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Research paper

Bioavailability of natural carotenoids in human skin compared to blood

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ABSTRACT

Skin functions and structure are significantly influenced by nutrients. Antioxidants protect the supportive layer of the skin against any damaging irradiation effects and the action of free radicals. A lack of suitable methods means that the pharmacokinetic properties of systemically applied carotenoids transferred into the skin remain poorly understood. In this study, a natural kale extract or placebo oil were given orally to 22 healthy volunteers for 4 weeks. Carotenoid bioaccessibility was evaluated using non-invasive resonance Raman spectroscopy on the palm and forehead skin. For the analysis of the blood serum, the standard HPLC method was used. The blood and skin levels of the carotenoids increased significantly during the study but compared to the blood serum values, increases in skin were delayed and depended on the dermal area as well as on the carotenoid. Lycopene, measured as being low in the extract, increases more in the skin compared to the blood indicating that the natural mixture of the extract stabilizes the antioxidative network in the skin. After supplementation had ended, the carotenoids decreased much faster in the blood than in the skin. The delayed decrease in the skin may indicate a peripheral buffer function of the skin for carotenoids.

1. Introduction

Metabolic processes, environmental conditions, inflammatory processes, and irradiation with UV and infrared light lead to the production of radicals in the body. High levels of free radicals can cause oxidative cell damage, skin aging, and cancer [1–4]. To avoid the effect of free radicals, the body has developed a natural antioxidative protective system consisting of carotenoids, vitamins, enzymes, and other active substances. Together they act synergistically as a protective chain, protecting each other from the destructive action of free radicals.

In the skin, carotenoids such as beta-carotene, lutein, and lycopene are considered to be of prime importance for the reduction in skin aging and the risk of cancer development [5–8]. The reaction of carotenoids with free radicals leads to their decomposition [9]. This results in the reduction in the protective chain in the body. However, as shown in previous studies, the oral uptake of antioxidative substances can raise the antioxidative potential [10,11]. The beneficial effects on skin of lutein uptake can be enhanced by topical application of antioxidants [12]. Until now, information has not been readily available concerning the uptake of antioxidants and their appearance, as well as clearance in the skin because of the lack of a rapid and non-invasive method to assess the antioxidative substances in the skin. The non-invasive Raman spectroscopic measurement provides an opportunity to measure carotenoids in the skin at different body sites [13,14]. To learn more about the kinetics and bioavailability of antioxidants in the skin, further investigations are necessary.

The discussion concerning the oral uptake of single synthetic substances with regard to health benefits is a controversial one. However, the uptake of vegetables and fruit has always shown a positive impact on the antioxidative potential of the skin [15–17]. In spite of significant benefits, to health, most people do not regularly consume fruit and vegetables. Here, the oral uptake of natural extracts could be an excellent alternative. These extracts deliver antioxidative agents in their natural combination and are available in the form of capsules or pills. Their non-varying ingredients make them well suited for clinical studies. In the past, various studies have shown that curly kale, sea-buckthorn oil and olive oil usually have constituents with a high antioxidative capacity [18–20]. One main component of kale is lutein, which is a powerful antioxidant. Besides lutein, it contains various other antioxidants such as beta-carotene, and phenolic compounds such as glycosinolates and flavonoids [21,20] in moderate concentrations. Olive oil is known to provide high amounts of phenolic and tocopherolic substances [22,23]. Less is known, however, about the bioavailability of single carotenoids in the skin, and there are very limited data on fruit or natural extracts containing a mixture of carotenoids at low concentrations. In contrast to synthetic

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antioxidant products, the natural mixture of antioxidants in the extracts may support the antioxidative network of the skin more efficiently.

The first aim of the study was to investigate the amount and kinetics of carotenoids in the skin after oral supplementation with a natural extract without any preceding antioxidant-depleted diet. The question is then whether the different carotenoids have an influence on each other in terms of bioavailability and whether low-dosed carotenoids may be protected by the scavenger effects of other antioxidants. These data could help to evaluate the hypothesis that fruit and vegetables, containing a mixture of moderately concentrated carotenoids, are more efficient than high doses of single carotenoids. Another aspect is whether various carotenoids show a homogeneous distribution and accumulation in the skin. The second aim was to evaluate the Raman technology for its suitability as a fast and reliable, non-invasive measuring method for carotenoids in the skin at two different sites after oral supplementation of extracts rich in antioxidants. Therefore, the bioavailability was measured in blood samples with the standard HPLC method and *in vivo* in the skin of the palm and the forehead using non-invasive Raman spectroscopy. These measurement sites were chosen because different studies have shown that the highest effects could be found in the palm and forehead [14,24]. Comparison of the blood and skin values may give detailed information about the different kinetics in uptake and clearing due to oral supplementation.

A placebo group was integrated into the study as the carotenoid concentration in the skin [25] varies with the seasons.

2. Materials and methods

2.1. Supplements

Two oral products (Lutex™ and placebo) were used, both produced as vegetable oils. The placebo oil was the olive oil, Royal del Sol (Fa. Reinhold GmbH Taunusstein, Germany) which contains low levels of carotenoids (<1 μg/ml). The Raman signal of the placebo oil was 0.12 a.u. and the vitamin E equivalents, using ESR investigations, were 0.39 g/L. The Lutex™ oil (BioActive Food GmbH, Bad Segeberg, Germany) consists of curly kale extracts (Brassica oleracea convar. acephala var. sabellica L), sea-buckthorn (Hippophae rhamnoides L.) and olive oil contained a high amount of carotenoids i.e. 1.5 mg/mL lutein, 0.5 mg/mL beta-carotene, and 0.13 mg/mL lycopene. The Raman signal resulted in 1.33 a.u and vitamin E equivalents of 3.3 g/L. A supplementation of 6 mL Lutex oil per day results in 9 mg lutein or 20 mg vitamin E equivalents per day. This is in the range recommended by Stahl and Krutmann to increase the internal skin photo protection [25]. By contrast, the placebo oil offers 2.3 mg vitamin E equivalents per day.

2.2. Study groups

The study protocol was submitted and approved by the local ethics committee of the Charité Universitätsmedizin – Berlin in accordance with the Declaration of Helsinki as revised in 1983. Twenty-two healthy volunteers aged between 22 and 59 years were included in the study protocol (8 females and 14 males) after having given their written informed consent. The median age was 42 years (range: 22–59) in the Lutex group ($n = 11$) and 42 years (range: 25–49) in the placebo group ($n = 11$) (Table 1). All volunteers had a skin photo type of II [26], an initial Raman palm signal below 0.8 a.u. and a body mass index (BMI) between 18 and 35 kg/m^2. The target group of supplementation are people with a low antioxidative potential. As the mean carotenoid value measured by Raman spectroscopy in the human palm in Germany is 0.5 a.u., volunteers with initial Raman values higher than 0.8 a.u. were excluded from the study.

Table 1
Volunteer characteristic at visit 1.

Parameter		Placebo	Lutex
Age	Mean	34.7	40.5
	Median	34.0	42.0
	Min	25	22
	Max	49	59
BMI	Mean	25.0	27.0
	Median	26.1	29.1
	Min	19	18
	Max	32	35
Gender	Male	8	6
	Female	3	5

Only volunteers with a stable lifestyle were included to minimise the effects of their lifestyle on the results. The volunteers had not taken any supplements during the last 2 months and were asked not to take any vitamin pills. Participants were advised to maintain their usual diet and physical activity during the trial.

2.3. Study protocol

On visit one (day 1), the volunteers were screened with the resonance Raman spectroscopy. The volunteers were included in the study, if their initial value of carotenoids was below 0.8 a.u. on the palm. Raman measurements were performed at two sites on the body, the forehead and the palm. Blood samples were taken from all volunteers, in order to analyse the total carotenoids, and beta-carotene, lycopene, and lutein individually. The supplements had been marked with numbers by the manufacturers and were handed out randomly and as a double-blind test. After screening, all volunteers started taking a daily dose of 3 mL oil together with their morning and evening meals for 28 days. After 14 days (visit 2) and 28 days (visit 3), blood sampling and skin measurements were carried out again. Fourteen days after finalizing the supplementation (visit 4, day 42), the same parameters were measured as for visits 1, 2, and 3.

2.4. Resonance Raman spectroscopy

Resonance Raman spectroscopy was used as a quick method for *in vivo* determination of the concentration of carotenoid antioxidant substances in human skin [24]. For the determination of cutaneous carotenoids, such as beta-carotene, lycopene, and lutein, excitation wavelengths at 488 nm and 514.5 nm were applied. The carotenoids showed comparable absorption behaviour in the blue range of the spectrum [13]. Therefore, blue light at 488 nm excites all the carotenoid substances with approximately the same Raman scattering efficiency [27]. Lycopene can be determined using an excitation wavelength of 514 nm [27,13]. The reproducibility of the Raman measurements can be influenced by inhomogeneous pigmentation, roughness, and the microstructure of the skin. The inhomogeneity of the skin pigmentation has a typical size of 1–2 mm. To reduce the influence of these factors a laser spot with a diameter of 6.5 mm on the skin surface was used in the measuring device [28]. In this way, the spread of the Raman values did not exceed 10%. Triplicate measurements were performed on the palm and forehead, and mean values were calculated for further analysis.

2.5. Blood analysis

The blood was centrifuged within 4 h; the supernatant (serum) was carefully removed and was stored at −18 °C. The carotenoids

(lutein, zeaxanthin, α-carotene, beta-carotene, β-cryptoxanthin, and lycopene) were separated and quantified by reversed-phased HPLC at the laboratories of BioAnalyt GmbH (Berlin, Germany) within 14 days [29]. In short, 200 µl of ethanol was added to 100 µl plasma diluted with 100 µl H_2O. After vortexing for 30 s, the plasma was extracted twice with *n*-hexane, 1 ml each time stabilized with 0.05% butylated hydroxytoluene (BHT), vortexed for 10 min and centrifuged for 10 min at 1500*g*. The supernatants were removed, pooled, and evaporated under nitrogen and reconstituted in 200 µl isopropanol and injected into the HPLC-system (Waters, Eschborn, Germany). For separation and quantification of compounds a C30 carotenoid column (5 µm, 250 × 4.6 mm; YMC, Wilmington, USA) in line with a C18 pre-column (Luna, Phenomenex, Germany) with a solvent system consisting of solvent A with methanol (Roth Chemicals Germany):water (90:10 v:v, with 0.4 g/l ammonium acetate in H_2O) and solvent B with methanol/methyl-tert-butyl-ether (Sigma Deisenhofen, Germany)/water (8:90:2 v:v:v, with 0.1 g/l ammonium acetate in H_2O) was applied as described in detail [29].

2.6. Statistical analysis

Relative mean data were calculated by dividing the individual data taken on visits 2, 3, and 4 by the data of visit 1 and then calculating the mean values.

For statistical analysis, the SPSS 16.00 for Windows (SPSS Inc., Chicago, Illinois) software was used. The effect of the treatment was statistically analysed by means of repeated measures ANOVA. The Friedman test was used for determining the variance within the individual groups, while the Mann–Whitney test was used for comparing the mean values between the groups.

3. Results

3.1. Skin measurements

The screening at visit 1 shows the typical broad distribution of carotenoids in the skin of the 22 volunteers. The volunteers were randomised into either the Lutex group ($n = 11$, taking Lutex oil) or the placebo group ($n = 11$, taking olive oil). At visit 1, both groups had similar mean values on the palm and forehead (Table 2). The repeated measures ANOVA ($p < 0.05$) proved the effect of the treatment with Lutex to be significant. The values of the placebo group remained stable within the error margin over the 42 days ($p > 0.05$, Friedman test). The volunteers of the Lutex group exhibited exclusively significant changes in the Raman values of their palms and foreheads ($p < 0.05$, Friedman test). The differences in the mean values between the placebo and the Lutex group were insignificant.

For better comparison, the relative changes of all data were calculated relating to the initial values at visit 1. The mean values of these relative carotenoid concentrations are shown in Fig. 1. Again, the placebo group shows no significant differences on all four visits.

In the Lutex group, the mean values increased by a factor of 1.17 on the palm and by 1.31 on the forehead. Fourteen days after supplementation this factors reduced to 1.13 and 1.23, respectively.

The mean relative concentrations between placebo and Lutex at the palms and foreheads on visits 2 and 3 and at foreheads on visit 4 were significantly different ($p < 0.05$, Mann–Whitney test). The placebo group exhibited no significant changes over the time (Friedmann $p > 0.05$) in contrast to the Lutex group (Friedmann $p < 0.05$).

The concentrations of lycopene in the skin were measured with Raman spectroscopy using an excitation wavelength at 514 nm [13]. The absolute values for the concentrations in a.u. are presented in Table 2. As expected, the absolute lycopene values were lower than the values of the total carotenoids. The relative values relating to the initial values on visit 1 are shown in Fig. 2. Lycopene

Table 2
Mean values ± SD for carotenoid skin concentration measured by Raman spectroscopy in a.u.

Time (days)	Total carotenoids (a.u.)				Lycopene (a.u.)			
	Palm[a]	±SD	Forehead[a]	±SD	Palm[a,b]	±SD	Forehead[a]	±SD
Placebo								
0	0.516	0.094	0.381	0.183	0.118	0.039	0.112	0.056
14	0.503	0.101	0.373	0.189	0.132	0.054	0.123	0.069
28	0.503	0.095	0.375	0.183	0.145	0.040	0.128	0.074
42	0.518	0.112	0.375	0.172	0.149	0.045	0.129	0.065
	Palm[b]		Forehead[b]		Palm[b]		Forehead[b]	
Lutex								
0	0.539	0.148	0.385	0.169	0.114	0.053	0.104	0.062
14	0.58[c]1	0.144	0.434[c]	0.196	0.150[d]	0.058	0.141	0.088
28	0.628[c]	0.170	0.492[c]	0.189	0.177[d]	0.057	0.164[c]	0.067
42	0.599	0.148	0.463	0.190	0.178[d]	0.047	0.157[d]	0.064

[a] Repeated measures ANOVA $p < 0.05$.
[b] Friedmann test $p < 0.05$.
[c] Differences between placebo and Lutex group $p < 0.05$ (Mann–Whitney test).
[d] Differences between placebo and Lutex group $p < 0.1$ (Mann–Whitney test).

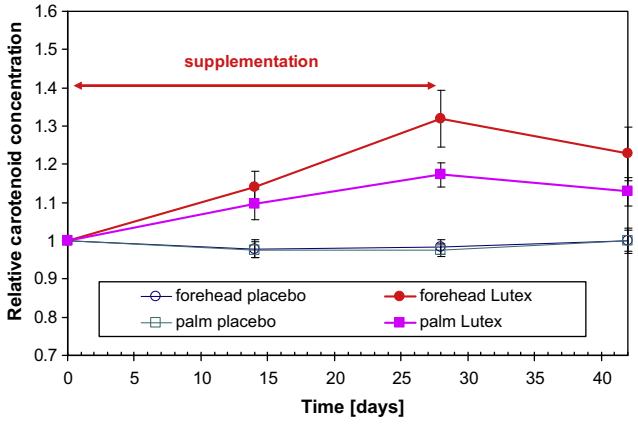

Fig. 1. Mean values ± SE of the relative carotenoid concentrations in the skin with standard errors on the palm and forehead for the placebo and Lutex groups. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

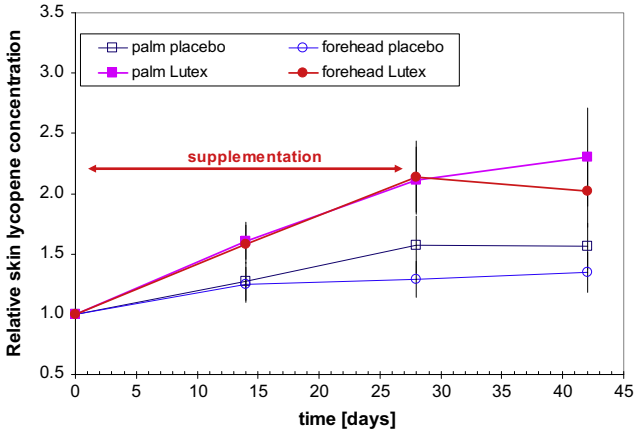

Fig. 2. Mean lycopene concentration ± SE in the skin relative to the concentration at visit 1. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

also increased from visit 1 to visit 3 by a factor above 2 and decreased at visit 4 only on the forehead. The values for the palm in the placebo group increased at visit 3 significantly; for all other values no significant changes have been found. On the forehead, the difference between placebo and Lutex at visit 3 was significant ($p < 0.05$, Mann–Whitney test).

4. Blood investigation

For comparison of the carotenoid concentrations in skin and blood, the concentrations of beta-carotene, lutein, and trans- and iso-lycopene were determined, as well as the total carotenoid concentration in the blood serum. The mean values of selected absolute concentrations are presented in Table 3.

The changes in relation to the initial values on visit 1 are shown in Figs. 3 and 4.

The mean concentrations of the carotenoids in blood on visit 3 increased by factors of 1.53–2.57 depending on the carotenoids. Fourteen days after supplementation, the concentrations decreased faster as observed for the skin values. The increase in relative concentration of total carotenoids was less than for the selected individual compound, as the latter also contained carotenoids such as zeaxanthin, canthaxanthin, beta-cryptoxanthin, alpha-carotene, trans-lycopene, which showed little or no changes at all.

The global test of the effect of the treatment with Lutex was shown to be significant using repeated measures ANOVA ($p < 0.05$) for lutein, beta-carotene, and total carotene. No significant effect could be observed for lycopene.

4.1. Beta-carotene

The Friedmann test resulted in significant changes over time ($p < 0.05$). The placebo values did not change during visits 1–4 ($p < 0.05$). For beta-carotene, the mean values between placebo and Lutex at visits 2 and 3 were significant ($p < 0,05$, Mann–Whitney test). The mean standard deviation (SD) amounted to 31%, the standard error (SE) to 11%.

4.2. Lutein

The Lutex and placebo groups showed significant differences in lutein at visits 2, 3, and 4 ($p < 0.05$, Mann–Whitney test). In contrast to beta-carotene and the other substances, the placebo values did not remain stable ($p < 0.05$, Friedmann). On average, the SD and SE amounted to 39% and 11%, respectively.

Table 3
Mean concentrations ± SD of carotenoids determined by HPLC in blood serum in µg/mL.

Time (days)	Lutein[a,b] (µg/mL)		Beta-carotene[a] (µg/mL)		Total carotenoids[a] (µg/mL)		Iso-lycopene (µg/mL)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Placebo								
0	0.105	0.049	0.133	0.111	0.468	0.159	0.0424	0.0220
14	0.081	0.035	0.137	0.146	0.439	0.202	0.0448	0.0201
28	0.080	0.028	0.144	0.157	0.437	0.189	0.0394	0.0146
42	0.071	0.026	0.145	0.147	0.425	0.183	0.0429	0.0140
	Lutein[b]		Beta-carotene[b]		Total carotenoids[b]			
Lutex								
0	0.081	0.042	0.172	0.132	0.534	0.255	0.0432	0.0254
14	0.151[c]	0.058	0.245[c]	0.122	0.707[c]	0.269	0.0553	0.0256
28	0.197[c]	0.102	0.278[c]	0.163	0.792[c]	0.357	0.0553[c]	0.0213
42	0.111[c]	0.056	0.214	0.232	0.592	0.391	0.0434	0.0170

[a] Repeated measures ANOVA $p < 0.05$.
[b] Friedmann test $p < 0.05$.
[c] Differences between placebo and Lutex group $p < 0.05$ (Mann–Whitney test).

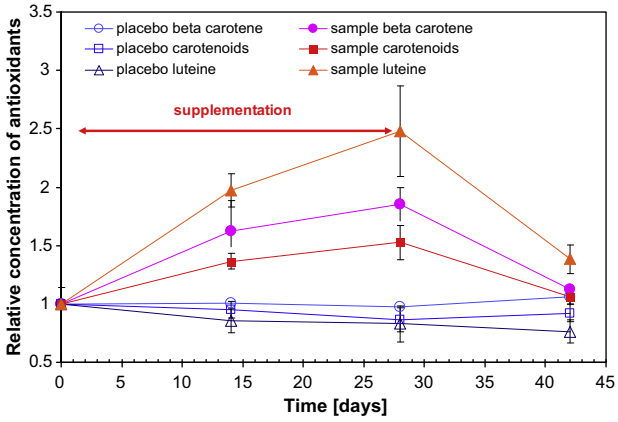

Fig. 3. Relative mean ± SE serum concentrations of carotenoids relating to the values of visit 1. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

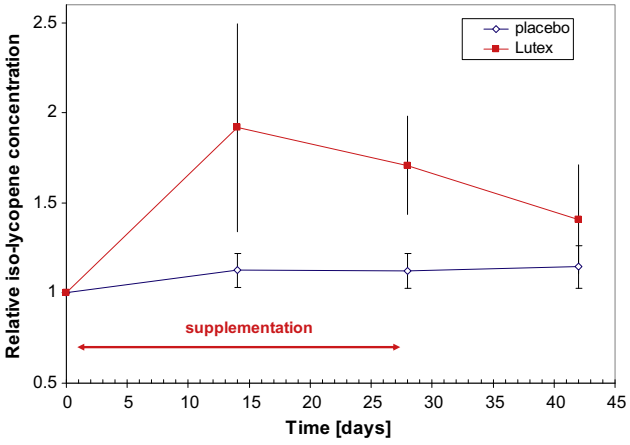

Fig. 4. Relative iso-lycopene concentration ± SE in blood serum. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

4.3. Total carotenoids

The total carotenoids show the same significant changes as beta-carotene. On average, the SD and SE amounted to 24% and 7%, respectively.

4.4. Lycopene

No significant changes between the visits could be found for iso- and trans-lycopene in the Lutex and placebo group (Friedmann, $p > 0.05$). Only the mean value of iso-lycopene increased significantly in the Lutex group in contrast to the value found in the placebo group on visit 3 ($p < 0.05$, Mann–Whitney test). The sum of both trans- and iso-lycopene values yields no significant changes.

5. Comparison of skin and blood values

A comparison of the palm carotenoids with the concentration of the total carotenoids in blood serum shows a correlation with $R = 0.77$ using the absolute data from both groups on visit 1. This

indicates that under stable conditions the blood and skin values correlate with each other.

The increase in relative carotenoid concentrations in the skin between visits 1 and 2 and visits 2 and 3 was almost constant due to the linear increase over the supplementation time. Even after 4 weeks of supplementation with Lutex, no saturation effect could be observed. The blood values increased faster in the first 14 days than in the second 2 weeks. This indicates the beginning of a possible saturation effect. After the end of supplementation, the carotenoid decrease was much faster in blood than in skin. In the skin, the carotenoids dropped to 28% of the total increase on the forehead and to 26% of the total increase on the palm. In blood, 85% of the enhanced beta-carotene, 74% of lutein, and 88% of total carotenoids had already vanished after 14 days without the supplementation with Lutex.

To evaluate possible correlations between the blood and skin values within the blood and skin values, Pearson's correlation coefficients were calculated.

In Table 4, the correlation coefficients of the mean values are listed. The correlations within the blood and skin data were high with R values above 0.98. The correlations between the blood and skin data were lower ($R < 0.79$) but still conspicuous.

Although the values on the palm and forehead increased and high correlations were obtained, the individual data did not, on average, really correlate ($R < 0.35$) with each other. Moreover, only slight correlations were found for individual blood and skin data ($R < 0.61$). When the absolute individual blood and skin data were compared, the correlation coefficient was found to have slightly increased but it remained below 0.64, except for visit 1, as mentioned earlier.

6. Discussion

The results have shown that the supplementation of a natural extract supplement to normal nutrition significantly increases the concentrations of carotenoids in the blood and the skin. This is in agreement with the results of previous studies [30,31]. The enrichment was much faster and higher in the blood than in the skin, but the reservoir function was superior in the skin. The reduced values in the skin are due to the fact that the substances were distributed not only into the skin, but they can also be transported into other parts of the body, especially adipose tissue [32]. Due to the different temporal distribution of the carotenoids, high correlations of the blood and skin values were not expected at the same time, with the exception of the data acquired at visit 1 prior to supplementation. Nevertheless, R-values up to 0.78 were obtained for blood and skin carotenoids. These data can be compared with the results of Stahl et al. [31] who acquired the data over an extended supplementation time administering a single carotenoid (beta-carotene) and using reflectance spectroscopy for the determination of the skin values.

The increase in blood beta-carotene caused by Lutex to a factor of 2.5 corresponds to the increase in plasma beta-carotene after the consumption of 8 portions of fruit or vegetables or rich in antioxidants per day, as shown by Watzl et al. [33]. This shows the potential of natural vegetable concentrates and natural extracts with regard to the bioavailability of carotenoids. The consumption could reduce risk factors caused by increased antioxidative stress such as sun irradiation, alcohol, or nicotine consumption and illness [34,35,3,36].

It has been reported that orally administered antioxidants are transported to the skin surface and the stratum corneum by the sebaceous gland secretion route [37]. The higher enrichment on the forehead, compared to the palm, could therefore be due to the high amount of hair follicles with sebaceous glands at this site. As the palms of the hands have a high sweat gland density, we assumed that the carotenoids were additionally transported via sweating. The long-term storage effect could be related to the stratum corneum, which is known to act as a reservoir, for example, for the storage of vitamins [38].

Previous investigations have shown that the oral uptake of lycopene significantly increases the values in blood serum by a factor of 3 after a 4-week supplementation [14]. However, the bioaccessibility to the skin was very limited. The statistical significance or tendency to statistical significance was only reached once during the 12-week supplementation. Thus, reduced lycopene uptake induces a slow but significant decrease, whereas a supplementation only tends to maintain the base line levels. This is in agreement with our findings that the carotenoid level was reduced by only 25% after 2 weeks, in contrast to the blood level which was reduced by approximately 80%.

The results of Stahl [31] showed a 3.1-fold increase for beta-carotene in serum and a factor of 2.4 on the forehead and 2.2 on the palm, which shows high correlations between the blood and skin values for the increase due to supplementation with carotenoids. The blood values were also increased faster than the skin values. The slower decrease in the skin values on the palm and forehead could be due to the fact that the present study was performed in the winter/spring time when the sun exposure is low.

With regard to the natural kale extract supplementation, the values of lycopene increase in the skin were at a higher level than in the blood serum, which is in contrast to the other supplemented carotenoids. The low increase in the blood is due to the low concentration of lycopene in the Lutex oil. The higher increase in the skin may possibly be caused by the fact that the antioxidant substances in the skin act as a network, protecting each other against degradation, caused by free radicals. An enhancement of several carotenoids protected the remaining ones which had not been additionally administered. Comparable results have been found in studies where lycopene was supplemented. In this case, the skin level of beta-carotene was increased but not in the blood plasma [14]. These data indicate that carotenoids may have an influence on the pharmacokinetic parameters of other antioxidants supporting the hypothesis that vegetables, fruit, and natural extracts, which contain a cocktail of different carotenoids, or in general antioxidants protect tissues such as the skin more efficiently than high doses of single synthetic carotenoids.

One conclusion of the study is that the application of the Raman spectroscopy shows that the plasma or serum values of carotenoids do not correlate exactly with the skin values, if status changes for example appear in nutrition. There are several parameters influencing the bioavailability in the skin such as location within the skin (e.g. palm vs. forehead), pharmacokinetic issues of plasma and skin influencing the concentration of different carotenoids. The skin, in comparison with blood, can serve as a long-term reservoir for carotenoids.

These results suggest that the consumption of a natural extract containing a natural mixture of carotenoids significantly increases the concentration of carotenoids in serum, as well as in skin, and may be an efficient support to the human antioxidative system.

Table 4
Correlation coefficients according to Pearson for various correlations of the mean values of the skin and blood data of the Lutex group.

	Blood β-carotene	Blood lutein	Blood total carotenoids	Forehead carotenoids
Blood lutein	0.988	1		
Blood total carotenoids	0.999	0.988	1	
Forehead carotenoids	0.684	0.786	0.685	1
Palm carotenoids	0.721	0.684	0.717	0.992

7. Conclusion

To evaluate the effect of nutrition on the antioxidative properties in the skin, the measured blood concentrations must not necessarily reflect the skin levels; they can be time delayed and less pronounced. Furthermore, the distribution and storage behaviour is dependent on the body site. Therefore, the Raman technology is highly suitable for recording the values on the skin. Natural extracts enhance the levels of carotenoids, including those not directly supplemented. This indicates that the antioxidants in the skin protect each other in an antioxidative network.

Conflict of interest and funding disclosure

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M.C. Meinke, M.E. Darvin, H. Vollert, and J. Lademann have no conflicts of interests.

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