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Alcohol Consumption Decreases the Protection Efficiency of the Antioxidant Network and Increases the Risk of Sunburn in Human Skin

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Key Words
Alcohol · Carotenoids · Sunburn · Skin cancer

Abstract
In recent years, epidemiological data has demonstrated that alcohol consumption is a risk factor for sunburn, melanoma and nonmelanoma skin cancer. We hypothesized that if the concentration of the antioxidants in the skin has already decreased due to alcohol consumption, then an adequate neutralization of the free radicals induced by ultraviolet light cannot be performed. Based on this hypothesis, we determined the carotenoid concentration in the skin and the minimal erythema dose (MED) of 6 male human volunteers before and after consumption of alcohol or alcohol and orange juice combined. The results showed a significant decrease in the carotenoid concentration in the skin and the MED after alcohol consumption, but no significant decrease after a combined intake of alcohol and orange juice.

Introduction

The occasional consumption of alcoholic beverages is a cultural habit, and for many people all types of festivities are unthinkable without the consumption of alcoholic drinks. Many studies have shown that a light to moderate consumption of alcohol can have positive effects, e.g., by preventing oxidation of lipoproteins [1] and decreasing the risk of cardiovascular diseases in the range of 25–30% [2]. To the contrary, both acute and chronic consumption of alcohol can have detrimental effects [3, 4]. Alcohol is an organic solvent, which in higher doses can exert both a direct and an indirect harmful influence on a large number of organs, such as the liver and brain where liver cirrhosis and dementia can be the consequences, respectively [3, 5]. The response of the body to acute or chronic consumption of alcohol has been shown to result in the generation of oxygen-derived free radicals in many tissues [6, 7]. The relationship between alcohol-induced oxidative stress and the development of liver pathology has been investigated intensively [8]. Ethanol-induced oxidative stress is the result of the combined impairment of antioxidant defenses and the production of reactive oxygen species (ROS) by the mitochondrial electron transport chain, the alcohol-inducible cytochrome P450 (CYP) 2E1 and activated phagocytes and hydroxyethyl free radicals generated during alcohol metabolism by CYP 2E1 [6, 9]. ROS, in turn, are able to damage or cause complete degradation of essential complex molecules in the cells, including lipids, proteins and DNA [6, 10–12].

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Table 1. Characteristics of the volunteers

Volunteer No.	Age, years	Skin type according to Fitzpatrick classification	BMI	Ethanol dose ml/kg of body weight
1	54	II	26.2	0.94
2	32	II	28.1	1.12
3	34	II	21.1	1.0
4	33	II	23.2	1.0
5	33	II	20.8	1.17
6	21	II	26.8	1.06

All living biological organisms such as humans, animals and plants have developed natural defense mechanisms against the destructive action of free radicals. The defense system of humans is based on the action of different antioxidant substances, which are able to neutralize the free radicals and especially ROS. Most relevant antioxidants are carotenoids (beta-carotene, lycopene, lutein and zeaxanthin), vitamins (A, C, D and E), enzymes (superoxide dismutase, catalase and glutathione peroxidase) and others (e.g., flavonoids, lipoic acids, uric acid, selenium and coenzyme Q10), which form an antioxidant network [13, 14]. The different antioxidant substances possess synergistic effects and protect each other from direct destruction in the reaction of neutralization of free radicals and in particular ROS [15–17], thus working as a 'protection chain'.

Several previous studies confirmed that alcohol consumers have significantly lower serum concentrations of beta-carotene than nonconsumers, probably due to a higher beta-carotene consumption because of alcohol-related radicals and an increased beta-carotene conversion to retinol, as well as malnutrition which is common in alcohol abusers [18, 19]. However, most of these studies were focused on the serum level or liver level of carotenoids or other antioxidant substances; to our knowledge, the carotenoid concentration in the skin after alcohol consumption has not yet been determined, although first observations published by our group showed a decrease in dermal carotenoids after the consumption of high amounts of alcohol [20]. Bearing in mind that the skin represents the barrier to the environment and is thus exposed to a multiplicity of harmful influencing factors, e.g., ultraviolet (UV) light [21], it could be of importance to determine if the natural defense system of the skin is compromised by alcohol consumption. Furthermore, in recent years, epidemiological data has demonstrated that alcohol consumption is indeed a risk factor for sunburn and associated with a risk of nonmelanoma skin cancer and melanoma [22].

There is evidence that several processes leading to a decrease in serum carotenoids also reduce the carotenoid concentration in the skin [23–26]. In the last decade, corresponding devices have been developed allowing the quick noninvasive determination of carotenoids in the skin [27, 28].

A decrease in the antioxidant concentration in the skin after alcohol consumption can have far-reaching consequences concerning the self-protection mechanism of the skin, in particular when alcohol is consumed outdoors and the skin is not protected from the sun. UV light leads to the formation of highly reactive free radicals in the skin [29–31] and sufficient amounts of antioxidants are required to neutralize these [32]. An adequate neutralization cannot be performed if the concentration of the antioxidants has already decreased on account of alcohol consumption.

We therefore hypothesized that: (1) alcohol leads – comparable to the serum levels – to a decrease in the carotenoid concentration in the skin, (2) the minimal erythema dose (MED) describing the UV dose necessary to initiate an erythema on the skin is lower after alcohol consumption, and (3) the parallel consumption of carotenoid-rich orange juice and alcohol can counteract the decrease of the carotenoids. This study investigated all three hypotheses.

Material and Methods

Volunteers

The investigations were performed on 6 male Caucasian volunteers (mean age 34.5 years). The characteristics of the volunteers are summarized in table 1. They were asked not to consume fruit or vegetables (including fruit juices) on the day of the experiment and to adhere to their normal lifestyle for 1 week prior to the experiment. They had breakfast and lunch as usual on the day of the testing. The experiments were all performed at the same time of day, i.e., in the afternoon.

Approval for this investigation was obtained from the local ethics committee of the Charité – Universitätsmedizin Berlin. All volunteers gave their written informed consent.

Study Design

The study consisted of three parts: A, B and C. In the frame of A, the basal MED of each volunteer was determined without alcohol consumption. Part B included the determination of the MED after the consumption of approximately 1 ml of ethanol per kilogram of body weight within a time span of 15–30 min. Part C investigated the MED after the consumption of this amount in

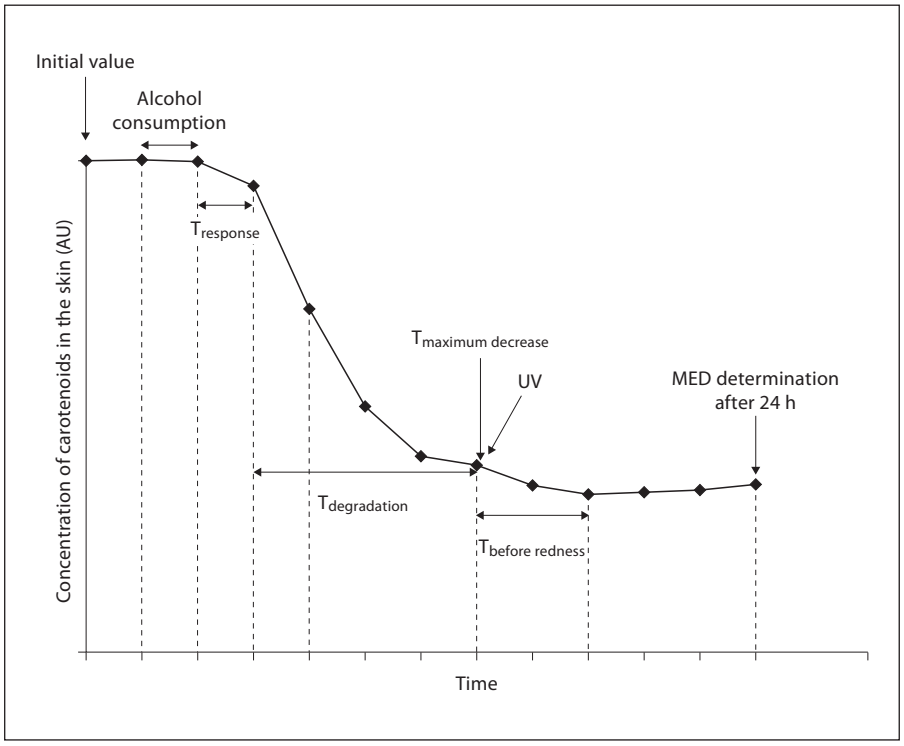

Fig. 1. Scheme of experimental time outline.

combination with orange juice (approx. 1 liter). All 6 volunteers participated in all 3 parts of the study, and at least 1 week of recovery was scheduled between parts.

Part A

On day 1 of the experiment, the basal MED was determined for each volunteer using the Dermalight® Erythemtester (Dr. K. Hönle Medizintechnik GmbH, Kaufering, Germany). This measuring device generates a dose gradient of UV light within an illumination slit of 1.5 × 8 cm. The radiation of an UV-emitting lamp is therefore bundled by reflectors in order to achieve a linear variation of the radiation intensity of 1:10 along the illumination slit.

The measuring device was placed on the inner forearm of the volunteers. By choosing the correct skin type on the device, radiation intensity and duration were settled automatically. The length of the erythema was then determined in millimeters after 24 h. Utilizing the provided table, the erythema length could be converted into the MED in mJ/cm^2.

Part B

At least 1 week after the determination of the basal MED, the volunteers were asked to drink approximately 1 ml of ethanol per kg body weight within a time span of 15–30 min, which corresponded to approximately 150 ml of vodka (Absolut, Absolut Company AB, Sweden, 40% ethanol), depending on the weight of volunteers. The individual ethanol doses are given in table 1.

Prior to alcohol consumption, the initial concentration of the carotenoid antioxidants was determined in the region of the palm of the hand by resonance Raman spectroscopic measurements. All measurements were performed in triplicate and mean values and standard deviations were calculated.

After termination of the alcohol consumption, the kinetics of the carotenoid antioxidants were determined. For this, the measurements on the palm were repeated again in triplicate every 20 min over 4 h. At the time point of the maximum decrease in dermal carotenoids, the experiment for the determination of the MED was repeated analogous to study part A.

In addition to the maximum decrease in percentage and the MED, the time until the decrease in the antioxidants started ($T_{response}$), the duration of the decrease ($T_{degradation}$) and the time before redness occurred on the skin after radiation ($T_{before\ redness}$) were determined in minutes. A scheme of the experimental time outline is shown in figure 1.

Part C

One week afterwards, the volunteers were asked to drink the same amount of vodka as in study part B and also to drink orange juice (hohes C Orange, Eckes Granini Deutschland GmbH, Nieder-Olm, Germany) at the same time ad libitum (approx. 1 liter).

The determination of the initial antioxidant concentration, the kinetics of the antioxidants and the MED determination were performed as described in study part B.

Resonance Raman Spectroscopic Measurements

The kinetics of the carotenoid concentration in the skin was determined noninvasively by the use of resonance Raman spectroscopy. Carotenoids are Raman-active molecules characterized by three prominent Stokes peaks measured at 1,005 cm^{-1} (rocking motion of the methyl group), 1,156 cm^{-1} (carbon-carbon single-

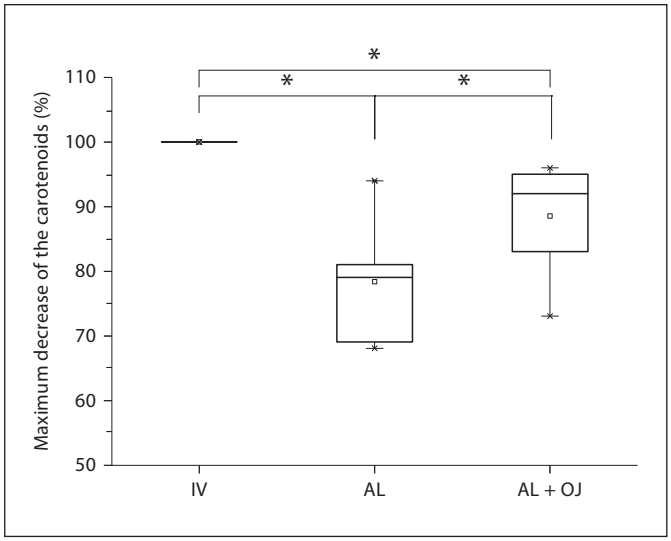

Fig. 2. Maximum decrease of the dermal carotenoids in percentage from the initial value (IV) after alcohol consumption (AL) and combined consumption of alcohol and orange juice (AL + OJ). * $p < 0.05$.

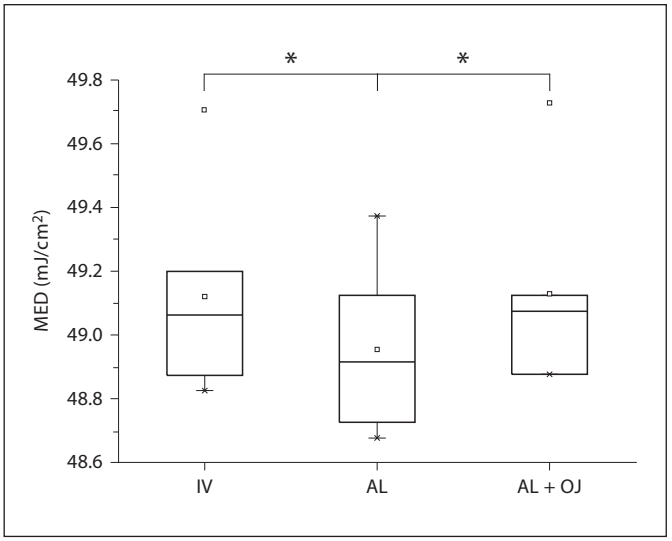

Fig. 3. Mean MED after alcohol consumption (AL) and alcohol consumption in combination with orange juice (AL + OJ) in comparison to the initial value of MED (IV). * $p < 0.05$.

bond stretch vibration of the conjugated backbone) and 1,523 cm^{-1} (carbon-carbon double-bond stretch vibration of the conjugated backbone) [33]. For resonance excitation of carotenoids, the laser wavelength should lie in the range of maximal absorption of carotenoids, i.e., in the blue-green range of the optical spectrum. To excite all dermal carotenoids simultaneously, the wavelength of 488 nm of an Ar^+ laser was used at a power density of 60 mW/cm^2 on the skin surface. The concentration of dermal carotenoids was determined by the intensity of a Raman peak measured at 1,523 cm^{-1}. The utilized Raman setup has been previously described in detail by our group [27]. Measurements were performed in triplicate on the marked area of the palm of the volunteer's hand. In between the different measurements, the measuring probe of the Raman device was removed from the skin and then replaced for the next measurement. The average value was used to determine the kinetics of dermal carotenoid concentrations.

Statistical Analysis

The statistical evaluation of the results was performed using the software program IBM SPSS Statistics 19 (IBM, Armonk, USA). Data are presented as mean ± standard deviation. The Wilcoxon test was used to compare related samples affording a significance of $p < 0.05$.

Results

The concentration of cutaneous carotenoid antioxidants of the volunteers was determined before and after the alcohol consumption, before and after the combined alcohol and orange juice consumption, respectively, as well as for 4 h after the corresponding consumption, in order to determine the maximum decrease. The results revealed a decrease in the antioxidant concentration after alcohol consumption ($p < 0.05$) and also after the consumption of alcohol and orange juice ($p < 0.05$). However, the maximum decrease after alcohol consumption was significantly higher than that after alcohol in combination with orange juice ($p < 0.05$). Obtained results are presented in figure 2.

The decrease in the antioxidant concentration ($T_{response}$) occurred on average 8.3 min after the end of the alcohol consumption and 46.7 min after the end of the alcohol and orange juice consumption. The difference in duration was not significant ($p > 0.05$). The duration of the decrease ($T_{degradation}$) was on average 71.7 min after alcohol consumption alone and 90 min after combined alcohol and orange juice consumption ($p > 0.05$).

The determination of the MED revealed that this was significantly reduced after alcohol consumption ($p < 0.05$), whereas after combined alcohol and orange juice consumption, the differences in MED were not significant ($p > 0.05$). The results are presented in figure 3. In addition, the time span until redness occurred on the skin was significantly shorter ($p < 0.05$) after alcohol consumption (on average 66.7 min) than in the experiments where either no alcohol was consumed (on average 101.7 min) or alcohol was consumed in combination with or-

ange juice (on average 96.7 min). No significant difference in the time until redness occurred on the skin was obtained between the combined consumption of alcohol and orange juice and the absence of alcohol consumption.

Discussion

In the frame of our study, we could confirm the hypothesis that alcohol consumption (approx. 1 ml of ethanol per kg of body weight) leads to a significant decrease in the dermal carotenoid concentration and in the MED; a reduced MED is accordingly associated with an increased risk of sunburn and UV-light-associated skin disorders and skin cancer. The redness of the skin, which is always associated with the start of inflammation processes, was visible significantly sooner ($p < 0.05$) after alcohol consumption than after combined consumption of alcohol and orange juice or no consumption of alcohol. These results clearly show the impairment of the antioxidant defense system of human skin by acute alcohol consumption.

An increased risk of sunburn after alcohol uptake has already been established in previous studies [22]. Warthan et al. [34] revealed that people consuming alcohol during time spent on the beach had a more severe sunburn than nondrinkers. Mukamal [35] conducted a survey on >300,000 adults and likewise confirmed that alcohol consumption was positively associated with increased sunburn.

Accumulative epidemiological data also suggest that alcohol consumption is a risk factor for sunburn and is associated with a risk for nonmelanoma skin cancer and melanoma [22]. However, the precise mechanisms by which alcohol contributes to cancer including skin cancer are still unknown. Saladi et al. [22] suggested that ethanol is converted to acetaldehyde which is a highly reactive chemical and serves as a photosensitizer and generates ROS upon exposure to UV radiation which, in turn, induces oxidative DNA damages, thus enhancing the binding of acetaldehyde to DNA and activating signal-transduction cascades and prostaglandin synthesis. Therefore, the combination of alcohol and UV exposure potentiates both the initiating and promoting activities of carcinogenesis.

The results of this study emphasize the 'ROS-centered' hypothesis of Saladi et al. [22]. For the first time, a decrease in the carotenoid concentration in the skin after alcohol intake could be measured directly. The carotenoid concentration, in turn, can be considered as a marker for the usage of the antioxidants for the neutralization of the massive numbers of free radicals, particularly ROS, upon alcohol consumption and UV irradiation.

Our study also revealed that the decrease in the carotenoids and the MED could be minimized when the alcohol consumption was combined with orange juice uptake, which is rich in carotenoids and other antioxidants, such as vitamin C. The decrease in MED was no longer significant when orange juice was consumed in combination with alcohol. Skin redness, however, occurred significantly later after combined consumption.

In this context, Moehrle et al. [36] found a significant rise in the MED after the consumption of red wine. The relatively small photoprotective effect was attributed to the polyphenols in the wine, which represent highly reactive antioxidants.

Therefore, it can be concluded that the harmful oxidative processes occurring during and after alcohol consumption can be partly inhibited if the antioxidant/oxidant balance is shifted towards the antioxidants by consuming antioxidant-rich food or drinks prior or parallel to the alcohol uptake. In this context, it would be of interest to investigate whether individuals possessing a high initial antioxidant status have either similar absolute or relative decreases in the carotenoid concentration and MED than individuals with lower initial values. Due to a relatively small number of volunteers in this pilot study, this effect could not be evaluated correctly. However, there are hints in the literature that for the same oxidative stress reaction, comparable amounts of antioxidants are utilized for neutralization, meaning that individuals with a higher initial value ultimately retain higher levels than individuals with lower initial values [37, 38].

All these aspects lead to clear recommendations of conduct:

(1) In order to strengthen their immune system defenses, people should increase their individual antioxidant status by means of healthy nutrition. Nutritional supplements cannot be generally recommended as concentrations and compositions are often not in a physiological range and can thus even have pro-oxidative effects [39–41].

(2) People should be aware of the fact that the consumption of alcohol in combination with UV light increases their risk of sunburn and therefore their risk of developing premature skin aging and even skin cancer. If the consumption of alcohol cannot be avoided, adequate sun protection measures should at least be considered. In addition, the consumption of alcohol in combination

with food or drinks rich in antioxidants is recommended, in order to reduce oxidative damage. Education is necessary to heighten people's awareness.

Conclusions

The obtained results indirectly confirmed the generation of free radicals and especially ROS in the skin, subsequent to the acute consumption of alcohol, and confirmed directly the epidemiological data that alcohol consumption serves as a risk factor for sunburn. It could be concluded that alcohol consumption in combination with drinks rich in antioxidants, such as orange juice, are helpful in reducing the oxidative damages to the skin induced by alcohol.

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