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# Food-derived nutricosmetic ingredients for combating skin aging: a critical review

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**ABSTRACT:** In recent years, the increasing demand for anti-aging solutions has led to rapid advancements in the skincare industry. Natural nutricosmetics, offering significant benefits for skin aging, have become a popular trend due to their safety and convenience. Despite this growing interest, the key active ingredients in nutricosmetics and their potential benefits remain underexplored. Therefore, this review aims to identify and classify the primary bioactive compounds found in food-derived nutricosmetics that alleviate skin aging, along with their underlying mechanisms. Nutricosmetic ingredients are categorized into peptides, polysaccharides, lipids, vitamins and phytochemicals based on their chemical structures. These compounds have been shown to play a significant role in improving skin hydration, reducing wrinkle formation, and alleviating erythema, as demonstrated in both *in vitro* and *in vivo* models. Additionally, the digestive absorption routes of these ingredients are discussed, along with the clinical evidence supporting their efficacy. Challenges related to oral bioavailability, dosage, and market restrictions in the nutricosmetic field are also addressed.

**Keywords:** Nutricosmetics; Bioactive compounds; Skin aging; Digestive absorption; Oral bioavailability

## 1. Introduction

Human skin is the barrier that segregates the body from the external environment and protects the body from mechanical damage, hazard substances, radiation and invasion of microorganisms. As an essential part of the immune system, skin also plays an important role in regulating body homeostasis by minimizing water loss and maintaining body temperature[1]. In addition to these biological functions, skin conditions intuitively reflect physical attractiveness and the degree of well-being.

Beauty, particularly in the context of dermatology, is often associated with youthful, healthy skin. Skin appearance is a key indicator of individual health and has held significance across various cultures and historical contexts. Additionally, it plays a vital role in shaping social attributes such as self-esteem and attractiveness. This association has fostered a growing consumer interest in interventions that address the

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visible signs of skin aging, such as wrinkles, dryness, and loss of elasticity. Skin aging itself is a complex biological process influenced by both intrinsic factors, such as genetics and hormonal changes, and extrinsic factors, including ultraviolet exposure and environmental stressors[2]. The increasing demand for beauty-related products that claim to mitigate or reverse the visible signs of skin aging has catalysed the development of a novel category of oral supplements. The specific bioactive ingredients in these supplements aim to improve skin health from within, by modulating cellular processes related to hydration, collagen synthesis and oxidative stress reduction, among others.

The term "nutraceutical", derived from "nutrition" and "pharmaceutical", refers to foods or food components that provide health benefits, including disease prevention or treatment[3]. Within this domain, nutricosmetics are ingestible, food-derived products or ingredients designed to enhance the health, function, and appearance of skin, hair, and nails. Rising demand for cosmetic solutions, particularly among females, drives substantial investment in products to enhance skin appearance and integrity, accelerating research into skin aging and its management. The global nutricosmetics market is projected to reach $7.9 billion by 2025, with a compound annual growth rate of 5.0%[4]. Increasing societal emphasis on skin health, linked to enhanced self-esteem, attractiveness, and social behaviour, has shifted consumer focus toward internal skincare solutions. Heightened awareness of personal health and safety further promotes the use of safer, naturally derived nutricosmetics, free from harmful substances, aligning with current industry trends toward novel, natural ingredients[5, 6].

Nutricosmetics, encompassing lipids, peptides, polysaccharides, vitamins, secondary metabolites, and botanical extracts, have been previously categorized by their general bioactivities or discussed within the broader context of food-cosmetic convergence, including topical applications, formulation strategies, skin penetration, sustainability, and green extraction[5, 7]. Nevertheless, existing works have not systematically organized food-derived nutricosmetic ingredients according to chemical class, nor have they fully integrated evidence on oral absorption and biotransformation with downstream signalling pathways in the skin and clinically validated outcomes. Although earlier studies emphasized analytical techniques and highlighted the promise of bioactive molecules, they did not provide a comparative synthesis of dose-response relationships across major ingredient families, nor did they consolidate emerging evidence into a unified framework for nutricosmetics[6, 8]. To address these gaps, this review systematically classifies food-derived nutricosmetic ingredients based on their chemical structures and examines their oral absorption pathways in relation to skin-targeted signalling and validated endpoints, drawing on the most recent *in vivo* and clinical data (**Figure 1**). It further distinguishes nutricosmetics from conventional cosmetics by highlighting differences in mechanisms and sites of action. Furthermore, this review evaluates efficacy and translational reliability by summarizing clinically applied ingredients and products, with attention to safe and effective dosing where available, and identifies persistent challenges such as the limited skin-targeting evidence for novel ingredients such as phytochemicals, thereby supporting the evidence-based development of high-value nutricosmetic products.

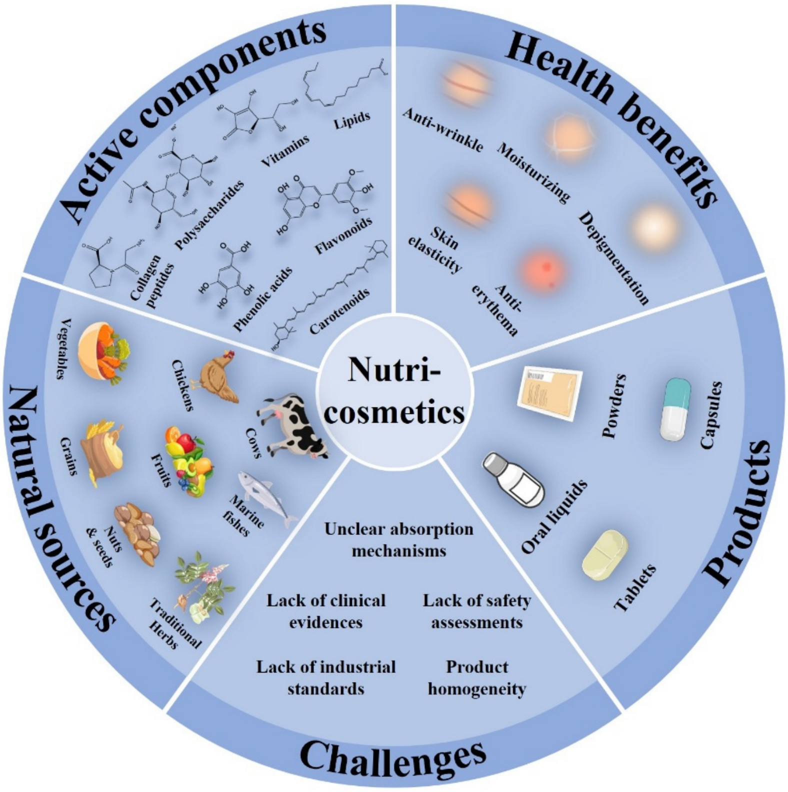


**Figure 1.** Brief summary on natural sources, active components, skin health benefits, product forms and current challenges for nutricosmetics.

### *1.1 Factors inducing skin aging and related signalling pathways*

The aging of organs begins from birth, and there is no exception for the skin. Several factors including nutrition deficiency, photoaging, hormonal disorders, and environmental factors, affect skin appearance and integrity. Skin aging is categorized into extrinsic and intrinsic aging. Intrinsic aging is determined by internal factors such as genes, hormones, and metabolism. Extrinsic aging is mainly caused by ultraviolet exposure and is characterized by degradation of skin structure and increase in thickness, sagging, roughness, wrinkle formation, dehydration and erythema[2]. Extrinsic aging occurs through exposure to ultraviolet adiation, generating reactive oxygen species (ROS) including superoxide anions, hydroxyl free radicals, and hydrogen peroxide, leading to cellular DNA damage, inflammatory responses, depletion of antioxidants, and degradation of collagen and elastin substrates by matrix metalloproteinases (MMPs). Skin aging is driven by interconnected biological processes. To provide a unified mechanistic context for this review, the principal pathways through which orally delivered nutricosmetic ingredients may confer protection are illustrated in **Figure 2**. Collagen metabolism plays a crucial role in wrinkle formation and the loss of dermal elasticity. Intracellular reactive oxygen species (ROS) induce the expression of MMPs such as MMP-1 in skin keratinocytes and fibroblasts, accelerating extracellular matrix (ECM) degradation. In parallel, the MAPK cascade (ERK, JNK, and p38) stimulates activator protein 1 (AP-1), further upregulating MMPs and promoting the breakdown of collagen and elastin that underlies wrinkle development[9]. Conversely, the transforming growth factor-β (TGF-β)/Smad signalling pathway supports procollagen transcription, collagen synthesis, and dermal matrix renewal, thereby counteracting structural decline. The NF-κB pathway drives the production of pro-inflammatory mediators, including TNF-α, IL-6, and IL-8, which lead to barrier impairment and erythema[10]. Besides, oxidative stress also activates the Nrf2 antioxidant defense system, which regulates genes such as HO-1 and NQO1 and counteracts reactive oxygen species, thereby mitigating skin inflammation[11]. Additionally, skin pigmentation is primarily regulated through melanogenesis[12]. Phosphorylation of p38 activates microphthalmia transcription factor (MITF), promoting melanin synthesis, while ERK activation inhibits melanogenesis by suppressing MITF expression via MAPK signalling pathways[13].

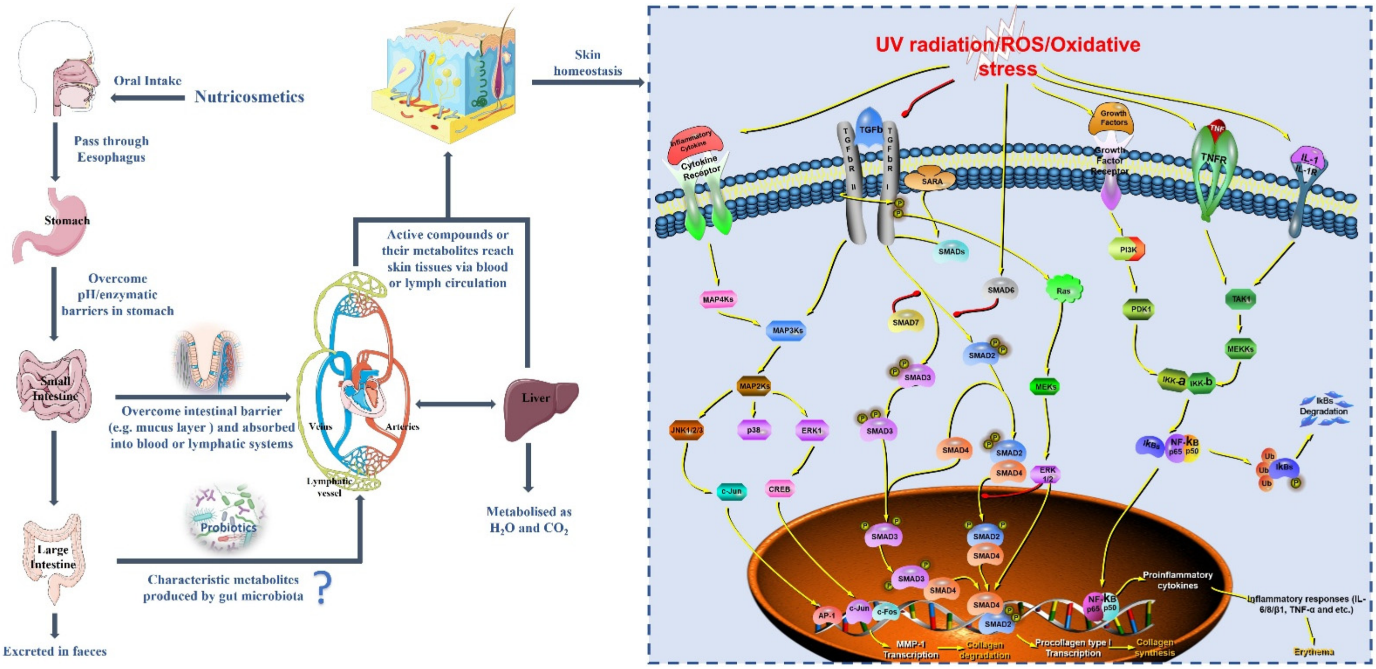


**Figure 2.** Plausible absorption and metabolism pathways of nutricosmetics, as well as signalling pathways related to skin issues involving winkle formation, epidermal thickening, dehydration elasticity loss and erythema: MAPK signalling pathway, TGF-β1/Smad signalling pathway and NF-κB signalling pathway regulation through ROS interaction. Oxygen reactive species (ROS); transforming growth factor-β (TGF-β); jun-N-terminal kinase (JNK); extracellular-regulated protein kinase (ERK); p38 mitogen-activated protein kinases (p38); activator protein 1 (AP-1); matrix metalloproteinase 1 (MMP-1); phosphorylation (P); tumor necrosis factor-α (TNF- α); interleukin 6 (IL-6); interleukin 8 (IL-8).

### *1.2 Comparisons between absorption pathways of nutricosmetics and cosmetics*

#### *1.2.1 Absorption of conventional cosmetics*

For percutaneous absorption of conventional cosmetics, the permeation pathways include three stages: into the stratum corneum, through the stratum corneum and into the bloodstream. Bioactive molecules in cosmetic formulation initially partition into the stratum corneum after directly applying to the skin surface. A lipophilic molecule from a hydrophilic preparation will favor this releasing process. Most molecules are then transported through the stratum corneum via three feasible pathways: the intercellular pathway, intracellular pathway, and trans-appendageal pathway[14]. The intercellular pathway through the lipid matrix is the principal route for the majority of small molecules. The shorter intracellular route is not preferred for most molecules to pass through the stratum corneum as it covers several partitioning-diffusion processes through hydrophilic and hydrophobic domains. Hydrophilic molecules with large molecular weights favour traversing through hair follicles or sweat ducts via the trans-appendageal pathway[15]. After bypassing the stratum corneum, molecules partition and diffuse through epidermal layers, followed by diffusing through dermal tissue to reach blood capillaries before partitioning into the blood stream. Penetrating through stratum corneum is the rate-determining step of the permeation process for most bioactive compounds that penetrate into the skin dermis or subcutaneous tissues to effectively take effect, but rarely enter the blood circulation.

*1.2.2 Absorption of nutricosmetics*

The gastrointestinal (GI) tract is commonly split into two segments. The upper segment is composed of mouth, pharynx, esophagus and stomach, while the lower segment consists of small intestine, large intestine and anus. After ingestion, nutricosmetics are dissolved and absorbed in the GI tract during digestive process. Absorption of nutricosmetics is remarkably restricted by the physical barrier of impermeable GI epithelium and biological barriers such as enzymatic degradation. During the digestion through the GI tract, the specific absorption site is determined by the nature of nutricosmetic compounds and regional distinctions such as enzyme activity, pH, thickness of mucosa and residence time. Nutricosmetics are mainly absorbed in the small intestine and the bioavailability of nutricosmetics primarily depends on the ability to traverse the intestinal mucus barrier and enter the blood or lymphatic circulation. Macromolecules such as proteins, polysaccharides and lipids prefer to be metabolized into smaller hydrophilic molecules by digestive enzymes in the GI tract before absorbed by protein-mediated active transport, $Na^+$-dependent active transport or endocytosis in the intestinal epithelium[16-18].

Unlike conventional cosmetics, the bioavailability of nutricosmetics is critical to their oral efficacy. Once ingested, bioactive compounds must overcome challenges related to stability, permeability, and the complexities of the gastrointestinal tract. Factors such as pH, transit time, digestive enzymes, and the intestinal barrier all significantly affect their absorption (**Figure 3**). Consequently, the solubility and stability of a nutricosmetic compound remarkably influences its bioavailability[19]. Lipophilic nutricosmetics such as carotenoids are initially released from the food matrix and are transferred into oil droplets, followed by transformed to mixed micelles and absorbed via passive diffusion in the small intestine after the micellar solubilization. Some insolubilized molecules travel forward in the gastrointestinal tract to be metabolized by microflora in the colon or eliminated. For hydrophilic bioactive compounds such as polyphenols, most of them are able to reach the small intestine due to their excellent stability in the stomach[20]. Flavonoids represent a class of polyphenols with a wide range of biological activities that commonly found in natural resources. However, poor aqueous solubility and low permeability significantly limits their bioavailability via oral ingestion[21]. A majority of flavonoids in edible resources are linked to one or more glucose, arabinose, galactose or rhamnose by glycosidic bonds. Flavonoid glycosides tend to be hydrolyzed and deglycosylated by endogenous enzymes such as lactases and β-glucosidases in the small intestine before absorption[22]. Non-glycosylated polyphenols such as catechins and procyanidins are absorbed in the small intestine without the critical deglycosylation, while a majority of them are degraded by gut microbiota in the large intestinal lumen[23]. After entering the blood stream, bioactive compounds are distributed and targeted to skin tissues before contributing to biological effects.

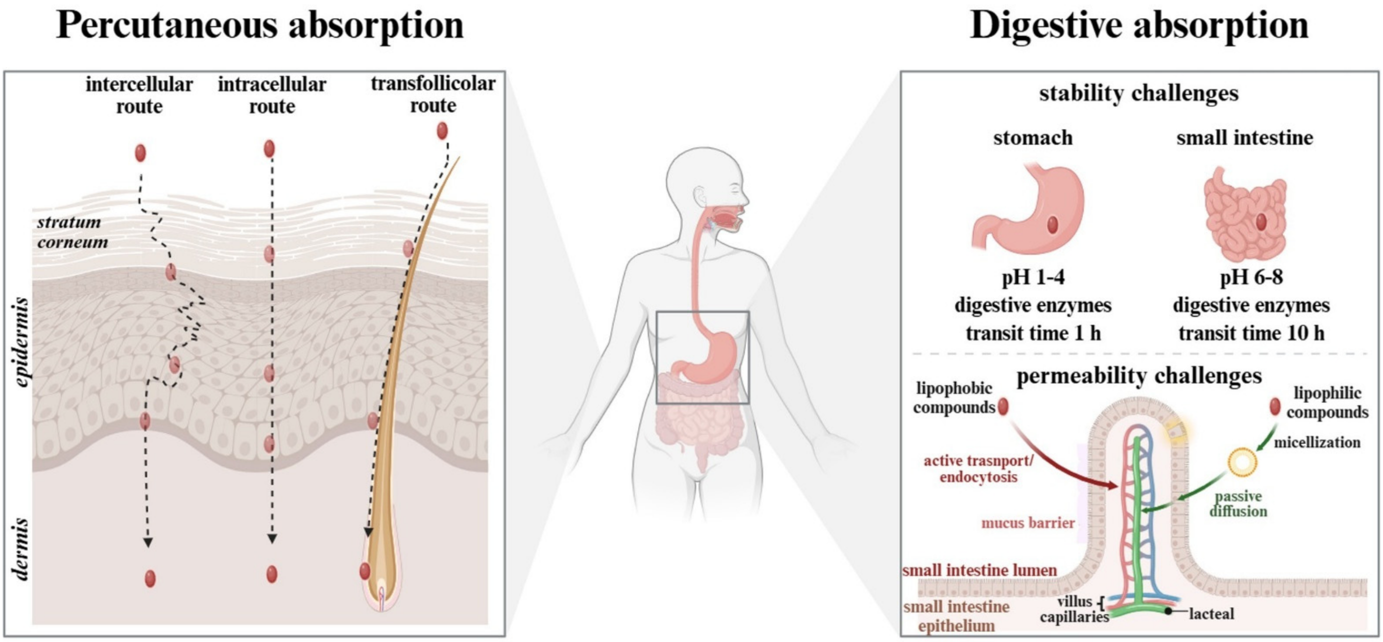


**Figure 3.** Key differences in absorption mechanisms between conventional cosmetics and nutricosmetics.

*1.2.3 Comparative advantages of digestive absorption over percutaneous absorption*

Comparing these two absorption pathways, oral delivery of nutricosmetics generally requires a longer period to be absorbed and take effect than topical preparations, thus they are not suitable for emergency situations. Besides, nutricosmetics are absorbed by the gastrointestinal tract and transported to the skin via blood circulation, and the dose required to achieve the ideal effect for skin beauty is usually higher because the bioavailability is restricted by the GI absorption barrier and metabolism. Despite these drawbacks, oral delivery strategy for nutricosmetics possesses remarkable superiorities compared with percutaneous absorption. Oral delivery is popular due to its better convenience and acceptance. Nutricosmetics are continuously distributed to skin tissues of the whole body via oral absorption, which tends to exert effects on skin beauty for a long period. In contrast, topical cosmetics are effective to the restrictive region of skin on which they are applied, and a regular application is required to maintain improved skin conditions. Most ingredients in topical preparations remain in the epidermis and are not capable of bypassing the stratum corneum barrier. Consequently, excessive use of topical cosmetics tends to cause skin problems such as skin thickening, clogged pores, acne and allergies.

*1.3 Common in vitro and in vivo models for efficacy assessment of nutricosmetics*

Normal human dermal fibroblasts (NHDFs), human fibroblasts (Hs68) and CCD-986sk cells are widely applied to evaluate beneficial effects of nutricosmetics on UVB-induced photoaging *in vitro*. Cell viability, intracellular ROS, elastase activity, levels of type I procollagen, MMPs and hyaluronic acids are measured to evaluate the effects on UVB-induced cell proliferation, ROS generation, skin inflammation, elastase activity and degradation of collagen[24]. In addition, human immortalized keratinocytes (HaCat) are also used to investigated UVB-induced damage by determining cell viability and the expression of type I collagen and HA[25]. UVB irradiation is considered to penetrate the epidermal and dermal layer of human skin, therefore, human keratinocytes and dermal fibroblasts are commonly selected as appropriate *in vitro* models for assessing cosmetic effects. However, evaluating skin beauty effects of nutricosmetics via *in vitro* cell models remains controversial. After oral ingestion, the absorption mechanisms in GI tract and following skin-targeted transport process of most nutricosmetics remain unclear so that whether active ingredients are capable of being transported to skin tissues or not is still ambiguous. Consequently, applying nutricosmetic ingredients directly on UVB-treated cells is incapable of mimicking real situations in animals with a weak correlation.

Hairless mice models (HOS:HR-1 and SKH:HR-1) are usually chosen for evaluation of nutricosmetics *in vivo*. SKH-1 hairless mice model of photoaging was initially developed by Stephen et al. and was considered to be close to the actual conditions of human photoaging skin[26]. UVB-induced wrinkle formation, TEWL, skin thickening, collagen degradation and synthesis were tested and these antiphotoaging effects associated with MAPK/AP-1 and TGF/Smad pathways were mechanistically explained by protein levels of MMP-1, procollagen type I and elastin, filaggrin, and mRNA expressions of IL-1β and IL-6, c-Fos and c-Jun[27]. Besides, zebrafish is recognized as an important vertebrate model in pharmacological studies[28]. Recently, an increasing number of researches utilize zebrafish model to evaluate bioactivities of topically-applied products, such as anti-wrinkle, anti-inflammatory and skin whitening[29]. The early-stage embryo absorbs substances diluted in the aqueous medias via skin and gills, while late-stage zebrafish prefers absorbing orally rather than percutaneously[30]. Therefore, late-stage zebrafish model is potentially suitable for *in vivo* evaluation of nutricosmetics.

## 2. Classification of nutricosmetic ingredients

### *2.1 Lipids*

Lipids, as the primary source of energy storage for body tissues, are commonly existed in the form of triacyl glycerides and phospholipids. Over 90% of ingested lipids prefer to be absorbed in the gastrointestinal tract. Formation of lipid micelles emulsified by bile acids and phospholipids in the intestinal lumen governs the rate of absorption via intestinal epithelial cells[31]. Dietary supplement of polyunsaturated fatty acids (PUFAs) or phospholipids significantly improves skin hydration and erythema, which is directly related to skin barrier functions, as shown in **Table 1**.

**Table 1.** Categories of food-derived ingredients with nutricosmetic potentials for skin antiaging.

| Nutricosmetic ingredients | Natural resources | Animal models | Doses of oral administration | Biological activities | References |
|---|---|---|---|---|---|
| **Lipids** | | | | | |
| Sphingomyelin-containing phospholipids | Milk | Eight-week-old male SKH-1 hairless mice | 50, 100, 150 mg/kg/day, 8 weeks | Level of hyaluronic acid, skin hydration, expressions of Nrf2 and HO-1 ↑; Skin thickness, level of TEWL, erythema index, expression of Keap1 ↓ | [37] |
| Sphingolipids-rich wheat extract oil | Wheat | Six-week-old SKH-1 hairless mice | 30, 60, 120 mg/kg/day, 12 weeks | Skin hydration, skin elasticity, Levels of collagen content, HA, ceramide and type I procollagen ↑; wrinkle formation, epidermal thickness, TEWL and level of MMP-1 mRNA ↓ | [24] |

| | | | | | |
|---|---|---|---|---|---|
| Linoleic acid/ α-linolenic acid | Flaxseed oil | Six-week-old male Kunming mice | 1:4 or 4:1 (v/v); 10 mL/kg/day | Epidermal hyperplasia, skin thickness, levels of IgE, Th1/2/17 cytokines, expression of JAK2 and STAT4 ↓ | [34] |
| Docosahexaenoic acid (DHA) | Marine fishes | - | - | Levels of adiponectin, PPARγ, C/EBPα, and SREBP-1a ↑; expression of MMP-1 ↓ | [35] |
| Eicosapentaenoic acid (EPA) | Marine fishes | HR-AD hairless mice | 600, 3000 mg/kg/day, 15 days | Skin hydration ↑; TWEL, epidermal thickening, scratching, level of thymic stromal lymphopoietin, IL-4 ↓ | [36] |
| **Peptides** | | | | | |
| Collagen peptides | Tilapia scale (*Oreochromis mossambicus*) | Four-week-old male SKH-1 hairless mice | 500, 1000 mg/kg/day, 9 weeks | Hyaluronic acid and stratum corneum water content, expression of HAS1, HAS 2, filaggrin and involucrin ↑; Wrinkle formation, level of TEWL ↓ | [42] |
| Low-molecular-weight collagen (Val–Gly–Pro–Hyp–Gly–Pro–Ala–Gly) | Tilapia gelatin | Five-week-old male SKH-1 hairless mice | 200, 400, 600 mg/kg/day | Wrinkle formation, epidermal thickness, expression of MMP-1/3/9, p-JNK, p-c-FOS and p-c-Jun ↓; expression of TGF-βRI, procollagen type I and collagen type I, activities of SOD, catalase and GPx ↑ | [43] |
| Collagen peptides | Fish skin | Five-week-old female SKH-1 hairless mice | 250, 500, 1000 mg/kg/day, 14 weeks | Epidermal thickness, wrinkle formation, TEWL, expression of HYAL2 ↓; Skin elasticity, expressions of MMP-1/13, HAS2, SOD1 and Gpx1 ↑ | [44] |
| Collagen peptide NS with Gly-Pro (low molecular weight) | Fish scale | Eight-week-old female CriOri: SKH1-Hrhr hairless mice | 300, 500 mg/kg/day, 12 weeks | Wrinkle formation, Epidermal thickness, TEWL, Level of MMP-1 ↓; Level of skin hydration, type I procollagen ↑ | [40] |
| Collagen tripeptides | Fish scale | Five-week-old male SKH-1 hairless mice | 100 mg/kg/day, 8 weeks | TEWL, wrinkle formation, epidermal thickness, expression of MMP-2/9/13, ↓; expression of TIMP-1/2, level of skin collagen fibres ↑ | [45] |
| Collagen peptide | Porcine placenta | Five-week-old female SKH-1 hairless mice | 25, 50, 100 mg/kg/day, 12 weeks | Wrinkle formation, roughness, level of TEWL, expression of MMP-1, ↓; skin hydration, levels of HAS1, HAS2, LCB1, GPx-1 and COL7A1↑ | [47] |
| L-glutathione | Wheat germ | Female BALB/c mice | 100 mg/kg/day, 2 weeks | Skin pigmentation, melanin content, tyrosinase activity ↓; Level of glutathione and MDA, and SOD activity ↑ | [46] |
| 5-amino-acid polypeptide | Oyster hydrolysates | Eighteen-week-old female SKH: HR-1 hairless mice | 50, 100, 200 mg/kg/day, 9 weeks | Wrinkle formation, epidermal thickness, expression of TNF-α, IL-1β, IL-6, MMP-1, -2, -3, -9, c-fos, c-jun and Smad-7 ↓; Activity of SOD, CAT, and GPx, expression of type I collagen, MDA, Tgf- β1 and TGF-β receptor type II ↑ | [48] |
| Hydrolysed collagen type II peptides | chicken sternum cartilage | Five-week-old female Hos: HR-1 hairless mice | 200, 600 mg/kg/day, 14 weeks | Skin elasticity, Hyaluronic acid content ↑; Level of TEWL, epidermal thickness, wrinkle formation, expression of MMP-1, MMP-2 ↓ | [49] |

| | | | | | |
|---|---|---|---|---|---|
| Whey peptides | Cow Milk | Four-week-old melanin-possessing male HRM hairless mice | 200, 400 mg/kg, twice/day, 17 weeks | Skin thickness, wrinkle formation, expressions of MMP-2, pro-MMP-9, Ki-67 and 8-OHdG ↓; Skin elasticity ↑ | [51] |
| Bovine lactoferrin | Cow milk | Seven-week-old male Hos:HR-1 hairless mice | 1600 mg/kg, six times/week | Level of TEWL, epidermal thickness, reduction in skin hydration, aberrant epidermal hyperplasia, cell apoptosis, expression of IL-1β ↓ | [52] |
| ACP and CCP with MW ＜ 1000 Da (abundant in Gly) | Bovine Bone | thirteen-month-old female SPF Kunming mice | 200, 400, 800 mg/kg/day, 8 weeks | Skin laxity, level of MDA ↓; Level of type I, II, III collagen, SOD and CAT ↑ | [50] |
| Elastin Peptide | Elastic tissues | BALB/C nude mice | 1.5, 5.0, 10 mg/ day, 6 times/week, 16 weeks | collagen content, level of skin elasticity, HA and Hyp ↑ | [53] |
| **Polysaccharides** | | | | | |
| Polysaccharide | *Saussurea medusa* Maxim | 45-day-old male SPF Kunming mice | 2, 6 g/kg/day, 30 days | Wrinkle formation, epidermal thickness, redness, pigmentation and level of MDA↓; skin elasticity, moisture, levels of superoxide dismutase, glutathione peroxidase, HYP↑ | [61] |
| | Peach gum | Five-week-old male SPF hairless nude mice | 200 mg/kg/day, 30 days | Wrinkle formation, epidermal and dermal thickness, keratinization and levels of MMP-1/3, ROS ↓; levels of SOD and CAT ↑ | [62] |
| Hyaluronic acid | Microbial fermentation and rooster combs | Six-week-old male HR-1 hairless mice | 200 mg/kg/day, 6 weeks | Epidermal thickness ↓; Level of skin moisture and expression of HAS2 ↑ | [58] |
| | | Female SKH-1 hairless mice | 10, 40, 160 mg/kg/day, 14 weeks | Expression of MMP-1, IL-1β and IL-6 ↓; Expression of Tgf- β1 ↑ | [59] |
| Proteoglycan with high molecular weight | salmon nasal cartilage | Eight-week-old male Hr-/Kud hairless mice | 0.5 ml prepared sample solution, six times/week, 11 weeks | Level of hydration ↑; epidermal and dermal thickness, Level of TEWL, expressions of TNF-α, IL-1β, and IL-6 ↓ | [60] |
| **Vitamins** | | | | | |
| Mixture of vitamin C and vitamin E | Vegetable oil and seeds | Nine-week-old female SKH-1 hairless mice | 700 mg/kg/day, 10 weeks | Wrinkle formation, Expressions of AP-1, c-Jun, MMP-3, MMP-13, type I procollagen and TGF-β2 ↓ | [65] |
| Vitamin C, L-ascorbic acid | Vegetables and fruits | Five-week-old male ICR mice | 50 mg/ day twice daily, 12 weeks | Skin redness and roughness ↓; skin elasticity, level of type I collagen ↑ | [66] |
| α-tocopherol, a main vitamer of vitamin E | Vegetables, fruits and nuts | Five-weeks-old female Hos; HR-1 Hairless female mice | 20 IU including diet, 20 weeks | Formation of 8-OHdG, expression of HNE-modified protein, nitro-tyrosine and PCNA ↓ | [67] |

As an important component of lipids, any fatty acid or aliphatic acid is a class of carboxyl acids linked with a long hydrocarbon chain. The majority of fatty acids are unbranched in natural resources such as fishes, crops and dairy products. According to the number of unsaturated double bonds, fatty acids are categorized as saturated fatty acids, monounsaturated fatty acids and PUFAs. Essential PUFAs are only acquired from diet or supplementation rather than endogenous biosynthesis in the body. Two primary categories of PUFAs, the omega-3 and omega-6 PUFAs, are abundant in rapeseed oils and marine fishes[32]. Short or medium-chain fatty acids are absorbed into bloodstream in the form of albumin complexes via intestinal lumen, while long-chain fatty acids tend to be transported in the form of chylomicrons wrapped with apolipoproteins via lymphatic systems[31]. PUFAs and their metabolites regulate various biological processes such as inflammation and immune responses[33]. Omega-3 PUFAs, especially eicosapentaenoic acid (EPA) and its precursor α-linolenic acid, are confirmed to alleviate skin damage after oral intake. In an UVB-irradiated hairless model, dietary supplantation with a mixture of linoleic acid and α-linolenic acid (v/v, 4:1 or 1:1) at a dose of 10 mL/kg per day ameliorates symptoms and progression of atopic dermatitis in DNFB-induced AD mice by modulating levels of PGE2, LTB4 and Th1/Th2/Th17, as well as by downregulating the expression of IFN-γ-related STAT4 signalling[34]. Docosahexaenoic acid is confirmed to inhibit UVB-induced skin aging by inducing adipocyte differentiation, adiponectin production and suppressing the expression of MMP-1 in Hs68 fibroblasts[35]. Another study indicates that in a diet induced AD hairless mice model, daily administration of EPA (600 or 3000 mg/kg) for 15 days significantly ameliorated skin dehydration, TEWL and scratching, through suppressing levels of thymic stromal lymphopoietin and IL-4[36].

Phospholipids represent a class of lipids that consist of a glycerol backbone connecting with two fatty acids and one phosphate-derived functional group. According to the difference of glycerol skeleton, phospholipids are divided into glycerophospholipid and sphingolipid. Hydrophilic phospholipids extracted from milk are mainly composed of sphingomyelin, phosphatidylcholine and phosphatidylethanolamine. In a UVB-irradiated hairless mice model, daily intake of milk phospholipids (100 mg/kg) for eight weeks markedly improves TEWL, skin hydration and erythema. Level of hyaluronic acid (HA) in the skin tissue was increased by regulating the expression of hyaluronic acid synthase and hyaluronidase correlated with HA synthesis and degradation. An ROS regulator named heme oxygenase-1 (HO-1) was controlled to alleviate ROS levels as well via nuclear factor erythroid-2-related factor 2 (Nrf2) pathway. Therefore, milk phospholipids helped recover skin barrier functions damaged by photoaging by reducing ROS levels and remaining HA content in skin[37].

Besides, Ceramides represent one of the major sphingolipids in stratum corneum, playing an important role in skin hydration and epidermal functions. Dietary sphingolipids are confirmed to be hydrolysed and passively transported to blood circulation in the form of chylomicrons via brush border membrane of small intestine[38]. Glucosylceramide is a representative of phytoceramide-enriched wheat extract oil. Daily ingestion of wheat extract oil (60 mg/kg) significantly improves skin hydration, elasticity, wrinkle formation, as well as the level of type I procollagen, collagen, hyaluronic acid, and ceramide. Theses beneficial effects are mechanistically interpreted by suppressing mRNA levels of MMP-1 in CCD-986-sk human dermal fibroblast cells[24].

*2.2 Peptides*

Bioactive peptides with specific short chains of amino acid are generally derived from natural resources via enzymatic fermentation. Initially, ingested peptides are partially digested by pepsin and gastricin in the stomach, and further degraded by elastases in the small intestine. Small peptides and amino acids are generated in the presence of aminopeptidases and dipeptidases on brush border membrane[39]. The following absorption occurs via passive diffusion or active transport after overcoming the mucus barrier in the intestinal lumen. Small peptides are delivered through enterocytes via peptide transporters PepT1, while oligopeptides can diffuse passively through hydrophobic channels of epithelia. Comparing to high-molecular weight peptides, short-chain peptides with low molecular weights are sometimes degraded by intestinal peptidases as well. Two studies found that after ingestion of gelatin-derived or collagen peptides, the major peptide components in serum and plasma were small peptides containing Hyp[40, 41]. These include the tripeptide Gly-Pro-Hyp and the dipeptides Pro-Hyp and Gly-Pro. It can be hypothesized that the extent of peptide degradation depends on their amino acid sequences, and specific small peptides such as dipeptides and tripeptides are absorbed into bloodstream. Oligopeptides are easily metabolized within a few minutes during blood circulation, while Pro-Hyp are considered the most stable and abundant form in the plasma[40]. Ingestion of peptides including whey peptides, elastin peptides, bovine lactoferrin, and especially collagen peptides derived from marine resources can significantly improve wrinkle formation, and attenuate skin dehydration and thickening. Nevertheless, compared with other categories of nutricosmetic ingredients, it generally requires a high dose of over 100 mg/kg per day for ingested peptides to observe obvious effects on skin, which is probably due to the high degradation ratio in the gastrointestinal tract, low intestinal permeability and short half-life periods in plasma.

Collagen is a structural protein of connective tissues in skin, cartilages and bones. Gelatin and collagen peptides are derived from collagen hydrolyzation via aqueous extraction or enzymatic degradation. The most studied peptides with beneficial effects for skin are prepared from fish scale and skin (**Table 1**). In a UVB-irradiated hairless mice model, daily ingestion of collagen peptides (1000 mg/kg) hydrolysed from tilapia scale dramatically improved skin hydration, wrinkle formation and TEWL by enhancing hyaluronic acid production via regulation of hyaluronic acid synthases (HAS-1/-2) and hyaluronidase (HYAL-1/-2)[42]. Another study also indicated that daily intake of low-molecular-weight collagen (Valine-Glycine-Proline-Hydroxyproline-Glycine-Proline-Alanine-Glycine) (200 mg/kg) derived from tilapia gelatine markedly improved UVB-induced wrinkle formation, epidermal thickening and loss of type I procollagen and collagen[43]. Besides, daily supplement of fish-skin collagen peptides (1000 mg/kg) significantly improved wrinkle formation, skin hydration, TEWL and epidermal thickness via MAPK signalling pathways in UVB irradiated mice[44]. More specifically, 800 Da collagen peptides hydrolysed from fish scale collagens, predominantly consisting of dipeptide Gly-Pro and oligopeptides[40]. Daily supplement of this novel short-chain peptides (300 mg/kg) observably alleviated UVB-induced wrinkle formation, epidermal thickening and TEWL, as well as improved skin hydration by regulating MMP-1 production and type I collagen synthesis in hairless mice. Dipeptides Gly-Pro and Pro-Hyp were considered as bioactive peptides due to their dramatic increase in plasma concentration directly after peptide administration[40]. Oral intake of collagen tripeptides hydrolysed from fish or pig skin showed obvious amelioration in wrinkle formation, TEWL and skin thickening via inhibiting activities of collagenases and gelatinase such as MMP-2, -9 and -13[45]. Interestingly, daily administration of L-glutathione (100 mg/kg), a hydrophilic endogenous tripeptide with excellent antioxidative activity, dramatically inhibited tyrosinase activity and melanin content in UVB-treated mice, which contributed to depigmentation[46].

Apart from those derived from marine fishes, collagen peptides with nutricosmetic potentials can be extracted from other natural resources as well (**Table 1**). Daily administration of porcine placenta peptides (25, 50 or 100 mg/kg) significantly improved wrinkle formation, skin hydration, roughness and inflammation in a UVB-induced skin photoaging mice model, which was mechanistically interpreted by upregulated expressions of HAS1, HAS2, LCB1 and GPX-1, as well as downregulated MMPs levels and the activation of p38 MAPK and JNK pathways[47]. Besides, it was found that in a UVB-irradiated hairless mice model, daily intake of a characteristic pentapeptide extracted from oyster hydrolysate (200 mg/kg) was effective in alleviating wrinkle formation, collagen degradation and epidermal thickening, promisingly due to the regulation of MMPs, proinflammatory cytokines, as well as synthesis and degradation of collagen via modulating MAPK/AP-1 and TGF-β/Smad pathways[48]. Daily intake of hydrolysed collagen type II peptides (200 mg/kg) extracted from chicken sternum cartilage notably improved wrinkle formation, TEWL, hyaluronic acid content and elasticity of dorsal skin in UVB-irradiated mice via down-regulating expression of MMP-1 and MMP-2[49]. Additionally, in the presence of alcalase and collagenase, collagen peptides hydrolysed from bovine bone gelatine with an average molecular weight smaller than 1000 Da were abundant in Gly, as well as other amino acids such as Pro and Glu. Daily ingestion of these peptides (400 mg/kg) greatly attenuated skin laxity and collagen fibre loss in a chronically aged mice model, probably due to the enhancement of antioxidative enzyme such as superoxide dismutase (SOD) and catalase (CAT)[50].

In addition to collagen peptides, there are still a few different types of peptides that are capable of refining skin aging as well (**Table 1**). Peptides with an average MW of 356 Da derived from whey proteins are primarily composed of Glu, Leu, Asp, and Lys. Oral administration of whey peptides significantly increased skin elasticity while attenuated wrinkle formation and skin thickness by reducing expression of MMP-2 and pro-MMP-9 in the skin of UVB-irradiated mice[51]. Bovin lactoferrin, an 80-kDa glycoprotein extracted from milk, was conductive to suppress skin dehydration, TEWL and epidermal thickening after daily ingestion with a dose of 1600 mg/kg for seven weeks. It could be explained by inhibiting the expression of proinflammatory cytokine IL-1β via NF-κB signalling pathway[52]. Furthermore, daily ingestion of elastin peptide (5.0 mg/kg) markedly increased skin elasticity, level of hyaluronic acid, Hyp and contents of collagen, especially type III and IV collagen in a UV-induced photoaging mice model[53].

*2.3 Polysaccharides*

Polysaccharides are naturally occurring polymers composed of more than ten monosaccharide units linked by glycosidic bonds, exhibiting a wide range of bioactivities. Aa a representative polysaccharide, hyaluronic acid has received much attention and has been deemed as one of the most popular nutricosmetic ingredients over a few years. Hyaluronic acid (HA) is a glycosaminoglycan polymerized by disaccharide units of D-glucuronic acid and N-acetyl-D-glucosamine with typical molecular weights of over 1 MDa, and is widely distributed in extracellular matrix and connective tissues of skin. Hyaluronic acids applied in cosmetic industry are widely prepared from microbial fermentation and rooster combs. In 2008, it was firstly reported that high-molecular-weight HA labelled with $^{99m}$technetium (Tc) was decomposed by microbiomes in large intestine, and only a small portion of it reached connective tissues via systemic blood circulation in mice[54]. Another study found that $^{99m}$Tc-HA was predominantly distributed in the liver after intravenous administration in mice[55]. In another mice model, it proved that about 90% of ingested $^{14}$C-HA was metabolized in liver as an energy source or utilized by skin tissues after intestinal absorption[56]. Later on, orally ingested HA was confirmed to be absorbed through the portal vein or the lymph in the large intestine and transported to skin tissues in the form of small oligosaccharides such as disaccharides and tetra-saccharides[57]. In short, orally administered HA was most likely to be digested and absorbed to bloodstream in the form of small oligosaccharides, while only a small proportion was transported to skin tissues due to rapid metabolism in liver.

Daily intake of HA (200 mg/kg) with molecular weight less than 10 kDa significantly alleviated epidermal thickening and dehydration on the skin of UVB-irradiated mice via upregulating the expression of HAS-2[58]. In another wrinkle-induced mice model, daily supplement of HA (160 mg/kg) obviously enhanced collagen synthesis in skin tissues by downregulation the expression of MMP-1 and proinflammatory cytokines such as IL-1β and IL-6[59]. Besides, daily administration of an especial high-molecular-weight proteoglycan extracted from salmon nasal cartilages improved UVB-induced skin erythema, TEWL, dehydration and epidermal thickening by the inhibition of excess inflammatory cytokines in skin tissues and plasma[60].

Furthermore, polysaccharides derived from edible plants and herbal medicines exhibited promising antiaging activities via oral administration. It was reported that daily intake of polysaccharide extracted from *Saussurea medusa* Maxim (6 g/kg) for thirty days improved wrinkle formation, epidermal thickness, skin elasticity, redness and pigmentation by upregulating the levels of superoxide dismutase, glutathione peroxidase and hydroxyproline and inhibiting MEK/ERK signalling pathways in photoaging mice[61]. Another study showed that daily intake of polysaccharide derived from peach gum (200 mg/kg) for 30 days significantly alleviated wrinkle formation, epidermal and dermal thickness and keratinization through elevating the levels of SOD and CAT, while inhibiting the levels of MMP-1/3 and ROS[62].

### *2.4 Vitamins*

Vitamins are trace organic substances that people can only uptake from exogenous sources to maintain physiological functions. Vitamin E, existed in the form of tocopherols or tocotrienols, is an essential micronutrient for maintaining human health, owning to its anti-inflammatory and free-radical scavenging abilities. Hydrophobic vitamin E are primarily found in vegetable seeds and oils, and α-tocopherol is the most common vitamer with the highest biological activities in nature[63]. After oral ingestion, vitamin E is initially dissolved and emulsified into lipid droplets, followed by approaching the brush border membrane of the enterocytes in the small intestine. After that, vitamin E is promisingly diffused through enterocyte apical membrane or mediated by cholesterol transporters such as scavenger receptor class B type I, and is secreted to bloodstream or lymphatic system in the form of chylomicrons. As for hydrophilic vitamin C or ascorbic acid, it commonly exists in fruits and vegetables, and is vital for maintaining normal immune functions due to its ROS scavenging activities, as well as regulating iron/copper metabolism and collagen synthesis. Dietary vitamin C tends to be absorbed in the small intestine via specific sodium-dependent processes mediated by the sodium-dependent vitamin C transporter-1 and the sodium-dependent vitamin C transporter-2, respectively[64].

Vitamins are especially beneficial for recovering skin laxity and wrinkle formation by dietary supplementation (**Table 1**). Oral intake of a mixture mainly composed of vitamin C and E (700 mg/kg) per day markedly improved wrinkle formation and type I procollagen by downregulating the expression of MMPs related to AP-1 activation and upregulating transforming growth factor- β2 (TGF-β2) in a UVB-irradiated hairless mice model[65]. Moreover, daily uptake of L-ascorbic acid (100 mg/kg) drastically improved UVB-induced redness, roughness, and reduction in elasticity of hairless mice skin [66]. Besides, oral supplement of α-tocopherol exhibited preventive effects on UVB-induced skin photo-carcinogenesis in hairless mice via decreasing the expression of expressions of the oxidative stress marker (8-OHdG), ROS-induced damage marker (HNE-modified protein) and peroxynitrite marker[67].

**Table 2.** Categories of phytochemicals derived from edible plants and herbs with nutricosmetic potentials for skin antiaging.

*2.5 Phytochemicals*

Botanical extracts containing complex metabolites of phytochemicals with different structures and functionalities have been used in cosmetics and skin care product for a long period. Classification of phytochemicals based on their structures is important for understanding their biological functions. Phenolic compounds with at least one phenolic functional group are the most abundant category of phytochemicals, which can be further separated to flavonoids, phenolic acids and etc. (**Figure 4**). Flavonoids mainly include flavanols, flavones, flavanones, flavanonols, isoflavones, and anthocyanins[68]. Besides, carotenoids are isoprenoid-derived hydrophobic pigments synthesized in plants, and generally exist in the form of free xanthophylls and carotenoid esters.

The absorption of phytochemicals through the gastrointestinal tract is primarily dependent on their chemical properties and forms of ingestion[69]. Compared with hydrophilic phytochemicals, hydrophobic ones favors more efficient absorption via simple diffusion or transporter-mediated active processes in general [21]. After ingestion, carotenoids initially are released from food matrix by mechanical or enzymatic disruption, followed by forming lipid droplets of gastric emulsions. After the solubilization in mixed micelles in the presence of bile salts, biliary phospholipids and dietary lipids, carotenoids are absorbed by the intestinal cells in the form of chylomicrons and secreted to the lymphatic system for circulation[70]. The intestinal absorption of carotenoids is greatly influenced by food matrix and dietary composition. Flavonoids linked with O-glycosides tend to be enzymatically hydrolyzed before absorbed in the gastrointestinal tract[21]. Phenolic acids are primarily transported via small intestinal epithelial cells by paracellular and transcellular passive diffusion, because there are few binding receptors for carrying phenolic acids. Due to the poor aqueous solubility and gastrointestinal stability, absorption rate and bioavailability of phenolic acids is relatively low[71] .

### *2.5.1 Flavonoids*

Hesperidin and narirutin were identified as two primary flavonoids in immature *Citrus unshiu* (**Table 2**). These two flavonoids have been assessed to possess antioxidant, anti-inflammatory activities and protective effect against apoptosis. Daily intake of immature citrus powder (200 mg/kg) improved skin hydration, TEWL and epidermal thickness in UVB-irradiated hairless mice by reducing ROS and MMPs generation[72]. Furthermore, another study found that oral administration of dihydroflavone hesperidin with a dose of 100 mg/kg per day markedly ameliorated UVB-induced wrinkle formation, epidermal thickness and collagen degradation by regulating expression of MMP-9, MEK and ERK via mitogen activated protein kinase (MAPK) pathways in hairless mice plausibly[73].

**Table 2.** Categories of phytochemicals derived from edible plants and herbs with nutricosmetic potentials for skin antiaging.

| Bioactive compounds | Natural resources | Animal models | Doses of oral administration | Biological activities | References |
|---|---|---|---|---|---|
| **Flavonoids** | | | | | |
| Hesperidin (dihydroflavone) |  Immature *Citrus unshiu* | Six-week-old male Hos/HR-1 hairless mice | 100 mg/kg, 5 days/week, 12 weeks | Wrinkle formation, TEWL, epidermal thickness, expression of MMP-9, MEK, ERK, TNF-α and IL-8 ↓ | [73] |
| Proanthocyanins |  Grape seed (*Vitis vinifera L.)* | brownish guinea pigs | 1% of extract in diet, 8 weeks | Levels of skin pigmentation, activity of mushroom tyrosinase, rate of melanogenesis in cultured B16 mouse melanoma cell, and number of DOPA-positive melanocytes, 8-OHdG, Ki-67 and/or PCNA-positive melanin-containing cells ↓ | [74] |
| Genistein and daidzein (isoflavones) |  Soy beans | Six-week-old female albino SKH: HR-1 hairless mice | 150 mg/kg, six times/week, 5 weeks | Wrinkle formation, skin roughness, epidermal thickness, expression of MMP-1 ↓; Level of type I procollagen ↑ | [77] |

| | | | | | |
|---|---|---|---|---|---|
| Anthocyanins |  *Vaccinium uliginosum* | Four-week-old male SKH-1 hairless mice | 122 mg/kg/day, 5 weeks | Wrinkle formation, skin thickness and cytokines, TEWL, expression of MMP-2, MMP-9, p-JNK, p-ERK and p-p38 ↓; level of collagen fibres, expression of TIMP-1, TIMP-2, SOD1, GPx and collagen type I alpha 1 chain (COL1a1) ↑ | [75] |
| Rutin (Flavanol) |  Azuki bean (*Vigna angularis*) | Six-week-old male SKH:HR-1 hairless mice | 1% or 5% of extract in diet, 10 weeks | Wrinkle formation, epidermal thickness, level of TEWL and EI and expression of MMP-1 ↓; Level of SC hydration and expression of TGF-β1, elastin, and procollagen type I ↑ | [76] |
| Tricin (Flavone) |  Rice bran | Six-week-old female SKH-1 hairless mice | 0.3 mg/kg/day, 14 weeks | Erythema, keratinization, wrinkle formation, epidermal thickness, expression of MMP-1, -13 ↓; Skin moisture, level of type I procollagen ↑ | [79] |
| **Carotenoids** | | | | | |
| β-Cryptoxanthin |  Citrus fruits (*Citrus unshiu*) | Four-week-old male HOS: HRM2 hairless mice | 0.1, 1.0, 10 mg/kg/day, 2 weeks | Skin pigmentation, production of melanin, phosphorylation of CREB, expression of tyrosinase, COX-2, CREB, MC1R and Tyrp1 ↓ | [92] |
| Xanthophyll (Lutein/zeaxanthin) |  Corn and green leafy vegetables | Six to eight-week-old SKH-1 hairless mice | 0.4% in diet, 16 weeks | Skin fold thickness, supra-papillary plate thickness, dermal mast cell density and desmosine content ↓ | [94] |
| Fucoxanthin |  Brown algae such as Kombu (*Laminaria japonica*) and Wakame (*Undaria pinnatifida*) | Four-week-old male Guinea-pigs; Four to five-week-old male HOS; HRM2 hairless mice | 0.001% in diet, 2 weeks for pig; 0.1, 1.0, 10 mg/kg/day, 2 weeks for mice | Skin pigmentation, production of melanin, expression of COX-2, p75NTR, EP1 and MC1R ↓; Expression of ET-1 and NT-3R ↑ | [95] |
| **Phenolic acids** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| Caffeic acid |  Rich in yerba-mate (*Ilex paraguariensis* A. St.-Hil., Aquifoliaceae), coffee and berries | Eight-week-old male C57BL/6J mice | 100 mg/kg/day, 8 days | Epidermal thickness, skin dermatitis, skin pigmentation, number of DOPA-positive Melanocytes, level of α-MSH, expression of p-MAPK, p-ERK, p-CREB and MC1R ↓; Level of β-endorphin ↑ | [82] |
| Gallic acid |  Rich in green tea, chestnuts and berries | Six-week-old male SKH:HR-1 hairless mice | 0.1% in diet, 10 weeks | Wrinkle formation, TEWL, Erythema index, expression of MMP-1 and IL-6 ↓; Level of type I procollagen, elastin, type I procollagen, TGF-β1, c-Fos and c-Jun ↑ | [84] |
| Chlorogenic acid and ferulic acid |  *Foeniculum vulgare Mill* seeds | Seven-week-old male albino HR-1 hairless mice | 0.1% or 1% of extract in diet, 10 weeks | Wrinkle formation, epidermal thickness, expression of MMP-1, p-ERK and p-p38 ↓; Production of collagen, expression of procollagen type I, elastin, TGF-*β*1, Nrf2 ↑ | [85] |
| 5-(3',4'-dihydroxyphenyl)-γ-valerolactone |  Cacao beans | Six-week-old female albino SKH-1 hairless mice | 39.1 or 156.3 mg/kg/day, 8 weeks | Wrinkle formation, collagen degradation, expression of MMP-1, cathepsin G and activity of AP ↓ | [87] |
| Hydrangenol |  *Hydrangea serrata* (Thunb.) Ser. (Leaves) | Five-week-old male HR-1 hairless mice | 20, 50 or 100 mg of extract/kg/day, 10 weeks | Wrinkle formation, skin thickness, TEWL, expression of MMP-1/3, TNF-α, IL-1, IL-6, IL-8, AP-1 subunits c-Fos and c-Jun ↓; Level of elastin, procollagen type I, collagen fibres and epidermal water content ↑ | [88] |
| Eugenol |  Clove (*S. aromaticum L.*) | Six-week-old male SKH: HR-1 hairless mice | 0.1% or 1% of extract in diet, 9 weeks | Wrinkle formation, level of roughness and erythema index, expression of MMP-1 and MMP-3, IL-6, p-c-juns, p-c-fos, NFATc1, NF-κB signalling ↓; Level of skin hydration, elastin and filaggrin, expression of procollagen type I mRNA, Nrf2, HO-1, NQO1, p-NFATc1 ↑ | [86] |
| **Others** | | | | | |
| Resveratrol |  Grape peel | Six-week-old male ICR mice, | 2, 10, 50 mg/kg/day, 6 weeks | Wrinkle formation, epidermal thickness, expression of MMP-1, -9, HO-1 and Nrf2 ↓ | [96] |

| | | | | | |
|---|---|---|---|---|---|
| betaine |  Widely distributed in plants such as *Beta vulgaris L.* and *Lycium chinense* | Six-weeks-old male HR-1 hairless mice | 100 mg/kg/day, 12 weeks | Wrinkle formation, epidermal thickness, collagen fibre damage, expression of MMP-9 and phosphorylation of MEK and ERK ↓ | [99] |
| Suberic Acid |  Castor, *Hibiscus syriacus*, and *Vernonia galamensis* | Six-week-old female albino SKH-1 hairless mice | 0.05, 0.1, 0.2% in diet | Wrinkle formation, epidermal thickness, expression of MMP-1, -3, -9, p-p38, p-ERK, p-JNK, p-c-Fos and p-c-Jun ↓; Level of hyaluronic acid, collagen fibre density, expression of TGF-β, p-SMAD 2/3, COL1A1, COL1A2, COL3A1, HAS1, HAS2, and HAS3 ↑ | [98] |
| Penta-1,2,3,4,6-O-Galloyl-β-D-Glucose (PGG) |  *Rhus verniciflua.* | Five–week–old female SKH-1 hairless mice | 4, 20 mg/kg/day, 10 weeks | Wrinkle formation, epidermal thickness, TEWL, degradation of type I collagen and expression of MMP-13 ↓ | [97] |

Grapes are rich in polyphenols and the majority of flavonoids are existed in grape seeds. Proanthocyanidins, as the primary species of grape seed flavonoids, were confirmed to exhibit promising antioxidant and free radical scavenging activities (**Table 2**). Oral administration of grape seed extracts (1g/kg) containing 89.3% proanthocyanidins per day apparently alleviated UV-induced skin pigmentation in guinea pigs. The lightening effect was validated by inhibiting melanogenesis and ROS-induced proliferation of melanocytes and melanin-containing keratinocytes in a B16 mouse melanoma cell model[74].

*Vaccinium uliginosum L.* belongs the genus Vaccinium (family Ericaceae) and was believed to possess excellent antioxidative activities due to high content of anthocyanins (**Table 2**). Daily ingestion of V. uliginosum anthocyanin-enriched ethanolic extract (122 mg/kg) significantly improved skin hydration, TEWL, wrinkle formation, and epidermal thickness in UVB-irradiated hairless mice by suppressing pro-inflammatory cytokines via upregulating expression of antioxidant-related genes, as well as inhibiting the expression of MMPs, ERK and JNK via MAPK signalling pathways[75].

Azuki beans (*Vigna angularis*) are one of the most important crops in China, Korea, and Japan. Rutin, as the representative hydrophilic flavanol in azuki beans, has been studied extensively due to its promising biological activities such as antitumor and antiallergic (**Table 2**). Dietary supplementation of 1% azuki bean extract in diet suppressed wrinkle formation, skin thickness, skin dryness and skin roughening by promoting the expression of elastin, procollagen type I, and TGF-β1 in UVB-irradiated hairless mice. Besides, rutin drastically inhibited MMP-1 production in UVB-irradiated normal human dermal fibroblast (NHDF) cells, indicating its potential in reliving photoaging[76].

Recently, isoflavones have been broadly studied due to their multiple health-promoting activities. Soy isoflavones, such as genistein and daidzein, were supposed to have moderate antioxidant activities (**Table 2**).

A study showed that in a UV-irradiated hairless mice model, daily intake of isoflavone-enriched soy extract (500 mg/kg) improved skin roughness, wrinkle formation, epidermal thickness and type I procollagen content. These antiaging effects was partially due to the regulation of collagen degradation via suppression of MMP-1 expression in human fibroblasts Hs68 cells[77]. Interestingly, a metabolite of the soybean isoflavone daidzein named coumestrol, inhibited wrinkle formation and collagen degradation in a 3D human skin equivalent model, which was due to suppression of MMP-1 expression regulated by AP-1 activity via FLT3 kinase targeted Ras/MEK/ERK and Akt/p70$^{S6K}$ pathways[78].

Tricin (4’,5,7-trihydroxy-3,5’-dimethoxyflavone), a flavone commonly exists in rice bran and sugarcane, was reported to possess anti-inflammatory, antioxidative and antiallergic activities (**Table 2**). In a UVB-induced photoaging hairless mice model, daily supplementation of tricin (0.3 mg/kg) for 14 weeks considerably attenuated skin erythema, hydration, wrinkle formation and epidermal thickness. In both UVB-irradiated mice skin tissues and HDF cells, inhibition of collagen degradation-related enzymes such as MMP-1 and MMP-3 by regulating the phosphorylation of MAPKs via NF-κB/AP-1 signalling pathways provided plausible mechanistical interpretation for these observations[79].

*2.5.2 Phenolic acids*

Phenolic acids, as aromatic secondary metabolites widely distributed in plants, are generally defined as polyphenols with one carboxylic acid functional group. Hydroxybenzoic, hydroxycinnamic and hydroxyphenyl acetic acids are classified as major subclasses of phenolic acids according to their structures and number of phenol groups[80].

Caffeic acid is a dihydroxycinnamic acid with two phenol groups abundant in some herbs such as yerba mate and thyme, and was identified as the main phenolic component in coffee[81]. Daily intake of caffeic acid (100 mg/kg) effectively alleviated skin inflammation and pigmentation via suppression of MAPK and cAMP microphthalmia-associated transcription factor pathways in UVB-irradiated mice[82].

Gallic acid is a hydroxybenzoic acid with three phenol groups naturally distributed in edible plants such as green tea, possessing biological activities such as anti-oxidative and anti-inflammatory effects[83]. Daily intake of gallic acid (0.1% in diet) significantly suppressed wrinkle formation and skin dryness via upregulating the level of type I procollagen and elastin via TGF-β1 pathway and downregulating the expression of MMP-1 and IL-6[84].

*Foeniculum vulgare Mill.* seed extract mainly contained two dihydroxycinnamic acid derivatives named chlorogenic acid (44.1%) and ferulic acid (36.1%), respectively (**Table 2**). A diet containing 0.1% phenolic acid-enriched extract significantly increased the production of collagen, elastin and TGF- β1 levels, while blocked matrix metalloproteinases production via MAPK and Nrf2 pathways, contributing to attenuate wrinkle formation and collagen loss in UVB-irradiated hairless mice[85].

Eugenol is a major phenolic compound (72%–90%) in the essential oil of *S. aromaticum L.* (**Table 2**). Dietary clove extract was found to recover wrinkle formation and skin dryness in UVB-irradiated hairless mice. Eugenol increased collagen synthesis by stimulating the TGF-β/Smad signalling pathways and reduced collagen breakdown by diminishing MMP-1 and MMP-3 activity through the MAPK/AP-1 signalling pathways.[86]

Cacao beans with excellent antioxidative activities was proved to be beneficial for regulating skin structure and microcirculation, as well as protecting skin against UVB-induced oxidative damage[87]. Long-term intake of flavanol-enriched cacao was previously confirmed to improve skin hydration and density. In a UVB-induced photoaging mice model, daily supplementation of cacao powder (39.1 mg/kg) attenuated UVB-induced wrinkle formation and collagen degradation by the regulating expression of genes involved in dermal matrix production and maintenance[87]. 5-(3’, 4’-dihydroxyphenyl)-γ-valerolactone, identified as a major bioactive metabolite of epicatechin and procyanidins in plasma after digestion, potentially inhibited wrinkle formation by suppressing MMP-1 expression and AP-1 activity via MAPK pathway[87].

Hydrangea (*Hydrangeaceae*) leaves with bioactivities including anti-inflammatory have been consumed as a tea in East Asian countries for a long time (**Table 2**). Daily administration of Hydrangea extract (25mg/kg) markedly reduced wrinkle formation, epidermal thickening, dehydration and collagen loss in dorsal skin tissues of UVB-irradiated mice by suppressing AP-1 activation via MAPK pathways[88]. Hydrangenol, as a distinctive phenolic acid in Hydrangea leaves, enhanced the production of type I procollagen and HA by inhibiting expression of MMP-1/-3 and HYAL-1/-2 in UVB-irradiated Hs68 fibroblasts, as well as inhibited the activation of AP-1 by suppressing phosphorylation of p38 and ERK[89].

*2.5.3 Carotenoids*

Carotenoids are tetraterpenoid natural pigments present in fruits, vegetable and algae, as well as some bacteria, that potentially have photoprotective activities via topical treatments. β-cryptoxanthin is a typical carotenoid that possesses various biological benefits including antioxidative and anticarcinogenic, and is widely distributed in citrus fruits[90]. It was reported that ingested β-cryptoxanthin was able to enter blood circulation via gastrointestinal tract and influence serum cholesterol and apolipoproteins, as well as to be dispersed in different organs[91]. Daily intake of β-cryptoxanthin (10 mg/kg) dramatically ameliorated skin pigmentation via in UVB-irradiated hairless mice. It was interpreted by inhibition of melanogenesis induced by melanogenic stimulators including prostaglandin E2, endothelin-1 and melanocyte-stimulating hormone, as well as expression of melanogenic molecules such as Cyclooxygenase-2 and endothelin-1 receptors in human melanocytes[92].

Lutein and zeaxanthin are two isomeric xanthophyll carotenoids that selectively accumulate in eye tissues and protect against age-related macular degeneration and skin photodamage as antioxidants[93]. In the nature, they commonly existed in plants including corns and green leafy vegetables (**Table 2**). Dietary supplementation of lutein and zeaxanthin (0.4% in diet) markedly improved epidermal thickness, desmosine content and reduced photo-carcinogenesis in UVB-irradiated mice [94].

Fucoxanthin is a carotenoid derived from edible brown algae such as *Laminaria japonica* and *Wakame Undaria* pinnatifida (**Table 2**). Biological activities of fucoxanthin including anti-cancer and anti-allergic have been studied in previous papers[95]. Oral administration of fucoxanthin with 10 mg/kg per day significantly alleviated UVB-induced skin pigmentation by suppressing melanogenesis via inhibition of prostaglandin synthesis and expression of melanogenic receptors in melanocytes of hairless mouse skin[95].

*2.5.4 Others*

Resveratrol is a phytoalexin polyphenol abundant in grape peel, possessing biological activities such as chemo-preventive effect (**Table 2**). Daily supplementation of resveratrol (2000 mg/kg) drastically alleviated wrinkle formation and epidermal thickening on UVB-irradiated mouse skin by downregulating the expression of MMP-1 and MMP-9 plausibly via activation of nuclear factor-like 2 (Nrf2) signalling pathway[96].

Penta-1,2,3,4,6-O-galloyl-β-D-glucose (PGG) is a a gallotannin polyphenol naturally consisting in fermented *Rhus verniciflua* with several biological activities including chemo-preventive effect[97]. Daily uptake of PGG (4 mg/kg) improved wrinkle formation, epidermal thickening and type I collagen in dorsal skin of UVB-irradiated mice by suppressing the expression of p21-activated kinase (PAK1) and c-Jun N-terminal kinases (JNKs) via MAPK pathway[97].

Suberic acid is a crystalline dibasic acid that is widely distributed in *Hibiscus syriacus*, and *Vernonia galamensis*[98]. In a UVB-exposed hairless mice model, Daily uptake of suberic acid (0.2 % in diet) significantly improved wrinkle formation, moisturization and epidermal thickness of skin tissues by regulating MAPK and TGF-β signalling pathways[98].

Betaine, a naturally occurred trimethyl derivative of the amino acid glycine, is abundant in plants and herbs such as *Lycium chinense* (**Table 2**). It was found that oral administration of betaine (100 mg/kg) per day significantly inhibited wrinkle formation, collagen loss and skin thickening in UVB-treated hairless mice by reducing the expression of MMP-9 via suppression of MEK and ERK in MAPK signalling pathways[99].

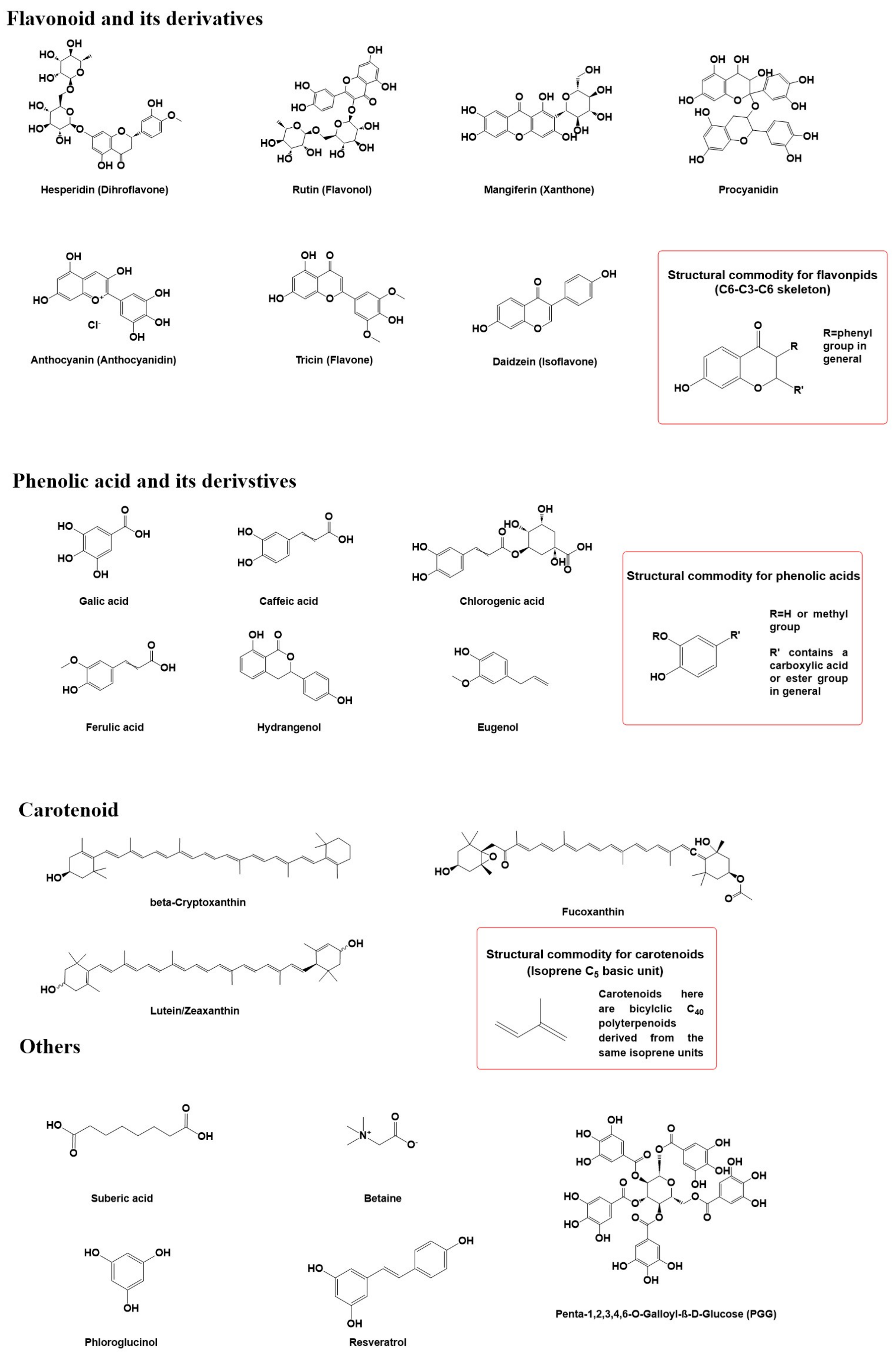


**Figure 4.** Chemical structures of phytochemicals derived from natural plants with nutricosmetic potentials and their structural commonalities.

## 3. Clinical studies

Bioactivities of nutricosmetic ingredients are well confirmed via typical cell and animal models, but their application values are required to be further confirmed by clinical trials. The current clinical studies based on nutricosmetics have not received sufficient attention. Published clinical studies conducted to evaluate the improvement of skin conditions are primarily focused on collagen peptides, hyaluronic acids, ceramides, phytochemicals and their related commercialized products.

In the case of collagen peptides, several recent randomized, double-blind, placebo-controlled clinical trials have confirmed their efficacy against skin aging. In a trial with 100 female participants aged 30–60 years, daily supplementation with 1,650 mg of collagen peptide containing dipeptides Gly-Pro and Pro-Hyp for 12 weeks significantly improved wrinkles, desquamation, elasticity, and hydration compared with placebo[100]. Besides, a clinical study with 64 female participants aged 40-60 years was conducted to confirm that oral supplement of low-molecular-weight collagen peptide derived from sutchi catfish's skin (*Pangasius hypophthalmus*) with 3% of Gly-Pro-Hyp tripeptide (1 g/day) for 12 weeks efficiently improved skin hydration, wrinkling and elasticity.[101] In another randomized double-blind placebo-controlled clinical study, ingestion of collagen hydrolysates with a high content of dipeptides Pro-Hyp and Hyp-Gly originated from fish gelatin (5g/day) for 8 weeks improved skin moisture, roughness, elasticity and wrinkle formation on facial skin of 85 female Chinese aged 35-55 years[102]. Furthermore, in an 80-participant trial, intake of low-molecular-weight collagen peptides (2.5 g/day) for 6 weeks led to a marked reduction in facial wrinkles and a significant increase in hydration[103]. Consistent findings were reported in another 8-week trial with 66 female participants aged 35–55 years, where ingestion of bovine-derived collagen peptides (2.5 g/day) significantly reduced periorbital wrinkle volume and improved skin elasticity and moisture[104]. Collagen peptides or hydrolysates are generally derived from fish scale, fish skin and chicken sternal cartilage for commercial purpose. Previous studies indicated that orally-administered collagen peptides or gelatin hydrolysates were absorbed into plasma in the form of dipeptides such as Pro-Hyp and Gly-Pro[40]. In combination with clinical evidences, oral supplementation of collagen peptides, especially those with low molecular weights such as dipeptides and tripeptides, is capable of improving skin conditions as a potential nutricosmetic.

Hyaluronic acid (HA) is a polysaccharide found in the extracellular matrix. Nearly half of body HA was present in the corium layer of skin tissues, playing an important role in regulating skin hydration and elasticity[105]. Recent clinical trials highlight its role in reinforcing hydration and barrier function. In a randomized double-blind study with 129 female participants, oral HA (300 kDa) supplementation for 2–8 weeks significantly enhanced stratum corneum hydration across different age groups and skin types[106]. Likewise, a 12-week clinical trial in 60 female participants aged 35–65 years found that daily intake of 60 mg of a hyaluronic acid matrix improved hydration, smoothness, and several biophysical skin-aging parameters[107]. In another randomized, double-blind, controlled study, 61 female volunteers orally administered capsules containing 120 mg of HA with mean molecular weights of 300 kDa or 800 kDa per day.

Skin moisture, wrinkling, brightness and softness are improved after intake of both HA for 6 weeks[108]. Moreover, a separate 12-week intervention with 120 mg/day of HA in adults aged 35–64 years reduced wrinkle depth, improved hydration and elasticity, and decreased transepidermal water loss compared with placebo[109]. Comparing the above clinical studies, it is obvious that oral intake of hyaluronic acids with molecular weight ranged from 2 kDa to 1 MDa always possess the bioactivity to ameliorate skin conditions with negligible differences. A previous study confirmed that about 90% of HA intake was absorbed in gastrointestinal tract and a small portion of HA with unclear molecular weights did reach the skin, but the bioavailability of HA was low as it was mainly metabolized to carbon dioxide by the liver. Combining clinical and experimental evidences, it can be hypothesized that hyaluronic acids with various molecular weights would be ultimately digested and degraded to HA with low molecular weights, which were further absorbed and transported to skin via blood circulation or lymphatic system. As a consequence, the efficacy of HA with molecular weights over a wide range remained consistent.

Recent clinical trials also underscore clinically meaningful barrier and photoaging benefits with oral ceramides. A 12-week, randomized, double-blind, placebo-controlled study of milk ceramides (600 mg/day) in female participants aged 30–65 years with crow's-feet reported significant improvements in periocular wrinkle/roughness indices, lower TEWL, and higher hydration and elasticity, with no serious adverse events[110]. Complementing these findings, a 12-week randomized trial of wine lees–derived ceramides and glucosylceramides in healthy adults significantly reduced TEWL and was well tolerated, supporting barrier reinforcement from sustainable plant sources[111]. In addition, a 4-week randomized, double-blind, placebo-controlled trial reported that oral intake of a rice-derived glucosylceramide (0.6 mg/day) improved TEWL and stratum corneum water content, further substantiating dose-efficient phytoceramide activity in human[112].

Phytochemicals refer to a large group of non-nutritious secondary metabolites with low molecular masses derived from fruits, vegetables, grains and etc. A 12-week, randomized, double-blind, placebo-controlled trial of fermented bilberry extract (100 mg/day) in female participants with visible "crow's feet" wrinkles, mild-to-moderate slackness, and uneven tone showed significant reductions in wrinkle depth, improvements in elasticity, firmness, brightness and antioxidant efficacy versus placebo[113]. Similarly, an oral four-botanical blend (pomegranate, sweet orange, *Cistanche*, *Centella asiatica*; 225 mg/day) produced early (4-week) and sustained (12-week) improvements across hydration, TEWL, elasticity, firmness, roughness, thickness, and dark spot pigmentation, with good tolerability[114]. Furthermore, in a randomized, double-blind, placebo-controlled clinical trial with 99 healthy females, wrinkle formation at the edge of eyes, skin elasticity and thickness, as well as the stratum corneum water content in the check and forearms were significantly improved in a dose-dependent manner after daily ingestion of a drink containing 25 mg of lingonberry extract and 30 mg of amla fruit extract for 12 weeks[115]. In another randomized, placebo-controlled study conducted on 44 healthy candidates aged 20-60-year-old, oral consumption of Lycii Fructus extracts (900 mg/day) with a high content of polyphenols for 8 weeks obviously inhibited erythema formation and promoted erythema dissipation due to its antioxidative activity[116].

## 4. Commercialized nutricosmetic ingredients and products

Nutricosmetic industry is booming in Europe and Asia due to the non-negligible increase in personal demand for skin beauty. Nutricosmetic commodities are developed in the form of tablets, pills, powders and liquids in general. The major bioactive compounds claimed as nutricosmetic ingredients in products are collagen peptides, hyaluronic acids, and phytochemicals. Selected novel ingredients and commercial products attract the most attention in nutricosmetic market and the nutricosmetic potentials of most of them are well confirmed by clinical trials as shown in **Table 3**.

**Table 3.** Summary of prevalent nutricosmetic ingredients and products in the current market.

| Ingredients/products | Manufacturers | Active components | Functions | References |
|---|---|---|---|---|
| VERISOL® Collagen powder | GELITA AG, Germany | Specific collagen peptides with MW of 2.0 KDA | Improve skin elasticity, hydration, roughness and wrinkle formation | [117] |
| POLA® White Shot Lotion LX | POLA ORBIS HOLDINGS, Japan | Dexpanthenol | Skin whitening ability of whole body | [118] |
| Yep® Sodium Hyaluronate Fruit Drink | By-health, China | Sodium Hyaluronate | Improve skin hydration | [120] |
| Swisse® Beauty Grape Seed Tablets | H&H group, China | procyanidins-rich grape seed extracts | Supports collagen formation and skin health | [121] |
| Nutroxsun® | Monteloeder, America | Polyphenol-rich extract from Mediterranean grapefruit and rosemary | Improve sun protection and skin beauty | [122] |
| DracoBelle™ Nu | Mibelle group, Switzerland | water-soluble extract from Moldavian dragonhead (*Dracocephalum moldavica L.)* | Improve skin hydration, elasticity and collagen repair | [123] |
| CERAMOSIDES™ | SEPPIC, France | Phytoceramides | Improve skin hydration, elasticity and wrinkle formation | [125] |

GELITA AG is a worldwide market leader in the field of collagen peptides and gelatin founded in Germany. A representative product Verisol® with specific collagen peptides of an average molecular weight of 2.0 kDa was extracted from either porcine, bovine or marine origins. Oral supplementation of Verisol® in a dose of 2.5 g/day for 8 weeks was validated to effectively improve skin elasticity, hydration, roughness and wrinkle formation by two clinical trials[117]. In Japan, POLA® white shot liquid containing active component dexpanthenol claims to possess the skin whitening ability for the whole body[118]. INRYU®, an inner beauty premium brand from Shiseido®, launched a combo of 3 SKUs containing Siberian Ginseng extract with the function of stabilizing leaks of blood capillary based on their Nutri-Vessel Network Technology™. Besides, BENEFIQUE®, another high-end brand from Shiseido®, launched 4 SKUs of supplements containing Black Ginger extract with the function of strengthening the intestinal barrier function[119]. Overseas brands have dominated the domestic nutricosmetic market in China for a long period. In recent years, domestic enterprises such as By-health and Swisse are developing rapidly in China. For example, Yep® Sodium Hyaluronate Fruit Drink developed by By-health containing sodium hyaluronate with molecular weight smaller than 600 kDa as a major functional ingredient claims to improve skin hydration confirmed by clinical trials [120]. Swisse® Beauty Grape Seed Tablets containing procyanidins-rich grape seed extracts and vitamin C claims to supports collagen formation and skin health due to its strong antioxidant activity[121].

Apart from the most popular nutricosmetic ingredients such as collagen peptides and hyaluronic acid in the market, novel nutricosmetic ingredients, especially those extracted from natural plants with promising bioactivities, are emerged along with the state-of-the-art delivering strategies. Monteloeder is an American enterprise in providing innovative ingredients with proven benefits and efficacy for skin beauty. Nutroxsun® developed by Monteloeder is a natural ingredient combination of grapefruit and Mediterranean rosemary extracts rich in polyphenols. A recommended daily intake of 100 mg of Nutroxsun® was confirmed to prevent skin photoaging and photodamage by clinical trials[122]. Mibelle Biochemistry was founded in 1991 to discover naturally-derived compounds for nutraceutical industry. DracoBelle™ Nu is a representative water-soluble powder extracted from the aerial parts of Moldavian dragonhead (*Dracocephalum moldavica L.*). Dietary supplement of flavonoid-glucuronides-rich DracoBelle™ Nu was clinically confirmed to enhance skin hydration, elasticity and collagen repair via AMPK/ FOXO pathways[123]. Curcumin is a polyphenol isolated from the rhizome of turmeric (*Curcuma longa*) with a wide range of pharmacological activities such as antioxidant, anti-inflammatory and antiaging effects. However, low bioavailability of hydrophobic curcumin is an inevitable challenge. HydroCurc® is a branded curcumin ingredient developed by Pharmako Biotechnologies in Australia. It applies a patented delivery system named LipiSperse® with a cold-water dispersion technology to enhance bioavailability after oral ingestion [124]. Besides, an oral phytoceramides CERAMOSIDES™ extracted from natural origin was developed by Seppic, a French healthcare company established in 1986. In a randomized double-blind placebo-controlled clinical study with 80 candidates, intake of CERAMOSIDES™ powder at a low dose of 30 mg/day remarkably improved skin hydration, elasticity and wrinkle formation after two months[125].

## 5. Conclusion and future perspective

In this review, we summarized food-derived nutricosmetic compounds from natural resources, classifying them into collagen peptides, hyaluronic acids, lipids, vitamins and phytochemicals based on their chemical structures. Meanwhile, we clarified their primary bioactivities for skin beauty as well as relevant mechanisms related to skin aging and depigmentation via oral administration in *in vitro* and *in vivo* models. Furthermore, we illustrated the most popular nutricosmetic ingredients and products in the current market, of which the skin-targeting benefits were clinically confirmed. Generally, they were exploited in the form of tablets, pills, powders and liquids, which mainly consisted of collagen peptides, hyaluronic acids, and novel phytochemicals. Although sufficient studies have been done on effectiveness, oral bioavailability and skin-targeting ability for collagen peptides and hyaluronic acid, a range of other natural compounds with promising bioactivities were lack of scientific and long-term clinical evidences for their effectiveness, toxicity and oral bioavailability.

The nutricosmetic market continues to be popular, but the rapid development also faces a series of challenges including strict legal and regulatory requirements, uncertainty of efficacy and homogenization of products. The National Standard for Food Safety Prepackaged Food Labeling General Rules (GB 7718-2011) and the Advertising Law stipulate that those products that have not been certified as “health food” cannot directly claim the functions of the product in labeling and advertising. Nutricosmetics belonging to health food list have strict requirements for functional claims, and only improvement of acne, chloasma and skin moisture was allowed to be claimed for nutricosmetics, which cannot satisfy demand for customers anymore. In addition, the whole development cycle for a nutricosmetic compound requires tedious process research and animal experiments with a general development period of 2 to 4 years, which cannot satisfy the fast-growing market. Therefore, it is a great challenge for enterprises to develop nutricosmetic products efficiently and legally. Most of the nutricosmetic products in the market are developed from natural food resources and are lack of sufficient evidences for their effectiveness. In addition, the essence of functional food is a long-term nutritional supplementation, it is impossible to observe apparent improvement in a short time as medicines, which leads to considerable uncertainty of effectiveness as well. Meanwhile, lipophilic and lipophobic nutricosmetics are absorbed by gastrointestinal tract with different mechanisms influenced by food matrix, which greatly affects their bioavailability. Hyaluronic acid and collagen peptides have been confirmed to reach skin tissues after oral ingestion, and their skin-targeting abilities have been well verified in clinical trials. A range of phytochemicals and botanical extracts with promising nutricosmetic potentials have been widely studied in recent years, but the effectiveness is still controversial due to the lack of long-term clinical studies. Most of nutricosmetics has been confirmed to be eventually absorbed or metabolized into blood circulation after digestion, whereas the study on the skin-targeting mechanisms received limited attention. Besides, an increasing amount of liver injury cases induced by herbal and dietary supplements has been reported. In a randomized, placebo-controlled, double-blinded phase II clinical study with 1021 candidates, level of alanine aminotransferase and aspartate aminotransferase increased after daily intake of green tea extract for 12 months, which implicated the adverse injury effect of high-dose green tea extract on liver enzyme elevations[126]. These current situations result in barriers to customer trusts and acceptances. Consequently, further clinical studies are required to confirm the safety and efficiency of intaking nutricosmetics for improving skin conditions after a long-term supplement. It is also necessary to develop specific delivering systems with suitable skin-targeting carriers to enhance bioavailability of different types of nutricosmetics in the future. Looking forward, anti-glycation represents a particularly important frontier. Advanced glycation end products accelerate collagen crosslinking and oxidative injury, thereby intensifying skin aging. Future studies should prioritize elucidating related signalling pathways, establishing standardized biomarkers for clinical trials, and identifying natural bioactives with anti-glycation potential. Equally critical are translational approaches that improve bioavailability, explore synergistic formulations, and validate long-term efficacy and safety in human populations. By advancing these directions, novel nutricosmetic ingredients can evolve into an evidence-driven, mechanism-based strategy for mitigating skin aging and shaping the next generation of functional food products.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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