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Mini Review on Dietary Supplements

Supplemental Use of the Carotenoids Lutein and Zeaxanthin

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Abstract

Lutein and zeaxanthin, commonly referred to as the macular pigments, are carotenoid antioxidants that provide protection against reactive oxygen species in the eyes and skin. This review article discusses the health effects of these carotenoids, their role in the pathogenesis of age-related macular degeneration (AMD), supplemental use and bioavailability, dosing, safety and drug-nutrient interactions.

Keywords: Lutein; Zeaxanthin; Carotenoid; Antioxidant; Age-related Macular Degeneration; Macular Pigment Optical Density; Marigold; Bioavailability; Form; Dosing; Safety; Drug-Nutrient Interactions

Abbreviations

AMD: Age-related Macular Degeneration;

MPOD: Macular Pigment Optical Density;

ADI: Acceptable Daily Intake;

GRAS: Generally Recognized As Safe

Introduction

Lutein and zeaxanthin are two yellow-colored carotenoids known as xanthophyll carotenoids. Over 600 carotenoids have been discovered, with only about 40 of these having been found in human serum and tissues. Lutein accounts for approximately 20% and zeaxanthin 3% of total serum carotenoids [1]. Zeaxanthin and lutein are isomers of one another; they have the same chemical components and differ only slightly in structure and function [2]. They are often found together in nature, imparting a yellowish color to many foods such as corn, peppers, melons, carrots, oranges, squash and eggs and are also present in leafy greens. Serum carotenoid levels can be measured as a tissue marker for a fruit- and vegetable-rich diet [2]. Unlike some other carotenoids, lutein

and zeaxanthin do not convert into vitamin A in the body [3].

Health Effects

The yellow color of lutein and zeaxanthin is related to their ability to filter and absorb short-wave blue light, the visible light most damaging to the eye [2]. In addition, lutein and zeaxanthin have been found to improve vision and act as antioxidants by scavenging reactive oxygen species [1]. The antioxidant effects of lutein and zeaxanthin may also positively benefit the skin, reduce signs of premature aging and exert profound effects in the eye [2]. Both lutein and zeaxanthin, commonly referred to as macular pigments, concentrate in the macula lutea, a yellow spot located in the retina of the human eye [1,3]. Oxidative stress, aging, smoking and

exposure to UV or blue light have been known to contribute to the development of cataracts and age-related macular degeneration (AMD), and research has associated both lutein and zeaxanthin with decreased incidence of these factors [1]. Additionally, consuming a high-lutein and high-zeaxanthin diet in combination with supplementation has been shown to raise serum levels of these carotenoids and increase the macular pigment optical density (MPOD). Low density of pigment in the macula is a risk factor for AMD, and increased intake of lutein and zeaxanthin can directly increase MPOD in humans [3]. Therefore, lutein and zeaxanthin may combat the oxidative stress implicated in AMD pathogenesis and may prevent or reverse the development of AMD, improving overall visual function [4]. Studies also suggest that lutein may play a role in the immune response. Individuals with low serum lutein and zeaxanthin and children with acute infections may exhibit high levels of C-reactive protein and elevated white blood cell counts, indicating a mechanism of action affecting immunity [2].

Bioavailability/Form

Supplemental lutein and zeaxanthin are most commonly extracted from marigold flowers and are available in either free or esterified form. Carotenoids are generally hydrophobic and are not soluble in water-based medium of the human digestive tract, therefore, dietary fat is required for optimal bioavailability and proper absorption [1]. The esterified forms require an even higher amount of dietary fat for proper absorption because the fatty acid groups attached to the carotenoids must be cleaved by pancreatic enzymes most likely secreted as a result of fat ingestion [2]. Processing and the supplement medium also affect the bioavailability of these carotenoids. One in vitro study showed that fruits and sweet potatoes transfer nearly 100% of their lutein and zeaxanthin, while spinach and broccoli transfer between 19% and 38% [1]. Therefore, a medium that mimics the matrix of fruit or sweet potatoes, compared to that of spinach or broccoli, may increase bioavailability of supplemental lutein and zeaxanthin. The lipoprotein profile of the consumer also plays a role in absorption, since lutein and zeaxanthin are transported by HDL and LDL particles through the blood to target tissues, including the macula as well as skin, cervix, brain, breast and adipose tissue [1,2]. There is also research suggesting that lutein and zeaxanthin may exert more powerful antioxidant effects when taken in combination with vitamins C and E [3].

Dosing

Some experts consider lutein and zeaxanthin conditionally essential because low serum levels of these carotenoids have been associated with age-related macular degeneration, breast cancer, prostate cancer, colon cancer, cervical cancer, HPV persistence, type 2 diabetes, impaired glucose metabolism, chronic cholestatic liver diseases and all-cause mortality [2]. A joint

committee of the Food and Agriculture Organization and the World Health Organization established the acceptable daily intake (ADI) of marigold- and zeaxanthin-derived lutein at 0-2mg/kg of body weight. The Panel on Food Additive and Nutrient Sources Added to Food established a marigold-derived lutein ADI of 1mg/kg of body weight daily. Generally, serum levels of lutein and zeaxanthin can be expected to rise 1% with each 10% increase in consumption of dietary lutein or zeaxanthin [2]. Studies show that large amounts of lutein, zeaxanthin and β -carotene administered together affect serum, tissue and retinal concentrations. Retinal concentrations of lutein and zeaxanthin increased 128% and 116% respectively when a cohort was fed a diet high in these carotenoids for 28 days (27.2mg/kg lutein and 15.3mg/kg zeaxanthin) [1]. Additionally, supplemental lutein at 3.7mg and zeaxanthin at 0.8mg significantly increased MPOD and serum concentrations over 8 weeks [1]. Concentrations of these carotenoids tend to be lower in smokers, younger people, those with low non-HDL cholesterol, those who consume high amounts of alcohol, people with high BMIs, and those who malabsorb fat-soluble vitamins [2]. These populations may benefit from supplemental lutein and zeaxanthin, although these carotenoids may not be strong enough antioxidants to combat the oxidative stress caused by smoking alone [3]. Lutein and zeaxanthin are available in supplement form from several manufacturers, with doses generally ranging from 6mg to 20mg [5].

Safety/Health

Purified crystalline lutein is generally recognized as safe (GRAS) and is likely safe when used at doses of up to 40mg daily for up to nine weeks or 15mg three times weekly for up to two years [5]. Caution should be taken when supplementing lutein and zeaxanthin in patients at risk for cardiovascular disease, cancer and hypoglycemia [5]. Supplementation should be avoided in patients hypersensitive to lutein or zeaxanthin. There is no information regarding lutein or zeaxanthin safety for use during pregnancy in the National Institute of Health's Lactation and Toxicology Database (LactMed), although increased plasma lutein has been associated with decreased pre-eclampsia risk [5].

Drug/Nutrient Interactions

Those taking simvastatin, cholestyramine, cardiovascular medications, hyperglycemic medications, stanols, sterols and drugs metabolized by cytochrome P450 enzyme pathway should be cautious with supplemental use of lutein and zeaxanthin [5]. Use of the cholesterol medication colestipol for six months has been shown to reduce blood levels of carotenoids [6]. Several nutrients have been shown to have health-positive effects when taken simultaneously with lutein or zeaxanthin including bilberry extract, omega-3 fatty acid-rich fish oil and DHA, black currant extract, iron and retinol. There is inconclusive evidence regarding the effects of supplementation with

other carotenoids along with lutein and zeaxanthin [5].

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