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Astaxanthin and Canthaxanthin Are Potent Antioxidants in a Membrane Model

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When the conjugated keto-carotenoids, either astaxanthin or canthaxanthin, are added to rat liver microsomes undergoing radical-initiated lipid peroxidation under air, they are as effective as α-tocopherol in inhibiting this process. This contrasts with the effect of β-carotene, which is a much less potent antioxidant when added in this system, without the addition of other antioxidants. © 1992 Academic Press, Inc.

Although early epidemiological studies considered the protective effect of dietary β-carotene as being equivalent to vitamin A (1), increasing evidence suggests that carotenoids may be protective against cancer by a mechanism independent of their conversion to vitamin A (2). It has been shown that canthaxanthin, which lacks retinol activity, delays development of UVB-induced skin tumors in mice (3) and causes regression of oral carcinomas in hamsters (4). In addition, carotenoids effectively quench free radical species in liposomes (5), lipoproteins (6), membranes (7), cells (8), and animal models (9–14), as well as quenching singlet oxygen (15, 16).

The observations cited above lead to the hypothesis that carotenoids may act as anticarcinogenic agents by an antioxidant mechanism. However, this *in vivo* mechanism remains unclear, particularly when the carotenoids are compared with the classical fat-soluble antioxidant, α-tocopherol (17). Much evidence has accumulated that α-tocopherol functions as a chain-breaking antioxidant by virtue of its ability to donate a hydrogen to a peroxyl radical, thus inhibiting the chain-propagating step in lipid peroxidation. The results with carotenoids are less clear, and appear to be strongly influenced both by the oxygen concentration (17–21) and by interactions with other antioxidants, such as α-tocopherol (22). The importance of the carotenoid structure in determining antioxidant activity has been also demonstrated. Where contributions of various carotenoids to radical scavenging have been compared, β-carotene was commonly less effective than those carotenoids that possess keto groups at the 4 and 4′ positions in the β-ionone ring, such as canthaxanthin (4,4′-diketo-β-carotene) and astaxanthin (3,3′-dihydroxy-4,4′-diketo-β-carotene) (13, 23, 24).

We have previously shown that the efficiency of α-tocopherol in inhibiting azo compound-induced lipid peroxidation in solution (21) or in a membrane model (7) is markedly greater than the efficiency of β-carotene. To evaluate the *in vitro* antioxidant activities of astaxanthin and canthaxanthin in comparison with β-carotene and α-tocopherol in a membrane model, we have exposed rat liver microsomal membranes to either chelated iron (Fe^{3+}/ADP) and a reducing component (NADPH) or the water-soluble azo-initiator 2,2′-azobis(2-amidinopropane) (AAPH)[2] and measured lipid peroxidation in the presence and absence of the antioxidants.

Our data provide supporting evidence that both astaxanthin and canthaxanthin are as effective as α-tocopherol as radical-trapping antioxidants in biological membranes.

MATERIALS AND METHODS

Reagents. α-Tocopherol and β-carotene were obtained from Fluka Chemica-Biochemica (Buchs, Switzerland); astaxanthin and canthaxanthin were obtained from F. Hoffmann–La Roche (Basel, Switzerland); 2,2′-azobis(2-amidinopropane) from Polysciences, Inc. (Warrington, PA); β-nicotinamide adenine dinucleotide phosphate (β-NADPH), adenosine 5′-diphosphate (ADP), thiobarbituric acid, and butylated hydroxytoluene from Sigma Chemical Company (St Louis, MO); and ferric chloride, trichloroacetic acid, and hydrochloric acid from Fisher Scientific Company (Fair Lawn, NJ). The solvents were of HPLC grade and used without purification.

Microsomal preparation. Liver microsomes were prepared from Sprague–Dawley rats according to (25) and suspended in 0.1 M potassium

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[2] Abbreviations used: AAPH, 2,2′-azobis(2-amidinopropane); MDA, malondialdehyde.

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