Nutrition and enhancing youthful-appearing skin

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Abstract The use of nutrition, including vitamins and antioxidants, to enhance youthful-appearing skin is presented. The most current references in the area are included, but much of the material discussed has not been well studied. The use of nutricosmetics is supported by testimonial, assumption, inference, and vague language. This contribution provides an overview of the current nutricosmetic marketplace and also substantiates the lack of available scientific data.

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Introduction

The newest trend in skin care is the use of diet and oral supplements to produce an appearance benefit. Healthy skin is a manifestation of overall health and as such can be influenced by the consumption of oral substances, including vitamins and antioxidants. This approach to antiaging is termed the “inside-out” approach, because oral food supplements and topical agents are synergistically combined to enhance efficacy. Although it has generally been assumed that good nutrition is the key to a long, healthy life and beautiful skin, no double-blind placebo-controlled studies have been conducted to verify this concept. Certain essential vitamins are necessary in the diet to allow the body to function, but the concept that ingesting large quantities of these substances or applying them topically to the skin results in enhanced health benefits has never been confirmed. Yet, marketing products with the inside-out philosophy abounds because foodstuff are considered safe, the raw materials are inexpensive, and the concept has widespread consumer appeal.

This inside-out approach has led to the developing of a new product category labeled the “nutricosmetic.” Nutricosmetic can be added to the other nebulous terms that describe this undefined appearance-related category. Cosmeceutical was coined to define products that were classified as cosmetics, yet attempted to deliver benefits more along the line of a pharmaceutical. Nutraceutical describes oral supplements that claim to deliver health benefits beyond a traditional vitamin tablet. And finally, nutricosmetic describes the synergistic use of oral and topical agents to improve skin appearance. In some instances, this may mean that a skin cream is sold in the same packaging as an ingestible. Is this really a valuable concept or simply a new marketing twist?

This contribution examines the use of nutrition to enhance youthful-appearing skin. The most current references in the area are included, but much of the material presented is not well studied. The use of nutricosmetics is supported by testimonial, assumption, inference, and vague language. Thus, this should be read as an overview of the current nutricosmetic marketplace and not scientific fact. The review will begin with vitamins and then examine antioxidants, including flavonoids and polyphenols.

Vitamins

The term nutricosmetic combines the words nutrition and cosmetic. Many of the new food introductions at the
grocery store are nutricosmetics of a sort. Traditional yogurt, for example, is not vitamin D-enriched like milk. A new line of yogurt contains vitamin D and inulin, a nonabsorbable fiber to aid in elimination. A competing yogurt contains probiotic organisms, which are bacteria designed to recolonize the gut, resulting in improved elimination and better overall health from the inside-out. This is an important marketing tactic, because it allows existing foods to be made “new” with the addition of one ingredient to the existing recipe sold in the existing packaging. An old food with sagging sales can be reinvigorated in the marketplace with little up-front cost.

This section examines the use of vitamins, which are used both orally and topically to improve skin health. Although the oral route is far superior to topical use, topical vitamins do perform in cosmeceuticals. Vitamins are frequently used as specialty ingredients in creams due to their excellent safety, low cost, and high consumer acceptance.

**Vitamin D**

Vitamin D is important in skin health because it maintains the bony architecture over which the skin is draped. Vitamins D and A were used in some of the oldest marketed skin care preparations (A&D Ointment) to aid in wound healing. Thus, vitamin D is used both orally and topically; however, its topical application is largely for its ability to function as a humectant, which increases the capacity of the skin to hold water.

Vitamin D is a fat-soluble vitamin manufactured by the body when exposed to sunlight. The inhibition of vitamin D manufacture by sunscreens and sun avoidance has been a controversial topic in the popular media, with some advocating discontinuing sunscreen use and deliberate sun exposure to prevent vitamin D deficiency. Vitamin D deficiency, the cause of rickets in children, was virtually eliminated when milk was enriched with 400 IU of vitamin D per quart in the 1930s. One cup of milk supplies 25% of the recommended daily allowance of vitamin D in adults; however, the current recommended daily allowances are probably too low. The daily recommendation is 200 IU from birth to 50 years, 400 IU from 51 to 70 years, and 600 IU for 71 years and older.

Only drinking milk is enriched with vitamin D. Cheese, yogurt, and ice cream are not required to include vitamin D enrichment; however, a new trend in some of the nutricosmetic yogurts, mentioned previously, is to add vitamin D. A few foods are rich in vitamin D, including fatty fish, such as salmon, sardines in oil, and mackerel, and fish oils, such as cod liver oil. Consuming too much vitamin D results in toxicity because the vitamin is stored in the fat of the body. Toxicity presents as nausea, vomiting, poor appetite, constipation, weakness, and weight loss.

The importance of vitamin D in appearance is the preservation of the facial bones. Vitamin D is necessary to maintain calcium homeostasis, promoting bone mineralization. Proper mineralization of the facial bones is necessary. Bone loss with maturity occurs commonly in the gingival bones, especially in edentulous persons. This loss of bone leads to wrinkling of the skin around the mouth and inward turning of the lips. Dermatologists should consider obtaining levels of 1,25-dihydroxy vitamin D for all female patients aged older than 50 to look for deficiency, especially if they are fair complected, petite, and have a family history of osteoporosis. Several vitamin D replacement protocols are available, depending upon the degree of deficiency. One commonly used replacement strategy is to take 50,000 IU of vitamin D once weekly for 1 month, followed by 50,000 IU monthly.

Vitamin D is being studied for its ability to modulate the skin’s immune response. It appears that vitamin D3 may be a major factor in the regulation of cathelicidin expression, which may be abnormally processed to forms that induce cutaneous inflammation in rosacea, producing a cosmetically unattractive red face. Other researchers have linked vitamin D to the regulation of p53, a tumor suppressor protein important in skin cancer. This has led to a speculation that there is a relationship between vitamin D deficiency and melanoma. It may be that oral vitamin D supplementation is worthwhile to prevent skin cancer, which is at one end of the cutaneous aging spectrum.

**Vitamin C**

Vitamin C, also known as ascorbic acid, is used both orally and topically for skin benefits. Topically, ascorbic acid is used in cosmeceuticals for hyperpigmentation because it interrupts melanogenesis by interacting with copper ions to reduce dopaquinone and blocks dihydrochinindol-2-carboxyl acid oxidation. Orally, nutricosmetic formulations use vitamin C, in the form of L-ascorbic acid, to function as an antioxidant by scavenging and quenching free radicals and by regenerating vitamin E from its radical form. That vitamin C is necessary for wound healing is well established. It is a cofactor for lysyl and prolyl hydroxylase, which stabilize the triple-helical structure of collagen. Whether oral or topical supplementation of vitamin C enhances wound healing is controversial.

The value of vitamin C oral supplementation is theoretically to maintain the body reservoir of 1500 mg, which is rapidly depleted when the body is exposed to ultraviolet (UV) light. Some researchers believe that natural dietary sources of vitamin C, such as vegetables and citrus fruits, are the best method of restoring body reserves. Other researchers have concluded that the poorly ripened fruits now sold in grocery stores are deficient in vitamin C and believe that synthetic vitamin supplementation is important.

Vitamin C can function as an oxidant in the presence of iron in vitamin supplements. Oral vitamin C is necessary to prevent scurvy, a disease with many skin manifestations, including skin fragility, gingivitis, and corkscrew hairs. Vitamin C may also promote fibroblast proliferation,
migration, and replication-associated base excision repair of potentially mutagenic DNA lesions.\textsuperscript{15} These activities are necessary to maintain youthful-appearing skin.

Even though much is available in the popular press about the merits of topical vitamin C, little has been published in the peer reviewed dermatologic literature. Some investigators have demonstrated enhanced cutaneous vitamin C levels after topical application of 10% L-ascorbic acid; however, this work was performed on a porcine model.\textsuperscript{16} Other human studies have demonstrated a decrease in the minimal erythema dose and less erythema after UVB exposure in individuals treated with topical 10% L-ascorbic acid, but the sample size was limited.\textsuperscript{17} Vitamin C has also been purported to produce lightening of skin dyspigmentation in the form of magnesium L-ascorbyl-2-phosphate, but no well-controlled studies exist.\textsuperscript{18} The challenge remains for researchers to embark on large-scale double-blinded placebo-controlled studies to demonstrate the value of topical vitamin C.

**Vitamin E**

Vitamin E is the most popular topical vitamin in cosmeceuticals and a common nutricosmetic. Vitamin E, like vitamin C, is a naturally occurring endogenous antioxidant. Even though the concentration of vitamin E in the epidermis is extremely small (1.0 nmol/g)\textsuperscript{19} it is the most important lipid-soluble membrane-bound antioxidant in the body.\textsuperscript{20} Vitamins E and C work synergistically: vitamin E can regenerate its antioxidant capabilities in the presence of vitamin C.\textsuperscript{21} The form of vitamin E with the most biologic activity is \( \alpha \)-tocopherol, which functions to terminate lipid radical chain reactions. It stabilizes membranes against damage by phospholipase A, free fatty acids, and lysophospholipids.\textsuperscript{22} Vitamin E may also protect membrane proteins containing selenium or sulfur.

The body’s stores of vitamin E are maintained through the intake of vegetables, oils, seeds, corn, soy, whole wheat flour, margarine, nuts, and some meats and dairy products.\textsuperscript{23} These stores must be maintained by continuous consumption or lipid peroxidation and collagen cross-linking occurs, which become accelerated with aging skin.\textsuperscript{24} Oral vitamin E intake has also been linked to immunoglobulin (Ig) E levels and the clinical manifestations of atopy.\textsuperscript{25}

Again, the value of topical application awaits further study. A review of the literature yielded articles that demonstrated \( \alpha \)-tocopherol could inhibit UVB-induced edema and erythema, conferring a sun protection factor of 3 after multiple applications.\textsuperscript{26} This is thought to be due to its ability to marginally absorb light and function as a free radical-quenching, lipid-soluble antioxidant\textsuperscript{27}; however, oral vitamin E did not confer any photoprotective effects.\textsuperscript{28} Topical vitamin E may also function as a penetration enhancer for other active ingredients by intercalating within the lipid bilayer region of the stratum corneum and altering membrane characteristics.\textsuperscript{29}

**Carotenoids (vitamin A)**

From the antioxidant vitamins, the discussion now turns to the carotenoids, another important nutricosmetic to prevent premature aging. Carotenoids are derivatives of vitamin A and have found widespread use in nutricosmetics and in cosmeceuticals due to the established topical antiaging benefits associated with the prescription retinoid tretinoin. The carotenoids are a large family of orange-, red-, and yellow-appearing substances that perform vital antioxidant roles when ingested but are less well established as topical antioxidants. The currently popular nutricosmetic carotenoids include astaxanthin, lutein, and lycopene.

**Astaxanthin**

Astaxanthin is a pink carotenoid found in high concentration in salmon and accounts for the characteristic pink color of the fish. This is the rationale for antiaging diets that recommend a serving of salmon five times weekly.\textsuperscript{30} For topical application purposes, astaxanthin is obtained from the marine microalgae *Haematococcus pluvialis*. The efficacy of astaxanthin is attributed to its cell membrane, composed of two external lipid layers, which has been touted to possess stronger antioxidant abilities than vitamin E.\textsuperscript{31} It is both water- and oil-soluble and is only produced when the algae are exposed to intense UV radiation.

Few topical studies exist to confirm the topical effect of astaxanthin,\textsuperscript{32} but it has been studied extensively as an oral supplement.\textsuperscript{33} It is used as a homeopathic treatment for macular degeneration because, unlike canthaxanthin, another carotenoid, it does not crystalize in the eye. It crosses the blood-brain barrier and has been studied in brain dysfunction, including spinal cord injuries and Parkinson disease.\textsuperscript{34} Although other carotenoids, such as \( \beta \)-carotene, have been proven ineffective in reducing the oxidative stress associated with cardiovascular disease, astaxanthin is currently undergoing further investigation.\textsuperscript{35}

Astaxanthin in concentrations of 0.03% to 0.07% produces a pink-colored cream. This limits the concentration that can be used, but no topical adverse reactions have been associated with this carotenoid. The topical antioxidant benefits of astaxanthin have not been established.

**Lutein**

Another nutricosmetic carotenoid is lutein, which is naturally found in green leafy vegetables, such as spinach and kale. Lutein is an antioxidant in the plant kingdom known for absorbing blue light. In the animal kingdom, lutein is found in egg yolks, animal fats, and the corpus luteum. It is a lipophilic molecule, not soluble in water, characterized by a long polyene side chain composed of conjugated double bonds. These double bonds are degraded by light and heat, a universal characteristic of carotenoids to a greater or lesser degree.\textsuperscript{36}

Lutein is used as a natural colorant due to its orange-red color resulting from the absorption of blue light. Its largest use
is as a food supplement for chickens, which results in more vivid yellow yolks. In humans, lutein is concentrated in the macula and has been linked to the prevention of macular degeneration.\textsuperscript{37} It has been available as a nutritional supplement since 1996 and can be administered as a sublingual spray for elderly patients with macular degeneration. The results of most of the well-conducted studies that have evaluated the benefit of lutein for macular degeneration have been inconclusive.\textsuperscript{38} No recommended daily allowance has been established for lutein, but 6 mg/d has been published.\textsuperscript{39} Most of the lutein used for food additives is derived from marigolds.

The question of whether topical lutein is of value remains. Again, data are lacking, but excess lutein intake can result in carotenodermia, and excess topical application results in bronzing of the skin. It may be of interest that lutein fed to chickens results in the characteristic yellow appearance of chicken skin, which is thought to be more attractive than the natural white skin.

**Lycopene**

Lycopene is another potent carotenoid that is found in most fruits and vegetables with a red color, including, tomatoes, watermelon, pink grapefruit, papaya, gac, red bell pepper, and pink guava. The highest lycopene-containing food is ketchup, but lycopene is not an essential human nutrient. The Mayo Clinic Web site rates as “C” the evidence for the use of lycopene as an antioxidant, because it is not clear if lycopene has these effects on the human body. Lycopene oral supplements have been purported to reduce the risk of prostate cancer, but the U.S. Food and Drug Administration (FDA) has concluded there is little scientific evidence to support this claim.\textsuperscript{40} Lycopene is a highly unsaturated hydrocarbon containing 11 conjugated and 2 unconjugated double bonds, which makes it a longer molecule than any other carotenoid. This makes its absorption into the skin doubtful. It undergoes cis-isomerization when exposed to sunlight. Even though lycopene was the new oral supplement added to many commercial multivitamins this year, its topical value has never been documented.

**Retinol**

Retinol is the most important of all the topical carotenoids because it is necessary for vision and possesses a well-characterized skin receptor.\textsuperscript{41} The amount of vitamin A in an oral supplement is measured in retinol activity equivalents (RAE). Many supplements contain β-carotene that can be split to yield two active units of vitamin A. Vitamin A is a fat-soluble vitamin with the recommended daily allowance of 700 RAE for women and 900 RAE for men. Foods that are high in vitamin A include sweet potatoes, kale, carrots, mango, turnip greens, spinach, and papaya. Low-fat and skim milk, margarine, and cereals are commonly enriched with vitamin A.

Ninety percent of the body’s vitamin A reserve is found in the liver, with 1% in the plasma. The liver vitamin A level in a well-nourished adult is approximately 100 μg/g.\textsuperscript{42} Adequate dietary vitamin A is necessary not only for vision but also for the prevention of chemical carcinogenesis in the epithelial tissues of the bronchi, trachea, stomach, uterus, and skin.\textsuperscript{43} Outside of the retina, 9-cis-dehydroretinoic acid and di-dehydroretinoic acid are more important because they trigger gene expression by binding to nuclear retinoid receptors.\textsuperscript{44} The mean concentrations per protein of carotene, retinol, and dehydroretinol in the back skin of healthy individuals were 13, 0.4, and 0.4 μg/g, with no difference found with variations in sex and age.\textsuperscript{45}

It is theoretically possible to interconvert the retinoids from one form to another. For example, retinyl palmitate and retinyl propionate, chemically known as retinyl esters, can become biologically active after cutaneous enzymatic cleavage of the ester bond and subsequent conversion to retinol. Retinol is the naturally occurring vitamin A form found in red, yellow, and orange fruits and vegetables. It is the pigment responsible for vision, but is highly unstable. Retinol can be oxidized to retinaldehyde and then oxidized to retinoic acid, also known as prescription tretinoin. This cutaneous conversion of retinol to retinoic acid is responsible for the biologic activity of some of the new stabilized over-the-counter vitamin A preparations designed to improve the appearance of benign photodamaged skin.\textsuperscript{46} The skin can only convert small amounts of retinyl palmitate and retinol, accounting for the increased efficacy seen with prescription preparations containing retinoic acid.

The topical benefit of retinol has been documented by well-controlled studies.\textsuperscript{37} It is commonly believed among dermatologists that retinol is of benefit in improving the appearance of aged skin.\textsuperscript{48,49}

**Vitamin F (essential fatty acids)**

Essential fatty acids are sometimes referred to as vitamin F in the nutricosmetic and cosmeceutical literature. The essential fatty acids cannot be synthesized by the body and must be consumed in the diet. They are long-chain polyunsaturated fatty acids derived from linolenic, linoleic, and oleic acids. The two families of essential fatty acids are ω-3, derived from linolenic acid, and ω-6, derived from linoleic acid, with the number indicating the position of the first double bond continuing from the terminal methyl group on the molecule.\textsuperscript{50}

The principal ω-3 fatty acid is α-linolenic acid, which is converted to eicosapentaenoic acid and then into docosahexaenoic acid. The ω-3 fatty acids are used in the formation of cell walls, and deficiency leads to decreased mental abilities, poor vision, diminished immune function, increased triglycerides, increased low-density lipoprotein cholesterol, hypertension, and skin disease resembling eczema. The highest concentration of ω-3 fatty acids are found in flaxseed oil, but other sources include canola oil, hemp seed oil, walnuts, sesame seeds, avocados, salmon, and albacore tuna.\textsuperscript{51} Linolenic acid has been studied for its health benefits in
Antioxidants

Antioxidants are one of the most popular nutricosmetic ingredients. Most are derived from plants because oxidation protection is necessary in the UV-rich outdoor environment. The classes of antioxidants present in plants are flavonoids and polyphenols. Flavonoids are aromatic compounds, frequently with a yellow color, that occur in higher plants. Researchers have identified 5000 flavonoids with a similar chemical structure, possessing 15 carbon atoms and a variety of biologic activities. Flavonoids can be divided into flavones, flavonols, isoflavones, and flavanones, each with a slightly different chemical structure. Currently, the most common isoflavones incorporated into cosmeceuticals are daidzein and genistein, derived from soybeans. Other sources of flavonoids include curcumin, silymarin, pycnogenol, and gingko. These will be discussed next.

Soy

Genistein and daidzein are soybean-derived isoflavones that function as phytoestrogens when orally consumed and have been credited with the decrease in cardiovascular disease and breast cancer seen in Asian women. These isoflavones are present when the soy is fermented. Other purported systemic benefits include improvement in immunity, reduction of prostate cancer, and improvement in cognition. Some of the cutaneous effects of soy have been linked to its estrogenic effect in postmenopausal women. Topical estrogens have been shown to increase skin thickness and promote collagen synthesis. Although genistein increases collagen gene expression in cell culture, there are no published reports of this collagen-stimulating effect in topical human trials. Genistein has also been reported to function as a potent antioxidant, scavenging peroxyl radicals and protecting against lipid peroxidation in vivo. The only studies that document the ability of soy to protect against UVB-induced skin damage are in mice, where a topical application of non-denatured soy extracts reduced UVB-induced cyclooxygenase-2 expression, prostaglandin-E2 secretion, and inhibited p38 mitogen-activated protein kinase activation.

Curcumin

Curcumin is a popular natural yellow food coloring that is used in everything from prepackaged snack food to meat. It is sometimes used as a natural yellow coloring in skin care products that claim to be free of artificial ingredients. Curcumin comes from the rhizome of the tumeric plant and is consumed orally as an Asian spice, frequently found in rice dishes to add yellow color the otherwise white rice. Tetrahydrocurcumin, a hydrogenated form of curcumin, is off-white in color and can be added to skin care products as a skin antioxidant and to prevent the lipids in the moisturizer from becoming rancid. The antioxidant effect of tetrahydrocurcumin is said to be greater than vitamin E by cosmetic chemists. It is said to provide antioxidant skin benefits by quenching oxygen radicals and inhibiting nuclear factor-κB. Oral ingestion in rodents has produced correction of cystic fibrosis defects and inhibition of tumor proliferation, but human trials are lacking.

Silymarin

Another plant antioxidant is silymarin, an extract of the milk thistle plant (Silium marianum), which is in the aster...
family of plants, including daisies, thistles, and artichokes. The plant is named milk thistle because the oldest recorded use of the extract was to enhance human lactation and the plant produces a white milky sap. The extract consists of three flavonoids—silybin, silydianin, and silychristine—derived from the plant’s fruit, seeds, and leaves. Homeopathically, silymarin is used to treat liver disease, but it is a strong antioxidant that prevents lipid peroxidation by scavenging free radical species. Its antioxidant effects have been demonstrated topically in hairless mice by the 92% reduction of skin tumors after UVB exposure.72,73 The mechanism for this decrease in tumor production is unknown, but silymarin decreased the formation of pyrimidine dimers in a mouse model.74 It also improved the healing of burns in albino rats.75

**Pycnogenol**

Pycnogenol is an extract of French marine pine bark (*Pinus pinaster*), which grows only on the southwest coast of France in Les Landes de Gascogne. The extract is a watersoluble liquid that contains several phenolic constituents, including taxifolin, catechin, and procyanidins, as well as several phenolic acids, including *p*-hydroxybenzoic, protocatechuic, gallic, vanillic, *p*-coueric, caffeic, and ferulic.76 It is a trademarked ingredient that is sold for oral consumption as a preventative for cardiovascular disease,77 a treatment for diabetic microangiopathy,78 and a pain reliever for muscle cramps.79 It is a potent free radical scavenger that can reduce the vitamin C radical, returning the vitamin C to its active form.80 The active vitamin C in turn regenerates vitamin E to its active form, maintaining intact the natural oxygen scavenging mechanisms of the skin.

Pycnogenol is the ideal antiaging additive because it demonstrates no long-term toxicity, no mutagenicity, no teratogenicity, and no allergenicity.81 It is consumed orally to enhance the production of nitric oxide, which inhibits platelet aggregation in coronary artery disease; thus, it is also deemed safe for topical use. Its use for skin indications is less well documented, however. In B16 melanoma cells, it was shown to inhibit tyrosinase activity and melanin biosynthesis.82

**Ginkgo**

*Ginkgo biloba*, also named the maidenhair tree, is the last member of the *Ginkgoaceae* family, which grew on earth some 200 to 250 million years ago. For this reason, ginkgo contains flavonoids not found in other botanicals. It possesses bilobalide (a sequiterpene), ginkgolides (diterpenes with 20 carbon atoms), and other aromatic substances such as ginkgol, bilobol, and ginkgolic acid. It is a plant with numerous purported benefits and has been a common part of homeopathic medicine in the Orient for 4000 years. The plant leaves are said to contain unique polyphenols, such as terpenoids (ginkgolides, bilobalides), flavonoids, and flavonol glycosides that have anti-inflammatory effects. These anti-inflammatory effects have been linked to antiradical and antilipoperoxidant effects in experimental fibroblast models.83 Ginkgo flavonoid fractions containing quercetin, kaempferol, sciodipitysin, ginkgetin, and isoginkgetin have been demonstrated to induce human skin fibroblast proliferation in vitro. Increased collagen and extracellular fibronection were also demonstrated by radioisotope assay.84

Another family of antioxidants, which is a subset of flavonoids, are polyphenols commonly derived from teas and fruits. Green tea and pomegranate juice are examples of the currently popular skin health drinks containing polyphenols.

**Green tea**

Tea (*Camellia sinensis*) is a botanical that has been used topically and orally in in the Orient for 5000 years. Teas are a rich part of the Oriental culture, used to stay alert during extended meditation. An Indian legend tells of Prince Siddhartha Guatama, the founder of Buddhism, who tore off his eyelids in frustration over his inability to stay awake during meditation. A tea plant is said to have sprouted from where his eyelids fell, providing the ability to stay awake, meditate, and reach enlightenment. Tea reached Western cultures during the 6th century from Turkish traders.

Several different types of tea are available: green, black, oolong, and white. The different teas come from the same plant, but different processing imparts different properties. Green tea is made from unfermented tea leaves and contains the highest concentration of polyphenol antioxidants.85 Black tea leaves are fermented days before heating. Oolong tea originates in the Fukien province of China and the leaves are treated much like black tea, except the withering and fermentation times are minimized. White tea comes from young tea leaves that are harvested for a few days each spring when the plant emerges from the ground. These leaves are said to be very high in antioxidants. The highest quality white tea is obtained from buds that are just ready to open, known as needles or tips.

The evidence to support the anticancer benefits of topical and oral green tea use was felt to be inadequate by the FDA. On June 30, 2005, the FDA concluded, “There is no credible evidence to support qualified health claims for green tea consumption and a reduced risk of gastric, lung, colon/rectal, esophageal, pancreatic, ovarian, and combined cancers.” The FDA denied these claims; however, the FDA concludes, “there is very limited credible evidence for qualified health claims specifically for green tea and breast cancer and for green tea and prostate cancer, provided the claims are appropriately worded so as not to mislead consumers.”86 The evidence to support cardiovascular benefits was also inadequate. On May 9, 2006, in response to “Green Tea and Reduced Risk of Cardiovascular Disease,” the FDA stated, “there is no evidence to support qualified health claims for green tea or green tea extract and a reduction in a number of risk factors associated with cardiovascular...
disease.\textsuperscript{87} Some FDA advisers have voiced concern that teas may contain high levels of pesticides and heavy metals.

Green tea is manufactured from both the leaf and bud of the plant. Green tea that is consumed orally is said to contain beneficial polyphenols, such as epicatechin, epicatechin-3-gallate (GTP), epigallocatechin, and epi/gallocatechin-3-gallate (EGCG), which function as potent antioxidants.\textsuperscript{88} EGCG, the most potent of the polyphenols, is sold as a white caffeine-free powder.\textsuperscript{89} Studies of oral consumption of EGCG demonstrated increased fat oxidation and improvements in heart rate and serum glucose levels with 300 mg. Other alkaloids present in green tea include caffeine, theobromine, and theophylline.

A study has demonstrated the anti-inflammatory effects of topical green tea application on C3H mice. A topically applied green tea extract containing (\textsuperscript{-})GTP reduced UVB-induced inflammation as measured by double skin-fold swelling.\textsuperscript{90} The researchers also found protection against UV-induced edema, erythema, and antioxidant depletion in the epidermis. This work was further investigated by applying GTP to the back of humans 30 minutes before UV irradiation, which resulted in decreased myeloperoxidase activity and decreased infiltration of leukocytes compared with the untreated skin.\textsuperscript{91}

The application of topical green tea polyphenols before UV exposure decreased the formation of cyclobutane pyrimidine dimers.\textsuperscript{92} These dimers are critical in initiating UV exposure decreased the formation of cyclobutane pyrimidine dimers.\textsuperscript{92} These dimers are critical in initiating UV-induced mutagenesis and carcinogenesis, which represent the end stage of the aging process. Thus, green tea polyphenols can function topically as antioxidants, anti-inflammatories, and anticarcinogens, making them a popular nutricosmetic.\textsuperscript{93,94}

**Pomegranate**

Another skin health drink is pomegranate juice. Pomegranate, botanically known as Punica granatum, is a deciduous tree bearing a red fruit native to Afghanistan, Pakistan, Iran, and northern India.\textsuperscript{95} It was brought to California by the Spanish settlers in 1769 and is commercially cultivated for its juice. The pomegranate became famous in Greek mythology when Persephone was kidnapped by Hades and taken to the Underworld to be his wife. Persephone had consumed four pomegranate seeds while in the Underworld and thus had to spend 4 months every year in Hades, during which time nothing would grow. This gave rise to the season of winter.

Pomegranate juice, commonly consumed in the Middle East, provides about 16% of the adult requirement of vitamin C per 100 mg serving. It also contains pantothenic acid (vitamin B\textsubscript{5}), potassium, and antioxidant polyphenols. These substances have been demonstrated to protect against UVA- and UVB-induced cell damage in SKU-1064 human skin fibroblasts.\textsuperscript{96} Pomegranate juice has also been purported to reduce oxidative stress, affect low-density lipoprotein, and platelet aggregation in humans and in apolipoprotein E-deficient mice.\textsuperscript{97,98} It has also been studied for improving hyperlipidemia in diabetic patients.\textsuperscript{99}

**Conclusions**

The value of vitamins and antioxidants in skin health is a controversial area. Controlled studies are difficult to conduct because it can be argued that such studies would violate the rights of human participants. Ideally, a study would consist of several arms, each evaluating a different vitamin. Participants in each arm would eat a diet devoid of a vitamin to observe the progressive effects of deficiency on the skin and general health. The vitamin would then be reintroduced in slowly escalating doses to determine the minimum amount required for health, and then the dose would be pushed higher to observe the effects of toxicity and determine the toxic dose. This should be done for all vitamins and antioxidants, but the problems with such human research are obvious. The studies could not be ethically conducted.

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