β-Carotene and Protection Against Photosensitization in Plants and in Humans

Micheline M. Mathews-Roth, M.D.
Channing Laboratory, Department of Medicine, Brigham and Women's Hospital
Harvard Medical School, Boston, MA, USA (*mmmathroth@rics.bwh.harvard.edu*)

One of the functions of carotenoid pigments in green plants and photosynthetic bacteria is to protect them against the damage caused by photosensitization by the organisms' own chlorophyll. Sistrom, Griffiths and Stanier (1) were the first to demonstrate this protective function. They studied the photosynthetic bacterium *Rhodopseudomonas spheroides* and a carotenoidless mutant of this organism: they found that when both strains were grown in the presence of light and air, the mutant was killed, but the wild-type, with its carotenoid pigments, survived. They showed that the cells' bacteriochlorophyll was responsible for killing the mutant, that both oxygen and light were needed for the killing reaction to occur, and that the carotenoid pigments were functioning as protective agents against this lethal photosensitization. Their finding that carotenoids can protect against chlorophyll photosensitization has been confirmed in other photosynthetic bacteria, algae and green plants (2).

Kunisawa and Stanier (3) investigated a non-photosynthetic carotenoid-containing bacterium, *Corynebacterium poinsettiae,* and its carotenoid-less mutant, and found that when these bacteria were exposed to light and air in the presence of an exogenous photosensitizer, (toluidine blue), the mutant was killed, but the wild-type, with its carotenoid pigments, was not killed. However, they could not demonstrate that the cells contained an endogenous photosensitizer, and so were not sure what value carotenoid photoprotection was to the cells.

Sistrom and I (4,5) demonstrated that non-photosynthetic bacteria do indeed contain endogenous photosensitizers: we exposed wild-type *Sarcina lutea*, another non-photosynthetic carotenoid-containing bacterium, and its colorless mutant to natural sunlight in air for 4 hours, we found that, at these high light intensities, the mutant was killed and the wild-type was not, and that here also, oxygen was needed for killing to occur. Other workers have since confirmed the protective function of carotenoids in non-photosynthetic bacteria (6).

Since carotenoids could prevent photosensitization by chlorophyll, the molecule of which contains protoporphyrin, I hypothesized that carotenoids might be able to lessen photosensitization in patients who have a genetic disease called: erythropoietic protoporphyria (EPP) (7). EPP is a form of porphyria: in this disease, protoporphyrin accumulates in the patient's red blood cells, leaks out of the cells, and causes photosensitivity in the sun-exposed skin, which results in itching and burning of the exposed skin. But first I had to test my hypothesis in an animal model. Eighteen to 24 hours before light exposure, a suspension of 3 mg beta-carotene in Tween-80 (8) was given intraperitoneally to one group of mice, and the equivalent volume of Tween-80 alone was given intraperitoneally to a second group of mice. Just prior to light exposure, each mouse in both groups received 1 mg of hematoporphyrin derivative (9) intraperitoneally. I found that significantly more animals which had received the beta-carotene survived the treatment with hematoporphyrin and light exposure than did those which had not received the beta-carotene (10). Thus, beta-carotene was effective in mice in preventing the lethal photosensitivity induced by injection of hematoporphyrin and exposure to visible light.

With the success of the study in mice, I now felt that we could try carotenoid therapy in erythropoietic protoporphyria. We first treated 3 EPP patients, two adults and an 11-year old girl, with 10% beta-carotene "beadlets" (Former Roche Vitamin, currently owned by DSM Nutritional Products, Basel, Switzerland), a highly bioavailable form of beta-carotene, which allowed the patients to develop high levels of beta-carotene in their blood. We exposed a small area of their skin to a carbon arc light (340-640 nm) before they started taking their beta-carotene pills, and at intervals while they were taking them. We found that all three tolerated longer exposure to the lamp without developing photosensitivity symptoms once they were taking the beta-carotene pills. They also were able to tolerate longer exposures to sunlight (11, 12).

I then set up a collative study in 1970, including additional EPP patients of my original collaborators, Drs. Harber and Fitzpatrick (11, 12), as well as EPP patients of physicians who had read our papers, and then contacted me concerning the use of beta-carotene in their EPP patients. By the summer of 1975, we had treated 133 EPP patients with beta-carotene, using a standard protocol adhered to by all participating physicians. We found that the majority of the patients increased their tolerance to sun exposure while taking beta-carotene. In July, 1975, the U.S. Food and Drug Administration approved the use of beta-carotene for the treatment of EPP, and we terminated the collaborative study at this time and published the results of our study (13).

To treat EPP successfully, it is important for EPP patients to take beta-carotene beadlet formulation. Through the years, other doctors have also reported in the medical literature the successful use of beta-carotene, and in some cases, canthaxanthin, treatment in EPP (13: page 130).

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