# Dietary Lutein Reduces Ultraviolet Radiation-Induced Inflammation and Immunosuppression

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**Ultraviolet radiation (UVR) promotes skin cancer development by mutagenic, immunosuppressive, and oxidative-stress-inducing mechanisms; however, certain antioxidants may counteract and prevent UVR-induced photodamage. Lutein is a xanthophyll carotenoid with potent antioxidant activity. Because reactive oxygen species (ROS) are believed to have a role in UVR-induced skin damage, we investigated whether lutein can modify UVR effects including the tissue swelling response to midrange UVR (280–320 nm, ultraviolet B (UVB) radiation) and UVB suppression of contact hypersensitivity (CHS) in both the local and the systemic models of UV-induced immunosuppression. We found that compared to mice fed the standard laboratory diet, mice fed dietary lutein demonstrated significant inhibition of ear swelling owing to UVB radiation. Mice exposed to 1700 J per $m^2$ UVB radiation four times at daily intervals and then sensitized to dinitrofluorobenzene at the site of irradiation showed a decreased CHS response upon challenge. This suppression by UVB radiation was significantly inhibited by lutein feeding. When UVB radiation was given at a single dose of 10,000 J per $m^2$ to inhibit the induction of CHS at a distant, nonirradiated site, no effect of lutein was seen. Finally, lutein accumulated in the skin of mice following diet supplementation and was shown to decrease ROS generation following UVR exposure. Thus, lutein modulates the skin's response to UVR and may contribute to the defense against some of the deleterious effects of solar radiation.**

Key words: antioxidant/ultraviolet radiation/immunology.
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Exposure to ultraviolet radiation (UVR) induces a variety of biologic effects including inflammation, sunburn cell formation, immunologic alterations, and photoaging (Taylor *et al*, 1990; Hruza and Pentland, 1993). Exposure to ultraviolet B (UVB) radiation (290–320 nm) suppresses the immune system (Kripke, 1984) and is the primary cause of nonmelanoma skin cancer in humans and animals (Urbach, 1997). UVB radiation critically damages cellular macromolecules and induces the formation of reactive oxygen species (ROS) (Fuchs, 1992). Ultraviolet A radiation (320–400 nm) contributes up to 95% of total UV exposure and is a significant source of oxidative stress in human skin (Tyrrell, 1991; Parisi and Wong, 2000). UVR-induced ROS include superoxides, singlet oxygen, and hydroxyl radicals and are believed to contribute to skin cancer formation, certain photodermatoses, sunburn, and photoaging (Black, 1987; Darr and Fridovich, 1994). To protect cells from UV-induced damage, the skin has an elaborate antioxidant system consisting of enzymatic and nonenzymatic components to quench reactive oxygen intermediates. Nevertheless, excessive exposure to UVR overwhelms and depletes the cutaneous antioxidant supply leading to a state of oxidative stress (Fuchs, 1998).

In recent years, the use of supplementary antioxidants as photoprotective agents has been explored. UV-induced erythema in humans is reduced following supplementation with an antioxidant combination that includes β-carotene, vitamin C, and vitamin E (Gruel *et al*, 2002) and following topical application of green tea polyphenol extracts (Elmets *et al*, 2001). The soybean isoflavone genistein inhibits UVB-induced oxidative events in murine skin (Wei *et al*, 2002), and trace minerals such as zinc, with antioxidant properties, are also reported to be photoprotective (Rostan *et al*, 2002). Despite the numerous antioxidants being investigated as potential protective agents, currently only β-carotene has been shown to be effective against visible light sensitivity and is thus recommended for the treatment of erythropoietic protoporphyria (Mathews-Roth, 1998; Rhodes, 1998). Carotenoids are lipophilic micronutrients with the ability to quench ROS and inhibit free radical reactions (Sies and Stahl, 1995). Epidemiologic studies show that a high intake of carotenoid-rich foods is associated with a reduced incidence of many forms of cancer and suggest that this association is due to the antioxidant properties of these compounds (Block *et al*, 1992). Carotenoids are present in the epidermis and dermis and are believed to play an

Abbreviations: CHS, contact hypersensitivity; DHR, dihydrorhodamine; DNFB, dinitrofluorobenzene; ROS, reactive oxygen species; UVB, ultraviolet B; UVR, ultraviolet radiation.

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