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Antioxidants

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Abstract

Antioxidants are chemicals that can prevent oxidative stress or slow cell damage. Natural antioxidants are mainly found in fruits and vegetables, marine plants, and some seafood that eat marine plants. Most commonly used antioxidants in vitiligo are; vitamin C, vitamin E, ginkgo biloba, vitamin A, polypodium leucotomas extract, polyunsatured fatty acids, quercetin flavonoids, tea polyphenols, soy isoflavones, resveratrol, curcumin, capsaicin, gluthathione, alpha lipoic acid, phenylalanine, cucumis melo, minerals.

Keywords: Antioxidants; Vitiligo; Oxidative stress

Introduction

According to autocytotoxic hypothesis; oxidative stress has been suggested to be the initial pathogenic event in melanocyte degeneration and loss with H_2O_2 accumulation in the epidermis of patients with active disease [1]. Significantly higher levels of Superoxide Dismutase (SOD) has been observed in the skin [2], erythrocytes [3,4], peripheral blood mononuclear cells [3,5] and serum [6,7] of vitiligo patients. Reduction in catalase (CAT) activity has been demonstrated in the epidermis [8,9], peripheral blood mononuclear cells [3] and in melanocytes [1].

In vitiligo patients lower levels of total antioxidant activity, superoxide dismutase, glutathione peroxidase, catalase, vitamin E, vitamin C and higher levels of oxidative stress indicators cause oxidative stress. There is imbalance of Reactive Oxygen Species (ROS) system in vitiligo melanocytes. Reactive oxygen species cause lipid peroxidation of cellular membrane of melanocytes. Consequently increased levels of ROS are capable of bleaching constitutional melanin and causing membrane lysis through lipid peroxidation reactions [10-13].

Increased oxidative stress and depletion of antioxidants reserves cause skin oxidative damage.

Antioxidants are chemicals that can prevent or slow cell damage. Antioxidant is not a substance; it's a behavior. Antioxidant properties can donate electrons and counteract free radicals. Natural antioxidants are mainly found in fruits and vegetables, marine plants, and some seafood that eat marine plants. There are thousands of antioxidant compounds, the most common dietary ones are vitamins A, C, and E and beta-carotene. Antioxidants can also be produced artificially and consumed in supplement form [14] (Table 1).

Vitamin C

Vitamin C is essential co-factor for collagen synthesis. Topical L-ascorbate improves epidermal barrier function. It has anti-aging effects and photoprotection from UV A and B. It causes neocollagenesis, inhibition of melanogenesis and improvement of a variety of inflammatory skin disorders [15,16] (Table 2).

Studies demonstrate; Oral combination of vitamins C and E in high doses provide protection against UV induced erythema [17].

Oral vitamins C, E, A, B12, folic acid and broadband UVB, has been followed by definite repigmentation in vitiligo patients [18].

Vitamin E

Vitamin E exists in 8 forms: 4 tocopherols and 4 tocotrienols. α-tocopherol is the most represented in humans.

Topical α-tocopherol reduces photo-aging and photo-carcinogenesis. It prevents UV-induced erythema, lipid peroxidation and immunosuppression.

Lin et al. demonstrate an increase in protection against UV-induced damage after oral administration of vitamin E combined with vitamin C [19] (Table 3).

Studies demonstrate; oral vit E has shown to increase narrow band-UVB effectiveness in vitiligo patients [20].

Ginkgo biloba

Ginkgo Biloba is one of the oldest tree species and the leaves of this herb has antioxidant effects. *Ginkgo biloba* contains bioactive constituents mainly flavonoids and some diterpene trilactones. A recent study has reported an association between daily ingestion of *Ginkgo biloba* with a significant improvement in total VASI (Vitiligo Area Scoring Index) and VETF (Vitiligo European Task Force) staging in vitiligo patients [21].

While the mechanism of *Gingko biloba* in the treatment of vitiligo

Vitamin C	Quercetin flavonoids	Glutathione
Vitamin E	Tea polyphenols	Alpha lipoic acid
Ginkgo Biloba	Soy isoflavones	Phenylalanine
Vitamin A	Resveratrol	Cucumis melo
Polypodium Leucotomas Extract	Curcumin	Minerals
Polyunsatured Fatty Acids	Capsaicin	……

Table 1: Most commonly used antioxidants in vitiligo.

Orange	Lime	Strawberry	Mandarin
Lemon	Cranberry	Cauliflower	Mango
Melon	Tomato	Garlic	Blackberry
Kale	Blueberry	Grapefruit	Potato
Passion fruit	Pineapple	Raspberry	Broccoli
Spinach	Papaya	Kiwi	

Table 2: Natural sources of vitamin C.

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Wheat germ oil	Tomato products	Nuts	Mangoes
Sunflower oil	Pumpkin	Nut oils	Broccoli
Safflower oil	Asparagus	Sweet potato	Avocados
Green leafy vegetables	Papayas	Rockfish	

Table 3: Natural sources of Vitamin E.

is unknown, ginkgo's immunomodulatory, antioxidant, and anxiolytic properties may be of benefit to vitiligo sufferers [22,23].

Vitamin A

Includes retinol and carotenoids (α/β/γ-carotene, lycopene and the xanthophylls lutein and zeaxanthin). Vitamin A is fat-soluble and can be stored in keratinocytes as retinyl esters. Carotenoids are useful to protect against UV-induced damage [24] (Table 4).

Studies demonstrate; daily oral β-carotene (30 mg) can prevent and repair photoaging and increases synthesis of procollagen type I [25]. Topical β-carotene (2 mg/cm^2) provides protection against reactive oxygen species in the human skin exposed to infra-red radiation [26].

Oral supplementation with vit A plus vit C and vit E, and minerals promoted vitiligo lesion repigmentation in the mice settings [27].

Polypodium Leucotomos (PL)

Polypodium leucotomos extract comes from a tropical fern plant grown in Central and South America. Recently, clinical research has shown that it has antioxidant and photoprotective properties PL acts as a scavenger to mop up free radicals and Reactive Oxygen Species (ROS), PL inhibits the depletion of Langerhans cells. PL reduces the number of sunburn cells. PL protects DNA by inhibiting the formation of cyclobutane pyrimidine dimers induced by UVB radiation. PL preserves skin tissue structure by inhibiting the infiltration of mast cells into skin [28,29].

Omega-3(three) Polyunsatured Fatty Acids

Omega-3(three) polyunsatured fatty acids are antioxidants and inhibitors of pro-inflammatory cytokines and free radicals. They protect auto-immunity by enhancing antioxidant enzymes. The enrichment of cell membranes with Omega-3 has been reported to increase the glutathione (GSH) peroxidase activity [30]. High doses of Omega-3 have been shown to decrease UVB-induced erythema [31]. Omega-3 seem to influence depressive disorders, that affect many patients with vitiligo [32] (Table 5).

Flavonoids and Green Tea Extracts

Flavonoids are the antioxidants most commonly found in the diet. Common sources of flavonoids in the diet are: wine, beer, tea, vegetables, fruit, and soy products. Both quercetin and green tea extract were found to have strong cytoprotective effects on H_2O_2 induced cell death [33].

Quercetin

Quercetin is a member of the flavonoids. In vitro studies demonstrate that quercetin can efficiently prevent keratinocyte oxidative damage induced by H_2O_2 exposure [34]. Topical application of the quercetin has been shown to prevent UVC-induced liposome peroxidation, UVB-induced myeloperoxidase activity and glutathione depletion [35] (Table 6).

Soybeans

Soybeans and associated food products are a rich source of flavonoids. Genistein is an oestrogen that occurs naturally in soya beans. Oral genistein is shown to decrease UVB-induced skin photoaging, carcinogenesis, inflammation and immunosuppression in a rodent model [36]. Topical genistein reduces erythema and histologic inflammation induced by PUVA in mice [36].

Genistein has collagen-stimulating effects, by increasing collagen (COL1A2) gene expression [37].

Green Tea Polyphenols

The term green tea polyphenols is used to refer to several potent antioxidants that appear in green tea leaves. The most (60-80%) polyphenols contained in green tea leaves are cathechins: epicatechin, epicatechin-3-gallate, epigallocatechin [38].

Epigallocatechin-3-gallate (EGCG) is the most important molecule. As antioxidants, cathehins are more potent than vitamins C and E. Cathechins are able to regenerate oxidized vitamin E. Epigallocatechin-3-gallate (EGCG) has photo-protective, anti-inflammatory, anti-carcinogenic effects and it can inhibit collagenase activity. Several studies demonstrate that, oral administration of EGCG significantly increases the minimal erythema dose to UV and improves microcirculation [39]. Topical application of EGCG inhibits carcinogenesis and selectively increases apoptosis in UVB-induced skin tumors [40].

Resveratrol

Resveratrol is a type of natural phenol. Its benifical effects: anti-oxidant, anti-inflammatory, anti cancer, blood sugar-lowering. Studies demostrate that oral resveratrol can prevent UV-induced tumorigenesis and cutaneous inflammatory disorders and increases cell survival [41]. Topical use of resveratrol on hairless mice before UVB; decreased erythema, reactive oxygen species production and inflammation [42] (Table 7).

Curcumin

Curcumin; a polyphenol derived from *Curcuma longa*, is an active

Liver (beef, pork, chicken, turkey, fish)	Papaya	Broccoli leaf	Collard greens
Sweet potato	Mango	Butter	Cheddar
Cheese	Pea	Kale	Melon
Cantaloupe	Broccoli	Spinach	Egg
Apricot	Carrot	Pumpkin	Milk

Table 4: Natural sources of Vitamin A.

Cold water	Flaxseeds	Brussel sprouts
Oily fish (salmon, herring, mackerel, anchovies, sardines)	Nuts	Blackberry
Fish oil	Eggs	Raspberry

Table 5: Natural sources of Omega-3(three) polyunsatured fatty acids.

Apples	Leafy green	Whortleberry	Rowanberry
Onions (++red onion)	Vegetables	Lingonberry	Raspberry
Red grapes	Lovage	Cranberry	Broccoli
Citrus fruit Tomato	Legumes	Chokeberry	Caparis spinosa plant

Table 6: Natural sources of Quercetin.

Grapes	Peanuts	Apples	Chocolate
Wines	Mulberries	Cocoa	
Pinot noir	Blueberries	Powder baking	

Table 7: Natural sources of Resveratrol.

ingredient in the spice turmeric. In the recent studies; Curcumin has anti-oxidant, anti-proliferative, anti-inflammatory, antiviral, antibacterial and antifungal properties. It reduces wound-healing time, improves collagen deposition and increases fibroblast and vascular density in wounds. Curcumin could be effective in treatment of different skin diseases (Phototoxic dermatitis, vitiligo, psoriasis, chronic inflammatory diseases…) [43,44].

Capsaicin

Capsaisin is an active component of chili peppers, which are plants belonging to the genus *Capsicum*. Capsaicin is a potent anti-inflammatory agent which has been used for: pain and itch relief, because of its desensitization property. It's benefits; cancer prevention, cardiovascular diseases, weight reduction. High antioxidant and anti-apoptotic potential of capsaicin have been recently described.

Becatti et al. demonstrate; Pre-treatment with capsaicin inhibits keratinocytes apoptosis in peri lesional vitiligo skin, increases cellular total antioxidant capacity and improves mitochondrial activity and cell metabolism [45].

Gluthatione

Glutathione (GSH) is a tripeptide and contributes to the functional vitality and morphological integrity of cells. GSH provides efficient protection against UVB-rays damages [46]. A severe GSH depletion has been documented inside keratinocytes after UV irradiation [47]. A few studies demonstrate; GSH supplementation is providing intrinsic wide-spectrum photo protection, cancer prevention and anti-aging effect [48].

Alpha Lipoic Acid

Alpha-lipoic acid or ALA is a naturally occurring compound that's made in the body. It serves vital functions at the cellular level, such as energy production. ALA is an antioxidant! There are food sources of ALA such as yeast, organ meats like liver and heart, spinach, broccoli, and potatoes. The study of Dell'Anna et al. demonstrate; Oral supplementation of alpha-lipoic acid before and during NB-UVB significantly improves the clinical effectiveness of NB-UVB and reducing vitiligo associated oxidative stress [49].

Phenylalanine

Phenylalanine is an α-amino acid and a precursor for tyrosine. Phenylalanine is found naturally in the breast milk of mammals. Some studies demonstrate phenylalanine antioxidant effects on vitiligo with or without UVA [50,51].

Cucumis melo

Cucumis is a plants genus in the Cucurbitaceae family, which includes the cucumber, muskmelons, the horned melon, and the West Indian gherkin. *Cucumis melo* exctract is a rich antioxidant that naturally contain a high superoxide dismutase activity [52].

Minerals

The best minerals with antioxidant effects are Manganese, Selenium, and Iodine. These minerals either act as antioxidants on their own or act in conjunction with other cells in the body to stimulate the production of antioxidants. A few studies demonstrated minerals antioxidants efficacy in vitiligo [53-55].

Consequently antioxidants may play an adjuvant role in the management of vitiligo in addition to specific therapies. Up to date there are no definite dosing regiments for antioxidants. More studies are needed to determine their side effect profile.

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