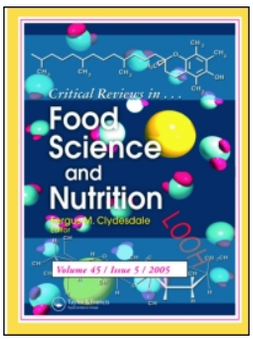

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A review on factors influencing bioaccessibility and bioefficacy of carotenoids

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ABSTRACT

Vitamin A deficiency is one of the most prevalent deficiency disorders in the world. As shown by many studies plant food based approaches have a real potential on prevention of vitamin A deficiency in a sustainable way. Carotenoids are important as precursors of vitamin A as well as for prevention of cancers, coronary heart diseases, age-related macular degeneration, cataract etc. Bioaccessibility and bioefficacy of carotenoids are known to be influenced by numerous factors including dietary factors such as fat, fiber, dosage of carotenoid, location of carotenoid in the plant tissue, heat treatment, particle size of food, carotenoid species, interactions among carotenoids, isomeric form and molecular linkage and subject characteristics. Therefore even when carotenoids are found in high quantities in plant foods their utilization may be unsatisfactory because some factors are known to interfere as negative effectors.

KEYWORDS

Carotenoids; bioavailability; bioaccessibility; bioefficacy; bioconversion; dietary factors

Introduction

Vitamin A deficiency is one of the most prevalent micronutrient deficiency disorders in the world. According to the National surveys vitamin A deficiency prevalence has remained high in pre-school children in much of the less developed world (IVACG, 2003; IVACG, 2004). Vitamin A plays a key role in vision, immunity, cell differentiation, maintenance of cell membrane integrity, embryonic development and growth & reproduction (Garrow et al., 2000). Vitamin A deficiency is the leading cause for the blindness among approximately 350,000 of pre-school children in each year (Garrow et al., 2000). As well, more than 250 million children suffer from sub-clinical vitamin A deficiency worldwide (IVACG, 2003). In addition to that marginal vitamin A deficiency has been reported from low-income countries and nearly 25% of children affected from that condition. The prevalence rate is highest in Asian countries (Mason et al., 2004). According to the documentary facts vitamin A deficiency is a global threat.

Carotenoids are natural plant pigments responsible for most of the yellow, orange, and red colors found in all over the natural world including the plant kingdom, giving those brilliant colors to fruits, vegetables, and flowers. Depending on the structural characteristics carotenoids can be categorized as pro-vitamin A carotenoids; e.g., β-carotene, α-carotene, γ-carotene, β-cryptoxanthin, and non pro-vitamin A carotenoids; e.g., Lutein, zeaxanthin, astaxanthin, violaxanthin. The necessary structural requirement to have vitamin A activity is that the carotenoid molecule must consist of at least one unsubstituted β-ionone moiety with a polyene chain of at least eleven carbon atoms (Rodriguez-Amaya, 1999).

In addition to the pro-vitamin A carotenoids, non pro-vitamin A caotenoids also exert their antioxidant activity by singlet oxygen quenching and free radical scavenging effects thereby they possess a range of important protective mechanisms for human health. This involves protection against the pathogenesis of degenerative diseases especially coronary heart diseases, cancers and an array of other free radical-mediated conditions (Krinsky, 1989; Halliwell, 1997; Kritchevsky, 1999).

Lutein and zeaxanthin usually referred to as "macula pigments" are known to provide the protection against age-related macular degeneration mediated by their ability to scavenge harmful reactive oxygen species formed in the photoreceptors. In addition, they can act as blue-light filters and may protect the macula from blue-wavelength photons (Landrum and Bone, 2001).

During digestion, due to chewing in the mouth partially disrupted food matrix enters to the stomach. In the stomach caroteno-protein complexes are dissociated into carotenoids by the action of pepsin. Further digestion takes place in the small intestine by proteolytic enzymes. Once the carotenoids are released in the stomach they associate with the dietary lipids. Bile salts emulsify the lipid containing carotenoids (Hedren, 2004). Carotenoids incorporated into mixed micelles are then absorbed intact. Absorption takes place in the small intestinal mucosal cells by passive diffusion along a concentration gradient. Within the intestinal epithelium, part of the pro-vitamin A carotenoids is converted into retinal by the enzyme 15–15′-carotenoid dioxygenase which can be subsequently reduced into retinol (Goodwin, 1986).

Food-based approaches are known to have a long-term solution to vitamin A deficiency worldwide (Tang et al., 1999; de Pee et al., 1998; Takyi, 1999; Wasantwisut et al., 2000; Drammeh et al., 2002). Therefore encouragements to ingest foods

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rich in pro-vitamin A carotenoids is one of the intervention strategies in prevention and controlling of vitamin A deficiency.

With regard to carotenoids, "bioavailability" is the fraction of ingested carotenoids available for normal physiological functions and storage. "Bioaccessibility" is the capacity of the digestive process to release carotenoids from the food matrix. This step assumed the key step in the bioavailability of carotenoids. "Bioconversion" is defined as "the proportion that is converted into retinol from the absorbed pro-vitamin A carotenoids " and the "bioefficacy" is the efficiency with which ingested carotenoids are absorbed and the fraction of that which is converted into retinol in the body (van Lieshout et al., 2001; van Lieshout et al., 2003).

Bioaccessibility and bioefficacy are governed by various factors. Therefore even when carotenoids are found in high quantities in the plant foods their consumption may be unsatisfactory to meet the requirement of vitamin A because some factors are known to interfere as effectors. The factors that influence bioavailability are grouped in the mnemonic "SLAMENGHI" and elucidated as, Species of carotenoids, molecular Linkage, Amount of carotenoids consumed in a meal, Matrix in which the carotenoid is incorporated, Effectors of absorption and bioconversion, Nutrient status of the host, Genetic factors, Host-related factors and mathematical Interactions (de Pee and West, 1996; Castenmiller and West, 1998). But Castenmiller and West (1998) reported that different carotenoids seem to have their own manner in absorption, plasma transport, and metabolism. van Vliet (1996) who reported that absorption occurs in a relatively nonspecific fashion, but absorption kinetics, and plasma transport seem to differ among carotenoids depending on polarity.

However, awareness on factors affecting bioaccessibility and bioefficacy of carotenoids is extremely important as in the case of some factors necessary precautions could be taken in order to increase the bioavailability of carotenoids in the target population.

The effect of dietary factors on bioaccessibility and bioefficacy of carotenoids

Dietary effectors

Fat

Among the dietary factors fat is a key positive effector on bioaccessibility and bioefficacy of carotenoids. Fat directs its effect in three different ways; stimulating bile salt secretion, giving a hydrophobic environment for the released carotenoids and promoting micelles formation.

Several studies have been shown that the positive effect of fat on carotenoid absorption in different ways. Brown et al. (2004) observed that the appearance of carotenoids in plasma chylomicrons had increased with ingestion of salads with reduced-fat salad dressing, compared to ingestion of salads with fat-free salad dressing. Authors further noticed that the appearance of carotenoids in plasma chylomicrons was higher after the intake of salads with full-fat than the reduced-fat salad dressing. Prince and Frisoli (1993) carried out a study on the effect of fat on accumulation of β-carotene in serum and skin. The absence of dietary fat resulted in no detectable changes in serum β-carotene levels with the administration of a single 51 mg dose of β-carotene. But the same dose administered with 200 g of fat had increased serum β-carotene concentration 2.5-fold at 40 h. Results of Unlu et al. (2005) revealed that addition of avocado (half or whole fruit, equivalent to 75 and 150 g avocado, respectively) significantly enhanced carotenoid absorption from salsa and salad and they concluded that the positive effect of avocado in enhancing carotenoid absorption is due to the presence of high amount of lipids in avocado. The comparison of avocado fruit with added avocado oil indicated that the lipid component of the avocado fruit is the significant variable enhancing carotenoid absorption and the fruit matrix has no negative effect on lipid release. The study included a new view regarding enhancing carotenoid absorption by showing the possibility of using a lipid-rich fruit instead of added fat/oil to increase the absorption of carotenoids.

Deming et al. (2000) showed the effects of dietary fat level at 10 or 30% of total energy and fiber type on β-carotene bioavailability. Results indicated increasing dietary fat resulted in higher vitamin A and lower β-carotene stores in the liver. Authors explained that this observation is due to fat enhanced bioconversion of β carotene into vitamin A. Roodenburg et al. (2000) showed that the effect of dietary fat on the bioavailability of lutein is different from the effect on α-carotene and β-carotene. The optimal uptake of α-carotene and β-carotene was similar when these carotenoids are consumed with a low-fat meal ($\approx$3 g fat) or a high-fat meal ($\approx$36 g fat), while the bioavailability of lutein esters was considerably lower when lutein esters were consumed as a part of a low-fat meal. Authors discussed this result was unpredicted as lutein is less lipophilic than α-carotene and β-carotene, therefore a great influence of the amount of dietary fat would be expected for the more lipophilic carotenoids. On the other hand, the lutein used in the above study was in esterified form and it is likely that lutein esters are more lipophilic than α-carotene and β-carotene. It can thus be assumed that in the presence of only little amounts of fat, the emulsification of lutein esters in the intestine is less than that of α-carotene and β-carotene. Further when lutein is not present as its ester form the quantity of fat required for its absorption may be less than the lutein esters.

The significance of dietary fat in bioaccessibility and bioefficacy of carotenoid is clearly mentioned by many authors. But the quantity of dietary fat needed for optimal bioavailability of carotenoids is not much clear. It is suggested that essentially a minimum quantity of fat is required for carotenoid absorption and the minimum amount for optimum absorption was 5 g of fat per day (Castenmiller and West, 1998). This observation is supported by the study of Ribaya-Mercado (2002). Depending on serum retinol or β-carotene response to meals including carotenes and different amounts of fat, it has been suggested that only a small quantity of fat may be needed to ensure carotene utilization in humans, 5 g of fat in a meal containing 40 g of cooked spinach (with 1.2 mg β-carotene) or 3 g of fat for 8 mg of α-carotene and β-carotene supplements consumed with a meal. But Roodenburg et al. (2000) proposed that different carotenoids require different amounts of fat. An experiment carried out on homogenized carrot showed that addition of 20% oil per gram dry matter increased the *in vitro* accessible β-carotene to a significant level. But when increased further up

to 60% there was only a slight increase (Hedren et al., 2002). Rock (1997) stated in a review that the level of fat does not affect tissue carotenoids concentration, suggesting a threshold effect for fat.

The conclusion on type of dietary fat on bioaccessibility and bioefficacy of carotenoids is uncertain. However Borel et al. (1998) investigated the effect of the ingestion of β-carotene with medium-chain triglycerides or long-chain triglycerides on the bioavailability of β-carotene in humans. The results showed chylomicron β-carotene response is obviously reduced when β-carotene is absorbed with medium-chain triglycerides instead of long-chain triglycerides. The possible reason for above observation is due to the reduced chylomicrons secretion with the present of medium-chain triglycerides. Further the results of the same study showed that medium-chain triglycerides had no adverse effect on bioconversion of β-carotene.

Outcomes of *in vitro* studies carried out by Priyadarshani and Chandrika (2007) indicated that addition of fat (scraped coconut and coconut milk) improved the percentage *in vitro* accessible β-carotene abut five-fold from carrot salad and about six-fold from carrot curry compared to the raw carrot.

According to Noakes et al. (2002) consumption of an additional daily serving of a high-carotenoid vegetable or fruit when consuming spreads containing sterol or stanol esters facilitates maintaining of plasma carotenoid concentrations while lowering LDL-cholesterol concentrations significantly.

Zhi et al. (1996) assessed the influence of orlistat, a lipase inhibitor, on the absorption of β-carotene. They observed that orlistat treatment had reduced the absorption of β-carotene by approximately one-third.

Fiber

Soluble dietary fiber has a negative effect on absorption of carotenoids in humans. Rock and Swendseid (1992) demonstrated that pectin has an inhibitory effect on plasma β-carotene response to a single dose of purified β-carotene administered with a meal. These data clearly indicated that the occurrence of dietary fiber in the food is the reason for decrease in plasma β-carotene response that has been observed after administration of carotenoid-rich foods compared to the purified β-carotene supplements. They further noticed that in the presence of pectin there was a 42% reduction in plasma β-carotene concentration in humans compared to control group. There are two possible explanations for this inhibition. One effect occurs due to soluble fibers diminishing micelle formation by increasing faecal excretion of bile acids. This is believed to be due to interaction of soluble fibers with bile acids (Yeum and Russell, 2002). Other role is that soluble dietary fiber can interfere the contact of micelle with intestinal mucosal cells by increasing the viscosity of the intestinal contents (van den Berg et al., 2000).

Water-soluble dietary fiber types (pectin, guar, and alginate) significantly reduced the absorption of β-carotene compared to the water-insoluble fibers. The same effect was observed for canthaxanthin also. Though both water-soluble and water-insoluble types of fiber reduce the absorption of lycopene and lutein there was no distinct difference in absorption of lycopene and lutein by both types of fiber (Riedl et al., 1999).

Deming et al. (2000) found that the effect of soluble fiber on hepatic vitamin A storage is based on fiber type. They showed consumption of citrus pectin decreases hepatic vitamin A stores and increases hepatic β-carotene stores. Authors explained that the above observation is due to less conversion of β carotene into vitamin A. In contrast, consumption of oat gum resulted in increased hepatic vitamin A and decreased β-carotene stores compared to citrus pectin. The study confirmed that citrus pectin has a negative effect on β carotene bioavailability but oat gum does not have such adverse affect on above process. This study further revealed that the level of dietary fat consumed with soluble fiber had no interactive effects on hepatic vitamin A, β-carotene or α-carotene stores but β-carotene bioavailability is independently affected by dietary fat level and type of soluble fiber.

Contrary to the most of the other studied carried out on effect of dietary fiber on absorption of carotenoids Unlu et al. (2005) demonstrated that no inhibitory effect on absorption of carotenoids from the dietary fiber present in avocado fruit though avocado is a good source of dietary fiber (6.8 g fiber/100 g edible portion) and 72% of these are insoluble fibers such as cellulose, pectin, and hemicelluloses. Authors discussed it is difficult to compare this effect with other studies as different studies have been used various types of dietary fibers. In addition to that, in this study intact carotenoid content has been quantified in the plasma triacylglycerol-rich lipoprotein (TRL) fraction during the 9.5 h after consumption of the test meal. Authors further discussed dietary fibers might show a marked negative effect on absorption of carotenoids as measured in plasma during long-term absorption studies compared to the TRL responses due to increased fecal excretion of carotenoids.

However, Castenmiller et al. (1999) reported that there was no inhibition of carotenoid absorption when dietary fiber was added to liquefied spinach. Authors suggested that this may be due to once the cell wall components are disrupted, addition of dietary fiber in quantities previously present in the food, has no effect on absorption of carotenoids.

Dosage of carotenoid

Serum β-carotene concentration depends on the amount of β-carotene in the meal. In general, less efficient absorption was noted with the administration of higher doses, which were not specified by authors (Castenmiller and West, 1998). Prince and Frisoli (1993) showed that administration of β-carotene daily in three divided doses with meals raised the serum β-carotene concentration three times as high compared with the same total dose administered once a day. Authors further mentioned that β-carotene has a therapeutic application but it's difficult to predict the optimal dose and regimen for each of its potential applications. van het Hof et al. (1999a) concluded that there is a marked difference in the bioavailability of β-carotene and lutein among different vegetables. In addition to that, the same study revealed that even though the spinach contains 10-fold higher β-carotene content compared to broccoli or green peas the total increase in plasma β-carotene levels were shown with the consumption of broccoli and green peas and not by the spinach. Authors discussed that the reason for above observation is due to the considerable difference among the different vegetable types in their efficacy to increase plasma levels of

β-carotene and the effectiveness of absorption of β-carotene and bioconversion of β-carotene into retinol may decrease with increasing intake. It was evident that when the carotenoid content of digested fruits or vegetables is higher, the transferring of carotenoids into the micelles becomes lower. Red grapefruit which contained the highest contents of lycopene and β-carotene showed only 4.9% and 2.1% transferred to the micelles, respectively. Spinach which had the highest content of lutein had the lowest bioaccessibility (18.9%) (O'Connell et al., 2007).

Daily administration of 15 or 45 mg β-carotene significantly increased the plasma β-carotene levels. The degree of increase and the pattern of plasma β-carotene levels showed extensive inter individual variation (Dimitrov et al., 1988).

Food matrix

The first step of carotenoid bioavailability is the mechanical and chemical disruption of the food matrix and the release of the carotenoids from the matrix where they were embedded and from protein complexes (Britton, 1995).

Location of carotenoids in plant tissue

Carotenoids exist in various forms within cell. When they are located in chromoplast they can exist in different ways such as crystalline form e.g., carrot and tomato, dissolved in oil droplets e.g., pumpkin. In such cases carotenoids are far more bioaccessible during digestion than when they are complexed to proteins in chloroplasts such as green leafy vegetables (de Pee et al., 1995; Castenmiller and West, 1998).

de Pee et al. (1995) carried out a study in order to find out that the effect of an extra daily portion of dark-green leafy vegetables on vitamin A and iron status in women with low hemoglobin concentrations (<130 g/L) who were breastfeeding a child of 3–17 months. The study population was given an additional daily portion of dark-green leafy vegetables. Authors noted that there was no improvement in vitamin A status, but a similar quantity of β-carotene from a simpler matrix showed a strong improvement of vitamin A status.

An intervention study was conducted on healthy men and they were administered four lutein doses including lutein supplement, lutein ester supplement, spinach and lutein-enriched egg for 9 days. All lutein doses contained 6 mg lutein except for the lutein ester dose, which contained 5.5 mg lutein equivalents. The results indicated that on day 10 baseline and dose-adjusted lutein response in serum was significantly higher with the consumption of egg than other lutein treatments. This observation is due to the presence of cholesterol in the egg yolk where in egg yolk, lutein is located in the digestible lipid matrix, which consists of cholesterol, triglycerides, and phospholipids (Chung et al., 2004).

According to an *in vitro* study carried out by O'Connell et al. (2007) transferring of xanthophylls to the micelles from fruits was higher than that of dark green leafy vegetables and therefore has a greater possibility for intestinal absorption.

Heat treatment

Raw plant foods are suggested to be less bioaccessible compared to thermally processed foods. Heat treatment causes softening and disrupting of the cell membranes and plant cell walls, also suggested to disrupt further the protein-carotenoid complexes (Erdman et al., 1988). As a result digestive enzymes can be more effective during the digestion process.

Consumption of thermally processed and pureed carrot and spinach on each day over a 4-week period produced a three-fold increase in plasma β-carotene concentration compared to the consumption of the same quantity of β-carotene from the same vegetables but in raw form (Rock et al., 1998). According to the Hedren et al. (2002) *in- vitro* accessible β-carotene content released from homogenized carrot pulp was 21% and cooking the pulp increased the accessibility to 27%. The similar trend was observed for α-carotene as well.

According to the *in vitro* study carried out on raw and boiled carrot showed that heat treatment improved the release of β-carotene from boil carrot about six-fold compared to raw carrot (Priyadarshani and Chandrika, 2007).

Contrary to the above studies a study in ferrets showed no significant increase in β-carotene level after consumption of thermally processed carrot. However, consumption of thermally processed carrot juice and thermally unprocessed carrot juice & isolated carrot chromoplasts showed no significant difference in β-carotene responses. These results imply that pectin-like fibers in the food matrix and the crystalline form of carotenoids in carrot chromoplast reduce the bioavailability of carotenoids from carrot juice. (Zhou et al., 1996).

Particle size

Mechanical and chemical disruptions are important as resulting reduced particle size improves bioaccessibility of carotenoids by increasing the surface area available for enzymes to act and thereby to release the carotenoids from food matrix. This has been evident in several studies (Torronen et al., 1996; Gartner et al., 1997; Furr and Clark, 1997; Hedren et al., 2002).

The study carried out by Castenmiller et al. (1999) showed that the bioavailability of β-carotene from liquefied spinach was higher than that of the whole leaf or minced spinach. Authors concluded that the bioavailability of β-carotene and to a lesser extent of lutein, was affected by the food matrix as processed spinach had an effect on the matrix and thereby on the bioavailability of β-carotene from spinach. The reason why lutein bioavailability was less affected by the food matrix from spinach, lutein is a dihydroxycarotenoid, is about 0.1% as lipophylic as β-carotene and the matrix in which lutein is embedded in spinach does not decrease lutein absorption as it does the absorption of β-carotene.

On the other hand increased plasma response to lutein is observed with the disruption of the matrix of spinach but this mechanical disruption did not affect the plasma response to β-carotene. The possible reason is lutein is more hydrophilic than β-carotene and this assists in improving the release of lutein from the chloroplasts in the cytosol during the disruption of the cell structure (van het Hof et al., 1999a).

Ornelas-Paz et al. (2008) investigated the impact of stage of ripening of mango on bioaccessibility of β-carotene. They used pulp from "slightly ripe", "moderately ripe," and "fully ripe" mangoes and they were digested *in vitro* in the absence and presence of processed chicken which was used as the source of exogenous fat and protein. The amount of β-carotene transferred to the micelle portion during simulated digestion greatly

increased as the fruit ripened and when chicken was mixed with mango before digestion.

van het Hof et al. (2000), concluded that bioavailability of carotenoids is determined by the intactness of the cellular matrix of tomatoes. According to this study it is evident that food processing has an obvious positive effect on both in the carotenoid response in triglyceride-rich lipoproteins (TRL) after single consumption and in fasting plasma after 4 days consumption of the tomato products. Homogenization had improved the lycopene levels significantly both in TRL and in plasma. Extra heat treatments are likely to increase the lycopene responses in TRL and plasma. Similar trend has been noted in the case of β-carotene as well. This study further showed that compared to homogenization at normal pressure, homogenization at high pressure is more effective in releasing carotenoids from the food matrix. The high-pressure destroys a greater part of the cell structures which remained intact after mild homogenization.

Carotenoid type

Species

Moving of carotenoids from emulsified lipid to micelles is dependent on hydrophobicity of the carotenoid. Polar carotenoids are more easily absorbed than less polar carotenoids as former are incorporated into the outer parts of lipid droplets while the latter are in the core. Therefore polar carotenoids transfer into mixed micelles is easier (Borel et al., 1996; Tyssiander et al., 2001; Tyssiander et al., 2002). Chitchumroonchokchai et al. (2004) in an *in vitro* study showed that micellarization of lutein and zeaxanthin in Caco-2 human intestinal cells exceeded that of β-carotene.

According to the findings of Khachik et al. (1992) epoxy carotenoids such as neoxanthin, violaxanthin, lutein epoxide, and carotenol fatty acid esters are shown to be missing in the nonpolar solvent extractions from human plasma even though their concentrations are high in the diets. Authors put forwarded that though the pathways of metabolism are unknown, absorption and metabolism of these epoxy carotenoids are different from the other routinely found carotenoids such as hydroxy and hydrocarbon carotenoids in plasma. The parent compounds of carotenol fatty acid esters have been found in the plasma and assumption was made that they undergo enzymatic hydrolysis. According to the observations of Asai et al. (2004) dietary neoxanthin is converted into stereoisomers (R/S) of neochrome by intragastric acidity before absorption.

However, the bioavailability of more hydrophilic lutein is five times greater than that of β-carotene. But the difference in relative plasma response between these two carotenoids may not reflect the true differences in absorbability. This is due to bioconversion of part of the absorbed β-carotene and this phenomenon does not occur in lutein, as it is not a pro-vitamin A carotenoid (van het Hof et al., 1999b).

Interactions among carotenoids

Conclusions of some supplement trials have indicated that unfavorable interactions among carotenoids. Kostic et al. (1995) observed a turn down in plasma lutein concentration with β-carotene supplementation. On the other hand van den Berg and van Vliet (1998) showed that lutein but not lycopene adversely influence β-carotene absorption but it appears that no effect on β-carotene cleavage when administrated at the same time. But results of van Vliet et al. (1996) indicated that according to the *in vitro* study, lutein but not lycopene may meddle adversely with cleavage activity. In addition Castenmiller and West (1998) reviewed the decrease in plasma levels of lycopene and canthaxanthin with β-carotene supplementation but an increase in plasma concentration of α-carotene. This observation was supported by the investigation of van het Hof et al. (1999b); they showed consumption of pure β-carotene and lutein supplements induced a significant reduction in plasma lycopene concentration. Authors suggest that this may be due to carotenoid supplements compete with lycopene for absorption or transport in plasma.

Isomeric form

According to the plasma response all-*trans*-β-carotene was shown to be absorbed preferentially with a higher amount incorporated into chylomicrons compared to 9-*cis*-β-carotene (Gaziano et al., 1995; Stahl et al., 1995). But lycopene from tomato juice showed *cis* isomers were better absorbed than all-*trans* form (Stahl and Sies, 1992). The possible reason may be due to better solubility of *cis* isomers from lycopene. This observation was supported by the findings of Boileau et al. (2002). In plant foods, about 90% of lycopene present as all-*trans* isomer form, but according to the research evidences the main isomer form found in human tissue is *cis* isomers. There are several clarifications for this observation; *cis* isomeric form of lycopene exhibits a better absorption than all-*trans* form as a result of the shorter length of *cis* isomer, better solubility of *cis* isomers in mixed micelles than *trans* isomers and the lower tendency of *cis* isomers to aggregate. A study carried out with ferrets showed that after a dose of lycopene the stomach and intestinal contents contained 6–18% *cis*-lycopene, whereas the mesenteric lymph secretions contained 77% *cis* isomers. This result clearly indicates that *cis* isomers are far more bioavailable then all-*trans* lycopene. According to the *in-vitro* studies carried out *cis* isomers are more soluble in bile acid micelles in the intestine and therefore more bioavailable than all-*trans* isomers.

Data of Deming et al. (2002) concluded that the value of isomeric form of β-carotene in assessing the vitamin A value of foods. Authors suggested that both 9-*cis* and 13-*cis* isomeric forms of β-carotene have lower vitamin A biopotencies than all-*trans*-β-carotene and these isomers assigned vitamin A value of 38 and 62%, respectively, relative to all-*trans*-β-carotene. Authors discussed that the lower value could be due to destruction or slower absorption in the intestine.

Molecular linkage

Castenmiller and West (1998) reviewed that human intestinal tract has a high efficiency of cleaving ester bonds from lutein diesters. Therefore lutein esters would have similar or better bioavailability than lutein. Richelle et al. (2004) demonstrated that supplementation with plant sterols, either free or ester form can reduce the bioavailability of β-carotene by $\approx$50% in normocholesterolemic men. The reduction of β-carotene

bioavailability was significantly less with plant free sterols compared to plant sterol esters.

The effect of subject characteristics on bioavailability of carotenoids

Bioavailability is primarily determined by the nutrient status of the subject. In humans vitamin A level can be increased by ingestion of β-carotene rich foods only when vitamin A status is initially low (Charoenkiatkul et al., 1985). The distinct differences in bioavailability and bioconversion of carotenoids were observed among the individuals with the administration of identical doses of carotenoids (Micozzi et al. 1992; Parker, 1996).

Zinc affects bioavailability of carotenoids while synthesizing retinol-binding protein as well converting β-carotene into vitamin A by influencing enzyme retinal reductase (Castenmiller and West, 1998). Intestinal parasites, fat maldigestion, and malabsorption were reported to be impaired carotenoid absorption (Castenmiller and West, 1998; Rock, 1997). The discrepancies in bioavailability could be attributed to genetic factor, season, sex, age, alcohol intake and smoking habits of the subject (Castenmiller and West, 1998).

An *in vitro* study carried out by Goñi et al. (2006) showed that colonic fermentation is a significant factor in availability of carotenoid in the gastro-intestinal tract. In the small intestine, bioaccessibility levels of lutein, β-carotene, and lycopene were 79, 27, and 40%, respectively. In the large intestine, same amounts of lycopene and β-carotene had released from the food matrix (57%), with the small amount of lutein (17%). The results signified that a larger portion of β-carotene, lutein, and lycopene present in plant foods is available in the gut after the completion of digestion process as the release of carotenoids from the food matrix is first done by digestive enzymes and afterward by enzymatic activity from intestinal microbiota.

Conclusion

Amongst the dietary factors fat, heat treatment and reduced particle size have a noticeable positive effect whereas dietary fibers have a negative effect on bioaccessibility and bioefficacy of carotenoids. It seems that higher carotenoid doses reduce the absorption of carotenoids. Location of carotenoid is extreme of important in releasing of carotenoids from the matrix. Carotenoids located in the chromoplasts can more easily released from the matrix compared to the chloroplasts. Polarity of carotenoid is imperative in transferring of carotenoids from emulsified lipid to micelles. All-*trans* β-carotene has a greater biopotency than *cis* isomeric form. But *cis* isomers from lycopene showed a greater absorption than the *trans* form. However, different carotenoids seem to have their individual behaviors in absorption and metabolism.

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