REVIEW

Photoprotection by dietary carotenoids: Concept, mechanisms, evidence and future development

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Carotenoids are micronutrients present mainly in fruits and vegetables, and they are ingested from these sources with the diet. They exhibit specific antioxidant activity but also influence signaling and gene expression at the cellular level. β-Carotene and lycopene, the colorants of carrots and tomatoes, respectively, are among the most prominent members of this group of lipids, and they are usually the dominating carotenoids in human blood and tissues. Both compounds modulate skin properties when ingested as supplements or as dietary products. There is evidence that they protect the skin against sunburn (solar erythema) by increasing the basal defense against UV light-mediated damage. Their photoprotective efficacy, however, is not comparable to the use of a sunscreen. In vitro data show that also other carotenoids are efficient photoprotectors. Among them are lutein and structurally unusual phenolic polyenes like 3,3′-dihydroxyisorenieratene.

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1 Introduction

Skin as the outer barrier of our organism protects us against external noxae. Among other functions, skin plays a role in water homeostasis, regulation of body temperature and vitamin D synthesis. A balanced diet is required to maintain proper skin function and health [1]. Hence, nutritional habits affect the risk for skin diseases, premature skin aging, cutaneous structure and texture and thus overall skin appearance [2, 3]. Nutritional science, medicine, pharmacology, food technology and cosmetics are actively researching the interplay of diet and skin in order to understand the role of selected nutrients and their mechanisms of action. Upon systemic application, cutaneous effects of vitamins, secondary plant constituents, e.g. carotenoids, polyphenols or essential fatty acids, have been studied in the last decade [4, 5]. Nutracosmeticals, cosmeceuticals, and functional food with claims on skin effects are already on the market. Among them are products providing the carotenoids, β-carotene, lycopene, lutein, zeaxanthin, or astaxanthin as active principle aiming to protect exposed tissues against light-induced damage. Fruits and vegetables provide most of the carotenoids in our diet, and we are adapted to a continuous supply as we make use of some of them as precursors for vitamin A, essential for vision and cell signaling. Carotenoid pigments protect the photosynthetic apparatus in plants by dissipating excess energy, and several lines of evidence support the idea that carotenoids also protect human skin against UV-induced lesions. Increasing the carotenoid content in plants thus may also improve the nutritional quality of foods derived thereof because fundamental cellular signaling processes and protective mechanisms are usually highly conserved in nature [6].

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Abbreviations: DHIR, 3,3′-dihydroxyisorenieratene; **MMP-1,** matrix metalloproteinase-1; **ROS,** reactive oxygen species

Various fruits and vegetables of green, orange, or red color contain considerable amounts of different carotenoids [7] and are the most important sources of pure hydrocarbon carotenoids (carotenes) and oxo-carotenoids (xanthophylls). Xanthophylls are in part conjugated with different fatty acids, which further decrease their solubility in aqueous compartments. β-Carotene and lutein are widespread in nature and are present in a number of different kinds of plants. In contrast, considerable amounts of other carotenoids are synthesized only by a few plant species, and only low levels are found in others. For example, the major sources for lycopene are tomatoes and products thereof; zeaxanthin is a structural analogue of lutein but as dominating xanthophyll found only in corn (*zea mays*). Due to genetic differences as well as growth and storage conditions, the amount and composition of carotenoids in the same type of a plant may vary within a broad range (see Table 1).

2 Skin carotenoids

The bioavailability of carotenoids depends on a number of factors either related to properties of the source or consumer-dependent variation [7, 8]. Parameters influencing liberation of the compound from the food matrix, its absorption in the gastrointestinal tract, as well as its distribution, metabolism, and excretion in the organism determine overall exposure. Food matrix-associated influences on bioavailability can be categorized as interaction with other matrix constituents, structural effects of the matrix, presence or absence of enzymes improving release, interference with co-ingested food, storage form of the compound within the matrix or its subcellular location.

In addition to the characteristics of the food matrix and properties of the formulation, individual factors such as lifestyle (smoking, alcohol), individual supply and status, gender, age, or disease state affect bioavailability of carotenoids. Major interindividual differences strongly modulating bioavailability are associated with genetic variations in proteins directly or indirectly affecting absorption, distribution, and metabolism of a compound within the body [9].

Carotenoid uptake from the diet follows the pathway of lipophilic nutrients. Dietary fat consumed together with the carotenoids improves their absorption. In the blood, carotenoids appear initially in the chylomicron and VLDL fraction, whereas the levels in other lipoproteins such as LDL and HDL rise at later time points. The major vehicle of hydrocarbon carotenoids is the LDL particles, whereas the polar xanthophylls are more equally distributed between LDL and HDL. Circulating carotenoids are delivered to all tissues including the skin where they can be determined by HPLC methods from punch biopsies or non-invasively by reflection spectrometry or Raman spectroscopy [10–12].

In a study with 27 healthy adults, correlations of dermal carotenoid and plasma levels were reported [13]. Lycopene in plasma was significantly correlated with lycopene in skin and a strong positive trend between β-carotene in plasma and β-carotene in skin was determined. In contrast, plasma–skin correlations were lower and not statistically significant for lutein, zeaxanthin, and β-cryptoxanthin. Carotenoids are not equally distributed in the different skin areas, with the highest levels occurring in the skin of the forehead and in the palms of the hands and less in dorsal skin, inside of the arm, or back of hand [12, 14]. After supplementation with an algal extract providing 24 mg/day of β-carotene for a period of 12 wk, considerable increases in carotenoid skin levels were determined within the first 4 wk

Table 1. Carotenoid content of fruits and vegetables (μg/100 g wt)

Food source	Lutein		Zeaxanthin	β-Carotene	Lycopene
Apricot	120–190		0–40	590–3800	50
Broccoli		710–3300[a)]		290–1750	n.d.
Carrot		250–510[a)]		4350–8840	n.d.
Cornflakes	0–50		100–300	n.d.	n.d.
Cucumber	460–840			110–270	n.d.
Endive	2060–6150		–	1340–4350	–
Kale	4800–11 470		–	1020–7380	–
Lettuce	1000–4780		–	870–2960	–
Orange[b)]	–		–	170–480	
Pepper (green)	90–910		0–40	0–340	n.d.
Pepper (red)	250–8510		590–1350	1440–2390	–
Spinach	5930–7900			3100–4810	n.d.
Tomato		50–210[a)]		320–1500	800–12 700
Watermelon	–		–	310–780	4770–13 520

Modified from [7].
a) Lutein and zeaxanthin were analyzed together.
b) A major carotenoid in oranges is cryptoxanthin (70–140 μg/100 g).
n.d., not determined.

of application, further slightly increasing from wk 4 to week 12. Cessation of treatment led to a decrease in skin carotenoids in all areas within a period of 2 wk [12]. In a human study with lycopene at a dose of 25 mg/day for 12 wk, it was shown that lycopene skin levels are less responsive to oral supplementation than plasma levels. Preceding supplementation, a low lycopene diet induced a slow but significant decrease of skin levels, whereas upon supplementation baseline levels were restored and maintained [10]. In this study, β-carotene plasma concentration was hardly affected by lycopene intake, but β-carotene skin levels increased under lycopene supplementation. It was discussed that antioxidant lycopene protects β-carotene from oxidation and thus preserves the provitamin-A carotenoid. It has been shown that more skin lycopene is destroyed compared to β-carotene when skin is exposed to UV light, suggesting a role of lycopene in mitigating photooxidative damage in tissues as discussed above [15].

As mentioned above, xanthophylls with a hydroxyl group may occur in plants as fatty acid esters, and the major parent carotenoids are lutein, zeaxanthin, cryptoxanthin, capsanthin, or violaxanthin. Carotenyl esters have been identified in apricots, peaches, pink grape fruit, oranges, or peppers. There is evidence that the fatty acid esters are hydrolyzed prior to release into the systemic circulation; no esterified carotenoids have yet been reported in blood. However, low amounts of carotenyl esters are present in human skin [16]. Eighteen different fatty acid esters were separated in extracts from human skin samples by HPLC. Lutein, zeaxanthin, 2′,3′-anhydrolutein, α-cryptoxanthin, and β-cryptoxanthin were the major parent carotenoids and several carotenyl mono- and di-fatty acid esters were tentatively assigned, conjugated to linoleate, palmitate, oleate, myristate, or stearate. However, skin levels of carotenyl esters are low, in the range of pmol/g of human skin, which is several orders of magnitude lower than that of β-carotene.

Histologically, skin is divided into two main layers, epidermis and dermis, with the latter attached to underlying subcutaneous connective and adipose tissue. The subcutaneous layer contains sweat glands, hair follicles, blood vessels, and fat. The outer layer of the epidermis is the *stratum corneum* (horny layer), which is formed by dead and peeling cells, mainly keratinocytes, filled with mature keratin playing an important role in the barrier function of the skin [17]. There are different ways of how carotenoids may be transported and distributed to and within the different layers of our skin [18]. It has been suggested that subcutaneous tissue is a storage for carotenoids, and that it is involved in skin coloration observed after long-term intake of β-carotene, lycopene or canthaxanthin. Little is known yet about the availability of carotenoids from this apparently deep compartment. It has been suggested that carotenoids are loaded into the epidermal keratinocytes, which are continuously generated at the basement membrane and then migrate to the skin surface, transporting with them the carotenoids to the upper layers. From human photoprotection studies with carotenoids, it is known that at least 6 wk of supplementation are required to observe any effect. This is approximately the time that keratinocyte migration lasts from basal layer to the surface.

Raman spectroscopy was applied to study the distribution of carotenoids in human skin. In untreated skin, the major fraction of the carotenoids was located in the upper part of the stratum corneum [14]. Here, the authors discuss the hypothesis that carotenoids are secreted via eccrine sweat glands and/or sebaceous glands and are delivered by this way to the skin surface. A similar concept has been proposed and proven by analytical data for vitamin E [19].

3 β-Carotene and lycopene in photoprotection

UV light penetrates the different skin layers and affects specific biological structures at all levels. Penetration depth is dependent on the wavelength and on structural features, molecular patterns, and pigmentation, with influence on absorption, reflection, and light scattering [20]. With longer wavelength, the depth of penetration of UV light increases; UVA light reaches the dermis and to some extent also the subcutis, whereas UVB does not pass beyond the epidermal layer. UVB combines tissue targeting and damaging properties in a way that most of the severe consequences of UV exposure are attributed to this wavelength range [21, 22]. However, UVA radiation is involved in processes of photoaging and photocarcinogenesis.

In tissues, UV light interacts with a suitable chromophore which is either photochemically modified or acts as a sensitizer. Adjacent thymines in DNA may undergo light-induced cyclization to yield dimeric photoproducts. Such processes are mainly initiated by UVB light. In photosensitization reactions, endogenous compounds such as porphyrins, flavins, or amino acids act as sensitizing molecules. The excited photosensitizer may react in either Type I or Type II reaction sequences to produce reactive oxygen species (ROS) including radicals, hydroperoxides or excited state molecules, e.g. singlet oxygen capable of damaging DNA, lipids and proteins, followed by cellular responses such as modified gene expression.

Photoprotective effects of carotenoids have been investigated in human intervention studies with β-carotene, lycopene, canthaxanthin, lutein, and natural/dietary sources of those carotenoids including tomato products, carrot juice, algal or petal extracts. Extended reviews on study results have already been published [12, 23–26]. A number of studies investigated the effects of β-carotene on the prevention of sunburn, i.e. solar erythema formation. The solar erythema occurs as a physiological response of the skin after overexposure to UV light. Diminished erythema responses have been reported following the ingestion of synthetic β-carotene [27, 28], extracts of natural sources rich in β-carotene [29, 30] or antioxidant mixtures with

β-carotene as a major constituent [30–32]. Other studies with similar design could not prove this effect [33–36]. Based on a meta-analysis that evaluated seven human β-carotene supplementation studies on the protection against UV light-induced erythema, it was concluded that the protection against UV light-induced erythema formation requires a minimum of 10 wk of β-carotene supplementation, which was not the case in most of the studies that showed no effects [37]. Further evaluation of the literature implies that doses of about 10 mg/day are required to provide photoprotection. All the studies performed so far in this context included only a small number of subjects. None of the human intervention studies provided unequivocal evidence that photoprotection (prevention of sunburn) is mechanistically linked to the antioxidant properties of β-carotene.

Tomatoes and tomato products are major sources of lycopene. Following ingestion of dietary products rich in lycopene, photoprotective effects have been demonstrated. After 10–12 wk of intervention, a decrease in the sensitivity toward UV-induced erythema was observed in volunteers. Ingestion of synthetic lycopene for a period of 12 wk also led to a decrease in erythema. However, the difference between weeks 0 and 12 was statistically not significant [38–40]. Plant-based sources of carotenoids also contain other constitutents that might contribute to photoprotection. In this context, UV-absorbing properties of the non-colored carotenoids phytoene and phytofluene have been discussed. It has been suggested that *cis*-isomers of lycopene may play a role in context with UV absorption. *cis*-Isomers of carotenoids are frequently found in human tissues and they exhibit an additional absorption band around 350 nm for lycopene [41]. The extinction coefficient at these wavelengths depends on the location of the bond within the molecule and is highest in 15,15′-*cis* isomers.

In contrast to lycopene, the all *trans* form of β-carotene is the dominating isomer in blood and tissue, which exhibits no additional absorption band in the UV range. Thus, filtering of UV light is not a major mechanism of action for this carotenoid, which is in accordance with a study performed in hairless mice, demonstrating that β-carotene does not act as an optical filter in the skin [42].

It should be noted that non-carotenoid compounds like polyphenols, which are also constituents of many dietary products, absorb in the UV range and may be operative in photoprotection.

For critical evaluation, it should be considered that in most of the studies reported until now, diminished erythma development was used as a measure of protection. Sunburn is a physiological response of cutaneous tissue to UV-induced cell damage. Inflammatory reactions of a tissue are primarily desired and beneficial. A major question that has not been answered yet is whether carotenoids prevent inflammation or suppress it. Protecting the tissue against damage in absorbing light or scavenging ROS before they react with target structures and thus preventing erythema is desired. However, it is debatable whether the scavenging of ROS, which are generated as a part of the inflammatory sequence, is beneficial. Additional markers of UV-induced damage including, e.g. formation of sunburn cells (apoptosis), DNA damage, or changes in extracellular matrix components would provide further information to evaluate the mechanism of action.

In addition to the erythemal response, some of the latter parameters were studied in a group of healthy premenopausal women who ingested lycopene from tomato paste over a period of 12 wk [43]. The protective effect of lycopene against UV-induced erythema was comparable to previous studies. After supplementation with tomato paste, UV-induced expression of matrix metalloproteinase-1 (MMP-1), which degrades interstitial collagen, was lowered in the dermis. Concomitantly, the induction of MMP-1 was accompanied by a small increase in the deposition of procollagen I in the papillary dermis. Mitochondrial DNA (mtDNA) damage is a result of UV exposure, and it likely plays an important role in the mechanisms of photoaging including damaging reactions related to the generation of ROS. Accordingly, the preventive effects of the tomato supplement on UV-induced mitochondrial DNA deletion were here attributed to the role lycopene and/or other antioxidants as scavengers of ROS.

The concept of endogenous photoprotection using dietary constituents such as carotenoids requires further research. Studies performed up until now were small in number of participants, and usually only a selected population, e.g. younger people, women, volunteers with a specific skin type, was studied. Doses of β-carotene beyond the physiological range were applied in the treatment of light sensitivity disorders. For over 30 years, carotenoids have been successfully used to ameliorate photosensitivity disorders of the skin, e.g. in patients suffering from erythropoietic protoporphyria [44–46]. It is generally accepted that singlet molecular oxygen and/or molecules in the excited triplet state are responsible for the lesions and that β-carotene acts as a quencher of this excited species.

Effects of antioxidant supplements on skin structure and texture have been investigated in a human intervention study with a mixture containing β-carotene as an ingredient [47]. However, there is yet no proof that the effects observed are unequivocally attributable to β-carotene.

4 Considerations and concerns

Based on recommendations of the International Agency for Research on Cancer (IARC) and the World Cancer Research Fund (WCRF), the use of β-carotene in photoprotection has been criticized, and possible adverse effects were discussed in the literature [48, 49]. Relatively high doses of β-carotene, above 10 mg/day, are required to ameliorate an UV-induced erythemal response of the skin. Such doses are still lower than those applied in long-term intervention studies aimed to prevent cancer and cardiovascular diseases, but need to be

scrutinized. In two of these controlled intervention studies performed with smokers and asbestos workers, both populations at high risk for lung cancer, it was shown that β-carotene supplementation unexpectedly increased lung cancer rates [50]. There are a number of hypotheses concerning the interaction of β-carotene and tobacco smoke constituents responsible for the observed adverse effects [51]. Modulation of retinoid metabolism and related signaling pathways, interaction with phase I metabolizing enzymes or prooxidative properties of β-carotene under specific conditions have been suggested to play a role. In vitro experiments provide evidence that β-carotene may act as a prooxidant especially at high oxygen tension [52]. Oxidative damage of DNA may underlie procarcinogenic activity [53]. Low ascorbate and tocopherol levels in smokers were discussed as a reason for the outcome of intervention studies mentioned above. It was suggested that sufficient vitamin C and E is required to scavenge intermediate β-carotene radicals. However, in vitro data are contradictory. Based on one-electron transfer rate constants different reactivity of various carotenoids with vitamin E were determined [54]. It is also not clear whether such interactions occur in vivo, and none of the supposed reactions has yet been clearly identified as a relevant mechanism of action [55, 56]. Such adverse effects as for β-carotene have not been reported for any other carotenoid.

The antioxidant properties of β-carotene in vitro and in cell culture [57] are apparently dose-dependent, and prooxidant effects have been observed at higher dose levels [58]. It is not yet known whether prooxidant behavior is relevant for the human organism.

One strategy to avoid high doses could be to substitute a part of the β-carotene dose with other carotenoids, preferentially non-provitamin A compounds, or other photoprotective dietary constituents, e.g. polyphenols [59]. It has been demonstrated that a high dose of β-carotene can be substituted by a mixture of different carotenoids retaining photoprotective effects [32]. With a carotenoid mixture consisting of β-carotene, lycopene, and lutein, 8 mg of each compound, photoprotective effects were comparable to those of 24 mg β-carotene alone. Erythema intensity in response to UV irradiation was diminished in both groups and was significantly lower than baseline after 12 wk of supplementation.

Several studies have been performed to investigate a correlation between carotenoid intake and skin cancer risk. However, overall, the present data suggest that carotenoids, especially β-carotene, have no effect, positive or negative, on the risk of either basal cell carcinoma or squamous cell carcinoma [60]. Randomized controlled trials have also failed to demonstrate a correlation between risk of nonmelanoma skin cancers (NMSC) and β-carotene supplementation. As a result of the Physicians Health Study, no beneficial effect of 12 years of β-carotene supplementation on the risk of NMSC was documented [61]. Furthermore, no association was found between plasma levels of β-carotene or vitamin A and the risk of NMSC.

5 Other carotenoids

Lycopene and β-carotene are the dominating carotenoids in the organism, and most of the human intervention studies on photoprotection were performed with them. However, there are many other carotenoids that are constituents of the human diet, but human data on their biological efficacy are scarce. As already mentioned, phytoene and phytofluene have been addressed as possible photoprotectants due to their UV-absorbing properties. They are the common carotenoid precursors to the carotene products found in plants and are conceivably present to some degree in a large spectrum of carotenoid-containing foods [62]. High levels are found in tomatoes and tomato products. In a tomato juice phytofluene and phytoene levels were around 5–10 mg/kg and the lycopene level was about 75 mg/kg. In a tomato paste product, phytoene and phytofluene were 45 and 26 mg/kg, respectively with lycopene levels of around 400 mg/kg (Stahl et al., unpublished work). After consumption of tomato-based products, photoprotective effects correlated not only with increasing lycopene levels but also with elevated concentrations of phytoene and phytofluene. At the end of 12 wk of intervention, phytofluene levels in serum were in the same range as those of lycopene or even higher [38]. However, this is no proof for photoprotective properties of these compounds. In vitro studies with primary human fibroblasts and HaCaT cells showed no significant effect of a mixture of phytoene and phytofluene on UV-induced expression of MMP-1 and IL-6 (Stahl et al., unpublished work).

Astaxanthin and canthaxanthin were studied in human dermal fibroblasts exposed to moderate doses of UVA [63]. Apoptosis, increased levels of ROS, decreased antioxidant enzymes activities, membrane perturbation, and elevated expression of heme oxygenase-1 were measured as markers of UVA response. In this model, astaxanthin exhibited a pronounced photoprotective effect and counteracted all of the above-mentioned UVA-induced alterations to a significant extent. Canthaxanthin had no effect on oxidative damage, except for an increased HO-1 expression. Further, astaxanthin attenuated UVA-induced up-regulation of matrix-metalloproteinase-1 and elastase in human dermal fibroblasts [64].

Evaluation of carotenoid data on photoprotection in cell culture is hampered by the fact that there are apparently optimal levels for photoprotection [57]. At optimal levels of lycopene, β-carotene, and lutein, a decrease in UV-induced lipid oxidation was determined. Below that level, antioxidant activity was lower, and beyond that level prooxidant effects were measured. The dependency of antioxidant properties on carotenoid levels has not been studied in complex organisms, and it is not clear whether such

concentration-dependent chemical properties play a role in vivo in the human.

Anti-pigmentation activity has been described for fucoxanthin, a carotenoid derived from edible sea algae [65]. In mice, fucoxanthin inhibited tyrosinase activity, melanogenesis in melanoma, and UVB-induced skin pigmentation after topical or oral application. The effect was suggested to be due to suppression of prostaglandin E2 (PGE2) synthesis and melanogenic stimulant receptors.

Recently, a very interesting carotenoid with an unusual structure has been studied for antioxidant activity and photoprotection in model systems and cell culture. 3,3′-Dihydroxyisorenieratene (DHIR) is a carotenoid with a polyenic backbone of nine conjugated double bonds substituted with phenolic end groups. DHIR is present in the bacterium *Brevibacterium linens*, which is used in the dairy industry for the production of various red smear cheeses [66]. The bacteria synthesize two other aromatic carotenoids, which are precursors of DHIR, 3-hydroxyisorenieratene, and the parent unsubstituted renieratene.

DHIR is a red-colored compound with an absorption maximum around 460 nm [67]. Both aromatic end groups participate only partially in the conjugation system because they are twisted out of plane. The methyl groups in the *ortho* position of the phenyl ring increase the steric repulsion between the ring and the polyene chain. Thus, its spectral properties closely resemble those of β-carotene. DHIR can be readily oxidized to the corresponding two-electron oxidation product isorenieratene-3,3′-dione (DHIRQ); see Fig. 1. This oxidation leads to drastic changes of the electronic and geometric properties with the quinoid end groups of DHIRQ fully integrated into the conjugation system. As a result, the absorption maximum is bathochromically shifted to about 560 nm, corresponding to a blue color. Under basic conditions DHIR is deprotonated accompanied by a small bathochromic shift of about 10 nm.

The antioxidant activity of the compound exceeds that of other carotenoids like astaxanthin, cryptoxanthin, zeaxanthin, or lutein. Due to the presence of a polyenic and phenolic substructure, DHIR acts as a bifunctional radical scavenger and quenches singlet molecular oxygen [68]. The second-order rate constant (kq) of quenching of singlet molecular oxygen for DHIR is around $9.7 \times 10^9\,M^{-1}\,s^{-1}$ and thus in the range of quenching constants measured for other carotenoids with kq between 10^9 and $10^{10}\,M^{-1}\,s^{-1}$. Lower second-order rate constants have been determined for polyphenols, indicating that the polyenic system rather than the phenolic ring is the structural element responsible for efficient quenching.

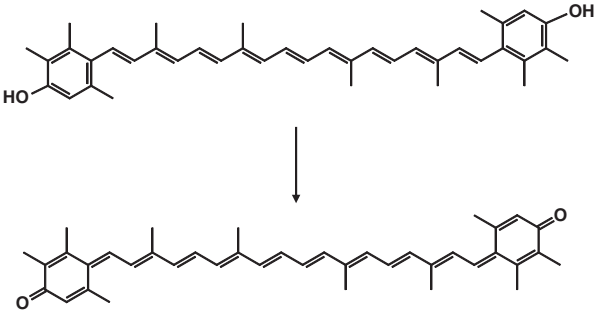

Figure 1. Oxidation of 3,3′-dihydroxyisorenieratene (DHIR) to the corresponding two electron oxidation product isorenieratene-3,3′-dione (DHIRQ).

Effects of DHIR on UV-induced photooxidation was studied in a liposomal model in which the carotenoids are in incorporated into multilamellar liposomes composed of egg yolk phospholipids. Irradiation with UV light (UV-A or UV-B) initiates lipid oxidation, and malondialdehyde was determined as a measure of oxidative lipid decomposition.

When liposomes were loaded with increasing amounts of DHIR, UV-induced malondialdehyde formation decreased significantly compared to control (Fig. 2). This photoprotective effect was more pronounced as in liposomes loaded with lutein at the same levels, where only moderate effects were observed. It can be speculated that both the phenolic structure and the conjugated system of double bonds contribute to radical scavenging via the formation of stable intermediate radicals and/or stable oxidation products like DHIRQ. The oxidation product itself is still equipped

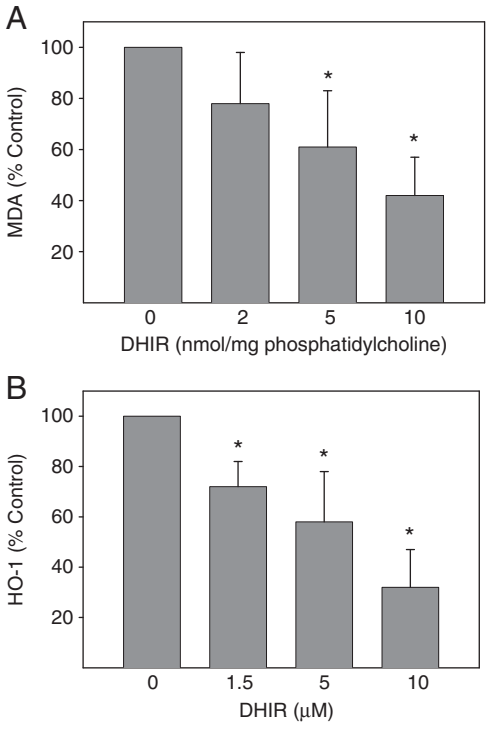

Figure 2. Effect of DHIR on markers of photoxidative damage. (A) Malondialdehyde (MDA) formation in liposomes is diminished when the particles are preloaded with DHIR and lipid oxidation is induced with UV-A (10 J/cm^2). (B) Preincubation with DHIR inhibits heme oxygenase-1 (HO-1) expression in human dermal fibroblasts stimulated with UV-A irradiation (20 J/cm^2).

with an intact conjugated system suitable for radical scavenging and quenching.

Following UV-A exposure, the expression of the enzyme heme oxygenase-1 is increased in human skin fibroblasts, which is taken as biomarker of photooxidative damage. Upon preincubation of cells with DHIR, heme oxygenase-1 expression was significantly lowered; only little effects were observed with lutein [68].

Zinc is an essential mineral required for a great number of biological processes. Numerous zinc proteins have been characterized, and among them are the zinc finger proteins, which represent a specific type of transcription factors and various enzymes. Complexation of the Zn^{2+} ion in zinc proteins is most common with cysteine and histidine residues, thus stabilizing the protein structure. Intracellular Zn^{2+} levels are strictly controlled, and almost all of the intracellular zinc is protein-bound. However, zinc homeostasis is disturbed under prooxidative conditions and the level of ''free'' zinc increases upon UV irradiation [69, 70]. DHIR prevents the UV-induced intracellular release of zinc ions from proteins in cell culture, e.g. human dermal fibroblasts [71]. The effect is correlated with decreased formation of intracellular ROS. It has been suggested that the intracellular zinc release upon UV irradiation is due to oxidative modifications of the zinc ligands in proteins (e.g. cysteine) and that protection by DHIR is due to intracellular scavenging of ROS generated in photooxidation.

A major DNA damage following UV-B exposure is the photochemically induced formation of cyclobutane pyrimidine dimers. Subsequent to exposure of human fibroblasts to UV-B light, thymidine dimers are formed, which can be visualized with specific antibodies. In cells preincubated with DHIR, less dimer formation was observed compared to the irradiated solvent control [68]. Because the formation of pyrimidine dimers is a typical photochemical reaction in DNA strands and not related to photooxidation, it is likely that UV-B absorbing properties of the phenolic end groups in DHIR are responsible for the effect. In addition to the major absorption band in the UV–visible range around 460 nm, which is responsible for the orange color of the carotenoid, DHIR exhibits a further, somewhat weaker absorption band with a maximum of about 290 nm.

The experiments underline the multifunctional properties of DHIR as a radical scavenger, quencher of singlet oxygen, and UV absorbing compound. However, further studies are needed to evaluate the possible use of this compound in humans.

6 Concluding remarks

β-Carotene, lycopene, and dietary products that provide these mediate moderate photoprotective effects against UV-induced erythema and thus provide an example for dietary constituents with effects on skin. Whether these effects are beneficial has to be assessed. Protection against sunburn is by far not comparable to the use of a sunscreen. However, a suitable diet may contribute to basal protection and thus increase the defense against UV light-mediated damage to skin. Apart from the major carotenoids found in the human diet, other members of this class of compound exhibit, at least in vitro, promising properties.

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