Review Article

Enhancing Skin Health: The Role of Nutraceutical Synergies in Counteracting the Signs of Aging

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ABSTRACT

Skin is the largest organ of the human body which is affected by aging. The objective of this review-paper is to briefly highlights the factors responsible for skin changes in aging and the role of nutraceutical synergies in counteracting the signs of aging. Ageing is a multifaceted biological process impacting skin health through intrinsic genetic programming and extrinsic environmental factors. Intrinsic ageing, characterized by hormonal changes and fibroblast dysfunction, and extrinsic factors, such as reactive oxygen species and advanced glycation end-products, compromise skin structure and function. Modern lifestyles, including poor nutrition, environmental pollutants, and UV exposure exacerbate oxidative stress and accelerate skin ageing. Nutraceutical interventions demonstrate significant potential in mitigating these effects, including collagen peptides, hyaluronic acid, nicotinamide mononucleotide, and trace elements like zinc and copper. These bioactive compounds promote collagen synthesis, enhance hydration, and reduce oxidative stress, improving skin elasticity, hydration, and resilience. This study emphasizes the efficacy of a multi-nutraceutical approach, which synergistically addresses ageing pathways, providing a promising avenue for personalized, effective anti-ageing strategies. Future research is recommended to focus on long-term, population-diverse studies to validate these findings and expand their applicability.

Keywords

Skin health, Aging, Nutraceutical, Counteracting skin sign in aging

INTRODUCTION

The skin is the largest organ of the human body, composed of three layers: epidermis, dermis and hypodermis[1]. The primary structural component of the dermis is collagen, which provides essential mechanical support. Dermis also contains another important element elastin, contributing to the skin's resilience and elasticity[1]. With ageing, collagen fibrils undergo progressive loss and fragmentation showing visible signs of aging manifested prominently as skin wrinkling, diminished elasticity, noticeable loss of hydration, appearance of dark spots and thinning of the blood vessel walls that significantly impact one's appearance[1,2]. The aging of our skin is significantly influenced by

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a complex interplay of intrinsic genetic changes and external environmental factors, along with our dietary choices and lifestyle habits. Together, these elements play a crucial role in shaping the health and appearance of our skin over time[3].

Changes of Skin in Aging

Intrinsic Factors

Intrinsic ageing is a natural, genetically determined process characterized by hormonal changes, fibroblast dysfunction, and a gradual decline in collagen production[4], which leads to thinner, less resilient skin with reduced hydration and elasticity. There is also a decline in key molecules such as hyaluronic acid (HA) and nicotinamide adenine dinucleotide (NAD+) that further diminishes the skin's ability to retain moisture and energy metabolism, compounding visible signs of ageing[5,6].

Extrinsic Factors

On the other hand, extrinsic ageing is driven by external factors such as ultraviolet rays and pollution, which induces ROS production, leading to the activation of matrix metalloproteinases (MMPs) enzymes and the breaking down of collagen, resulting in fragmented collagen fibres and compromised dermal structure[4,7-10]. Free radicals are constantly produced in our body as a by-product of normal aerobic respiration, metabolism and inflammation. Excess free radicals damage the skin stem cells, resulting in a decrease in collagen production by fibroblasts[11], and ultimately showing hallmarks of skin ageing, such as loss of elasticity and wrinkle formation[2]. Other factors such as lifestyle choices, including smoking and poor dietary habits, cause deficiencies in vitamins, trace metals, and amino acids that exacerbate oxidative stress and reduce the skin's natural ability to repair itself[8,9]. Furthermore, sedentary habits and the widespread use of processed foods exacerbate nutritional deficiencies. Socioeconomic disparities also limit access to effective antiaging interventions, leaving many individuals without adequate preventive or restorative measures[12].

Nutraceutical interventions have emerged as promising tools to counteract the effects of ageing. These bioactive compounds promote collagen synthesis, enhance hydration, and reduce oxidative stress, improving skin elasticity, hydration, and resilience. Blends of collagen peptides and multiple active ingredients have been shown to restore skin hydration and elasticity and to reduce fine lines and wrinkles. This review highlights the effectiveness of using nutraceuticals as potential anti-aging ingredients for skin rejuvenation, representing a promising pathway for personalized and effective anti-aging strategies.

NOVEL NUTRACEUTICAL INTERVENTIONS IN COUNTERACTING THE EFFECT OF AGING

The term "nutraceutical" is obtained by combining the terms "nutrition" and "pharmaceutical" by Dr Stephen DeFelice in 1989, founder and chairman of the Foundation for Innovation in Medicine (FIM), Cranford, New Jersey[13]. According to the 1996 definition by Dr Stephen DeFelice, nutraceuticals are "food or food ingredients providing medical and health benefits, including prevention and/or treatment of diseases"[13,14]. Such products include isolated nutrients, dietary supplements, genetically engineered 'designer' foods, functional foods and herbal extracts" According to the above definition, all foods or food supplements can be defined as nutraceuticals[15]. A number of nutraceuticals having benefit on ageing skin are described here.

Bioactive Peptides (Collagen peptides)

Peptides are short polypeptidic chains formed by amino acids, have low molecular weight, and are usually under three kDa. Peptides used for nutraceuticals are typically derived from collagen with improved bioavailability and solubility[16]. Collagen peptides play a pivotal role by stimulating fibroblast activity, enhancing collagen synthesis, facilitating cellular migration and improving skin elasticity and hydration[17-19]. In recent years, collagen supplements have been increasingly used, as they are advertised as a potential remedy against ageing[20]. Collagen obtained from livestock and poultry is a primary source of natural collagen and collagen peptides[21]. Marine-derived collagen has a homology with human collagen and is widely used for skin health and restoration[22].

Marine Collagen Type I

Marine collagen, primarily sourced from fish skin, scales, and cartilage, has become a highly effective nutraceutical for addressing age-related skin and hair changes. The underlying mechanism of action for marine collagen lies in its hydrolyzed peptides, which stimulate dermal fibroblast activity and promote the production of collagen and hyaluronic acid both essential for maintaining skin structure, hydration,

and elasticity. These peptides also inhibit the activity of matrix metalloproteinases (MMPs), enzymes responsible for the breakdown of collagen, thereby preserving the extracellular matrix (ECM) and, thus, enhancing skin hydration and elasticity and reducing wrinkle formation. The peptides in marine collagen also protect the skin against oxidative damage by suppressing MAPK signaling pathways[23], further supporting collagen preservation and enhancing skin regeneration[22].

One study showed that supplementation of fish collagen with low molecular weight at a dose of 1000 mg once daily for 12 weeks in a cohort of women aged 40–60 years has efficiently improved skin hydration as early as after 6 weeks of intake and skin wrinkling and elasticity after 12 weeks of intake[24]. A meta-analysis has demonstrated significant improvements in skin hydration and elasticity with oral fish collagen supplementation compared to placebo treatments[25]. Another meta-analysis showed that intervention with hydrolyzed collagen (2.5–10 g/day) vs. placebo for 2–12 weeks significantly improved skin hydration and elasticity[26].

Marine collagen supplementation is generally well-tolerated, with no significant adverse effects reported in clinical trials. However, individuals with fish or shellfish allergies should exercise caution due to potential allergenicity[25].

Sheep Collagen (Type I & III)

Sheep collagen, primarily extracted from sheep skin, sinews, and connective tissues, is rich in Type I and III collagen. It is a valuable ingredient in skin health because it enhances the extracellular matrix (ECM) and provides significant anti-ageing benefits. The hydrolyzed peptides in sheep collagen, such as Gly-Pro-Hyp, are quickly absorbed into the bloodstream and integrated into the dermal layers, stimulating fibroblast activity and promoting collagen and elastin production. Moreover, it causes inhibition of matrix metalloproteinases (MMPs), which degrade collagen. These actions are essential for maintaining skin structure, hydration, and elasticity[27,28].

Hyaluronic Acid

Hyaluronic acid (HA), a naturally occurring glycosaminoglycan polysaccharide, is essential for maintaining skin hydration, elasticity, and overall dermal health[29]. HA is a key component of the extracellular matrix (ECM) of the human body, with high concentrations in connective tissues such as skin, synovial fluid, and vitreous humour[30]. It plays a critical role in skin structure by exhibiting excellent moisturizing properties by binding water molecules due to its highly anionic properties[30]. Ageing causes loss of hyaluronic acid and collagen in the skin; thus, overlying wrinkles begin to form due to loss of viscoelastic properties. Hyaluronic acid counteracts ageing by replacing lost volume. In addition, hyaluronic acid fillers have also been shown to increase collagen production and affect fibroblast morphology[31]. The most common applications are cosmetics and intra-articular use, although many other ophthalmic and topical forms are also available[31]. HA can be prepared in various forms, such as creams, films, gels, serums, hydrogel, fillers, and plasma[32]. One study showed that daily use of a cream containing HA causes a significant improvement in skin firmness and a reduction in the depth of perioral and orbital wrinkles in all patients[33]. It is found that oral administration as a dietary supplement can counteract skin ageing and effectively improve skin condition by increasing skin hydration and improving skin dryness[34-39].

Nicotinamide Mononucleotide

Nicotinamide mononucleotide (NMN), a precursor to nicotinamide adenine dinucleotide (NAD+), has emerged as a promising supplement for combating age-related cellular decline. NAD+ is essential for physiological activities such as cellular energy metabolism, DNA repair, and oxidative stress regulation[23]. As age advances, the cellular concentration of NAD+ naturally declines across multiple human tissues, including skin, blood, liver, muscle, and brain, declining the energy production in mitochondria and affecting the activities of NAD+-dependent enzymes with redox reactions. The decline in NAD+ levels also influences the function of sirtuins, which are proteins that modulate ROS activity. As NAD+ levels decline and sirtuin activity reduces in ageing skin, the accumulation of ROS can lead to oxidative stress in the skin[40,41], promoting melanogenesis, contributing to the development of ageing and a range of age-related disorders[42].

The NMN supplementation has demonstrated the ability to replenish NAD+ levels, thereby improving biosynthesis pathways and overall cellular function, reversing the ageing process, physical performance and metabolic health[23]. Clinical studies have provided

robust evidence supporting the efficacy of NMN[43-45]. For instance, Yi et al. (2023)[46] observed significant increase in Blood NAD concentrations and physical performance among participants supplemented with NMN in doses ranging from 300 mg to 900 mg daily. Its safety profile is favourable, with no significant adverse effects reported in doses up to 1,000 mg per day. However, long-term safety data remain limited, and further research is necessary to confirm the effects of prolonged use[47].

Minerals

Vitamins and minerals are essential micronutrients that play a vital role in skin cell turnover. Minerals like zinc and copper help stabilize collagen structure, offer antioxidant protection, and support enzymatic processes necessary for skin repair and maintenance[48].

Zinc (As Zinc Gluconate)

Zinc is pivotal in promoting skin health, with functions spanning immune modulation, antioxidation, and support for dermal integrity[49]. Clinical studies have highlighted zinc's role in enhancing skin elasticity and hydration and reducing visible signs of ageing. One study demonstrated that zinc supplementation significantly reduced oxidative stress and inflammatory cytokines in elderly participants, improving immune function and skin health. It enhances collagen synthesis by activating fibroblasts and regulates inflammatory pathways by interacting with NF-κB signalling[48]. Additionally, zinc mitigates oxidative stress by promoting the activity of antioxidant enzymes like superoxide dismutase and catalase. This dual role in antioxidation and inflammation control is crucial for maintaining skin integrity and preventing premature ageing[49].

Copper (As Ghk-Cu)

Copper, particularly GHK-Cu (Glycyl-L-Histidyl-L-Lysine Copper), is pivotal in skin rejuvenation, wound healing, and antiaging processes. GHK is a naturally occurring tripeptide found in human plasma. This molecule has a high affinity for copper (II) and forms the endogenous chelate GHK-Cu. The plasma level of GHK is about 200 ng/ml at age 20 but declines to 80 ng/ml by age 60, reducing its regenerative and antioxidant properties in the skin[50]. Copper is essential for collagen synthesis, elastin formation, and the regulation of enzymes such as superoxide dismutase (SOD), which mitigate oxidative stress. Through its role in the extracellular matrix (ECM), GHK Cu helps maintain skin elasticity and hydration, essential for reducing wrinkles, skin texture, inflammation, and free radical damage[51]. Studies have demonstrated GHK-Cu's effectiveness in tissue remodelling, collagen production, and anti-inflammatory activity. A clinical trial showed that topical GHK-Cu reduced wrinkle volume by 55.8% and wrinkle depth by 32.8% over eight weeks, outperforming other cosmetic products[51]. It has shown the ability to increase cellular production of collagen and elastin by human adult dermal fibroblast cells, supporting skin regeneration and antiaging benefits[52].

Selenium

Selenium (Se) is a trace element that is essential for humans. It is widely distributed in various tissues and organs of the human body and animals[53]. Selenium, is present in nuts particularly Brazil nuts and seafood such as fish and shellfish. Other sources include meats (especially liver and kidneys), edible fungi, poultry eggs, broccoli, whole grains, purple sweet potatoes, garlic etc.[54]. The selenium ingested from food is absorbed by the digestive system and then transported through the bloodstream to various cells throughout the body, where it participates in multiple biological processes such as antioxidation and immune enhancement[53]. Selenium stimulates antioxidant enzymes glutathione peroxidase and thioredoxin reductase, and thus protects the skin against the oxidative stress induced by UV radiation[55]. Study showed that low doses of Se (30 nM) provide potent protection against UVA-induced cytotoxicity in young keratinocytes (from 20–30-year-old donors), while higher concentrations (240 nM) were required for protective efficacy in old keratinocytes (from donors 60-70 years old)[56].

Vitamins

Incorporation of vitamin-A and all of its derivatives, applied systemically or topically enhances skin elasticity and boosts the natural processes of collagen fibre regeneration and cellular repair[57]. Vitamin C and vitamin E are potent antioxidants. The biological function of vitamin C in the skin is its active role in collagen synthesis. Due to its antioxidant property, vitamin C protect the skin, especially the epidermis, against oxidants generated by ultraviolet radiation and other environmental factors[57]. Additionally, vitamin C plays a role in cholesterol synthesis and iron absorption and increases the bioavailability of selenium[58]. Topically, ascorbic acid is used in various cosmetic products, such

as lightening skin depigmentation, antiaging, and sun protection formulations[58]. Since the human body does not produce vitamin C naturally, obtaining enough of it through diet is crucial to maintain a healthy lifestyle[58]. Vitamin E complex is a group of lipophilic compounds known as tocopherols. As a fat-soluble, membrane-bound antioxidant, tocopherol serves as a formidable defence against oxidative damage and protecting the epidermis and dermis against oxidative stress induced by environmental factors[58].

Challenges to Modern Society

Modern lifestyles introduce significant challenges to combating aging. Poor dietary habits, including low intake of collagen-boosting nutrients, vitamins, and essential minerals, impair the bodies' ability to repair and regenerate skin tissue[17]. Chronic stress, environmental pollution, and prolonged UV exposure contribute to oxidative stress and cellular damage, intensifying the aging process[10]. Furthermore, sedentary habits and the widespread use of processed foods exacerbate nutritional deficiencies. Socioeconomic disparities also limit access to effective anti-aging interventions, leaving many individuals without adequate preventive or restorative measures[11]. These combined factors have led to an increase in the prevalence of early aging symptoms, highlighting the urgent need for accessible, scientifically-backed solutions. Achieving the best result in enhancing aging skin health through nutraceutical synergies, media communication plays a great role[59-60]. Good media communication is an art that determines compliance and adherence to therapy[59,61].

CONCLUSION

Modern lifestyles with multiple factors such as poor nutrition, environmental pollutants, UV exposure etc. exaggerate the oxidative stress and accelerate skin ageing. Nutraceutical interventions have emerged as promising tools to counteract the effects of aging. By addressing multiple biological pathways, the combination of bioactive peptides (marine collagen, sheep collagen), hyaluronic acid, nicotinamide mononucleotide, minerals (zinc, copper, selenium), and vitamins provides a scientifically strong and synergistic approach in combating the multifaceted visible signs of aging. The integrated approach ensures optimal outcomes, making it an ideal choice for those seeking long-lasting and transformative anti-aging benefits.

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Conflict of Interest

The authors declared no conflicts of interest.

Authors' Contribution

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