REVIEW

The contribution of β-carotene to vitamin A supply of humans

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Populations that administer highly restrictive diets using a strong dietary regime, excluding certain types of food, might be at risk of vitamin A insufficiency, even in developed countries. Thus, provitamin A carotenoids from plants represent an additional major dietary source of vitamin A for most of the world's population. Our aim was to estimate the contribution of β-carotene to vitamin A supply in industrialized countries using available data from the literature. A total of 11 studies from 8 countries were used, representing data of 121 256 participants. Intakes of total vitamin A, provitamin A carotenoids, including β-carotene were retrieved and used to calculate the retinol activity equivalents (RAE) utilizing current conversion factors. Mean total daily dietary intake of RAE was 1083 ± 175. The mean β-carotene intake was 3.9 mg/day. Preformed vitamin A accounts for nearly 65% of total vitamin A intake, carotenoids make up 35%. No statistical differences between men and women in total intake of retinol were observed. We conclude that a safe vitamin A intake in general cannot be reached by consuming only one component (vitamin A or β-carotene) alone, even in Western countries where animal products are commonly available.

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1 Introduction

Vitamin A refers to the compounds retinal, retinol and its esters, whereas provitamin A refers to the carotenoids β-cryptoxanthin, β-carotene and α-carotene, as these are the major vitamin A precursors in the diet [1]. Vitamin A is indispensable for cell differentiation, embryonic development and vision, besides many other roles (e.g. glycoprotein synthesis, carcinogenesis, growth hormone production) [2–5]. In developing countries, vitamin A deficiency still leads to thousands of cases of blindness, as well as increased morbidity and mortality [2].

Preformed vitamin A is present only in animal products, such as liver, kidney, fatty fish, dairy products and eggs. This preformed vitamin A is mostly consumed in the form of retinyl esters, which are easily hydrolyzed endogenously to form retinol. Vitamin A may also be converted endogenously from its dietary precursors β-carotene, α-carotene and β-cryptoxanthin, found mostly in green leafy and yellow-colored vegetables and orange-colored fruits [6]. Populations that administer highly restrictive diets, using a strong dietary regime, excluding certain types of food, even in developed countries, might be at risk of vitamin A insufficiency. Therefore, provitamin A carotenoids from plants are an additional major dietary source of vitamin A for most of the world's population [7].

Carotenoids are red and yellow fat-soluble pigments found in many fruits and vegetables. The major carotenoids with vitamin A activity in human plasma are β-carotene, α-carotene and β-cryptoxanthin, whereas the major carotenoids without vitamin A activity are lycopene, lutein and zeaxanthin [8].

β-Carotene is a commonly consumed plant pigment. Dietary sources of β-carotene include orange and bright green vegetables, such as carrot, sweet potato, pumpkin, broccoli and cabbage, as well as other foods like red palm oil and also vitamin supplements (Table 1).

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Abbreviations: FFQ, food frequency questionnaire; **24HDR,** 24-hour dietary recall; **RAE,** retinol activity equivalent; **RE,** retinol equivalent

Table 1. Sources of provitamin A carotenoids

β-Carotene	α-Carotene	β-Cryptoxanthin
Carrots	Carrots	Orange juice
Sweet potatoes	Sweet potatoes	Oranges
Pumpkin	Pumpkin	Bell peppers
Broccoli	Winter squash	Tropical fruits (e.g. papaya)
Cabbage	Green beans and peas	Tangerines
Red palm oil	Spinach	Physalis
Supplements	Broccoli	Apples
	Cabbage	
	Lettuce	

The amount of vitamin A formed from β-carotene depends on the source of β-carotene. β-Carotene in orange fruits and vegetables appears to be better absorbed and utilized, or more bioavailable, than β-carotene in leafy green vegetables [9], for detailed reviews on the bioavailability of carotenoids see [10–12]. Therefore, orange fruits and vegetables are better sources of vitamin A than leafy green vegetables with comparable β-carotene content. Carrots contain high amounts of β- and α-carotene. β-Cryptoxanthin is mainly derived from orange juice, oranges, bell peppers, some tropical fruits and tangerines/mandarines [8, 13, 14].

Carotenoids are hypothesized to exert other biological activities besides the provitamin A activity, including antioxidant capacity, immune modulation and regulation of cell differentiation and apoptosis, additionally β-carotene seems to play an important role in the control/reduction of body fat reserves [15–17]. But so far, the only clearly proven function in humans of β-carotene is its provitamin A activity [18].

Besides the positive effects and functions of β-carotene mentioned, one should also take into account the negative effects of β-carotene demonstrated in higher doses especially in smokers resulting in higher incidence of lung cancer and mortality [19, 20]; for reviews see [15, 21].

It is widely assumed that serum concentrations of carotenoids reflect, at least to some extent, the consumption of carotenoid-containing foods and, thus, serum carotenoid status is used as an index related to a healthy diet.

Due to its chemical structure, β-carotene can theoretically be centrally cleaved by β-carotene 15,15′-oxygenase to yield two molecules of vitamin A (retinol) [22], eccentric cleavage via β-carotene-9,10′-oxygenase yields only one molecule of retinol [22]. Other provitamin A carotenoids, thus can only yield one molecule retinol. Some authors suggest better bioavailability of the carotenoids β-cryptoxanthin and α-carotene compared with β-carotene leading to an overall better conversion rate for these two carotenoids than for β-carotene [23]. Practically, more than one molecule of β-carotene is needed to reach the activity of one molecule retinol. Compared with preformed vitamin A, β-carotene as well as other provitamin A carotenoids are relatively poor, but yet important sources of vitamin A.

Table 2. Factors influencing absorption, bioconversion and bioavailability of provitamin A carotenoids

Consumer specific characteristics (e.g. metabolism and absorption limit)	[51]
Dose	[52, 53]
Fat content of a meal	[26]
Food matrix	[54]
Food preparation and processing	[55]
Other carotenoids present in meal	[56, 57]

The recently accepted conversion factor for β-carotene is 12, for β-cryptoxanthin and α-carotene it is 24, meaning that 12 μg β-carotene and 24 μg β-cryptoxanthin or α-carotene, respectively, supposedly exert the activity of 1 μg vitamin A [24]. The retinol activity of carotenoids is indicated by retinol activity equivalents (RAE) [24]. In 2001, the US Institute of Medicine introduced this new conversion factor for β-carotene, replacing the former equivalent of 1 μg retinol (retinol equivalent; RE) = 6 μg β-carotene. So currently up-to-date estimation use the conversion factor as stated below

$$1\ \mathrm{RAE} = 1\ \mu\mathrm{g\ retinol},\ 12\ \mu\mathrm{g}\ \beta\text{–carotene},\ 24\ \mu\mathrm{g}\ \alpha\text{–carotene, or } 24\ \mu\mathrm{g}\ \beta\text{–cryptoxanthin} \tag{1}$$

The fraction of a dietary component that is capable of being absorbed and available for use or storage is called bioavailability [12]. There are various factors influencing the availability and the absorption and thus the conversion rate of provitamin A carotenoids (Table 2).

The maximum daily amount of β-carotene an adult intestine can cleave is approximately 2.5 mg [25]. The minimum amount of fat required for an optimal absorption of carotenoids is about 3–5 g per meal [26]. Determining the contribution of each factor to the vitamin A supply is important to understand the individual nutritional status of vitamin A supply. The bioavailability of carotenoids can also vary substantially depending on the presence of other carotenoids or other food components [27, 28]. Therefore, the amount of vitamin A obtainable from dietary carotenoids depends mainly on two factors: the bioavailability of the ingested carotenoids and the conversion of the carotenoids to vitamin A [16].

Burri et al. denoted that current conversion factors for α-carotene and β-cryptoxanthin were set at half the RAE for β-carotene only because the cleavage of one molecule of α-carotene or β-cryptoxanthin can theoretically only yield one molecule of retinol, instead of using data from α-carotene- and β-cryptoxanthin-rich foods [23]. The conversion rate of β-carotene may be less efficient when retinol is provided simultaneously from other dietary sources [29]. Interestingly, de Pee et al. suggest a β-carotene conversation factor of 1:21 for a mixed fruit and vegetable diet (ratio 1:4) [9].

In order to address our initial goal to test the contribution of carotenoids to vitamin A supply in industrialized countries, we performed a literature survey and used the available data for calculations.

2 Materials and methods

PubMed was searched for terms ''carotenoid intake'', ''retinol intake'', ''human'', ''diet'', and the results were reviewed for Western industrialized countries (e.g. North America, Europe, Australia). Inclusion criterions were at least the mean intake of preformed retinol and β-carotene, if possible also total vitamin A intake, α-carotene, and β-cryptoxanthin intake. Only articles available in English or German language were searched. Participant size of the study had to be minimum $n = 1000$. Intake of retinol and provitamin A carotenoids was measured by the method of dietary assessment, e.g. 24-h dietary recall (24HDR), food record (weight of foods eaten) or food frequency questionnaire (FFQ). Studies from 1998 to 2010 were searched that are mentioned in PubMed. Studies published before 1998 were often not conducted in Western populations, not in whole adult populations, did not indicate ''intake'', or did not show mean values (rather quintiles or odds ratios). Many studies were not included, as the number of participants was too small ($n < 1000$). Additionally, National Nutrition surveys in German and English language were searched, leading to the inclusion of the German and the Austrian Nutrition Report.

Provitamin A carotenoid intake was calculated as follows: 1 β-carotene+0.5 α-carotene+0.5 β-cryptoxanthin). Provitamin A carotenoid intake was then divided by 12 to calculate RAE (see and Eq. 2). If necessary, retinol intake data was calculated from total vitamin A intake: total vitamin A–(β-Carotene/6)–(other provitamin A carotenoids/12) to obtain retinol levels, as retinol intake was partly not given, some studies noted applying conversion factor 6 for β-carotene, this was then recalculated with the recent conversion factor 12.

$$\text{Retinol activity equivalents} = \mu\text{g retinol} + (\mu\text{g } \beta\text{-carotene}/12) + (\mu\text{g other provitamin A carotenoids}/24) \quad (2)$$

In the final stage, a total of 11 studies from 8 countries were used, including Italy, USA, Australia, the Netherlands, Austria, Germany, Ireland, Spain, and data from the EPIC study (European Prospective Investigation into Cancer and Nutrition which involves data from 10 European countries: Denmark, France, Greece, Germany, Italy, the Netherlands, Norway, Spain, Sweden and the United Kingdom). These studies represent data of 121 256 participants from 8 countries (Table 3).

The level of total vitamin A intake, which was recommended by most industrialized countries, was set to 800 μg/day, as it represents a good average of recommendations in Western countries [30–33]. The recommended intake levels vary from 700 μg/day (UK) to 1000 μg/day (Germany, Austria, Switzerland) for men and from 600 μg/day (UK) to 900 (Germany, Austria, Switzerland) for women.

It was not stated in each of the selected publications if supplements were included. We calculated total retinol and β-carotene intake from total intakes mentioned in each of the selected publications. In specific, two publications asked for supplement use and included this in the results [34, 35], all other publications supplements were either not inquired [14, 36–39], or inquired but not included in result calculations [40–43].

In particular, O'Brien included nutritional and supplement sources of retinol and states that retinol supplements contributed only 6.7 and 10.8% to total intake in men and women, respectively [34], Wang included reported supplement intake in the result calculations [35]. Goldbohm does not state any supplement intake [14], Garcia-Closas did not ask for/include supplements [36], Tavani only mentions common Italian foods and recipes and not supplements [37], Arancetas results are based only on dietary intake data, specifically excluding supplements [38], and Jenab presented only intake data from dietary sources and did not include supplement intake [39]. The questionnaire of Hodge covered supplement use, but supplement use was not quantified,

Table 3. Studies used in the analysis of vitamin A intake

Country	Participants	Women	Men	Method of dietary assessment	Reference
Spain[a)]	41 446	25 812	15 634	DHQ	[36]
Australia	3110	2024	1086	FFQ	[40]
Italy[b)]	1452	423	1029	FFQ	[37]
USA[c)]	4697	4697	–	Diet history questionnaire	[35]
The Netherlands	3123	1598	1525	Vitamin A intake: two-day-record; carotenoid intake: FFQ	[14]
Austria	2123	1345	778	24HDR, 3 day protocol	[42]
Germany	15 371	8278	7093	Diet history interview	[43]
Italy	2313	1245	1068	Estimated food record	[41]
Ireland	1379	717	662	7-Day estimated food diary	[34]
Spain	10 208	5480	4728	Repeated 24HDR	[38]
Europe (EPIC)	36 034	23 009	13 025	24HDR	[39]
Total	121 256	74 628	46 628		

a) Part of the Spanish EPIC cohort.
b) Controls and patients with non-fatal acute myocardial infarction.
c) Breast cancer risk patients and controls in non-Hispanic White and Hispanic women.

and thus not included in the results section [40], Sette specifically asked for supplement use and identified 5% of participants as supplement users, but the tables we used only included retinol and β-carotene intake from food and fortified food and excluded supplements [41], the Austrian Nutrition Survey showed that 37% of women and 45% of men consuming supplements used supplements containing vitamin A, and 30% of women and 26% of men consumed supplements containing β-carotene. In the analysis for the survey, supplements were not included, because brand and dose of supplementation were not specified [42]. The German Nutrition Survey showed that median intake of retinol supplements was 0.75 mg/day in men and women, median intake of β-carotene was 1.8 mg/day in women and 1.2 mg/day in men, respectively. Participants reaching reference values only rise by 1–4% by consuming supplements in the German Nutrition Survey [43].

The intake of carotenoids from colorants was not stated anywhere and thus we will not address this issue specifically.

3 Results

Figure 1 shows the mean dietary intake of RAE in the used studies, which might be taken as the representative of the general Western population. Mean total daily dietary intake of retinol activity equivalents is 1083 ± 175. Intake of preformed vitamin A (retinol) is 701 ± 362 RAE, β-carotene intake is 329 ± 144 RAE. α-Carotene and β-cryptoxanthin contribute 39.5 ± 14 RAE and 13.7 ± 5.8 RAE, respectively. Combined provitamin A carotenoids account for 382 ± 172 RAE (Fig. 1B).

As shown in Table 4, the total intake of provitamin A carotenoids is 5.2 mg/day. The mean β-carotene intake is 3.9 mg/day. The mean intake of β-carotene includes data from all mentioned studies, whereas intake of the other provitamin A carotenoids was only available in 5 studies (α-carotene) or 4 studies (β-cryptoxanthin), respectively.

Figure 2 shows the percentage of the daily contribution of intake of preformed vitamin A (retinol) and provitamin A carotenoids to total vitamin A intake. Total vitamin A intake was set to 100%. Preformed vitamin A accounts for nearly 65% of total vitamin A intake. Carotenoids only make up 35% (1.3% β-cryptoxanthin, 3.6% α-carotene and 30.4% β-carotene, respectively). Of the provitamin A carotenoids, β-carotene accounts for 86%, α-carotene for 10% and β-cryptoxanthin for 4%.

In order to test whether gender-related differences in the total vitamin A intake and in the contribution of the components of the vitamin A supply exist, we calculated the vitamin A supply for the male and the female population separately. Interestingly, both genders took up the same amount of RAE. About 68.4% of total vitamin A intake in men are ascribed to preformed vitamin A, whereas in women, preformed vitamin A accounts for some 63.8%

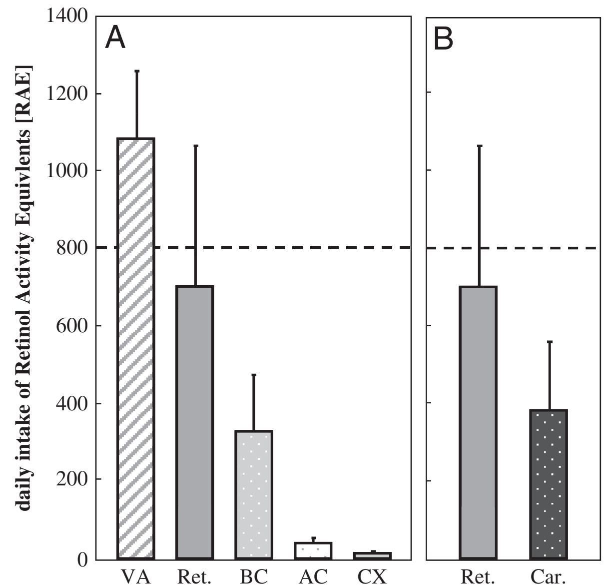

Figure 1. Mean dietary intake of retinol activity equivalents (RAE) or total vitamin A (VA), from preformed vitamin A (retinol = Ret.), β-carotene (BC), α-carotene (AC), and β-cryptoxanthin (CX). The average mean recommended dietary intake level (800 RAE) is shown by the dashed line. Columns show mean ± standard deviation. Retinol and β-carotene data were obtainable from 11 studies (n = 121 256), data for α-carotene and β-cryptoxanthin were obtainable from 5 and 4 studies, respectively (n = 53 828 and 50 705).

Table 4. Summarized carotenoid intake

	mg/day	n	Reference
β-Carotene intake	3.94 ± 1.7	121 256	[11, 28, 29, 44–51]
α-Carotene intake	0.95 ± 0.34	52 818	[11, 44–47]
β-Cryptoxanthin intake	0.33 ± 0.14	50 695	[44–47]
Total intake of provitamin A carotenoids	5.22		

(Fig. 3). Provitamin A carotenoids contribute 31.6% in men and 36.2% in women, respectively. The slightly elevated intakes of carotenoids in women are due to increased total intake of β-carotene, and not related to the other provitamin A carotenoids (intake of α-carotene: 32 RAE in men, 34 RAE in women, intake of β-cryptoxanthin: 20 RAE in men, 17 RAE in women, β-carotene: 265 RAE in men, 303 RAE in women). Interestingly, no statistical differences between the overall vitamin A intake levels in men and women were observed (886 versus 889 RAE).

4 Discussion

Our original aim was to judge the contribution of β-carotene to the vitamin A supply. Since it is obvious that various

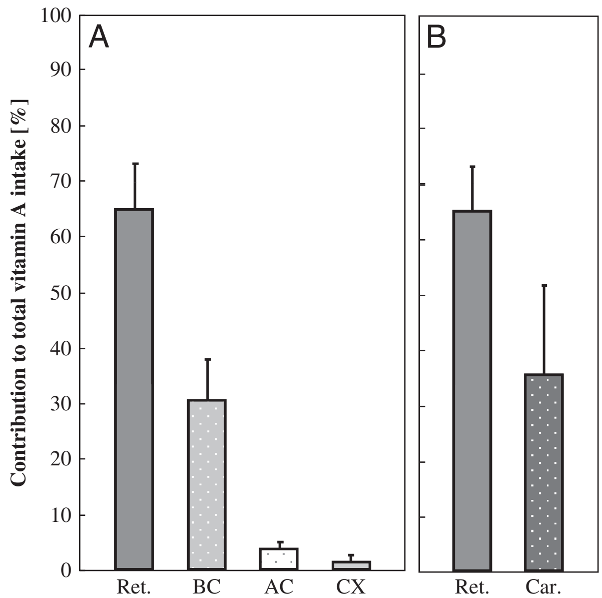

Figure 2. Percentage of mean daily contribution of preformed vitamin A (retinol = Ret.) and provitamin A-carotenoids (Car.) (β-carotene = BC, α-carotene = AC and β-cryptoxanthin = CX) to total vitamin A intake. Total Vitamin A intake was set at 100%. Columns show mean ± standard deviation. Retinol and β-carotene data were obtainable from 11 studies ($n = 121\,256$), data for α-carotene and β-cryptoxanthin were obtainable from 5 and 4 studies, respectively ($n = 53\,828$ and $50\,705$).

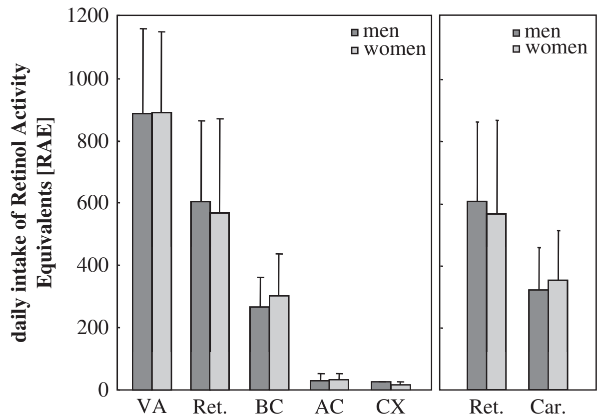

Figure 3. Contribution of preformed vitamin A (retinol = Ret.) and provitamin A-carotenoids (Car.) (β-carotene = BC, α-carotene = AC and β-cryptoxanthin = CX) to total vitamin A intake in men and women, respectively. Total Vitamin A intake was set at 100%. Columns show mean ± standard deviation. A total of 46 628 men and 74 628 women were included for retinol and β-carotene, whereas for α-carotene 19 274 and 34 554 women and for β-cryptoxanthin 17 749 men and 32 956 women were included.

populations do have differences in their nutritional habit, we limited our search of PubMed listed publications for studies performed in industrialized, Western countries, assuming a likewise nutritional style. Even so, only a limited number of PubMed listed publications were sufficiently large and included data on nutrient intake of carotenoids and retinol, whereas many others reported simply relative risk or OR levels. The number of studies was further restricted by the fact that a larger number of studies collected data on either carotenoid or retinol intake, but not of both.

Studies from single countries show varying results. In Germany, the mean daily intake of β-carotene is 5.1 mg for men and 5.4 mg for women, respectively [43], whereas in Austria (2.8 and 3.5 mg/day, male and female), and in the Netherlands (2.9 and 2.9 mg/day, male and female) the intake levels are considerably lower [14, 42]. Total vitamin A in the studies reviewed meets the averaged recommended dietary intake of 800 μg/day (or 800 RAE). The recommended intake levels vary from 700 μg/day (UK) to 1000 μg/day (Germany, Austria, Switzerland) for men and from 600 μg/day (UK) to 900 (Germany, Austria, Switzerland) for women. Therefore, in average this level cannot be reached by either preformed vitamin A or carotenoids alone in the whole population. Without preformed vitamin A, the requirements can hardly be met by carotenoids alone. In contrast, without provitamin A carotenoids, mean retinol intake also do not reach the average recommendation of 800 μg/day.

The total intake of provitamin A carotenoids is 5.2 mg/day. The mean β-carotene intake is 3.9 mg/day. This is in agreement with the recommended intake levels of 2–4 mg/day [31, 44]. Women take up somewhat more provitamin A carotenoids (36.2 versus 31.6% in men), which is due to elevated β-carotene intake. In men, on the other hand, 68.4% of total vitamin A intake attribute to retinol intake (versus 63.8% in women).

It should be mentioned that data for total and individual carotenoid intake obtained from different studies are difficult to compare due to differences in methodological approaches and the purpose of data collection. Methods of dietary assessment can be divided into records (keeping an active record) and recalls (recalling a specific period after a specific time). The record methods are, among others, the menu record, the estimated record, and the weighed record. The recalls include the diet history, the FFQ and the 24HDR. FFQs can be self-administered or conducted by an (professional dietitian) interviewer, their costs are comparably low (when self-administered) but limited by the fixed list of foods. 24HDR and diet histories can be more detailed by the ability of the interviewer to ask for portion sizes, snacks, etc, but are limited by the ability of participants to memorize meals. Weighed records are limited to a short time-period (often 1 day to 1 week) because of the burden for the participant. This method also is prone to changes in the dietary behavior due to the study burden. Methodological difficulties include furthermore random misclassification of dietary intake, un-/intentional underreporting of food consumption, and in the case of micronutrients as vitamin A or carotenoids incomplete data on their content in some foods in food composition tables and databases. Due to this complication often only one time point of data collection for carotenoid intake is performed. Based on correlations of dietary assessment and serum concentrations of carotenoids, the 7-day diet diary method is considered to be the most robust method of dietary assessment [45–47]. The FFQ method also shows moderate correlations with dietary carotenoid intakes of β-carotene, β-cryptoxanthin and zeaxanthin with serum concentrations [48]. All these methodological differences lead to hard to compare results concerning intake of carotenoids and vitamin A. As for our study, we tried to compare the intake data of adults living in Western countries, including different intake measurement methods and studies implying at least retinol and β-carotene data and preferably also data of provitamin A carotenoids.

It should be noted, that in the Western world, supplement use is widely spread and contributes to the carotenoid and vitamin A intake. In Germany, 12.4% of men, and 24.9% of women are considered as regular users of dietary supplements, in the UK, even 29% of men and 40% of women use supplements on a daily basis [49, 50].

Various countries recommend different dietary intake doses of RAE. The USA, Canada and Australia recommend a daily dietary intake of vitamin A of 700 μg for women and 900 μg for men, respectively [30, 33]. Germany, Austria and Switzerland recommend a higher intake of 800 μg for women and 1000 μg for men, respectively [44], whereas the UK recommends 600 μg for women and 700 μg for men, respectively [32]. This leads to varying interpretation of study results depending on which reference values are used. Therefore, it is difficult to reach a conclusion whether the recommended vitamin A intake is reached. However, since β-carotene contributes about 30% to vitamin A intake in Western countries, it can be stated that a safe vitamin A intake in general cannot be reached by consuming only one component (vitamin A or β-carotene) alone. Therefore, highly restrictive diets using a strong dietary regime excluding certain types of food might be accompanied by vitamin A deficiency.

The authors have declared no conflict of interest.

5 References

[1] Nomenclature policy: generic descriptors and trivial names for vitamin A and related compounds. *J. Nutr.* 1984, *114.* 643–644.

[2] Underwood, B. A., Arthur, P., The contribution of vitamin A to public health. *FASEB J.* 1996, *10*, 1040–1048.

[3] McCullough, F. S., Northrop-Clewes, C. A., Thurnham, D. I., The effect of vitamin A on epithelial integrity. *Proc. Nutr. Soc.* 1999, *58*, 289–293.

[4] Luo, T., Sakai, Y., Wagner, E., Drager, U. C., Retinoids, eye development, and maturation of visual function. *J. Neurobiol.* 2006, *66*, 677–686.

[5] Marceau, G., Gallot, D., Lemery, D., Sapin, V., Metabolism of retinol during mammalian placental and embryonic development. *Vitam. Horm.* 2007, *75*, 97–115.

[6] Simpson, K. L., Relative value of carotenoids as precursors of vitamin A. *Proc. Nutr. Soc.* 1983, *42*, 7–17.

[7] Bendich, A., Olson, J. A., Biological actions of carotenoids. *FASEB J.* 1989, *3*, 1927–1932.

[8] Chug-Ahuja, J. K., Holden, J. M., Forman, M. R., Mangels, A. R. et al., The development and application of a carotenoid database for fruits, vegetables, and selected multicomponent foods. *J. Am. Diet. Assoc.* 1993, *93*, 318–323.

[9] de Pee, S., West, C. E., Permaesih, D., Martuti, S. et al., Orange fruit is more effective than are dark-green, leafy vegetables in increasing serum concentrations of retinol and beta-carotene in schoolchildren in Indonesia. *Am. J. Clin. Nutr.* 1998, *68*, 1058–1067.

[10] Castenmiller, J. J., West, C. E., Bioavailability and bioconversion of carotenoids. *Annu. Rev. Nutr.* 1998, *18*, 19–38.

[11] Yeum, K. J., Russell, R. M., Carotenoid bioavailability and bioconversion. *Annu. Rev. Nutr.* 2002, *22*, 483–504.

[12] Maiani, G., Caston, M. J., Catasta, G., Toti, E. et al., Carotenoids: actual knowledge on food sources, intakes, stability and bioavailability and their protective role in humans. *Mol. Nutr. Food Res.* 2009, *53*, S194–S218.

[13] Mangels, A. R., Holden, J. M., Beecher, G. R., Forman, M. R. et al., Carotenoid content of fruits and vegetables: an evaluation of analytic data. *J. Am. Diet. Assoc.* 1993, *93*, 284–296.

[14] Goldbohm, R. A., Brants, H. A., Hulshof, K. F., van den Brandt, P. A., The contribution of various foods to intake of vitamin A and carotenoids in The Netherlands. *Int. J. Vitam. Nutr. Res.* 1998, *68*, 378–383.

[15] Bendich, A., From 1989 to 2001: what have we learned about the ''biological actions of beta-carotene''? *J. Nutr.* 2004, *134*, 225S–230S.

[16] Olson, J. A., The effects of iron and copper status and of dietary carbohydrates on the activity of rat intestinal beta-carotene 15,15′-dioxygenase. *Br. J. Nutr.* 2000, *84*, 3–4.

[17] Amengual, J., Gouranton, E., van Helden, Y. G., Hessel, S. et al., Beta-carotene reduces body adiposity of mice via BCMO1. *PLoS. One.* 2011, *6*, e20644.

[18] Grune, T., Lietz, G., Palou, A., Ross, A. C. et al., Beta-carotene is an important vitamin A source for humans. *J. Nutr.* 2010, *140*, 2268S–2285S.

[19] The alpha-tocopherol, beta carotene cancer prevention study group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *N. Engl. J. Med.* 1994, *330.* 1029–1035.

[20] Goodman, G. E., Thornquist, M. D., Balmes, J., Cullen, M. R. et al., The beta-carotene and retinol efficacy trial: incidence of lung cancer and cardiovascular disease mortality during 6-year follow-up after stopping beta-carotene and

retinol supplements. *J. Natl. Cancer Inst.* 2004, *96*, 1743–1750.

[21] Patrick, L., Beta-carotene: the controversy continues. *Altern. Med. Rev.* 2000, *5*, 530–545.

[22] Kiefer, C., Hessel, S., Lampert, J. M., Vogt, K. et al., Identification and characterization of a mammalian enzyme catalyzing the asymmetric oxidative cleavage of provitamin A. *J. Biol. Chem.*2001, *276*, 14110–14116.

[23] Burri, B. J., Chang, J. S., Neidlinger, T. R., Beta-cryptoxanthin- and alpha-carotene-rich foods have greater apparent bioavailability than beta-carotene-rich foods in Western diets. *Br. J. Nutr.* 2011, *105*, 212–219.

[24] Institute of Medicine. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc.* A Report of the Panel on Micronutrients, Subcommittees on Upper Reference Levels of Nutrients and of Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes Food and Nutrition Board, National Academy Press, Washington, DC, 2001, pp. 91–93.

[25] During, A., Smith, M. K., Piper, J. B., Smith, J. C., Beta-carotene 15,15′-dioxygenase activity in human tissues and cells: evidence of an iron dependency. *J. Nutr. Biochem.* 2001, *12*, 640–647.

[26] Roodenburg, A. J., Leenen, R., van het Hof, K. H., Weststrate, J. A. et al., Amount of fat in the diet affects bioavailability of lutein esters but not of alpha-carotene, beta-carotene, and vitamin E in humans. *Am. J. Clin. Nutr.* 2000, *71*, 1187–1193.

[27] Parker, R. S., Swanson, J. E., You, C. S., Edwards, A. J. et al., Bioavailability of carotenoids in human subjects. *Proc. Nutr. Soc.* 1999, *58*, 155–162.

[28] Granado, F., Blazquez, S., Olmedilla, B., Changes in carotenoid intake from fruit and vegetables in the Spanish population over the period 1964–2004. *Public Health Nutr.* 2007, *10*, 1018–1023.

[29] Tang, G., Bioconversion of dietary provitamin A carotenoids to vitamin A in humans. *Am. J. Clin. Nutr.* 2010, *91*, 1468S–1473S.

[30] Institute of Medicine, *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. A Report of the Panel on Micronutrients, Subcommittees on Upper Reference Levels of Nutrients and of Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes Food and Nutrition Board, National Academy Press, Washington, DC, 2001, pp. 113–115.

[31] Bundesinstitut für Risikobewertung (BfR). *Verwendung von Vitaminen in Lebensmitteln. Toxikologische und Ernährungsphysiologische Aspekte, Teil I*, 2004.

[32] Dietary reference values for food energy and nutrients for the United Kingdom. Report of the Panel on Dietary Reference Values of the Committee on Medical Aspects of Food Policy. *Rep. Health Soc. Subj.* (*Lond*) 1991, *41*, 1–210.

[33] Nutrient Reference Values for Australia and New Zealand Including Recommended Dietary Intakes. *National Health and Medical Research Council (NHMRC)*, 2006.

[34] O'Brien, M. M., Kiely, M., Harrington, K. E., Robson, P. J. et al., The North/South Ireland Food Consumption Survey: vitamin intakes in 18–64-year-old adults. *Public Health Nutr.* 2001, *4*, 1069–1079.

[35] Wang, C., Baumgartner, R. N., Yang, D., Slattery, M. L. et al., No evidence of association between breast cancer risk and dietary carotenoids, retinols, vitamin C and tocopherols in Southwestern Hispanic and non-Hispanic White women. *Breast Cancer Res. Treat.* 2009, *114*, 137–145.

[36] Garcia-Closas, R., Berenguer, A., Jose, T. M., Jose, S. M. et al., Dietary sources of vitamin C, vitamin E and specific carotenoids in Spain. *Br. J. Nutr.* 2004, *91*, 1005–1011.

[37] Tavani, A., Gallus, S., Negri, E., Parpinel, M. et al., Dietary intake of carotenoids and retinol and the risk of acute myocardial infarction in Italy. *Free Radic. Res.* 2006, *40*, 659–664.

[38] Aranceta, J., Serra-Majem, L., Perez-Rodrigo, C., Llopis, J. et al., Vitamins in Spanish food patterns: the eVe Study. *Public Health Nutr.* 2001, *4*, 1317–1323.

[39] Jenab, M., Salvini, S., van Gils, C. H., Brustad, M. et al., Dietary intakes of retinol, beta-carotene, vitamin D and vitamin E in the European Prospective Investigation into Cancer and Nutrition cohort. *Eur. J. Clin. Nutr.* 2009, *63*, S150–S178.

[40] Hodge, A. M., Simpson, J. A., Fridman, M., Rowley, K. et al., Evaluation of an FFQ for assessment of antioxidant intake using plasma biomarkers in an ethnically diverse population. *Public Health Nutr.* 2009, *12*, 2438–2447.

[41] Sette, S., Le, D. C., Piccinelli, R., Arcella, D. et al., The third Italian National Food Consumption Survey, INRAN-SCAI 2005-06 – Part 1: Nutrient intakes in Italy. *Nutr. Metab. Cardiovasc. Dis.* 2010.

[42] Elmadfa, I., Freisling, H., Nowak, V., Hofstädter, D. et al., *Österreichischer Ernährungsbericht 2008. Institut für Ernährungswissenschaften, Universität Wien*, 2009.

[43] Max Rubner-Institut Bundesforschungsinstitut für Ernährung und Lebensmittel. Max Rubner-Institut. *Nationale Verzehrs Studie II – Ergebnisbericht, Teil 2.* Karlsruhe, 2008.

[44] Deutsche Gesellschaft für Ernährung e.V.(DGE) et al., *D-A-CH. Referenzwerte für die Nährstoffzufuhr*, 2008.

[45] Scott, K. J., Thurnham, D. I., Hart, D. J., Bingham, S. A. et al., The correlation between the intake of lutein, lycopene and beta-carotene from vegetables and fruits, and blood plasma concentrations in a group of women aged 50–65 years in the UK. *Br. J. Nutr.* 1996, *75*, 409–418.

[46] Bingham, S. A., Welch, A. A., McTaggart, A., Mulligan, A. A. et al., Nutritional methods in the European prospective investigation of cancer in Norfolk. *Public Health Nutr.* 2001, *4*, 847–858.

[47] Day, N., McKeown, N., Wong, M., Welch, A. et al., Epidemiological assessment of diet: a comparison of a 7-day diary with a food frequency questionnaire using urinary markers of nitrogen, potassium and sodium. *Int. J. Epidemiol.* 2001, *30*, 309–317.

[48] Tucker, K. L., Chen, H., Vogel, S., Wilson, P. W. et al., Carotenoid intakes, assessed by dietary questionnaire, are associated with plasma carotenoid concentrations in an elderly population. *J. Nutr.* 1999, *129*, 438–445.

[49] Beitz, R., Mensink, G. B., Fischer, B., Thamm, M., Vitamins – dietary intake and intake from dietary supplements in Germany. *Eur. J. Clin. Nutr.* 2002, *56*, 539–545.

[50] Swan, G., Findings from the latest National Diet and Nutrition Survey. *Proc. Nutr. Soc.* 2004, *63*, 505–512.

[51] Lampen, A., Meyer, S., Arnhold, T., Nau, H., Metabolism of vitamin A and its active metabolite all-trans-retinoic acid in small intestinal enterocytes. *J. Pharmacol. Exp. Ther.* 2000, *295*, 979–985.

[52] Novotny, J. A., Harrison, D. J., Pawlosky, R., Flanagan, V. P. et al., Beta-carotene conversion to vitamin A decreases as the dietary dose increases in humans. *J. Nutr.* 2010, *140*, 915–918.

[53] Tang, G., Qin, J., Dolnikowski, G. G., Russell, R. M., Vitamin A equivalence of beta-carotene in a woman as determined by a stable isotope reference method. *Eur. J. Nutr.* 2000, *39*, 7–11.

[54] Lemke, S. L., Dueker, S. R., Follett, J. R., Lin, Y. et al., Absorption and retinol equivalence of beta-carotene in humans is influenced by dietary vitamin A intake. *J. Lipid Res.* 2003, *44*, 1591–1600.

[55] van het Hof, K. H., West, C. E., Weststrate, J. A., Hautvast, J. G., Dietary factors that affect the bioavailability of carotenoids. *J. Nutr.* 2000, *130*, 503–506.

[56] Kostic, D., White, W. S., Olson, J. A., Intestinal absorption, serum clearance, and interactions between lutein and beta-carotene when administered to human adults in separate or combined oral doses. *Am. J. Clin. Nutr.* 1995, *62*, 604–610.

[57] Van den Berg, H., van, V. T., Effect of simultaneous, single oral doses of beta-carotene with lutein or lycopene on the beta-carotene and retinyl ester responses in the triacylglycerol-rich lipoprotein fraction of men. *Am. J. Clin. Nutr.* 1998, *68*, 82–89.

