Dermatology Practical & Conceptual

Functional Foods in Dermatology

Emily Strouphauer[1], Milbrey Parke[2], Ariadna Perez-Sanchez[3], Evelyne Tantry[4], Rajani Katta[5]

1 Medical Student, Baylor College of Medicine, Houston, TX, USA
2 Department of Internal Medicine Resident, Tulane University School of Medicine, New Orleans, LA, USA
3 Department of Internal Medicine, University of Texas Health San Antonio, San Antonio, TX, USA
4 Graduate, Rice University, Houston, TX, USA
5 Clinical Professor of Dermatology, McGovern Medical School at UTHealth Houston, Houston, TX, USA

Key words: functional foods, diet, dermatology, photoprotection

Citation: Strouphauer ER, Parke MA, Perez-Sanchez A, Tantry E, Katta R. Functional Foods in Dermatology. *Dermatol Pract Concept.* 2023;13(4):e2023256. DOI: https://doi.org/10.5826/dpc.1304a256

Accepted: June 23, 2023; **Published:** October 2023

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

Corresponding Author: Rajani Katta, MD, 6750 West Loop South Suite 695, Bellaire, TX, 77401 Phone: 281-501-3150
Fax: 832-810-0072 Email: info@kattamd.com

ABSTRACT Functional foods, defined as whole foods that provide health benefits beyond their nutritional value, may provide multiple dermatologic benefits. Research studies have documented multiple benefits, including enhanced skin barrier function, improved wound healing, radiance, photoprotection, and hormonal regulation. Although the majority of research to date has involved small-scale human interventions or animal models, promising findings have been noted. A number of potential molecular mechanisms have been described, such as the ability of some foods to combat oxidative stress and thus reduce visible and histologic skin changes in response to UV radiation. Additional mechanisms have been described for wound healing, photo-carcinogenesis, and other outcomes. In this review, we discuss the potential dermatologic role of functional foods in order to advocate for larger-scale, evidence-based, human studies to expand this promising field.

Introduction

A growing body of research has explored the benefits of specific dietary approaches to improving skin health [1,2]. One approach centers on a diet rich in functional foods, which can be defined as foods that provide health benefits beyond their nutritional value [3]. These differ from dietary supplements in that functional foods are whole foods consumed as part of the usual diet, while dietary supplements are manufactured, individual biological compounds taken in addition to the diet [4]. There has been some overlap in terminology with the term "nutraceutical," though nutraceutical has traditionally been used to describe supplements [4,5].

A variety of different foods have been shown to serve as functional foods, including herbs, fruits, vegetables, and plant oils, among others. Many different studies, including human trials, population studies, and animal and laboratory studies have elucidated the benefits of specific foods for skin health. While the term "functional foods" has been used in different contexts to describe supplements and foods, here it is being used solely to describe foods.

The main advantage of functional foods over the traditional topical application of dermatologic products is their oral ingestion, which facilitates metabolism into active forms and absorption from the intestines to the bloodstream. This allows deposition of metabolically active compounds into multiple areas of the skin, including the subcutaneous tissue, dermis, epidermis, and sebum.[6] Another benefit is that functional foods may provide additive benefits to topical products, as with photoprotection [7].

Due to these factors, there has been an increasing interest in the role of functional foods in skin health. Research into specific foods has demonstrated antioxidant and signal modulation properties as well as effects on barrier function. These properties allow functional foods to impact the skin barrier, wound repair, radiance, photoaging, photoprotection, and photocarcinogenesis, among other effects.

Skin Barrier Function

Several human studies have documented the role of functional foods in improving the skin barrier. The skin barrier, composed of the stratum corneum, microbiome, immune system components, and chemical components, is the body defense against external insults and water loss [8,9]. Skin barrier function is commonly measured through transepidermal water loss (TEWL) and stratum corneum hydration. TEWL is considered a good indicator of skin barrier integrity, with higher values indicating impairments in barrier function [10].

Human Studies

Healthy oils with various lipid profiles, particularly flaxseed, hempseed, and argan oil, have resulted in TEWL improvements in several small-scale human studies. Consumption of flaxseed oil, rich in alpha-linolenic acid (ALA), resulted in significant improvements in TEWL and decreased skin sensitivity in response to nicotinate irritation in 2 separate studies. In one, healthy participants were randomly assigned to consume placebo- or flaxseed oil-filled capsules daily [11]. After 12 weeks of treatment, TEWL was decreased by about 25% within the flaxseed oil cohort (with no improvement in the placebo cohort), along with significantly decreased inflammatory skin response. A later study echoed these results, with significantly decreased TEWL and skin sensitivity, along with improvements in skin roughness and scaling, in those consuming flaxseed oil [12]. Another study compared the consumption of argan and olive oils in a group of 60 postmenopausal women and reported that argan oil, but not olive oil, significantly decreased TEWL and increased epidermal water content [13].

Dietary hempseed oil, which contains omega-6 and omega-3 fatty acids in a ratio of 2:1, has been studied in patients with atopic dermatitis (AD). One crossover RCT, using a 4-week washout period, compared outcomes in 16 individuals with AD who consumed either 2 tablespoons of hempseed oil daily or a control (olive oil) [14]. Despite no pronounced reduction in TEWL, participants consuming hempseed oil reported significant decreases in skin dryness and itchiness along with decreased usage of topical medications as compared to controls.

Fermented dairy products are another promising area of research. These are rich in probiotics, prebiotics, and bioactive compounds that interact with the gut microbiota to reduce oxidative stress and enhance epidermal differentiation [15-17]. Two separate studies observed skin barrier changes among healthy Japanese volunteers after 4 weeks of daily consumption of fermented milk containing Bifidobacterium breve strain Yakult (BbrY) and galactooligosaccharides (GOS) [17,18]. Both studies reported significant increases in keratinocyte differentiation compared to control cohorts, as well as improved skin hydration. There was also evidence of wrinkle reduction and improved skin clarity compared to controls, determined using a visual analog scale [17]. Additional small-scale human studies have found similar improvements in TEWL after consumption of milk fermented with Lactococcus lactis strain H61, conventional yogurt, and yogurt fermented with LB81 lactic acid bacteria [16,19].

Several other functional foods have been linked to enhanced skin barrier function, though research is limited. In a study of 33 healthy participants, the TEWL effects of oral turmeric, a turmeric-containing supplement, and a placebo were compared. The turmeric group showed a trend toward decreasing TEWL among participants with higher sebum concentrations, while the supplement group showed a statistically significant decrease in TEWL. Foods that contain polyphenols are another area of interest, such as green tea, coffee, and cocoa beans [20-23]. Extracted food polyphenols have shown promise in improving dry skin via impacts on skin barrier water homeostasis, but whole food studies are lacking. Table 1 summarizes human studies of selected functional foods and their associated dermatologic benefits.

Wound Healing

Wound healing occurs in a series of stages orchestrated by signaling molecules and chemical mediators. Damaged tissue leads to inflammatory changes involving catecholamines, reactive oxygen species (ROS), nitric oxide (NO), and tumor necrosis factor (TNF)-alpha, followed by fibroblast

Table 1. Human Studies of Functional foods in Dermatology (selected examples).

Function	Associated foods with evidence from human studies
Skin barrier function	Flaxseed oil: improvements in TEWL [12,61] Argan oil: Improvements in TEWL [13] Hempseed oil: decreases in skin dryness and itching in those with atopic dermatitis [14] Fermented dairy products: improved skin hydration [17,18] Fermented dairy products: improvements in TEWL [16,19]
Wound healing	Olive oil: decrease in duration of wound healing and hospitalization [25]
Radiance	Increased fruit and vegetable consumption over six weeks: documented increases in skin redness and yellowness and perceptions of increased health and attractiveness [32]
Anti-photoaging	Almonds consumed daily for four months: decreased wrinkle severity and width [33] Avocado, daily consumption for eight weeks: increases in forehead skin firmness and elasticity [34] A diet reported to be higher intake of monounsaturated fatty acids from olive oil: lower risk of severe photoaging [36] Reported consumption of higher intake of total dietary polyphenols from all sources: decreases in pigmented spots scores [35]
Photoprotection	Tomato paste: improvement in MED [42,43] High flavanol cocoa powder or chocolate: Improvements in MED [23,44,45]
Reduction of DNA damage	Cruciferous vegetables (broccoli, Brussels sprouts, watercress): potential benefit in reducing DNA damage [49-51] Tomato purée: protected DNA against oxidative damage [52] Kiwi fruit: increased efficiency of base excision repair activity [53] Tart cherry juice: increase in DNA repair activity [54]
Hormonal regulation	Spearmint tea derived from the plant *Mentha spicata*: decreased free and total testosterone levels [56] Green tea for 12 weeks in women with PCOS: decrease in free testosterone levels [59]

MED = minimal erythema dose; PCOS = polycystic ovarian syndrome; TWEL = transepidermal water loss.

proliferation, angiogenesis, and re-epithelialization [24]. Several rodent and human studies have investigated the role of olive oil and certain mushroom species in modulating the wound healing process.

Human Studies

The effects of olive oil ingestion were investigated in 100 hospitalized patients who had experienced second degree or higher burn wounds over 10-20% of their total body surface area [25]. Admitted patients were prepared salads with either olive oil or sunflower oil (control) dressing. Results showed a significant decrease in the duration of wound healing (7.2 days versus 8.7 days) and duration of hospitalization (7.4 days versus 8.9 days) in the olive oil group as compared to the control group.

Animal Studies

Rodent studies shed some light on potential mechanisms of action. In one mouse study, dietary supplementation with olive oil improved cutaneous wound healing in a stressful environment [26]. An excisional lesion was created, followed by 14 days of olive oil consumption in a stress-induced environment. This intervention significantly accelerated wound contraction and improved collagen deposition and angiogenesis, likely due to a decrease in ROS damage and catecholamine synthesis. A similar mouse study echoed these results, reporting that olive oil administration accelerated NO synthesis, reduced oxidative damage, and decreased expression of TNF-alpha, thereby improving the wound healing process in pressure ulcers [27].

Mushrooms have also exhibited wound-healing properties in diabetic rats. Administration of the mushroom Sparassis crispa for four weeks significantly accelerated wound closure by increasing macrophage and fibroblast migration, type I collagen deposition, and re-epithelialization in diabetic rats as compared to a control cohort [28]. Similarly, consumption of the polysaccharide of another mushroom, Ganoderma lucidum, (Gl-PS, 250 mg/kg) significantly accelerated wound closure by as much as 2 days in diabetic mice as compared to control mice.

Finally, while a number of traditional herbs have been shown to promote wound healing, and thus warrant further investigation into benefits and mechanisms of action, a full review of these is outside the scope of this review.

Radiance

Human Studies

Functional foods rich in phytochemicals, specifically carotenoids, promote the appearance of health and skin radiance by influencing skin coloration, luminance, and vascularization. Carotenoids cannot be synthesized de novo in the body and are primarily obtained through the consumption of fruits and vegetables [29]. The correlation between high dietary intake of fruits and vegetables and increased yellow and red facial pigmentation is well documented in the literature [29-31]. Carotenoids are thought to generate these observable changes due to their deposition in every skin layer, particularly the epidermis [31].

Individuals with greater yellow and red skin coloration are often perceived as being healthier, as presented in one study exploring cross-cultural consistency in preferences for skin yellowness [29]. In another study, increased fruit and vegetable consumption over 6 weeks resulted in perceptions of increased health and attractiveness, likely due to documented increases in skin redness and yellowness [32].

Anti-Photoaging

Human Studies

Although limited, a few human studies have investigated the role of functional foods in modifying photoaging. In one small randomized control trial (RCT) of 28 post-menopausal women, the group consuming 2 ounces of almonds daily for 4 months had decreased wrinkle severity and width as compared with controls [33]. In another small trial of 39 healthy overweight women, daily consumption of 1 avocado for 8 weeks significantly increased forehead skin firmness and elasticity [34].

Small cross-sectional survey studies have also identified some promising correlations.

In a survey of Japanese women in which food consumption was reported by patients, a correlation was noted between consumption of coffee (as well as total polyphenols from all sources) with a decrease in pigmented spot scores [35]. In a large-scale, cross-sectional study including 1264 women and 1655 men, reported diet was compared to severity of facial photoaging. After controlling for possible confounding variables, a lower risk of severe photoaging in both men and women was associated with higher intakes of monounsaturated fatty acids from olive oil (but not with intake via animal sources) [36].

Photoprotection

The cutaneous effects of ultraviolet (UV) radiation range from acute erythema to the clinical features of photoaging, to the molecular changes of photocarcinogenesis that increase the risk of skin cancer. Mechanistically, UV radiation induces oxidative stress and subsequent free radical production, primarily in the form of ROS. These unstable compounds cause damage to multiple skin components, including proteins, lipids, and DNA. In addition, ROS activate several inflammatory pathways, causing further damage to the epidermis and dermis [37].

Given the constant threat of free radicals, the body defense systems have evolved to provide multiple layers of protection. One of the key methods by which the body combats oxidative stress is through antioxidants, which may directly neutralize ROS or upregulate genes that encode neutralizing enzymes [38]. Antioxidants, found within the epidermis and dermis, include vitamin C, vitamin E, selenium, and carotenoids, as well as endogenous protective enzyme systems such as glutathione peroxidase [39,40]. These are depleted throughout the day and require constant replenishment from dietary sources. This has directed attention to functional foods and their role in enhancing photoprotection.

A number of human interventional studies have identified beneficial foods, while animal and laboratory studies have identified many other promising photoprotective foods and food components. Interventions studied have included tomato paste, high flavanol cocoa, grapes, and multiple individual food components.

Protection Against UV-Induced Erythema

Human Studies

Multiple studies have evaluated the effect of functional foods on the minimal erythema dose (MED), used to measure sensitivity to sunlight and which represents the lowest UV dose necessary to produce sunburn or redness. This visible erythema represents multiple biochemical and histologic skin changes [41].

In one RCT, researchers investigated a dietary source naturally rich in carotenoids. Over 10 weeks, volunteers ingested 40 grams of tomato paste in olive oil daily. At the end of the study, subjects demonstrated 40% lower erythema formation following UV exposure [42]. In another RCT, volunteers ingested 55 grams of tomato paste in olive oil daily for 12 weeks, resulting in significant improvement in the MED [43]. Biopsies taken following UV radiation at the end of the study demonstrated a significant reduction in matrix metalloproteinase-1 enzyme in the tomato paste group as compared to control participants. This enzyme, induced by oxidative stress from UV radiation, leads to the degradation of dermal proteins and plays a major role in the pathogenesis of photodamage [43]. It has been noted that the bioavailability of carotenoids from tomato paste is higher than that from tomato juice or fresh tomatoes, suggesting that the source of antioxidants may also influence improvements in MED [42].

Cocoa beans have also been studied, as they are rich in strongly antioxidant flavanol compounds. Researchers have specifically studied the effects of cocoa products with high flavanol content (ie products in which flavanol content was retained during the cocoa bean manufacturing process).

In one RCT, 2 groups of women consumed either high flavanol (HF) or low flavanol (LF) cocoa powder daily for 12 weeks. Those in the HF group experienced a 25% decrease in erythema from baseline following irradiation with a solar light simulator, with no change noted in the LF group [23]. In another RCT, subjects consuming 20 grams of high flavanol chocolate for 12 weeks also demonstrated significant improvement in MED [44]. Finally, another RCT found some improvements in MED in women consuming either 30 grams daily of either HF or LF chocolate [45].

Grapes, high in polyphenols, have also shown promise. In one study, 19 volunteers consumed California table grape (CTG) powder (reconstituted in water) 3 times daily for 14 days, with each serving equivalent to 1 serving (0.75 cup) of fresh grapes [46]. The MED improved in 11 volunteers and stayed in the same in 7. Eighteen participants underwent further biopsy for molecular biomarker studies, which demonstrated reduced markers of DNA damage, inflammation, and apoptosis [47].

Prevention of Photocarcinogenesis

Multiple RCTs of antioxidant supplements have failed to show benefit for the prevention of non-melanoma skin cancer [40]. On the other hand, although individual foods have rarely been studied, research on overall eating patterns has shown promise for the role of antioxidant-rich diets in skin cancer prevention, emphasizing the importance of additive and synergistic properties of foods [40]. This also highlights the need for additional studies of eating patterns as opposed to individual nutrients.

Animal Studies

A few foods have been evaluated for their role in prevention of photocarcinogenesis. Tea has shown promise, although current studies are limited to animal models. In one study, mice consumed black or green tea daily as their sole source of drinking fluid over 31 weeks of UVB treatment [48]. Administration of black, green, decaffeinated black, or decaffeinated green tea inhibited the number of carcinomas per mouse by 93%, 88%, 77%, and 72%, respectively. The mean concentration of tea leaves used in the study, 1.25 g/100 mL water, is comparable to that of tea brews ingested by humans.

Reduction of DNA Damage-Human Studies

DNA damage caused by oxidative stress is a major factor in photocarcinogenesis. Therefore, multiple studies have evaluated the role of fruits and vegetables that are rich in antioxidants and their role in reducing DNA damage. For example, cruciferous vegetables, including broccoli, Brussels sprouts, and watercress, contain high levels of antioxidants and have shown potential benefit in reducing DNA damage in several small human studies [49-51]. Tomato puree, high in the carotenoid lycopene, protected DNA against oxidative damage in a small human study, while kiwifruit increased the efficiency of base excision repair activity in another small human study [52,53]. Tart cherry juice was also shown to increase DNA repair activity in an RCT of older adults [54]. Further research into the effect of these functional foods on skin processes is warranted.

Nicotinamide, a form of vitamin B_3, has shown promise in skin cancer prevention. Its mechanism of action is not felt to be due to antioxidation properties but rather via promotion of DNA repair via the provision of extra energy stores. A large, multicenter, phase III trial demonstrated the benefit of oral nicotinamide in reducing the rates of actinic keratoses and non-melanoma skin cancer in a high-risk patient group [55]. As research to date has studied the effects of the isolated vitamin, further research is indicated on the role of foods rich in nicotinamide.

Hormonal Regulation

Functional foods may serve to modulate hormone bioavailability in certain disease states with dermatological manifestations. Polycystic ovarian syndrome (PCOS), characterized by hyperandrogenism, anovulation, and polycystic ovaries, increases the risk of hirsutism and acne in female patients [56]. A number of studies have evaluated the potential role of foods in combating hyperandrogenism [57].

Human Studies

Spearmint tea derived from the plant *Mentha spicata* has demonstrated anti-androgen effects in multiple human trials [56,58]. One RCT observed the effects of twice-a-day spearmint tea consumption in 41 women with PCOS compared to placebo tea [56]. After the 30-day treatment period, free and total testosterone levels were significantly decreased in the spearmint tea cohort. Although patient perception of degree of hirsutism was reduced in the spearmint cohort, there was no measurable reduction in objective hirsutism ratings. One shortcoming of the study, however, is its short duration, as hormonal alterations would need longer time to impact follicular hair growth.

Green tea and licorice have also been studied for their androgen-modulating effects. One RCT evaluated the effects of green tea consumption as compared to placebo in 60 overweight women with PCOS [59]. After 12 weeks, the group consuming green tea had significantly decreased free testosterone levels. Similarly, the effects of a commercial preparation of licorice (3.5 g) consumed daily throughout 2 consecutive menstrual cycles were observed in 9 healthy women [60]. Total free testosterone levels decreased from 27.8 ± 8.2 at baseline to 17.5 ± 6.4 ng/dL by the second month of licorice therapy. These hormonal improvements warrant additional study to evaluate clinical effects.

Conclusions

The past few decades have seen an increased focus on the effects of food on skin health. Numerous studies have identified promising functional foods, although the majority of research to date has involved small-scale human interventions or animal models. Larger human trials are warranted, especially to help elucidate populations that may benefit. In addition, trials examining eating patterns are important, as beneficial compounds in foods exhibit many additive and synergistic effects. Also important are further human, animal, and laboratory studies to elucidate the biochemical pathways and molecular mechanisms by which these observed clinical effects are achieved. Nevertheless, this overview highlights promising functional foods that have demonstrated benefits on skin barrier function, wound healing, radiance, anti-photoaging, photoprotection, and hormonal regulation. Additional research is encouraged, as functional foods represent an easily accessible option for patients interested in improving skin health.

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