise the fundamental sources of natural constituents. The efficacy of natural ingredients in skin care products is evaluated based on their *in vitro* and *in vivo* effectiveness and the type of dermatological basis utilized for inclusion. Plants served as the principal sources of all cosmetics before the adoption of synthetic chemicals with analogous capabilities and have historically been used for therapeutic purposes. Additionally, novel items comprising natural oils and herbs are anticipated to enter the market in the upcoming years (7). Herbal cosmetics, composed of diverse natural herbal ingredients, serve as a foundation for creating efficient herbal cosmetic products. The demand for herbal medicines has rapidly expanded due to their mildness on the skin and few adverse effects. Herbal cosmetics primarily benefit from being composed of pure herbs and shrubs, rendering them devoid of negative effects. Natural composition provides the body with nutrients and beneficial minerals, while also lacking adverse human impacts (8).

The application of cosmetics and cosmeceuticals commenced long ago when individuals saw beauty as a desirable attribute that provides sensory pleasure. In antiquity, before the advent of chemical research, individuals utilized natural substances for cosmetic enhancement, subsequently transitioning to the application of synthetic items following the discovery of diverse

chemical compounds (9). Cosmeceuticals, such as fairness creams and sunscreens, are utilized equally by both women and men; thus, they are regarded as some of the oldest items employed by humans, despite the perception that women mostly use them. Conversely, food and cosmetic chemistry synergistically enhance both internal and external bodily wellness. To address skin requirements and appendages, nutricosmetics enhance their condition and mitigate aging by optimizing the intake of nutritious microelements, hence aiding skin protection against environmental aging forces. Numerous studies have demonstrated a substantial association between adequate intake of nutritional microelement supplements, enhancement of both cosmetic and histological skin quality and expedited wound healing (10).

The review aims to provide a comprehensive understanding of natural cosmetics and medical treatments for skin anti-aging, with a particular focus on their molecular and cellular mechanisms.

Specifically, the review's objectives are to:

1. Ascertain the pharmacological effects of various plants on key aspects of skin aging, including wrinkle formation, oxidative stress, dermal pigmentation, photodamage and cutaneous hydration.
2. Compare natural skin anti-aging treatments with medical skin anti-aging treatments.
3. Highlight the main advantages and disadvantages of both oral and topical natural cosmetics.

This review is important for several reasons:

- **Addressing the complexities of skin aging:** It explores the complex aging process, which involves the degeneration of skin morphology and physiology influenced by hereditary factors, lifestyle choices and environmental impacts. Understanding the molecular and cellular mechanisms of these changes is crucial for developing effective anti-aging strategies.
- **Growing interest in natural products:** There is increasing interest and demand for natural compounds with beneficial properties, including anti-inflammatory, anticancer, antibacterial and anti-aging effects, across various industries. Herbal cosmetics, in particular, are gaining traction due to their perceived safety, compatibility with all skin types, reduced side effects and accessibility compared to synthetic components.
- **Informing treatment strategies:** By comparing oral and topical natural cosmetics and discussing the advantages and disadvantages of medical anti-aging treatments, the review

provides valuable insights for both consumers and practitioners. It emphasizes that pharmacological assessments of plant species are crucial for evaluating their potential in skin anti-aging.

- **Promoting holistic skin health:** The review also highlights the significant role of lifestyle factors such as nutrition, sleep quality, physical exercise, alcohol intake and smoking in enhancing skin health and postponing the effects of skin aging.
- **Guiding future research:** It suggests areas for future research, including investigating novel processes of skin aging, discovering new natural active substances, incorporating biological products and devising safer and more effective administration strategies with improved bioavailability or permeability.

### The historical trajectory and resurgence of natural cosmetics in skin anti-aging

The historical overview outlines the long-standing human use of cosmetics across ancient civilizations such as Egypt, China, India, Greece and Rome. Initially, cosmetics were composed of natural substances like minerals, herbs and animal-derived materials, serving both aesthetic and medicinal roles. Egyptian women used sour milk for skin exfoliation, Chinese royals applied herbal and pearl-based preparations and Indian traditions emphasized personalized herbal remedies. Over centuries, cosmetics became symbols of beauty and social status, leading to the widespread use of whitening agents and sometimes hazardous substances like lead. Despite evolving trends, the foundation of natural ingredients in skin care remains historically consistent and culturally significant (11). Natural cosmetics utilize ingredients derived from plants, minerals and animals, processed by physical or environmentally friendly methods rather than synthetic chemicals. These products are valued for their safety, effectiveness, skin compatibility and lower risk of side effects compared to synthetic alternatives. Plant extracts are especially prominent due to their rich content of bioactive compounds—such as antioxidants, vitamins and essential oils—that protect the skin from environmental damage, including UV radiation and free radicals.

Recent innovations in green cosmetics and nutricosmetics (oral beauty supplements) highlight a shift toward holistic approaches that integrate nutrition and skincare. These include capsules or syrups containing concentrated natural compounds like hyaluronic acid, vitamins and herbal extracts aimed at improving skin, hair and nail health from within. The therapeutic efficacy of natural ingredients is influenced by factors like plant part used, extraction method and metabolite content (primary and secondary).

Overall, the growing interest in plant-based cosmetics reflects a movement toward sustainable, safe and science-backed skincare solutions (12).

### Importance of history & natural cosmetics

- Begin by emphasizing the timeless human desire for beauty and health and how cosmetics have always played a significant role.
- Immediately establish that historically, these products were derived from natural sources.
- Transition to how this historical foundation informs current trends and research, particularly the renewed scientific interest in natural compounds for skin anti-aging.

### Historical overview (concise & thematic)

- Condense the historical details, focusing on key periods (e.g., ancient Egypt, China, India, Rome, Japan) that highlight the use of natural ingredients and their perceived benefits.
- Emphasize the shift from basic hygiene to symbols of wealth/status and the subsequent move towards synthetic compounds.
- Crucially, draw connections to elements that foreshadow modern discoveries (e.g., lactic acid from sour milk, pearl powder's benefits on collagen, herbal therapies in Ayurveda).

### Recent discoveries and our viewpoint

*Discuss cutting-edge research* on specific phytochemicals, advanced extraction techniques, or novel delivery systems for natural ingredients that enhance their efficacy and stability (e.g., nanotechnology in natural cosmetic delivery, new findings on specific plant extracts and their molecular targets).

**Integrate our point of view:** Based on the historical context and recent scientific findings, offer our perspective on the future of natural cosmetics. For example:

- The potential for discovering new bioactive compounds from unexplored plant sources.
- The challenges and opportunities in standardizing natural cosmetic formulations.
- The importance of rigorous scientific validation (linking back to the molecular and cellular mechanisms).
- How natural cosmetics fit into a holistic approach to anti-aging alongside lifestyle factors.

In short, this section bridges historical wisdom with contemporary science, providing cultural depth and supporting the central thesis that natural compounds offer credible, evidence-supported alternatives or complements to medical anti-aging interventions.

### Molecular and cellular mechanisms of natural cosmetics in skin anti-aging

#### Introduction to natural cosmetics' anti-aging potential

- Briefly reiterate the increasing interest in natural ingredients due to their perceived safety, efficacy and sustainability.
- Clearly state that this section will move beyond general benefits to explore the scientific evidence supporting their action at a biological level.
- Emphasize that many natural compounds are rich in secondary metabolites (e.g., phenolics, flavonoids, terpenes, vitamins) which are responsible for their anti-aging effects.

#### Key molecular and cellular pathways in skin aging

Before detailing specific natural ingredients, briefly (or refer to an earlier section if already covered) outline the main molecular and cellular processes involved in skin aging that natural cosmetics aim to counteract. These typically include:

- **Oxidative stress:** Role of reactive oxygen species (ROS) in damaging cellular components (DNA, proteins, lipids).
- **Inflammation:** Chronic low-grade inflammation contributing to matrix degradation.

- **Collagen and elastin degradation:** Activity of matrix metalloproteinases (MMPs) and reduced synthesis of structural proteins.
- **Glycation:** Formation of Advanced Glycation End Products (AGEs).
- **Cellular senescence:** Accumulation of senescent cells.
- **Melanogenesis/hyperpigmentation:** Overproduction of melanin.
- **Hydration/barrier function impairment:** Loss of hyaluronic acid, ceramides, etc.

#### Natural ingredients and their mechanisms (organized by mechanism or compound type)

For each natural ingredient or class of ingredients, you should explicitly describe its molecular and cellular mechanism of action related to anti-aging. Instead of just listing what they do, explain how they do it.

Examples based on our previous content:

- **Antioxidants (e.g., Vitamins C & E, Green Tea Polyphenols, Curcumin):** Explain how they neutralize free radicals, scavenge ROS, enhance endogenous antioxidant enzymes (like glutathione peroxidase, superoxide dismutase) and protect cellular components from oxidative damage.
- **Collagen promoters/protectors (e.g., Vitamin C, peptides from natural sources, some plant extracts):** Detail how they stimulate fibroblast proliferation, promote procollagen gene expression, inhibit collagenase/elastase enzymes, or protect existing collagen from degradation.
- **Anti-inflammatory agents (e.g., Curcumin, Green Tea):** Describe how they modulate inflammatory pathways, inhibit pro-inflammatory cytokines, or reduce inflammatory cell infiltration.
- **Anti-glycation agents (e.g., Jasminum sambac):** Explain how they prevent AGE formation or reverse glycation damage.
- **Tyrosinase inhibitors (e.g., Green Tea, Oryza sativa, Garcinia mangostana):** Explain their role in inhibiting melanin synthesis to address hyperpigmentation.
- **Hydration enhancers (e.g., Aloe Vera, Hyaluronic Acid (if plant-derived)):** Discuss how they improve skin barrier function, increase hyaluronic acid production, or enhance water retention.

#### Integration of oral vs. topical delivery (as per review aim)

Within this section, or as a concluding part of it, briefly touch upon how these molecular and cellular mechanisms are affected by the route of administration (oral vs. topical). This will link back to one of our review's main aims.

#### Recent discoveries and future directions (from a mechanistic perspective)

- Discuss new findings regarding previously unknown mechanisms of action for existing natural compounds.
- Highlight novel natural compounds being investigated for their anti-aging potential and their proposed mechanisms.
- Mention advancements in delivery systems (e.g., nano-encapsulation) that improve the bioavailability of natural compounds at the cellular level.

- Offer your viewpoint on the most promising areas of research for understanding and harnessing the molecular and cellular effects of natural cosmetics.

#### Characteristics and benefits of natural cosmetics

Natural cosmetics include a variety of products formulated primarily with ingredients derived from plants, minerals and other natural sources. These can be broadly categorized based on their main constituents, such as herbal extracts, essential oils, mineral components and natural emollients.

#### Vitamins

Skin aging results in a decline in fibroblast quantity, which is essential for collagen production and a decrease in vascular structures that provide nutrients, culminating in wrinkle creation due to heightened skin laxity. Skin aging transpires owing to several causes, including free radicals, glycation, the cell cycle and cellular and molecular processes of skin deterioration, as shown in Fig. 2. Natural goods functioning as antioxidants, including tocopherols, ascorbic acid, polyphenols and other free radical scavengers, are employed to avert and address both intrinsic and extrinsic skin aging, thus mitigating cellular damage (13). Moreover, cellular regulators such as botanicals, polyphenols and vitamin A derivatives employed in topical applications contribute to the prevention of skin aging. Their mechanism influences collagen metabolism, hence promoting the synthesis of collagen and elastic fibers. Moreover, phytochemicals such as quercetin, green tea extract and resveratrol are efficacious in decelerating the aging process (14).

Several natural antioxidants are utilized in the cosmetics industry and sourced from various plants, grains and fruits to safeguard products against oxidative damage and reduce oxidative stress on the skin. The antioxidant activity of enzymes or low-molecular-weight antioxidants involves donating an

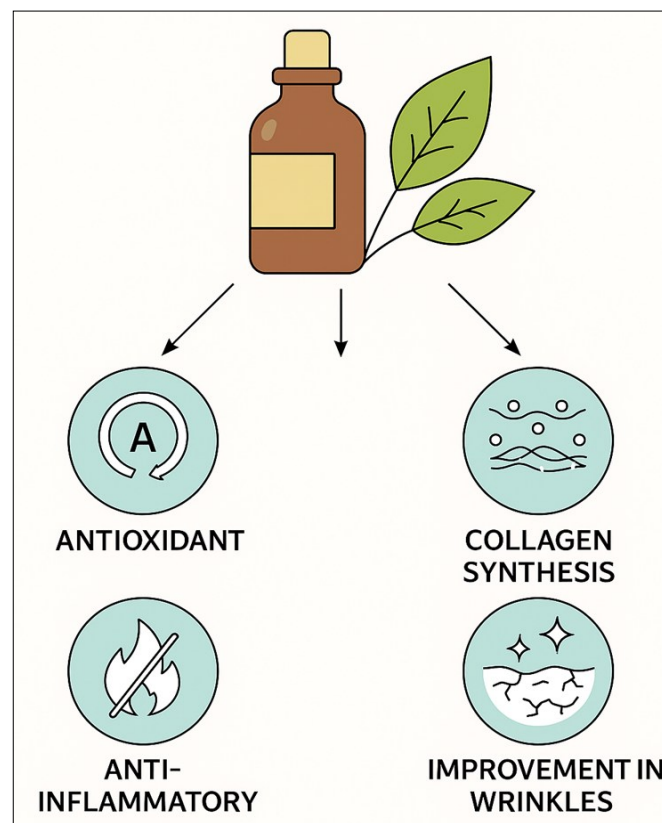


Fig. 2. Anti-aging effects of natural compounds.



electron to reactive species, thereby limiting radical chain reactions, lowering the formation of reactive oxidants, or serving as metal chelators, oxidative enzyme inhibitors, or enzyme cofactors. Moreover, antioxidant molecules may serve as stabilizers, inhibiting lipid rancidity. As most vitamins cannot be synthesized by the human body, they must be obtained from dietary intake. The primary vitamins utilized for the prevention of skin aging are natural goods such as vitamins A, C and E (15). Provitamin A ( $\beta$ -carotene), is one of the most important carotenoids, present in plants and a precursor of vitamin A in the human body. Vitamin A is a free, non-esterified type of retinoid. Retinoic acid is the biologically active molecule produced in the human body by a two-step conversion of vitamin A. Retinoids are crucial for skin renewal and several biological functions, including inflammation, differentiation, proliferation, vision, growth and apoptosis (16). Retinoids, such as retinol, are active compounds frequently utilized topically to combat skin aging. One potential mechanism is that retinol may enhance the creation of collagen, angiogenesis and the activation of procollagen genes. This can improve pore size, pigmentation, texture and skin tone. In the past, oral and topical retinoids significantly reduced hyperpigmentation and fine wrinkles (17). Retinoids ought to be regarded as the primary treatment and preventive measure for skin aging. Their application duration should be incrementally extended due to potential initial side effects such as erythema, irritation, desquamation and stinging.

Furthermore, retinoids must be applied at night and protected from sunlight using sunscreen. Vitamin C is a hydrophilic compound, with L-ascorbic acid being the most physiologically active and unstable variant. The inadequate penetration into the skin is attributable to the hydrophobic nature of the stratum corneum. It is a potent antioxidant possessing anti-aging, anti-pigmentary and photoprotective characteristics. It neutralizes free radicals in cells by donating electrons. Moreover, activating mRNA stabilizes collagen fibers, reduces their breakdown and directly encourages collagen synthesis (18). A recent double-blind, prospective, randomized clinical research administered 200 mg of vitamin C, with or without a cosmeceutical including growth factors, as a topical treatment to patients post-laser skin resurfacing. The study's results indicated a discernible decrease in the average depth of periorbital wrinkles and skin roughness following three months of treatment. Both groups exhibited improvement, with both growth factors and vitamin C, showing better results than those given with vitamin C alone (19). Numerous studies indicate that using vitamin C in cosmetics may alleviate signs of skin aging; however, the quantity of research is inadequate for definitive confirmation. The stability of vitamin C depends on its physical state and composition, with the primary fresh fruits and vegetables such as citrus fruits, blackcurrants, rose hips, guava, chili peppers and parsley being examples of natural sources (20).

Utilizing antioxidants is an effective approach to mitigate skin aging processes. Lipid-soluble vitamin E, often known as tocopherols, has antioxidant properties. It shields the skin from UV light and scavenges free radicals. Vitamin E promotes the synthesis of glutathione (GSH) in keratinocytes, which mitigates UVB-induced edema, erythema and lipid peroxidation, while also diminishing certain adverse effects of UVA. By blocking tyrosinase, it lessens the negative effects of collagenase, skin roughness and wrinkle depth.

By accelerating the healing process, it also treats burns, surgical scars and wounds. Whole grains, leafy greens (spinach), sunflower seeds, walnuts and vegetable oils (wheat germ) all contain this vitamin (21). Together, they protect against oxidative damage because vitamin C replenishes the oxidative form of vitamin E. Topical treatments may contain multiple active ingredients in a single formulation to give facial skin the best possible anti-aging and brightening effects. According to a recent study, the majority of skin aging symptoms, such as wrinkles, scaliness, radiance, smoothness, elasticity and darkening, can be improved by combining vitamin C and vitamin E in an encapsulated serum with raspberry leaf cell culture extract (22).

There is an increasing interest and demand for natural compounds possessing beneficial qualities, including anti-inflammatory, anticancer, antibacterial and anti-aging effects, across the pharmaceutical, cosmetic and food industries. Phenolics, flavonoids, terpenoids and saponins are the most intriguing categories of useful substances derived from plants. Regarding the effective and environmentally sustainable extraction of these chemicals from natural sources (23). For decades, the topical application of botanical preparations has been shown to facilitate skin regeneration and address dermatological issues, including ulcers, burns, persistent diabetic ulcers, pressure sores and non-healing lesions.

Diverse botanicals and natural pharmaceuticals exhibit considerable therapeutic potential for skin regeneration and wound healing via diverse mechanisms that augment normal skin repair processes. These processes encompass the manipulation of cytokine, growth factor, chemokine, or neuropeptide production by skin cells, as well as impacts on keratinocyte migration and proliferation rates, enhancement of fibroblast activity and stimulation of capillary vessel development (24). Numerous scientific studies demonstrate the significant influence of phytochemicals, such as triterpenes, alkaloids and flavonoids, as well as plants such as *Curcuma longa*, *Calendula officinalis*, *Althaea officinalis* and *Aloe vera*, on tissues and their capacity to expedite wound repair and enhance skin regeneration (25). In *Aloe* species, there has been a surge of interest, leading to several studies aimed at exploring the various properties of distinct aloe compounds. Aloe plants are the exclusive source of phytochemicals owing to their capacity to withstand arid, high-temperature environments. Consequently, they conserve bigger, succulent leaves, which contain water and essential chemical components (26).

Numerous natural phytochemicals, including Organic acids, proteins, polyphenols, alkaloids, amino acids, vitamins and hormones, are found in *Aloe* species. The majority of which possess the amine functional group, prevalent in all living organisms. Aloe activities are regarded as effective therapy, especially for various skin diseases, including skin inflammation and atopic dermatitis. They are utilized to enhance skin regeneration and wound healing. The efficacy of these remedies is attributed to the complex effects of various polysaccharides and anthraquinones, such as aloin and barbaloin (27).

The therapeutic effects of *Aloe vera* for preserving healthy skin have been examined in double-blind, randomized, placebo-controlled research. The research findings validated that the use of low dosages of aloe sterol enhance skin hydration by facilitating skin barrier function and dermal collagen synthesis, which is essential for sustaining healthy skin. In Japan, a daily oral aloe sterol at 8 weeks was administered by women over 40 years old, a significant

reduction in facial wrinkles by activating both hyaluronic acid and collagen production (28). From 2014 to 2019, two clinical trials were published regarding the efficacy of this medicinal herb, particularly in mitigating skin damage induced by radiation. The findings from both trials indicate that the topical use of *Aloe vera* in gel or cream form did not lead to any decrease in the prevalence or severity of dermatitis caused by radiotherapy and skin damage in women with breast cancer relative to the control group (29).

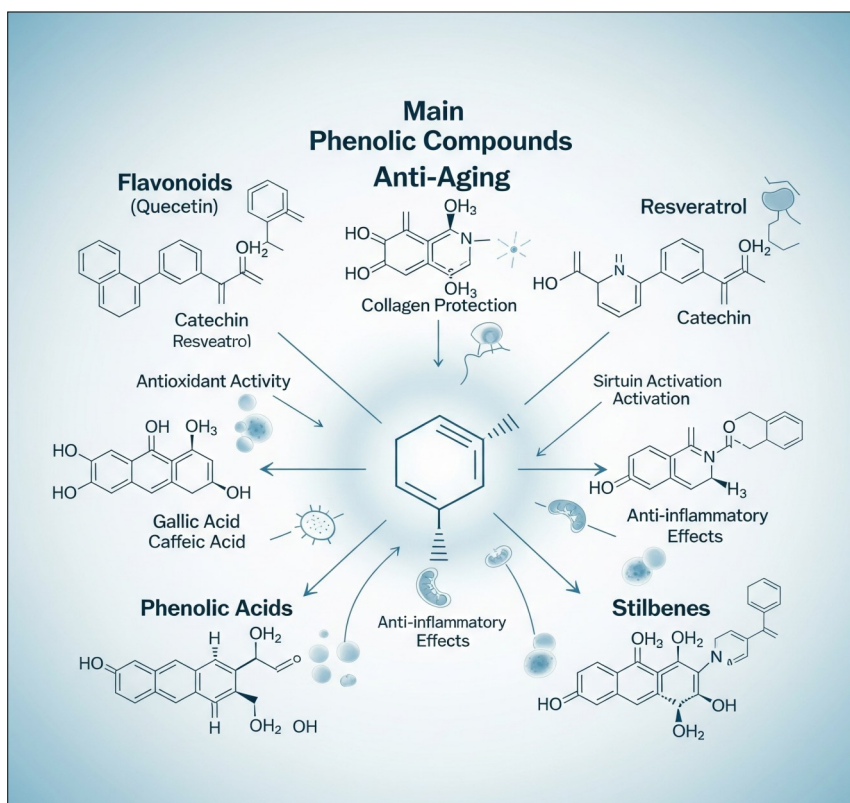
Curcumin is a chemical molecule derived from turmeric; a plant recognized for its therapeutic properties. Curcumin is a promising anti-aging molecule that is readily accessible and ideal for dietary incorporation, being both safe and cost-effective. Turmeric comprises around 12 active constituents; hence, turmeric powder contains curcumin (chemically identified as diferuloylmethane) at a maximum concentration of 3.14 % by dry weight of the powder. There is an increasing interest within the medical community in discovering new, safe and cost-effective molecules for the treatment of inflammatory and neoplastic illnesses (30). Evidence has increased indicating that curcumin is a beneficial medication for the treatment of several skin disorders. Research has been done on the possible use of curcumin topically and systemically to cure and prevent the aging of the skin, particularly concerning sun exposure, owing to curcumin's anti-inflammatory and antioxidant properties (31).

Forty-seven healthy adults participated in a randomized, double-blind, placebo-controlled study in which the hot water extract of *Curcuma longa* significantly decreased UVB-induced TNF- $\alpha$  and IL-1 $\beta$  at both the mRNA and protein levels as compared to the placebo group. This study showed that the extract, when provided, dramatically enhanced hyaluronan production in non-stimulated keratinocytes and subsequently increased the hydration level in the face epidermis. The study results indicated that curcumin may serve as an efficient moisturizing agent while also validating its anti-inflammatory properties (32).

Research has demonstrated that curcumin can enhance collagen synthesis, aesthetics and dermal health. Curcumin's antioxidant action significantly contributes to skin anti-aging, attributed to its phenolic and  $\beta$ -diketone functional groups. Curcumin can diminish indications of aging, like wrinkles and age spots, by functioning as a free radical scavenger and mitigating oxidative damage. Curcumin/turmeric is characterized as a benign and well-tolerated natural ingredient, making it a viable alternative to traditional medications, including antibiotics and corticosteroids (33). An *in vivo* study evaluated the possible antiaging effects of a nutricosmetic formulation, such as a cosmeceutical cream based on Curcuma and cream with a dietary supplement. Except for the hydration test, where they produced equal results, the nutricosmetic product outperformed the cosmeceutical one in most cases. The finest commercial curcumin extracts to use for experiments were determined by their curcuminoid level (34).

### Green tea

The fresh leaves of *Camellia sinensis* (L.) are heated to produce green tea, thereby inhibiting the oxidation of polyphenolic compounds by the inactivation of polyphenol oxidase and peroxidase, which are oxidative enzymes present throughout the tea leaves. The preservation of elevated amounts of tea polyphenols, primarily catechins constituting around 60–80 % of the total and L-theanine, which contributes to the characteristic astringency, umami and sweet aftertaste of green tea due to the absence of fermentation. Green tea-derived products have garnered significant interest over the years as potential nutraceuticals, owing to their notable bioactivities, particularly polyphenols such as 3-gallate epigallocatechin. Because of the many hydroxyl groups in its chemical structure, green tea has anti-inflammatory and antioxidant qualities, as illustrated in Fig. 3. This characteristic may be leveraged in the treatment of various diseases, including dermatological conditions, due to its interaction with reactive oxidizing species (35).



**Fig. 3.** Chemical structures of significant anti-aging phenolic compounds.

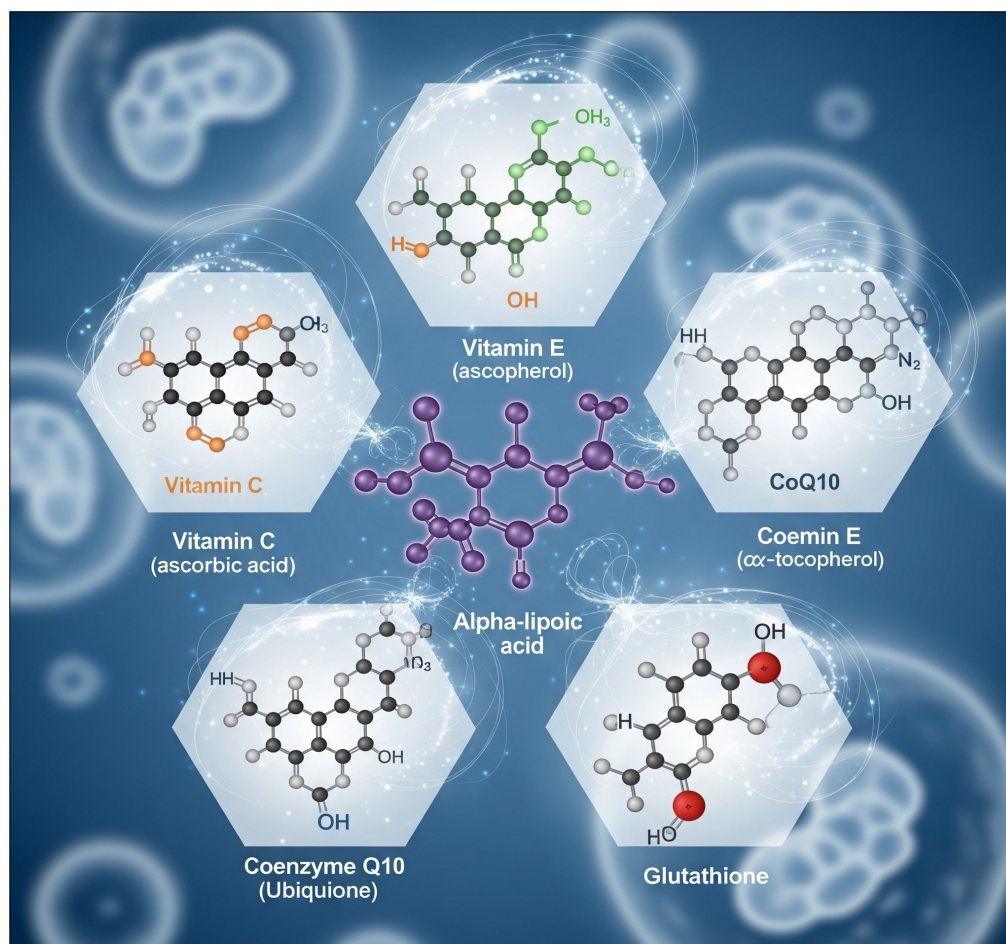
According to earlier research, using green tea topically and internally can help relieve skin conditions. Furthermore, it has been demonstrated that green tea polyphenols (GTPs) have anti-melanogenic, anti-wrinkle and anti-photoaging properties that are enhanced by tyrosinase inhibition. These properties may be linked to the GTPs' antioxidant capacity and their capacity to promote the synthesis of collagen and elastin while blocking the enzymes that break it down. A recent study concluded that a 3 % green tea extract cream enhances the look of *striae distensae* without unwanted effects, therefore qualifying it as an effective treatment for this condition (36).

### **Garcinia mangostana**

Mangosteen is a tropical arboreal species indigenous to Southeast Asia. Their fruits possess a notably distinctive flavor and have become prevalent supplements in botanical diets due to their acknowledged contribution to overall health enhancement. Iso-prenylated xanthenes, a category of secondary metabolites, are the primary phytochemicals Present in the species, demonstrating diverse physiologic effects, including hypoglycemia, anti-obesity, pro-apoptotic, anti-proliferative, antinociceptive, anti-inflammatory and neuroprotective properties. Mangosteen peel was previously recognized for its abundance of polyphenolic chemicals in the xanthone category (37). Research indicates that mangosteen fruit extracts may enhance skin elasticity and modulate inflammatory skin conditions by functioning as photoprotective agents against ultraviolet B (UVB) damage. Nonetheless, the biological targets and mechanisms of action of mangosteen fruit extracts employed in cosmetic formulations remain ambiguous, despite the fruit's dermatological advantages. Because there are so many different components to the phyto complex, it has been difficult to determine

which one is responsible for the dermatological symptoms that have been reported. A study assessed the dermatological properties of different organic mangosteen extracts and the effects of these chemicals on human keratinocytes, a commonly used cell line for studying skin damage *in vitro* (38). Pretreatment experiments demonstrate the molecular antioxidant potential of mangosteen. The studies showed a decrease in intracellular Production of reactive oxygen species and the suppression of Protein Kinase B (PKB), also referred to as Akt, extracellular signal-regulated kinase (ERK) and Tumor Protein (P53) pathways associated with cellular damage and the onset of apoptosis (39) as shown in Fig. 4.

Both chemical and physical numerous varieties of xanthenes, including  $\alpha$ -mangostin,  $\gamma$ -mangostin, garcinone C and garcinone D, garcinone E, gartanin and mitoxantrone-A, have been identified in mangosteen peel. The prenylated xanthenes  $\alpha$ -,  $\beta$ - and  $\gamma$ -mangosteens are the primary constituents in the fruit responsible for the antioxidant properties of mangosteen extracts. Both  $\alpha$ -mangosteen and mangosteen extract are associated with oxidative stress and age-related illnesses. Reduced myeloperoxidase activity, along with increased catalase and the formation of reactive oxygen species and malondialdehyde are suppressed by superoxide dismutase activity.  $\gamma$ -Mangosteen demonstrates considerable anti-tyrosinase and anti-hyaluronidase activity. Moreover,  $\alpha$ -mangosteen had considerable anti-collagenase activity, suggesting that mangosteen extract and its components may serve as antioxidant and anti-aging therapies (40). Successfully developed green herbal cosmeceuticals, including facial creams containing standardized mangosteen (*Garcinia mangostana*) peel extract, which is both dermally compatible and physically stable. The mangosteen-based



**Fig. 4.** Phytochemicals with antioxidant activity.



creams were unique since they didn't contain alcohol, parabens, sulfides, or sodium lauryl sulfate (SLS), all of which are known to irritate skin. Additionally, natural surfactants and scents must be used to enhance acceptability and stability. The creation of a green cosmeceutical herbal face cream derived from mangosteen will enhance the local economy and augment opportunities for international collaboration. Consequently, cream-based mangosteen is anticipated to serve as an alternative to synthetic antioxidants and whitening agents due to its safety and efficacy (39). A preclinical study concluded that daily oral administration of 0.1 mL water containing purified 100 mg/kg  $\alpha$ -mangostin by mice before UVB irradiation could effectively reduce skin damage. Specifically,  $\alpha$ -mangostin improves wrinkling processes induced by UVB irradiation (41).

#### ***Oryza sativa***

Phytic acid, ferulic acid and gamma-oryzanol are constituents of rice bran oil that possess excellent antioxidant properties. It has been utilized to address dermatological conditions within the beauty sector. Rice bran oil and extracts are available uses both unencapsulated and nano encapsulated forms to address skin issues and protection against UVB radiation damage. Furthermore, the bioactive compounds in rice bran have demonstrated the potential to mitigate skin aging and address alopecia (42). Gamma oryzanol, the primary component of rice bran, a common by-product of rice milling, may serve as a skin-brightening agent. Black rice bran extract contains ferulic acid (gamma oryzanol), which constitutes roughly 56-77 % of the total phenolic components, hence serving as the predominant phenolic acid in bran. Rice protein hydrolysates (RPHs) were found to have values of 8.91 mg/mL and 107.6 mg/mL that were 50 % effective in suppressing hyaluronidase and tyrosinase activity, respectively. Due to their antioxidant, anti-hyaluronidase and anti-tyrosinase characteristics, RPHs were shown to be suitable for potential future cosmetic uses in a previous study (43). Moreover, black rice bran comprises glucosides, protonic acid, vanillic acid and anthocyanins, which function as tyrosinase inhibitors. A previous study concluded that the application of a 10 % black rice bran extract lotion significantly reduced both melanin and erythema indices, indicating its potential as a natural skin-lightening product, as the formulation demonstrated no adverse effects on the skin, despite the recommendation for long-term safety studies on the 10 % black rice bran extract lotion (44). Plant fermentation is increasingly popular in the beauty industry. Fermented extracts derived from natural botanicals and microbiological cultures demonstrate their efficacy in enhancing the skin's intrinsic physiological processes and the microecology of the skin surface. A recent study determined that red rice ferment filtrate (RRFA) derived from the fermentation of *Aspergillus oryzae* had multiple skincare benefits, including antioxidant, anti-aging, repair, whitening and moisturizing activities *in vitro*. These statistics suggest a prospective application value in beauty and skincare. At present, RRFA has been mostly employed in dermatological healing and anti-aging compositions (45).

#### ***Jasminum sambac***

It is an upright or scandent shrub belonging to the Oleaceae family, capable of reaching heights of approximately 1-1.5 m and it does not occur naturally in tropical and subtropical countries. The manufacturing of cosmetics and fragrances sometimes incorporates value-added products derived from *J. sambac* flowers and beverages. Furthermore, various studies have demonstrated that

flowers have medicinal uses in treating conjunctivitis, dermatitis and stomach pain. The physiological and pharmacological properties of *J. sambac* flowers, including antioxidant, anti-aging, antibacterial activities and skin-whitening actions, are recorded (46). In contrast, there is no evidence of systemic biological toxicity or mortality linked to either extract of *J. sambac* flowers or the essential oils in the examined mice, suggesting their safety as functional components for widespread application in cosmetics, medicines and food (47). Furthermore, the antioxidant activity of *J. sambac* cell cultures, JasHEX, is accountable for the reduction of cytosolic ROS production in H<sub>2</sub>O<sub>2</sub>-exposed keratinocytes. The extract possesses antiglycation capability, which was assessed and validated by both *in vitro* and *ex vivo* experiments. JasHEX reduces the development of advanced glycation end products (AGE) in glyoxal-treated human dermal fibroblasts (HDF) and methylglyoxal-stressed skin explants, which serve as models to demonstrate the anti-glycation properties of natural compounds (48). Furthermore, JasHEX enhances an extracellular matrix effect, resulting in elevated formation of collagen type I, which is highly susceptible to glycation and whose levels are markedly diminished by oxidative stress. The previous study that JasHEX serves as a potent natural antioxidant against skin ageing caused by oxidative stress, with both its biological activity and chemical composition validated through *in vitro* and *in vivo* investigations (49). Furthermore, it is strongly suggested that a blend of extracts from *J. sambac* flowers at a ratio of 2:8 may serve as a potent antioxidant, whitening and non-toxic component applicable in several sectors, including pharmaceuticals, cosmeceuticals and the food industry. The ratio of this jasmine extract blend was deemed a viable commercial product due to its overall physiological and cytotoxic activities, as well as its acceptable flavor and cost-effectiveness. Prior research has concentrated on the inhibitory activity of tyrosinase in extracts of *J. sambac* flowers (50).

#### ***Hibiscus sabdariffa* L. (HS)**

It is a wild tropical plant from the Malvaceae family, commonly known as roselle. Due to its significant significance, this crop has been cultivated globally and features remarkable red calyces, originating from Asia, specifically India to Malaysia. *Hibiscus sabdariffa* L. (HS) possesses a lengthy history of medicinal and culinary applications, originating from regions including Egypt, China, Thailand, Indonesia and South America (51). Numerous investigations, *in vivo* as well as *in vitro*, demonstrate that HS has advantageous effects as either a food source or a medicinal agent. Nevertheless, fewer studies have concentrated on the significant significance of HS application in skin anti-aging therapy. A nitric oxide (NO)-Griess inflammatory assay is employed to assess their anti-inflammatory efficacy. Additionally, a significant anti-oxidative stress effect of hibiscus acid was identified by the creation of an oxidative stress model caused by hydrogen peroxide. Numerous studies indicate that hibiscus acid treatment can significantly reduce the secretion of extracellular adenosine triphosphate (ATP) and carbonyl protein production, while also preserving elevated levels of reduced/oxidized glutathione (GSH/GSSG) in skin cells, suggesting a potential mechanism through which hibiscus acid may counteract oxidative stress (52). The roselle drink significantly increased the hydration and redness of the subjects' faces. Additionally, over six months, oral consumption of roselle beverages significantly reduced blood pressure, raised antioxidant levels and positively impacted skin moisture and redness. The main ingredients in roselle that are probably responsible for its health advantages are phenolics and anthocyanins. Frequent consumption of roselle drink helps lower



blood pressure, boosts antioxidant levels and effectively regulates skin redness and wetness. A recent study demonstrated that the use of a cream containing 20 % rosella flower extract inhibited the decrease in skin collagen levels in Wistar rats following exposure to ultraviolet-B light (53).

### **Rosa**

The classification of the rose, a member of the Rosaceae family, as a blooming shrub, originates from the Latin term *Rosa*. More than 100 distinct species of the *Rosa* genus are widely dispersed in the Middle East, Asia, Europe and North America. The *Rosa* extract may be utilized for prophylaxis or management of many diseases. *Rosa rugosa*, a prevalent species in eastern Asia, has historically been utilized as an herbal remedy for ailments including abdominal pain, diabetes mellitus, diarrhea, menoxenia, pain and chronic inflammatory conditions. The most studied species of the genus *Rosa* in Europe is the dominant flower, *Rosa canina*, which has high levels of ellagic acid, vitamin C and quercetin. The Damask Rose, scientifically known as *Rosa damascena* Mill, is renowned for its exquisite smell and serves as a source of rose oil utilized in perfumery for the production of rose water. Roses and other medicinal plants use their petals, stems, leaves, buds, fruits, flowers and bark, among other parts, for therapeutic purposes (54). The ideal concentration for achieving optimum anti-aging and antioxidative benefits, the extraction method with the maximum flavonoid concentration is 50 % absolute ethanol (EtOH) extraction. The properties of a 50 % ethanolic extract of *Rosa gallica* petals showed significant antioxidant activity, anti-hyaluronidase, anti-elastase and anti-inflammatory potential. In contrast, a hydroalcoholic extract of *Rosa centifolia* showed strong inhibitory effects on tyrosinase activity, melanogenesis and solar ultraviolet-induced matrix metalloproteinase (55). The effects of *Rosa gallica*'s anti-wrinkle and skin-whitening petals on aging skin were examined. Among 16 herbal extracts, *Rosa damascena* extract had one of the highest levels of antioxidant activity and whitening effects, in addition to exhibiting modest anti-tyrosinase activity. It was applied topically in cosmeceutical formulations. According to a recent study, *Rosa rugosa* tea has several health advantages and the plant's aqueous polyphenol (RAP) may one day be used to create a bioactive anti-aging product (56).

### **Lavandula**

Lavender is a beneficial medicinal herb from the Lamiaceae family. Its indigenous home is the Mediterranean region, but it also flourishes in natural settings at lower mountain elevations. In several European nations, lavender is grown as a decorative plant, in China, Japan, Western Iran, Eastern India, North Africa and Southwest Asia. Only *Lavandula angustifolia* is recognized as a pharmacopeial raw material, despite the existence of 39 species within the *Lavandula* genus. Lavender is extensively employed as a fragrance in culinary uses and is frequently included in cosmetics because of its anti-inflammatory, antioxidant, antifungal and antibacterial qualities. Soaps, shampoos, eau de toilette, lotions and household cleaners infused with lavender essential oil. Furthermore, cosmetics that contain lavender essential oil do not need the addition of preservatives (57). The medicinal raw materials consist of Lavender flowers collected before the blossoming phase. The primary biologically active chemicals in lavender are triterpenes, phenolic compounds, sterols and essential oils. Terpenes such borneol, limonene, camphene, eucalyptol,  $\beta$ -ocimene, 1,8-cineol, camphor, fenchone, lavandulol acetate, lavandulol,  $\alpha$ -terpineol,  $\beta$ -

caryophyllene and geraniol are among the main components and  $\alpha$ -pinene, alongside non-terpenoid aliphatic compounds such as octanone, octenol, octenyl acetate and octanol. Polyphenols constitute a significant category of chemicals found uniformly in lavender flowers (58). Lavender oil is an essential oil derived from the flower spikes of specific lavender species, particularly *Lavandula limon officinalis*. It possesses antiseptic and anti-inflammatory properties and is utilized in cosmetics, perfumes and topical applications, as well as in the treatment of skin burns to alleviate pain and address skin infections. The cosmetic sector is the primary domain utilized for the production of bath salts, skin tonics, shampoos, cosmetic face masks and naturally formulated lotions, balms or toilet water. The study results indicate that the effect of lavender oil on the keratinocyte cell line synthesis of interleukin-6 (IL-6), interleukin-8 (IL-8) and vascular endothelial growth factor (VEGF) depends on concentration (59).

### **Punica granatum L**

Pomegranate fruit has become increasingly popular among consumers for addressing various health issues. It is the most ancient consumable fruit commonly utilized in traditional medicine. Furthermore, it is regarded as an effective natural bioactive component supplement. Market demands frequently arise due to the cosmeceutical components derived from plants that possess natural antioxidant properties. Pomegranate and its components contain over 100 bioactive ingredients, such as anthocyanins, flavanol-anthocyanin adducts, gallotannins, ellagitannins, flavonoids, phenolic acids and other phenols. Ellagitannins, one of the pomegranate constituents, are a class of polyphenols that include hydrolyzable tannins, subsuming punicalagin, punicalin and pedunculagin. Furthermore, the phytochemicals found within the pomegranate, according to many studies, have been reported. It makes sense to protect human skin fibroblasts *in vitro* against UVA and UVB-mediated cell damage and to reduce oxidative stress, DNA damage and cytotoxicity brought on by cytotoxic chemicals like hydrogen peroxide and methylglyoxal (60). The daily oral intake of 250 mg of pomegranate fruit extract, standardized to 75 mg of punicalagin, during four weeks in a double-blind, placebo-controlled clinical experiment will dramatically enhance various aspects of skin health. The reduction in average facial wrinkle severity is affected by a decrease in the forehead sebum secretion rate. The administration of a blend of pomegranate, osmanthus and olive extracts protects human skin from the damaging effects of ultraviolet light, demonstrating qualities such as skin whitening, antioxidative effects and anti-aging benefits. The inhibition of melanin formation is the mechanism of action of this mixture and may lead to a decrease in UV-induced photodamage. Numerous natural products have been determined to mitigate UV-induced skin damage, with their additional properties such as antioxidants, skin whitening and anti-aging effects (61).

### **Vitellaria paradoxa**

Commonly recognized as the shea butter tree, it is a member of the Sapotaceae family and is found in the semi-arid regions of sub-Saharan Africa, extending from Senegal in the west to Uganda. Shea butter is a lipid derived from the nut of the African shea tree. It is derived from the fat of the five main fatty acids found in *Butyrospermum parkii* kernels: stearic, palmitic, oleic, linoleic and arachidic acids. Approximately 85–90 % of these fatty acids are stearic and oleic. It is employed in cosmetic formulations and as a replacement for cocoa butter in the chocolate sector. Additionally, it

includes triterpene acetate and cinnamate esters, which demonstrate anti-inflammatory and anti-tumor-promoting properties. Shea butter melts at body temperature and remains solid at room temperature (62).

Consequently, it is beneficial for skin care due to its sunscreen characteristics, as well as its functions as a moisturizer and emollient. Shea butter has been applied topically to demonstrate both anti-inflammatory and anti-aging properties. The sun protection factor was only found to be provided by shea butter that contained 20 % triterpene esters. It is reported to as one of the plants that has medicinal value, especially in the preparation of skin ointment. A clinical study reported various prevented photo-aging signs that were diminished by shea butter. Also, in animal study, collagen production is boosted by shea butter. The principal structural proteins that confer resilience and volume to the skin are collagen and elastin. Moreover,  $\alpha$ -amyrin and lupeol, the triterpenes found in the shea butter's unsaponifiable portion, have been recognized as inhibitors of proteases, encompassing metalloproteases (such as collagenase) and serine proteases (such as elastase) (63).

### Predominant oils

#### Olive oil

The olive tree is a major component of Mediterranean cuisine, with Spain, Greece and Italy being the primary producers of olives and extra virgin olive oil (EVOO). The fruit and other plant components contain lipids derived from olive by-products, mostly utilized for their several health advantages, encompassing antioxidant, antibacterial and anti-inflammatory properties. The phenolic components of olives are predominantly found in mill wastewater (OMW), with around 98 % present there and only 2 % retained in the oil itself. A recent study has highlighted the potential therapeutic advantages of OMW compounds based on their biological characteristics, including dermatological uses (64). Numerous studies have emphasized the preventive role of olive tree chemicals, such as squalene (Sq) derived from olives, against skin aging, attributable to their influence on several systems involved in the skin aging process. An *in vitro* study using HaCat keratinocytes revealed that the use of a cosmetic cream enhanced with olive leaf extract enhances face rejuvenation by reducing wrinkles, minimizing trans-epidermal water loss and enhancing hydration (65).

#### Almond oil

*Prunus dulcis* is an almond tree that is a member of the *Amygdalus* subgenus of the *Prunus* genus, which is a member of the Rosaceae family and the Rosales order. Numerous studies have examined almonds as an important source of fatty acids, phytochemical polyphenols and antioxidant vitamins including vitamin E. They are also a noteworthy source of fiber, riboflavin, manganese, magnesium, copper and phosphorus. Sweet Almond oil (SAO) is a frequently employed natural seed oil, extensively used in healthcare, cosmetics and dermatological issues. Sweet Almond oil possesses a significant concentration of oleic acid, making it an exceptional carrier oil that enhances the penetration of its active constituents into the skin, as well as serving as a carrier for other lipophilic actives and soap compositions. Moreover, the oil is utilized in numerous cosmetic goods since it facilitates skin regeneration and preserves suppleness owing to its elevated levels of vitamins E and K. Almond oil is a widely utilized essential oil in aromatherapy and massage therapy due to its compatibility with all skin types (66).

A recent study assessed the impact of almond intake on wrinkle formation and skin pigmentation. This prospective randomized clinical investigation found that eating almonds substantially diminished the intensity of wrinkles in the intervention group. The consistent administration of almond supplements led to a reduction in the overall intensity of skin pigmentation. Significantly reduced the severity of wrinkles in the intervention group, it may reduce skin pigmentation and alleviate face wrinkles. Alpha-tocopherols, which are found in almonds, have antioxidant and photoprotective properties that may lessen uneven wrinkles and pigment formation. This could also explain why skin pigmentation decreased in the group who took almond supplements (67).

#### Jojoba oil

The Sonoran Desert is home to the evergreen shrub known as jojoba (*Simmondsia chinensis*). The United States, India, Chile, Peru, Argentina, Australia and Egypt are among the countries that cultivate jojoba. Jojoba oil is obtained through the cold pressing of seeds, yielding approximately 50 % liquid wax, which consists of esters of fatty acids and long-chain alcohols serving as an energy reserve in seed lipids. This extract is extensively utilized in cosmetic formulations as a protective film on the skin, preserving hydration and acting as a humectant. Ointments and lotions containing jojoba wax are used for dry, scaly skin, to mitigate aging and to safeguard and hydrate the skin. Moreover, hand cream employs Jojoba wax to substitute the hydrolipidic coating, particularly when external aggressors, such as detergent chemicals compromise it. Additionally, lotions containing jojoba wax are advantageous for preventing and combating wrinkles. There has been an increase in its application in pharmaceuticals, especially in topical formulations like sunscreens and moisturizers, which improve the absorption of topical medications (68). Furthermore, jojoba wax in topical formulations enhances pro-collagen and hyaluronic acid synthesis and may be advantageous in mitigating age-related diseases. The dermo-cosmetic efficacy of all jojoba wax formulations was evaluated *ex vivo* utilizing the human skin organ culture model, which simulates critical attributes of intact tissue (69).

### Other skin antiaging agents

#### Collagen

The main protein structure in many connective tissues is collagen, which is the main constituent of the extracellular matrix. It constitutes 80 % of the dry mass of human skin, providing mechanical support and regulating tissue development. The deterioration of skin quality with age is marked by reduced collagen production and diminished skin vascularity, resulting in decreased suppleness and the emergence of wrinkles. The aging process involves a decrease in enzymes essential for the post-translational modification of collagen and a reduction in the fibroblasts number responsible for collagen synthesis and the vascular supply to the skin. Consequently, dryness, diminished suppleness and a decrease in epidermal thickness are degenerative alterations that the skin experiences with aging. Various nutrients and supplements should be utilized to enhance and sustain skin health and beauty (70).

Collagen is a key ingredient designed to improve skin hydration and firmness in topical products. Hyaluronic acid fillers, as injectable substances, promote collagen production and provide immediate results through skin volumization. Notwithstanding the potential for unwanted consequences, including edema, contusions and infection, as well as its considerable expense. In contrast, the

most secure and cost-effective collagen supplements consist of hydrolyzed collagen peptides, rather than other collagen-based alternatives. Additionally, a significant advantage of collagen supplements is their oral administration, which allows for easy incorporation into daily routines (71). A recent study concluded that both oral and topical collagen contribute to the decrease or postponement of skin aging. Furthermore, they advised a thorough comprehension of the potential impacts of these two collagen types on the aging process, necessitating future epidemiological research to incorporate large sample sizes and follow-up assessments (72).

### **Hyaluronic acid (HA)**

One essential component of the extracellular matrix is hyaluronic acid (HA) and a biodegradable polymer. It is a substantial non-sulfated glycosaminoglycan with significant water retention capabilities, extensively found in joints and skin. HA derivatives can be employed to create various formulations such as fillers, lotions, gels and drops due to their diverse molecular weights. Due to its features like as mucoadhesion, biocompatibility and simplicity of chemical modification, research on HA-based drugs has recently experienced significant growth. These HA qualities have resulted in applications for tissue regeneration, anti-aging and anti-inflammatory therapies. Hyaluronic acid (HA) is the primary molecule responsible for skin hydration, as its migration to deeper layers contributes to moisture loss during skin aging. The initial clinical application of HA was established in the 1970s and 1980s for ocular surgery, after research that garnered interest in HA. Since then, there has been a notable rise in the utilization of hyaluronic acid in dermatology due to its hygroscopic, rheological and viscoelastic properties. Hyaluronic acid (HA) has been incorporated into cosmeceuticals for topical use and formulated into filler injections (73). Although numerous studies emphasize HA fillers as the predominant therapy for enhancing the appearance of aged skin, not all patients are prepared to initiate injectable treatments. Topical HA may provide supplementary advantages.

Numerous research has validated that topical HA-based cosmeceutical applications are effective in the anti-aging treatments administered by physicians, addressing indicators of skin aging and elasticity while enhancing skin moisturization. Large non-sulfated glycosaminoglycan with significant water retention properties (74). In a recent clinical study after taking 120 mg of HA daily for 8 and 12 weeks, 40 healthy Asian men and women between the ages of 35 and 64 showed a significant improvement in their skin condition compared to the placebo group. This improvement was measured by wrinkle assessment, stratum corneum hydration, trans-epidermal water loss and elasticity. According to the study's findings, oral intake of HA may help reduce wrinkles and improve skin conditions (75).

### **Glutathione**

Glutathione is a thiol-tripeptide with a low molecular weight, that serves as a significant antioxidant in preserving intracellular redox equilibrium. Furthermore, its endorsement as a skin-lightening agent following the identification of its anti-melanogenic characteristics has led to widespread use for this purpose among some ethnic groups. Nonetheless, there exists a conflict between evidence supporting its efficacy and safety. Prior research indicated that the supplementation of reduced glutathione (GSH, 500 mg/d) demonstrates skin-lightening effects in people. The glutathione effects in both reduced form (GSH) and oxidized form (GSSG) were

evaluated in this study. at dosages below 500 mg/d, on enhancing skin characteristics.

Oral treatment of 250 mg/d of both reduced and oxidized forms of glutathione dramatically alters skin features, based on a double-blind, randomized, placebo-controlled research. Moreover, both variants are highly accepted. Furthermore, in comparison to a placebo, both the oxidized (GSSG) and reduced (GSH) forms appear to enhance skin elasticity. No indication of harmful effects was observed during the trial, indicating that it is typically a safe substance for use as a dietary supplement (76). Preclinical studies on the acute toxicity of oral GSH in mice indicated that the lethal dose 50 (LD50) exceeds 5 g/kg, demonstrating that oral glutathione is safe and non-toxic. No significant adverse responses have been noted in numerous clinical trials. Wahab S et al. concluded in their study that both topical and oral glutathione are effective treatments for skin whitening. Moreover, combinations of topical and oral glutathione may prove more efficacious than monotherapy. *In vitro* studies have shown glutathione's role in melanogenesis. The processes elucidating the anti-melanogenic characteristics of GSH stem from the promotion of pheomelanin synthesis instead of darker eumelanin, its antioxidant actions and the disruption of the intracellular transport of melanogenic enzymes (77).

## **Medical skin antiaging treatment**

### **Soft tissue fillers**

For decades, injectable fillers have been employed to rectify age-related soft tissue deficiencies. Recently, the utilization of hyaluronic acid (HA)-based fillers as "skin boosters" for enhancing skin quality has gained favor, particularly among those seeking skin rejuvenation. The characteristics of an optimal injectable product include good biocompatibility, ease of injection due to advantageous rheological qualities and a sufficiently prolonged impact. Xenogeneic and allogeneic collagen materials have demonstrated extensive successful application, providing potential for enduring outcomes. Currently, existing HA-based injectables vary in their modification and stabilization methods, as well as in their rheological properties, sources and concentrations of HA (78).

### **Botox**

*Clostridium botulinum* synthesizes Botulinum toxin (Botox), consisting of seven neurotoxic variants; only varieties A and B are utilized in clinical settings. Botox A is utilized in medicine for many ailments, particularly in dermatological and cosmetic applications. It may be utilized as a remedy for conditions including hyperhidrosis, lichen simplex, pompholyx and acne vulgaris, as well as for diminishing the visibility of wrinkles in the top facial regions and elevating the eyebrows. A Botox injection consists of a modest dosage of type A Botulinum toxin, which inhibits muscular contraction. It can diminish the visibility of wrinkles; however, repeated treatments are essential.

This toxin can induce botulism, a condition that impacts the nervous system when administered in substantial quantities. Since the 1970s, Botox has been utilized in ophthalmology and its application has broadened across numerous medical disciplines, particularly dermatology, in the past two decades. Since 2002, Botox has been approved by the Food and Drug Administration (FDA) to treat glabellar frown lines (79). Additionally, blepharospasm, cervical dystonia, marionette lines, platysma bands in the neck, perioral wrinkles, hyperhidrosis and synkinesis after facial surgery can all be



treated with Botox injections. Botox's anti-wrinkle effect is achieved by affecting the neuromuscular junction. Following the injection, the toxin penetrates the tissue until it reaches the neuromuscular junction's presynaptic terminal, where it binds selectively and reversibly to the particular membrane protein that promotes acetylcholine secretion, preventing its release at the neuromuscular junction. This process causes localized muscles to relax quickly, which temporarily reduces the face (80).

#### **Dermabrasion and microdermabrasion**

Dermabrasion and microdermabrasion are facial rejuvenation methods that mechanically eliminate damaged or aged skin to facilitate re-epithelialization. Dermabrasion eliminates the epidermis and reaches the papillary or reticular dermis, facilitating the regeneration of the skin's structural proteins. Microdermabrasion (MDA) just facilitates the removal of the outermost layer of the epidermis, hence expediting the natural exfoliation process. Both approaches can yield clinically substantial enhancements in skin appearance and may gain relevance among practitioners as new uses emerge (81). Microdermabrasion is a minimally invasive epidermal resurfacing technique utilized for addressing irregular skin tone and texture, photoaging, stretch marks, melasma and other scars, including acne scars. Microdermabrasion has been utilized to enhance skin permeability for specific pharmaceuticals, yielding positive outcomes. This treatment diminishes fine lines and wrinkles, reduces hyperpigmentation and enhances skin texture, making it predominantly utilized for facial rejuvenation. Abrasive crystals are directed onto the skin using a handheld vacuum apparatus during this MDA. The crystals induce mild mechanical abrasion on the skin, thereby eliminating the stratum corneum layer of the epidermis. A new epidermis develops with improved aesthetics during the wound-healing process (82).

#### **Laser skin resurfacing**

Laser resurfacing technologies signify a significant advancement in the cosmetic surgeon's arsenal for enhancing skin tone, texture and pigmentation. It enhances the appearance of lentigines, rhytids, skin texture and various scars and promotes skin tightening. Laser resurfacing is not a replacement for a facelift or blepharoplasty. Lasers can be categorized as fractionated or non-fractionated and as ablative or non-ablative (83). Fractionated lasers focus on an evenly distributed portion of the targeted region, while non-fractionated lasers impact the entire surface area of the treated skin. The process of removing the epidermis and superficial dermis to lessen the obvious signs of photoaging is known as "ablative laser skin resurfacing". Actinic keratoses, seborrheic keratoses, face wrinkles and scarring are more indications for ablative Skin resurfacing using the laser. The targeted thermolysis of the epidermis and dermis during light energy application underpins ablative laser skin resurfacing. Melanin and water, the skin's main chromophores, absorb the laser's light energy and subsequently release heat energy, killing nearby tissue (84).

The process of removing the epidermis and superficial dermis to lessen the obvious signs of photoaging is known as "ablative laser skin resurfacing". Actinic keratoses, seborrheic keratoses, facial wrinkles and scarring are additional conditions for which ablative laser skin resurfacing is recommended. The precise thermolysis of the epidermis and dermis during light energy application is fundamental to ablative laser skin resurfacing. The primary chromophores of skin, melanin and water, absorb laser light energy and then emit thermal

energy, destroying adjacent tissue (85).

#### **Comparison between natural skin antiaging and medical skin anti-aging treatment**

Natural cosmetic components for skin anti-aging have fewer side effects, reduced irritation, enhanced skin absorption and superior biodegradability compared to synthetic counterparts. As a result, research efforts have been continuous in identifying anti-aging cosmetic components from various natural sources. There is increased interest in the research and development of highly functional natural cosmetic chemicals, particularly those aimed at preventing skin aging, including whitening and wrinkle reduction, which must be both safe and effective. Extensive research exists about synthetic substances, including allergic contact dermatitis, skin irritation, phototoxicity and photoallergic responses. Concerns remain about the detrimental consequences of artificial substances in anti-aging cosmetics; for instance, hydroquinone, a principal component in whitening products, has been designated as a carcinogen (86).

The rapid advancement of novel dermo-cosmetics, especially non-invasive products with fewer adverse effects compared to existing options, has been driven by heightened customer demand. Plant-derived natural chemicals and herbal formulations have gained popularity because of their diverse, safe active ingredients that operate through several mechanisms on multiple signaling pathways related to skin aging (87). Conversely, it is important to note that many natural substances may be allergic, toxic, or irritating, potentially leading to health issues, especially in cases of overdose. The principal botanical formulations with potential anti-aging properties, utilized as ingredients in skincare products, will be integrated into standard skincare regimens, provided these formulations exhibit high safety margins, substantial consumer acceptance, optimal affordability and minimal benefits to skin health (88).

The clinical trial results indicated a notable enhancement in face wrinkles following almond consumption, including a reduction in facial pigmentation severity, without unwanted effects. Furthermore, the significant benefits of natural dyes and plant-derived coloring compounds include their non-carcinogenic properties, safety (nontoxicity), absence of unwanted effects, environmental compatibility and cost-effectiveness. Consequently, they are garnering public interest due to their extensive use in the cosmetic business. Plant-derived colors serve as a substitute for synthetic dyes, which are derived from petrochemical substances, due to their poisonous, allergenic, carcinogenic and mutagenic properties that contribute to various skin and health issues (89).

Conversely, numerous drawbacks exist to medicinal interventions for skin aging. Research has demonstrated numerous side effects of dermal fillers, ranging from mild injection site issues, such as soreness and bruising, to serious consequences, including infections, tissue necrosis and retinal artery obstruction. These complications should be promptly acknowledged and effectively managed by the aesthetic provider. The potential side effects of dermal hyaluronic acid (HA) filler include bruising, erythema, edema, granuloma development, discomfort and delayed hypersensitivity (90). A diverse array of filler options with varying characteristics is accessible. The optimal outcome relies on appropriate indications and synergistic use of fillers. Training in the knowledge and procedures of fillers for skin aging is essential to prevent both trivial

and severe morbidity and mortality. Adverse reactions to fillers may arise from different types of fillers applied to particular facial areas, as substantiated by evidence.

Alongside the prevalent detrimental effect of foreign body granuloma, additional adverse lesions were identified, aggravating systemic illnesses accordingly (91). Complications encompass infection, scarring, dyschromia, milia and chronic erythema. The predominant etiological agents of postoperative infections following dermabrasion are *Staphylococcus aureus*, herpes simplex virus (HSV), or *Candida*. Usually appearing within the first 48 to 72 hr, staphylococcal infections cause erythema, edema and a honey-colored crust (92). Moreover, microdermabrasion has emerged as a compelling therapeutic alternative for numerous people with dermatological disorders. Tenderness, edema, erythema, petechiae and ecchymosis are the predominant consequences of microdermabrasion. Contact between the crystals and the conjunctiva may result in eye discomfort. The chance of reactivation of latent herpes simplex virus in an afflicted dermatome and autoinoculation of viral cutaneous sores is heightened. The skin exhibits heightened sensitivity to photodamage for several days post-treatment, while the loss of the stratum corneum transpires during MDA (93). Following a botulinum toxin injection, sequelae may manifest at any location, including pain, edema, erythema, ecchymosis and transient hypesthesia, which are linked to systemic and widespread diffusion of the toxin.

Transient and benign events represent two categories of unfavorable occurrences identified as potentially serious incidents. A hematoma, resulting from a blood vessel injury, constitutes a more serious consequence. Conversely, significant adverse consequences of botulinum toxin following cosmetic application encompass dysphagia, muscular weakness and allergic responses. Dysphagia and myasthenia are prevalent manifestations of botulism. It may manifest shortly after injection and may endure for an extended duration. Treatment of cervical lines and wrinkles with cosmetics generally requires increased dosages of botulinum toxin, augmenting the likelihood of significant adverse effects. Elevated dosages for senior individuals will augment the probability of targeted diffusion into deeper cervical tissues or direct injections of botulinum toxin. The diffusion range of botulinum toxin from the muscles that were injected to nearby muscles is 30-45 mm. Botulinum toxin may disseminate to cervical muscles, resulting in unintended muscular paralysis that can induce dysphonia, dysphagia or dystonia (94). Moreover, most ablative methods entail extended recovery periods and may induce more severe adverse effects, albeit their superior outcomes.

Conversely, non-ablative technologies typically demonstrated more moderate outcomes with reduced adverse effects and a simpler recovery process. Laser treatment carries potential dangers such as burns or other injuries from the laser's heat, scarring and alterations in skin pigmentation, resulting in areas of hyperpigmentation or hypopigmentation. These consequences arise from selective photo thermolysis and, in certain instances, may be advantageous to the doctor, particularly in mitigating hyperpigmentation in melasma. Conversely, the emergence of erythema, desquamation and skin fragility during the standard post-procedural period of CO<sub>2</sub> laser resurfacing may persist for as long as 3 months following the treatment. CO<sub>2</sub> lasers induce hypopigmentation, which is more prevalent than other laser modalities due to the extent of heat damage and ensuing

inflammation. This consequence can be difficult to manage (95).

### Healthy lifestyle factors

A healthy lifestyle is acknowledged as an evidence-based innovation that clarifies the impact of everyday activities and routines on disease prevention and treatment, acting as a vital complement to total health. An incremental approach can significantly influence individual health and well-being, particularly regarding skin health. The most conspicuous external indicators of age, especially in the face, cervical, manual, brachial and crural regions. While aging is inevitable, the impact of healthy lifestyle factors on preventing and treating age-related disorders has been extensively studied; nevertheless, this framework has been insufficiently applied to skin aging. Patient education, as a pivotal anti-aging treatment strategy, is essential for modifying a patient's lifestyle and ensuring adherence to treatment protocols. This includes smoking cessation, regular exercise, adequate hydration, consumption of a nutritious diet and stress reduction through relaxation techniques to avert skin damage (96).

### Diet

Numerous nutritional components, including, water, protein, trace elements such as (iodine, zinc, iron, copper and selenium), vitamins (A, B complex, C, D and E), along with dietary habits, daily activities and health-related lifestyle choices, are acknowledged to impact skin health. A study conducted in 2020 investigated the impact of a whole-food, plant-based (WFPB) diet on key markers of skin health. Ingesting plant-based foods in their entirety and unrefined state, including fruits, vegetables, legumes, entire grains, lentils, nuts and seeds and modest quantities of beneficial fats, is what defines the WFPB diet. Red meat, chicken, fish, dairy products, eggs, processed foods and confections were all prohibited. The study's findings indicated that the WFPB diet maximizes antioxidant capability by providing vital vitamins C, A and E to fight oxidative stress, methylglyoxal and advanced glycation end products (AGEs), resulting in telomere elongation that promotes youthful, healthy skin (97).

The formation of glycation products can result from high glycemic index foods, contributing to damage in collagen and elastin. Conversely, the consumption of foods with low glycemic index, adherence to the Mediterranean diet and metformin administration, as advised by a physician, when necessary, are recommended to mitigate glycation. An imbalance in nutrition and suboptimal dietary practices are significant contributors to skin aging, as demonstrated by contemporary scientific research. High-fat diets impede skin healing by exacerbating oxidative stress and inflammatory responses, diminishing protein synthesis and perhaps altering skin shape and matrix remodeling (98).

### Physical activity

Numerous health advantages, such as increased mental well-being, weight control and cardiovascular fitness, are linked to physical activity. Moreover, sustaining an active lifestyle may enhance skin health, as indicated by current studies. The beneficial outcomes and particular impacts of exercise on skin aging remain inadequately comprehended. Earlier research demonstrated that endurance exercise mitigates skin age-related alterations in both people and mice, identifying IL-15 produced by exercise as a new modulator of mitochondrial activity in aged skin. The study findings indicate that exercise partially regulates IL-15 expression via skeletal muscle AMP-activated protein kinase (AMPK), an essential metabolic regulator

and that the absence of muscle AMPK leads to the degradation of skin structure. Additionally, daily IL-15 therapy emulates specific exercise's anti-aging benefits on skin and muscle in mice models. Moreover, a recent study showed that resistance exercise rejuvenates aged skin by improving dermal extracellular matrices and diminishing circulating inflammatory markers (99).

### **Psychological stress**

In contemporary society, psychological stress is prevalent and indicative of the educational, occupational, financial and familial constraints confronting young women. The COVID-19 epidemic recently exerted a significant impact on psychological stress, especially among younger persons. Skin aging can be categorized into intrinsic, resulting from the passage of time and extrinsic, influenced by environmental variables. The primary focus of the study on extrinsic aging is photoaging, among additional factors like cigarette smoking and air pollution exposure that warrant consideration. The influence of psychological stress is among the most underexplored subjects related to extrinsic skin aging. Psychological stress is a reaction to external or internal stimuli that triggers physiological alterations through neural and endocrine mechanisms, including inflammation.

Prolonged activation of these pathways can lead to chronic immune dysfunction, heightened generation of reactive oxygen species and DNA damage, resulting in skin aging and other associated tissues, a phenomenon termed inflammaging (100). A novel notion denoting self-perceived indicators of skin aging that manifest in the early 20s to 30s, potentially induced by psychological stress, is referred to as aging skin. Perceptions regarding the relationship between stress and skin aging vary amongst young women and healthcare professionals (HCPs). Healthcare professionals advise that they regularly administer therapies to their patients to assist them in managing mental or emotional stress.

The predominant recommendations encompassed modifications to sleep patterns, meditation, physical exercise, increased outdoor activity, re-establishing connections with friends and family, massage therapy and prescription drugs. Recommendations from dermatologists and psychologists were substantially comparable, although dermatologists were more inclined to suggest antistress cosmetic treatments. The findings indicate that the proficiency of healthcare providers in treating patients with stress and comprehending activities can contribute to a reduction in stress levels (101).

### **High body fat, smoking, alcohol and body mass index (BMI)**

The two primary variables adversely affecting skin health are alcohol intake and smoking. Diuretic water loss, a reduction in inflammation and vitamins and minerals that increase peripheral vasodilation and oxidative stress all contribute to dehydration. These are the two primary effects of alcohol on the skin, which can adversely affect sleep quality and skin cell turnover and diminish antioxidant defense by modifying carotenoid concentrations (102).

Smoking offers no health advantages. The impact of smoking on the skin is contingent upon usage history and frequency, resulting in pronounced symptoms of aging such as wrinkles and diminished skin tone. Conversely, those with the briefest smoking history exhibit more evolved facial features and perceptual abilities reflect their actual age, especially in the regions around the eyes and lips. Moreover, both vaping and smoking exert identical detrimental effects on skin health and numerous studies have indicated that

vaping, akin to conventional cigarettes, leads to significant respiratory ailments, particularly among adolescents and young people (103).

Distinct correlations were identified between facial aging associated with skin and volume deterioration, tobacco consumption and excessive alcohol intake. Excessive alcohol use adversely impacts the body through vitamin inadequacies, tissue damage, altered inflammatory responses and reduced synthesis of type I collagen by skin fibroblasts. Studies have reported that alcohol abuse causes a reduction of fat mass, which might be responsible for the volume reduction in the midface reported by heavy drinkers. The reduction in midface volume may have exposed the suborbital fat pad, perhaps leading to an increase in under-eye puffiness.

Moreover, alcohol compromises the antioxidant defense system of the skin, making it more vulnerable to sunburn and UV light's aging effect. A positive link exists between cigarette smoking and photodamage, because the aryl hydrocarbon receptor, a transcription factor that mediates the toxicity of UVB-generated photoproducts in the body, is downregulated by smoking. The augmentation of under-eye puffiness may have resulted from the exposure of the suborbital adipose tissue, when the volume of the midface decreased. Furthermore, alcohol compromises the skin's antioxidant defense mechanisms, rendering it more susceptible to sunburn and the aging effects of ultraviolet light. A correlation exists between cigarette smoking and photodamage, as smoking diminishes A transcription factor called the aryl hydrocarbon receptor controls how harmful UVB-induced photoproducts are to the body (104). Dermatologists, supported by empirical research, advocate that patients can delay the beginning of face aging with lifestyle modifications, specifically by abstaining from smoking and moderating alcohol use. Young smokers should be counseled to cease smoking, as the severity of aging escalates with the quantity and length of tobacco exposure. Older individuals with significant alcohol intake and a smoking history seeking nonsurgical interventions for facial aging attributed to these external variables may necessitate earlier and more comprehensive treatment to mitigate the pronounced skin aging (105).

## **Conclusion**

Skin aging is a multifactorial and individualized process shaped by both intrinsic (genetic and chronological) and extrinsic (environmental and lifestyle) factors. Through the understanding of its underlying molecular, biochemical and structural changes, targeted interventions-whether natural or medical-can be designed to delay or reverse visible signs of aging.

This review has critically analyzed the efficacy and limitations of phytotherapeutic strategies such as natural cosmetics rich in plant extracts, essential oils and antioxidants, alongside medical interventions like retinoids, botulinum toxin, laser therapy and dermal fillers. While medical approaches often yield faster and more dramatic results, they may carry higher risks, costs and invasiveness. In contrast, phytotherapy offers a gentler, sustainable alternative with lower side-effect profiles and increasing scientific support for mechanisms such as collagen preservation, oxidative stress reduction and anti-inflammatory effects.

An integrative strategy, combining evidence-based natural products with selected medical treatments, appears most promising for long-term skin health and anti-aging effects. This combined



approach not only maximizes therapeutic benefits but also aligns with growing consumer demand for holistic and personalized skin care solutions.

In addition to external treatments, lifestyle and behavioral factors-including balanced nutrition, adequate hydration, physical activity, quality sleep, stress management and avoidance of smoking and alcohol-are crucial modulators of skin aging and should be incorporated into any anti-aging strategy.

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## Authors' contributions

ZA carried out the abstract, Introduction and survey of antiaging drugs' molecular and cellular mechanisms. DA participated in the design of antiaging natural medicines and the safety and efficacy of mixed medicinal plant preparations with medical treatment. ZA and DA participated in the design and coordination of the manuscript. All authors read and approved the final manuscript.

## Compliance with ethical standards

**Conflict of interest:** Authors do not have any conflict of interests to declare.

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