

The Role of Nutraceuticals In Skin Anti-aging

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ABSTRACT

The concept of anti-aging is becoming more popular. This is because more individuals are living longer. The world is becoming increasingly cosmetic with increasing interest in appearance and the subject of slowing down aging is increasingly becoming the focus of scientific research. Now, aging is no longer accepted as 'natural' as there are ways to influence it. The role of nutrition as a tool for anti-aging has become topical. This subject of the use of food for nutritional and medicinal purposes is referred to as nutraceuticals. Nutraceuticals function as antioxidants, lipid membrane stabilizers, enzyme inducers or inhibitors. The role of nutraceuticals in anti-aging is hereby presented.

INTRODUCTION

In 2010, the World Health Organisation (WHO) estimated that, 8% (524 million) of the world's population was aged 65 years and above.¹ It is estimated that by 2050, this age group will make up 16% (1.5 billion) of the world's population.¹ The result of this increased longevity is an increasing interest in how to slow down aging. This interest in anti-aging is compounded by the increasingly cosmetic world that we live in. The question now is, can we really slow down aging? Currently, there are a lot of studies in which skin aging is reported as the goal or target for biomedical and scientific interventions using nutrition.²⁻⁷

How do we age? Two independent, clinical and biological mechanisms (intrinsic and extrinsic) are responsible for skin aging.⁸⁻¹⁰ These two mechanisms combine to cause phenotypic changes in skin cells.⁸ They also cause structural and functional changes in extracellular matrix components such as collagen, elastin and proteoglycans which provide tensile strength, elasticity, and hydration to the skin.⁸

The intrinsic mechanism represents chronological aging and it is inevitable.^{8,9} Intrinsic aging results from a decline of biological functions and the action of reactive oxygen species (ROS) following cellular metabolism.^{9,10} Factors which contribute to this mechanism of aging include; cellular metabolism,

genetics, hormone and time (age).^{8,9} Histologically, intrinsic aging is most evident at the basal cell layer of the skin.⁸ Proliferation of the basal cell layer reduces with age and the epidermis becomes thinner reducing the contact surface area between dermis and epidermis.⁸ The result of this is increased frailty, loss of elasticity, thin dry skin, fine wrinkles and gradual dermal atrophy.⁸

The extrinsic mechanism is dependent on external factors and influenced by the environment.^{8,9} These factors include; smoking, inadequate sleep, sun exposure and UVR, environmental pollution, chemicals and toxins, poor nutrition.^{8,9} UV radiation increases matrix metalloproteinases (MMPs) expression in human skin.^{8,9} The stratum corneum which is mostly affected by extrinsic aging thickens because of failure of degradation of corneocyte desmosomes.⁸ The result of extrinsic aging is coarse wrinkles, loss of elasticity, laxity and rough textured appearance.⁸ This extrinsic mechanism is what is addressed in most anti-aging research and interventions.^{8,9} These intervention are done by way of a well regulated lifestyle, caloric restriction, physical exercise, reduction of stress /stressful conditions and a balanced diet rich in anti-oxidants.

Oxidative stress is defined as an imbalance between pro-oxidants and/or free radicals and anti-oxidizing systems.^{9,10} Following from this

definition, aging results from an excess of pro-oxidants. Cellular metabolism results in the production of reactive oxygen species.^{9,10} Reactive oxygen species (ROS) when produced in excess damage collagen, elastin, DNA and fibrosis of blood vessels.⁹ On the other hand, the generation of ROS following cellular metabolism, physical exercise, emotional stress, UV rays, toxic substances and cigarette smoke provides cell-protective and anti-aging effects. This is because ROS activation induces the expression and upregulation of the cell's own antioxidative enzyme system with the production of enzymes like superoxide dismutase, glutathione peroxidase and catalase.^{9,10}

This upregulation of the cell's own intrinsic antioxidative enzyme system prevents the cell from accumulating harmful cellular levels of ROS.¹⁰ These antioxidative enzymes depend on an adequate supply of microelements (selenium, copper, zinc, iron and manganese) to function.¹⁰ A failure of this protective function and consequent skin aging occurs when the supply of micronutrients, environmental pollution and constant stimulation of the immune system (allergies, infections, chronic diseases) overwhelms the antioxidative system.

The signs of skin aging are reported to be; coarse wrinkles, xerosis, dyschromias, loss of collagen and elastic fibers and a reduction in the synthesis of hyaluronic acid (HA).^{8,10} These signs are variously reported to improve following dietary intervention; the subject of nutraceuticals.^{3,4-5,11} The word nutraceuticals, derived from a combination of nutrition and pharmaceuticals was first put together by Stephen Defelice in 1989.¹² Nutraceuticals are said to be products which have both nutritional and medicinal properties.^{5,11,12} They are also defined as substances which have physiological benefit or provides protection against chronic diseases.¹¹ Nutraceuticals improve health and delay the aging process.^{2,13} Nutraceuticals functioning as antioxidants decrease the adverse effect of reactive oxygen and nitrogen species.⁹ They are derived from natural foods, antioxidants, dietary supplements, fortified dairy products, citrus fruits, vitamins, minerals, herbs, milk, and cereals.⁵ Nutraceuticals differ from normal foods as

they are used in prevention and treatment of illnesses while normal food is not.¹¹ They are regarded as important nutrients for slowing the ageing process. The advantage of this nutritional route of administration is delivery of nutraceutically bioactive compounds to all layers of the skin from the circulation.¹⁰ There are different dietary sources of nutraceuticals (Figure 1).

Nutraceuticals are grouped into: carotenoids, tocotrienols, and tocopherols; polyphenols; carbohydrates and their derivatives (ascorbic acid and fiber); minerals (i.e., selenium compounds) and micro-organisms (probiotics and prebiotics).¹⁴ They all function as antioxidants, enzyme inhibitors or enzyme inducers and membrane stabilizers.^{10,14} Discussed below are some nutraceuticals used in skin anti-aging.

NUTRACEUTICALS

VITAMIN C: Derived from citrus fruits, vegetables, blackcurrant, rose hip, guava, chili pepper and parsley.¹⁰ Stability of the vitamin C molecule is dependent on its condition and formulation. The metabolically active vitamin C is the L-ascorbic acid.^{10,15,16} L-ascorbic acid can be used orally and topically.¹⁰ Vitamin C functions as a cofactor for lysyl and prolyl hydroxylase to stabilize the structure of collagen.¹⁶ It also functions in iron absorption, cholesterol synthesis and in the bioavailability of the micronutrient, selenium.¹⁰ L-ascorbic acid specifically works as a free radical scavenger and in the recycle of oxidized vitamin E in the membranes.^{10,16} The indications for Vitamin C especially via the topical route are depigmentation, anti-aging and sun protection.^{10,15,16} Specifically, combinations of oral formulations of ascorbic acid and vitamin E improves UVB-induced epidermal damage.¹⁰ Apart from L-ascorbic acid, other formulations of vitamin C- based products which readily penetrate the skin exist.¹⁰ These formulations are however not converted to L-ascorbic acid the active vitamin C molecule. These topical or oral products do not result in the effects provided by L-ascorbic acid.¹⁰

VITAMIN E: Vitamin E are a group of 8 compounds called tocopherols.^{10,12} Tocopherols

are endogenous antioxidants.¹⁰ They function as fat-soluble membrane bound antioxidants and free-radical scavengers.¹⁰ They can be found in wheat, seed oil, nuts, beans, herbal oil, egg yolk, green leafed vegetables, vegetable oils (wheat germ oil, sunflower oil, safflower oil) seeds, corn, soy and meat.¹⁰ Following UV exposure, there is oxidation of cellular components and peroxidation of lipid membranes rich in polyunsaturated acids like arachidonic acid by UV-activated molecules.^{10,12} In this process, the antioxidant D- α -tocopherol is oxidized from its antioxidant form to the tocopheroxyl radical.¹⁰ Vitamin C acts synergistically with vitamin E to regenerate its antioxidant form of vitamin E.^{10,16} Other molecules which recycle vitamin E are glutathione and coenzyme Q10.¹⁰ Vitamin E prevents collagen cross linking and lipid peroxidation, which are both linked to aging of the skin.¹⁰ Also, vitamin E stabilizes the cell membrane by inhibiting the oxidation of polyunsaturated fatty acids (like arachidonic acid) of membrane phospholipids.^{10,17,18} When administered topically, vitamin E reduced erythema, sunburned cells and improves facial wrinkles, elasticity, dermal density and skin tone.^{17,18}

CAROTENOIDS: These are plant pigments which serve as potent ROS scavengers.¹² They include; β -carotene, astaxanthin, lycopene and retinol.¹⁰ Carotenoids function as antioxidants and photoprotectors.¹² The most important member of the group is β -carotene and there is no difference between naturally occurring and chemically synthesized β -carotene.¹⁰ Carotenoids function as inhibitors of free radical and singlet oxygen induced lipid peroxidation.^{10,12} They can be found in carrots, pumpkin, sweet potatoes, mangos and papaya.^{10,12} β -carotene is an endogenous photoprotector which prevents UV-induced erythema formation. β -carotene supplementation reduces the rate of mitochondrial mutation in human dermal fibroblasts after UV irradiation thereby, reducing wrinkling and irregular pigmentation of aging skin.^{10,12}

Photo protection following oral administration of β -carotene is dependent on dose and duration of

treatment. In a review article on discovering the link between nutrition and skin aging, Schagen et al reported that, at least 7 weeks of use of. β -carotene with doses > 12 mg/d is required for skin aging and that treatment duration of only 3–4 weeks was of no effect.¹⁰

Retinoids when used topically inhibit the UV-induced metalloproteinase (MMP) mediated breakdown of collagen and protect the skin against UV-induced decreases in procollagen expression.¹⁰ However, oral administration of retinol or retinal derivatives is not approved as an anti-aging treatment.¹⁰ This is because of the liver toxicity associated with high doses, increased risk of cell aging and tumor promotion.¹⁰

VITAMIN D: It acts as a prohormone and it is synthesized in the human skin.¹⁰ Vitamin D is found in skin, fatty fish, egg yolk, fortified foods (milk, cereals and margarine).¹⁰ It functions to protect human skin cells from UV-induced cell death, apoptosis and skin atrophy.^{10,19} This is done by the inhibition of the activation of stress-activated protein kinases and the suppression IL-6 production.¹⁰ Vitamin D prevents skin damage and carcinogenesis. With increasing age, the ability of the skin to produce vitamin D₃ and its protective effects declines.¹⁰ Vitamin D and calcium supplementation therefore become important as we age.¹⁰ Oral vitamin D treatment showed skin cancer prevention, which is linked to anti-aging effects.¹⁰ Oral dose of vitamin D 400 IU is recommended for those aged 50–70 years and 600 IU in those >71 years.¹⁰

POLYPHENOLS: They possess anti-aging and antioxidant properties.¹⁰ Sources include; Fruits, the skin of grapes (but not in the flesh), fruit juices, tea, coffee and red wine, vegetables (onions, tomatoes), cereals, chocolate and dry legumes.¹⁰ Oral intake can be as high as 1 g/day.¹⁰ Polyphenols protect the skin from UV radiation and pathogens.¹⁰ This group is divided into; phenolic acids, flavonoids, stilbenes, and lignans.¹⁰ Flavonoids are found in the bark of pear, apple, cherry and other fruit trees.¹⁰ Human studies on the effect of flavonoids on skin aging are rare.¹⁰

RESVERATROL: They function as antioxidants, chelating agents, radical scavengers and anti-inflammatory inhibiting IL-8.¹⁰ Resveratrol is indicated in skin anti-aging.¹³ They prevent cell death after exposure to free radicals in the skin, improve systemic oxidative stress and provide skin antioxidant power.^{10,13} Buonocore et al reported an improvement in skin moisturization and elasticity, decrease in skin roughness and depth of wrinkles following the administration of one capsule of resveratrol-procyanidin blend a day for a period of 60 days.¹³ One capsule contains; 133 mg grape (8 mg transresveratrol), 14.63 mg procyanidins, 0.67 mg anthocyanosides, 0.4 mg flavonoids, 1.3 mg other stilbenes, 125 mg pomegranate (3.75 mg procyanidins), 8.75 mg punicalagin-ellagic acid, 50 µg selenium, 26 mg silicon dioxide, and 45 mg maltodextrin.¹³

CURCUMIN: They are found in turmeric (member of the ginger family) and they reduce oxidative stress and inflammation.¹² Curcumin also act as an antioxidant, suppress ROS production, scavenge free oxygen radicals and inhibit lipid peroxidation.¹²

GREEN TEA: Topical or oral administration of green tea leads to inhibition of chemical carcinogens and UV radiation-induced skin carcinogenesis.²⁰ Green tea acts as an antioxidant and ROS scavenger in the epidermis to reduce the number of sun burn cells, DNA damage and antiaging.²⁰ There are 2 active molecules in green tea; green tea polyphenol (GTPP) epigallocatechin (EGC)-3-gallate (EGCG). These molecules were found to inhibit chemical carcinogenesis.²⁰ In humans, topical application of green tea is not effective due to poor epidermal penetration.²⁰ Green tea polyphenols result in histologic improvement in elastic tissue. Figure 2

UBIQUINOL (COENZYME Q10): Coenzyme Q10 (CoQ10) is a fat-soluble, vitamin-like antioxidant. It is found in the epidermis where it acts as barrier to oxidant assault in combination with other enzymatic and non-enzymatic substances.^{6,10} Sources of CoQ10 include oily fish (salmon and tuna), organ meats (liver), whole grains, a balanced diet, supplements (soft gel

capsules, oral spray, hard shell capsules, tablets).¹⁰ Zmitek et al demonstrated in a double blinded study of 34 participants for 12 weeks that, oral supplementation with CoQ10 improve dermal density and facial wrinkles.⁶ CoQ10 is also effective topically.^{6,21} Oral administration of vitamin E (50mg), coenzyme Q10 (50mg) and selenium (50mg) combined with topical biocosmetics increases stratum corneum CoQ10 after 15 and 30 days.²¹

ESSENTIAL FATTY ACIDS (EFA): Found in fish and shellfish, fish oil supplements, flaxseed, hemp oil, soya oil, canola oil, chia seeds, pumpkin seeds, sunflower seeds, leafy vegetables, walnuts, sesame seeds, avocados, salmon and albacore tuna.^{10,12} Fish oil supplements are made from mackerel, herring, tuna, halibut, salmon, cod liver, whale blubber, or seal blubber. Linoleic and oleic acids are the two essential fatty acids. Inadequate linoleic acid results in senile dryness and skin atrophy.¹⁰ Essential fatty acids inhibit UVB induced MMP production.¹² Dietary supplements of fish oil rich in omega-3 polyunsaturated fatty acids for 3 months has been reported to reduce UV-induced inflammation due to lowered prostaglandin-E2 levels.¹⁰ Oral administration of an antioxidant mixture containing vitamin C, vitamin E, pycnogenol and evening primrose oil inhibits wrinkle formation.¹⁰ Essential fatty acids can be combined with calcium, iron, or vitamins A, B1, B2, B3, C or D for oral administration.¹⁰

COLLAGEN PEPTIDES: Used as collagen or collagen hydrolysates either as food or as dietary supplements for the improvement of skin properties.^{2,4,22} Effective as low molecular weight collagen peptides (LMWCP) derived from fish.^{2,4,22} Kim et al in a case control study of 64 individuals using 1000 mg of LMWCP once daily for 12 weeks reported an improvement in hydration, elasticity and wrinkling.⁴ Collagen peptides are nutraceuticals derived from marine collagen peptides (MCPs) due to their high homology with human collagens, safety, bioavailability through gut.² They however, have the disadvantage of increasing the risk of oxidative stress connected with collagen synthesis and to ROS production by MCPs-stimulated phagocytes.² De Luca et al

reported an improvement skin moisture, elasticity and sebum production following intake of collagen peptides.² This was the result of a study involving 50 individuals using a combination of MCPs derived from skin of deep sea fish (MCPs, 570mg), grape-skin extract (10mg), coenzyme Q10 of plant origin (10mg), luteolin (10mg), and selenium (0.05mg) formulated in soft gelatine capsules.² Figure 3. In another study on 41 males, the daily use of a nutraceutical containing MCPs and polysaccharides, grape and tomato seed extracts, vitamin C and zinc can improve the signs and symptoms of skin aging.²

OTHER PLANT EXTRACTS: Natural remedies have recently gained the interest of the society. Increasingly, clinical studies on the role of plant extracts in anti-aging are being conducted.^{3,23} Following a case control study of 92 individuals, *Boesenbergia pandurata* a plant extract was found to improve skin hydration, gloss, wrinkling and elasticity after 12 weeks.³ In another case-control study by Choi et al in Korea on the protective effect of fermented honeybush on skin aging, skin wrinkles, elasticity and hydration improved on a daily dose of either 400 or 800mg/d after 12 weeks.²³

In a Dutch study of 2753 individuals by Mekic et al, a healthy diet resulted in less facial wrinkles in women but not in men.⁷ The reason for the gender difference was attributed to the difference in wrinkling pattern between males and females.⁷ A Red meat and snack-dominant diet is associated with facial wrinkling in women whereas a fruit-dominant diet is associated with fewer wrinkles.⁷

SIDE EFFECTS OF NUTRACEUTICALS:

Although nutraceuticals are beneficial in anti-aging, there are associated side effects. Nutraceuticals are unregulated and there is no regulation for complete disclosure of their contents.²⁴ Side effects due to unlabeled contaminants and preservatives have been reported.²⁵ Some of the constituents like ascorbic acid are associated with photodermatitis.²⁶ Liver toxicity is associated with excess vitamin A

derivatives and green tea.^{10,27} Excess vitamin A supplementation can cause intra-hepatic cholestasis, bone mineral density and increased fracture risk²⁸ Prolonged use of β -carotene supplementation is associated with lung cancer.^{12,29} High serum levels of vitamin D is associated with increased mortality, pancreatic cancer, cardiovascular events, falls and fractures in the elderly.¹⁰

Flavonoids are reported to have eostrogenic properties and to cause uterine hypertrophy, reproductive tract malformations, reduce testicular size, reduce fertility (due to inhibition of androgen production).²⁹ Vitamin E doses of 800–1200 mg/d can result in bleeding due to antiplatelet action.²⁹ In addition, vitamin E supplementation following radiation was found to result in increased cancer recurrence within the first 3.5 years of follow-up.³⁰ Interaction with prescribed medications is another adverse effect of nutraceuticals. In patients taking anticoagulant medications such as warfarin, nutraceuticals can potentiate the anticoagulation and promote bleeding.^{14,29}

CONCLUSION

The use of nutraceuticals in anti-aging is increasingly gaining ground in research with a number of proven effects. Nutraceuticals support the endogenous antioxidant system that are normally present in the skin. They are not without there adverse effects. A permanent intake of non-physiologically high dosages of isolated antioxidants should be avoided. The consumption of fruits and vegetables, avoidance of adverse environmental factors is necessary for a youthful skin.

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- v Figures 1-3, courtesy of Google Images. <https://www.google.com/search?q=nutraceuticalica> Site assessed 27th of October, 2020



Figure 1. Nutraceuticals.



Figure 2. Nutraceuticals. Green tea



Figure 3. Nutraceuticals: Collagen peptides in combination with polyphenols