Polyphenols against Skin Aging

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Contributor: Farid Menaa

Polyphenols représente a superfamily of diverse naturally occurring phytochemicals, which exert a particularly potent antioxidant activity, thereby contributing to delay skin aging.

Polyphenols Skin Anti-aging Antioxidant Inflammation Cosmetics

1. Introduction

Aging is associated with a gradual decline of physiological and cognitive functions.[1] Over the past two decades, significant progress has been made in elucidating the molecular mechanisms of aging,[2][3] an active but still challenging area. Hundreds of genetic factors, called longevity-related genes, have been identified to modulate lifespan and healthspan in model organisms ranging from yeast (e.g., Sacharromyces cerevisiae), worms (e.g., Caenorhabditis elegans), flies (e.g., Drosophila melanogaster), and rodents (e.g., Mus musculus, Rattus norvegicus). Among them, a large number of the longevity-related genes fall into three conserved nutrient sensing pathways: target-of-rapamycin (TOR), insulin/IGF-1-like signaling (IIS), and sirtuin pathways. [4][5] The recent studies have shed light on some of the mechanisms involved in aging processes, and provide valuable guidance for developing and promoting effective healthy skin aging interventions. [6]

Skin aging is a complex, progressive and inevitable biological process. Although it is primarily a physiological process (i.e., the so-called chronologic aging) involving our own genetic background, it may also become a pathological process (i.e., the so-called premature aging). Premature skin aging is manifested by accelerated induction of wrinkling, scaling, roughness, dryness, laxity, as well as mottled pigment abnormalities including hypo-pigmentation and hyperpigmentation, and can be caused by the detrimental effects of xenobiotics agents or environmental (e.g., chronic exposure to solar ultraviolet radiation-induced oxidative stress aka hotoaging, pollution, cigarette smoke, extreme temperature change). [7][8]

One of the major features of aging skin is the pro-gressive proteolytic degradation of cutaneous elastic fibers that cannot be adequately replaced or repaired by adult dermal fibroblasts. [9] In fact, the impact of both chronological aging and hotoaging on the skin appears particularly concerning when enhanced oxidative stress is involved. Interestingly, a recent study showed quantitative and qualitative differences in the oxidative stress generated either by chronological aging or by hotoaging in the skin of hairless mice. [10] Indeed, while the lipid peroxides level was increased in both skin types, and so would represent a good parameter to determine the oxidative stress, a difference in the decay capacity of lipid membrane turnover was noticed between chronological and hotoaging skin. [10] Importantly, neither superoxide dismutase (SOD), which remained unchanged, nor catalase, which increased with chronologic aging and decreased in irradiated mice, could have been considered as good biomarkers of oxidative stress. [10]

Plants are the source of important products with nutritional and therapeutic value. There is emerging evidence that topical application or oral intake of some polyphenol-rich plant extracts can reduce a number of degenerative diseases and skin conditions such as skin aging. [11][12] Polyphenols represent a superfamily of diverse naturally occurring plant chemicals, and are abundant micronutrients in our diet (e.g., vegetables, fruits, flowers, nuts, seeds). [13][14] The protective health effects exerted by polyphenols as neutraceuticals depend not only on the dietary intake but also on their systemic bioavailability. [13][14] Indeed, the most abundant polyphenols in our diet are not necessarily those that have the best bioavailability profile. [13] The bioavailability and sources of polyphenols and polyphenol-containing foods has been previously reviewed, [13][14] showing that it mainly depends on: (1) their intestinal absorption during which the microflora of each given individual plays an important role in the catabolism of polyphenols and the production of some active metabolites, (2) their chemical structure (e.g., glycosylation, esterification, and polymerization), (3) their inclusion in the food matrix, and (4) their excretion back into the intestinal lumen.

Globally, there are three main types of polyphenols: the flavonoids, the stilbenes, and the lignans, which are classified by the number of phenol rings they contain as well as the binding properties of the ring structures. [11][12][13][14] The phenol rings are comprised of phenyl and hydroxyl group structures that possess diverse biological activities such as anti-inflammatory, immune-modulatory and antioxidant properties. [11][12][15] Further, each class of these phytochemicals can be subclassified in accordance to the interactions of their respective phenyl rings to carbon, oxygen, and organic acid molecules. [13][14] Thereby, flavonoids represent a large class of edible polyphenols, and are divided into six main sub-classes: (1) flavonols (highly concentrated in onions, apples, red wine, tea, broccoli and Ginkgo biloba), (2) flavones (a good amount in the herb chamomile), (3) isoflavones (predominant in soy), (4) flavanones (largely present in citrus fruits), (5) anthocyanidins (abundant in berries and cherries), and (6) flavanols (i.e., catechins, mainly found in red wine, tea and apples), among which the most abundant is (2)epigallocatechin-3-gallate (EGCG), extensively studied because of its potent therapeutic effects in skin. [16][17] Stilbenes (aka stilbenic phytoalexins) are found in low quantities in the human diet, and are mainly represented by resveratrol that exist in both cis and trans isomeric forms, mostly glycosylated. Resveratrol has been detected in more than 70 plant species (e.g., red grapes, particularly in the fresh skin, berries, peanuts, red wine, grape juice), and presents potential benefit against premature skin aging. [13][14][18][19] Most lignans are naturally present in the free form, while their glycoside derivatives represent a minor form. They are also found in low quantities in the human diet (e.g., mainly present in linseed, nuts, and whole grain cereals). [13][14]

Being widely abundant and relatively inexpensive, the use of polyphenols is highly attractive to researchers as a cost-effective alternative or as a strategy to supplement current skin pharmacologic therapeutics, [20] skin protection agents (e.g., sunscreens) [21][22][23][24] and cosmeticesthetic techniques (e.g., microdermabrasion). [25]

2. Polyphenols Benefits on Skin Aging: An Overview

Skin, the largest organ of the body, is the organ in which changes associated with aging are most visible. The skin is made up of three main layers: the hypodermis, the dermis, and the epidermis. [26] The hypodermis is the deepest section of skin, and is primarily a place of connection and fat storage. [26] The epidermis is made up mostly of keratinocytes, is rich in reactive oxygen species (ROS), detoxifying enzymes and in low molecular weight antioxidant molecules, and also contains melanocytes, Merkel cells, and Langerhans cells. [26] The primary function of the epidermis is to provide a weather- and water-proof layer to protect the body.[26] The dermis contains most of the connective tissues of the skin, as well as nerve endings, sweat glands, and hair follicles. [26]

Similar to the entire organism, skin is subject to an unpreventable intrinsic aging process (e.g., respirationinduced oxidative stress). Intrinsic skin aging is characterized by atrophy of the skin with loss of elasticity and slowed metabolic activity. [27][28] Additionally, skin aging is influenced by exogenous/extrinsic factors (e.g., sunlight/UV radiation (UVR) and other atmospheric conditions) that can lead to premature skin aging, [29][30][31] resulting in hypertrophic repair response with thickened epidermis and increased melanogenesis, as well as even more striking changes in the dermis (i.e., massive elastosis, collagen degeneration, twisted and dilated microvasculature). [27][28]

In normal/unstressed cells, there is a constant pro- p0055 duction of ROS from the mitochondria, which is balanced by the production of antioxidant enzymes in the cell, such as SOD, catalase, and glutathione (GSH) peroxidase. [32] When a cell comes under stress, this balance is interrupted, and the ROS can overwhelm the cells and lead to a change in normal cellular behaviors. [33][34] Therefore, despite their morphological and pathophysiological differences, intrinsic and extrinsic aging (i.e., chronologic skin aging and skin hotoaging, respectively) share several molecular similarities. In summary, the central aspects of the skin aging are reflected by the intracellular and extracellular oxidative stress initiated by two main events: (1) the formation of ROS, and (2) the induction of matrix metalloproteinases (MMPs).

ROS (e.g., singlet oxygen, superoxide, peroxyl radicals, hydroxyl radicals, and peroxynitrite), [35] overbalances the antioxidant defense system potential of the skin structure (i.e., horny layer, epidermis and dermis). [36][37] ROS react with nucleic acids, proteins, glucids and fatty acids, causing oxidative damage (i.e., lipid peroxidation), [38] and contribute to chronologic skin aging, [35][38][39] pathogenesis of inflammatory processes and allergic responses in the skin, [27] as well as to skin hotoaging and skin cancer development (e.g., photocarcinogenesis). [38] The roles and mechanisms of ROS metabolism (i.e., generation and elimination) in the body, as well as the effects of ROS generated in the skin (e.g., free radical damage, cell-mediated responses associated with the mitogen-activated protein kinase (MAPK) activity), have been previously reviewed. [35][36]

The induction of MMPs, which leads to the accumulation of fragmented collagen fibrils, which prevents neocollagenesis and accounts for the further degradation of the extracellular matrix (ECM) by means of positive feedback regulation. [39] For instance, it is known that after UVR-induced ROS, MMP-1 (aka collagenase-I), -3, -9 levels are increased, causing collagen and elastin degradation before forming coarse wrinkles and sagging skin. [40]

In recent years, epidemiological and biochemical studies have shown that the occurrence of various diseases (e.g., cancer, degenerative and cardiovascular pathologies, premature skin aging) has been reduced, notably because of the antioxidative effects of polyphenols. Indeed, antioxidants such as flavonoids and phenolic acids play a main role in fighting ROS, and the inhibiting mechanisms of photoaging by polyphenols (e.g., inhibition of MMP-1, elastase and hyaluronidase) are being unraveled in order to develop agents able to slow down the aging process. [40][41]

In this regard, the evaluation of local polyphenolbased anti-aging therapy (e.g., polyphenol-rich sunscreens and skin care products), [21][23][25][37][38][40] as well as the potential benefit of dietary polyphenol, [16][19][22][41] remains an active but challenging field of research. Briefly, it is now well-accepted that topical polyphenol-rich products (i.e., cosmeceutics) can partially "reverse" the clinical and histologic changes in the epidermis and dermis induced by the combination of sunlight exposure and chronologic aging (e.g., repair of keratinocyte ultrastructural damage, distribution of melanin, deposition of new papillary dermal collagen, improvements in vasculature, normalization of hyperkeratinization, increased epidermal thickness and dermal glycosaminoglycan (GAG) such as hyaluronic acid). [23] Thus, the topical use of such agents may favorably supplement sunscreens providing additional anti-aging (and anticarcinogenic) skin benefits. [24][42] Besides, the protective effects on skin aging exerted by polyphenol-rich food products (i.e., neutraceuticals) depend not only on the dietary intake, the source plant, the polyphenolic content and nature in the food matrix, but also on the polyphenols systemic bioavailability. [13][14] Some herbs such as green tea (EGCGrich plant), [16][17] or some fruits such as grapes (resveratrol-rich plant), [18][19] have been shown as promising edible products against skin aging. Further, polyphenol-rich agents should strengthen the use of some esthetic techniques, supporting the role of topical antioxidants as antiaging factors. For instance, a recent study using adult female volunteers (n510), reported that the addition of skin polyphenolic antioxidant-based serum enhanced the dermatologic changes (i.e., increased epidermal and papillary dermal thickness, enhanced fibroblast density, increased hyalinization of the papillary dermis with newly deposited collagen fibers). This was seen following facial treatments using microdermabrasion, a reliable, non-invasive tool for facial rejuvenation. [25]

Nevertheless, one should also keep in mind that some polyphenols could be a double-edged sword for the human skin, exerting both protective (i.e., as antioxidants) and damaging actions (i.e., allergic reactions, contact dermatitis, phytodermatoses, photo-phytodermatoses, and enhanced UV-induced apoptosis). [34][35][43]

3. Conclution

The traditional use of plants in medication (e.g., skin anti-aging and associated diseases) or beautification (e.g., cosmetics) is the basis for active but challenging research, and should make new trends in cosmetics and medical therapy. Polyphenols are believed to have photo-protective anti-aging effects through decreasing inflammation and acting as a scavenger of free radicals. For many compounds, a large number of well-conducted clinical studies are required to prove their safety and efficacy before they are used as anti-aging cosmeceutics, anti-aging neutraceutics, or as adjuvant therapeutics. Besides, the complexity of polyphenol-rich extracts of the whole food product (e.g., mix of vitamins such as C and E, pigments such as carotenoids) or polyphenol-rich blends (e.g., sea buckthorn (Hippophae rhamnoides L.) fruit blend) might be more beneficial to treat skin conditions (e.g., skin aging) than the pure, selected polyphenols. However, highly purified polyphenols are important for the study of biological effects and in unraveling mechanisms of action. Essentially, clinical studies combining pure polyphenols, polyphenol extracts or polyphenolbased nano-formulations with other modalities (e.g., chemotherapeutics, sunscreens, techniques used in esthetics) in order to increase their respective efficacy, are lacking.

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