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Mammalian carotenoid absorption and metabolism*

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Abstract: Carotenoids are purported to provide widespread function in the biology and health of humans and other mammalian species. Provitamin A carotenoids, such as β-carotene, are valued in the diet of many mammals for their contribution as precursors of vitamin A and retinoids. Carotenoids may also function in the prevention of some chronic diseases by improving intercellular communication. enhancing immune response, and operating as antioxidants *in vivo.* It is widely known that humans and other mammalian species absorb and accumulate carotenoids in body tissues. However, the potential use of carotenoids as modulators of disease and in the prevention of vitamin A deficiency has been hindered by the limited progress in understanding carotenoid absorption and metabolism. In fact, major gaps in knowledge still exist in the fundamental pathways beginning with release from the food matrix and ending with distribution in body tissues and excretion. Continued development of assessment methods for humans, appropriate animal models for mechanistic studies, and analytical techniques for quantification and identification of compounds is needed to advance our understanding of these critical pathways. This review will discuss the current knowledge involving the fundamental pathways of absorption and metabolism of carotenoids in mammalian species. When applicable, emphasis will be placed on the human.

INTRODUCTION

The potential function of carotenoids in the biology and health of mammalian species, in particular humans, continues to stimulate extensive interest in the carotenoid field. β-Carotene is the most common carotenoid in the diet of mammalian species and has the highest conversion efficiency to vitamin A. However, the actual contribution of β-carotene to the vitamin A requirement in humans is not well understood. Approximately 124 million children worldwide are deficient in vitamin A [1].

Other carotenoids may function in the prevention of some chronic diseases by improving intercellular communication, enhancing immune response, and operating as antioxidants *in vivo*. In addition to its provitamin A activity, β-carotene may stimulate intercellular communication via gap junctions, which could be an important factor in the regulation of cell differentiation *in vivo* [2]. β-Carotene supplementation has also been reported to stimulate natural killer cell activity in the elderly [3]. The presence of oxidative metabolites of lutein and zeaxanthin in the retina suggests that these carotenoids may act as antioxidants to protect the macula of the eye against damage from light and oxygen [4].

Humans and other mammalian species clearly absorb and accumulate carotenoids in their tissues. Nevertheless, the potential use of carotenoids in the prevention of vitamin A deficiency and as modulators of disease is hindered by the limited progress in understanding how carotenoids are absorbed and metabolized. In fact, major gaps in knowledge still exist in the fundamental pathways regulating (a) the release of carotenoids from the food matrix; (b) the incorporation of carotenoids into mixed micelles in

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the intestinal lumen; (c) the uptake of carotenoids into intestinal mucosal cells; (d) the incorporation of carotenoids into chylomicrons; (e) the release and transport into the circulation; and (f) the distribution, metabolism, and recycling of carotenoids among tissues. Continued development of assessment methods for humans, appropriate animal models for mechanistic studies, and analytical techniques to quantify and identify isomers and metabolites is needed to advance our understanding of the critical pathways described above. This review discusses the current knowledge involving the pathways of absorption and metabolism of carotenoids in mammalian species with an emphasis on humans. The reader is directed to other recent reviews [5–9] which provide additional background to this paper.

LINKAGE BETWEEN STRUCTURE AND FUNCTION

Carotenoids are lipophilic molecules classified by structure as carotenes and xanthophylls (Fig. 1). Both classes share a common C_{40} polyisoprenoid structure containing a series of centrally located, conjugated double bonds. Some carotenoids are open chain polyene molecules, while others have closed end groups, such as a β-ionone ring. The carotenes (e.g. β-carotene, α-carotene, and lycopene) are non-polar hydrocarbons. The more polar xanthophylls (e.g. lutein, zeaxanthin, canthaxanthin, and β-cryptoxanthin) contain oxygen either as a hydroxyl or keto group contained in the end group.

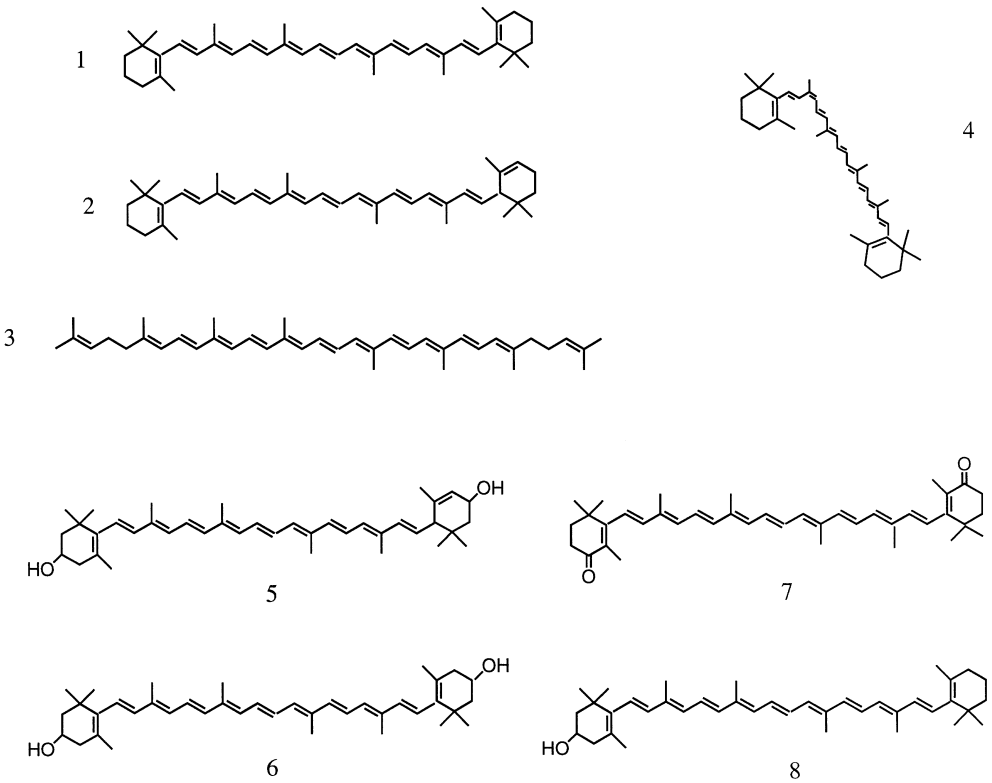

Fig. 1 Structures of common carotenoids. Carotenes: (**1**) all-*trans*-β-carotene, (**2**) α-carotene, (**3**) all-*trans*-lycopene, (**4**) 9-*cis*-β-carotene; xanthophylls: (**5**) lutein, (**6**) zeaxanthin, (**7**) canthaxanthin, (**8**) β-cryptoxanthin.

Most carotenoids are colorful yellow, orange, and red pigments synthesized by plants and some bacteria, algae, and fungi. Their conjugated double-bond structure is related to the most characterized function of carotenoids in biological systems, which is to absorb light during photosynthesis and protect cells from photosensitization [10]. Structure not only determines the color and light absorption properties of carotenoid molecules, but may also provide insight into their absorption, metabolism, and complex biological effects, which may be relevant to *in vivo* processes in mammalian species [11].

The six-membered β-ionone ring of β-carotene, α-carotene and β-cryptoxanthin provides these major dietary carotenoids with the capacity to be metabolized to vitamin A. The presence of a six-membered ring located at the end of the polyene structure has been associated with stimulation of intercellular gap

junctional communication [2]. Of the provitamin A carotenoids, only β-carotene has been shown to induce the gap junction protein, connexin [12]. Other non-provitamin A carotenoids, such as canthaxanthin, also contain the six-membered ring structure and are quite active in the induction of connexin [13]. Lycopene is an exception because it has the ability to induce connexin, but lacks the ring structure. The structure of lycopene, a straight chain polyene, may have additional biological activity related to its antioxidant properties [14,15].

Plant foods, in particular fruits and vegetables, are the primary dietary source of carotenoids for most mammalian species. While more than 600 carotenoids have been identified in nature, only 50 are commonly found in fruits and vegetables consumed by humans. Khachik *et al.* [16] have identified 34 of these 50 carotenoids in human serum and breast milk. Notably, most of these are geometrical isomers and metabolites of a few parent carotenoids. The carotenoids most prevalent in human serum are β-carotene, lycopene, lutein, α-carotene, zeaxanthin, and β-cryptoxanthin. Configurational (e.g. β-carotene and α-carotene) and geometrical (e.g. all-*trans*-lycopene and *cis*-lycopene) isomers of carotenoids are absorbed and metabolized differently by the body and among mammalian species [17].

PATHWAY OF CAROTENOID ABSORPTION AND METABOLISM

Carotenoids are lipid-soluble molecules that follow the absorption pathway of dietary fat (Fig. 2). Early in the digestive process, carotenoids are partially released from the food matrix by mastication, gastric action, and digestive enzymes.

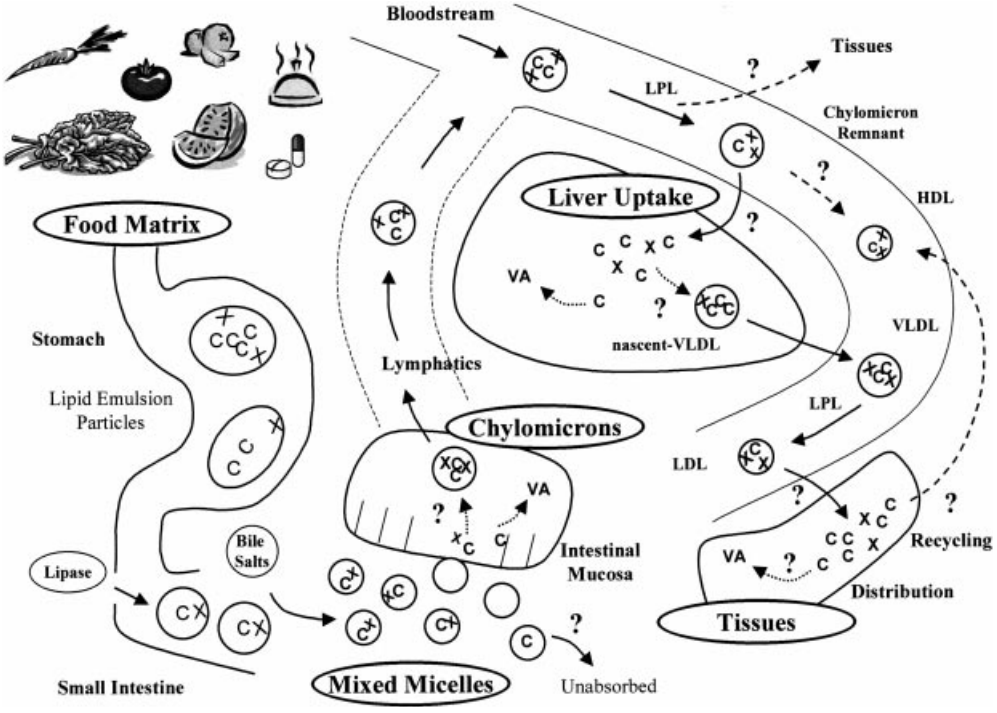

Fig. 2 Pathway of carotenoid absorption and metabolism: C, carotene; X, xanthophyll; LPL, lipoprotein lipase; HDL, high density lipoprotein; VLDL, very low density lipoprotein; LDL, low density lipoprotein.

Release from the food matrix

The extent of release from the food matrix is highly variable depending on whether carotenoids are complexed with other components, such as protein, or whether they are present in the crystallized state as in carrot root or dissolved in dietary oils as in corn or palm oils. As a result, the bioavailability of carotenoids from fruits and vegetables is quite variable and dependent upon the type of fruit or vegetable consumed, whether it is finely chopped or puréed, raw or cooked, and whether or not fat is consumed simultaneously.

In general, the relative bioavailability of carotenoids has been estimated to vary from less than 10% in raw, uncooked vegetables to 50% in oils or commercial preparations [9]. Previous studies have reported that crystalline β-carotene, the physical form in carrots [18], is less bioavailable than β-carotene dissolved in oil [19], which may explain the differences in the bioavailability of β-carotene from vegetables compared to supplemental forms [20,21]. More recently, de Pee *et al.* [22] reported that β-carotene from orange fruits was more available than that from dark-green, leafy vegetables. The results of this study have prompted the scrutiny of the recommendation to prevent and treat vitamin A deficiency with increased consumption of vegetables containing provitamin A carotenoids. Moreover, there has been a renewed interest in exploring how food processing can improve the bioavailability of carotenoids from vegetables.

Mechanical homogenization, heat treatment, and addition of fat during the processing of vegetables are feasible techniques to enhance the bioavailability of carotenoids [23]. Studies in humans support the use of these processing techniques to enhance the bioavailability of lycopene, the major carotenoid found in tomatoes. Lycopene bioavailability is greater from tomato paste than from fresh tomatoes. Higher concentrations of lycopene in chylomicrons resulted from the ingestion of a single dose of tomato paste with added oil compared to ingestion of fresh tomatoes [24]. Consumption of tomato juice, heated in the presence of oil, significantly increased serum lycopene in humans in contrast to unheated tomato juice [25]. Pateau *et al.* [26] recently reported that lycopene was equally bioavailable in humans after 4 weeks of consumption of tomato juice and supplements, each providing 70–75 mg lycopene/day. The tomato juice, tomato oleoresin capsules, and lycopene beadlets used in this study were manufactured from a proprietary, lycopene-rich, tomato variety and were consumed with 4.5 g of fat at mealtimes.

Carotenoids are present in the all-*trans* configuration in raw fruits and vegetables. While lycopene is relatively stable to heat processing, this technique can promote isomerization of all-*trans*-β-carotene to various *cis* isomers of β-carotene. All-*trans*-β-carotene appears to be absorbed preferentially to 9-*cis*-β-carotene in animals [27] and humans [28] after supplementation of equal amounts of both isomers. *Cis* isomers of β-carotene resulting from the heat processing of vegetables are also less bioavailable than the all-*trans* form. Rock *et al.* [29] reported increased plasma response of total and all-*trans*, but not *cis*, isomers of β-carotene in humans after ingestion of heat-processed and puréed carrots and spinach. Some carotenoids may be less affected by changes in the food matrix than others. The relative bioavailability of lutein versus β-carotene was reported to be less affected by the food matrix in spinach [30].

While mild heating (e.g. steaming) increases carotenoid bioavailability, excessive heating (e.g. boiling) causes isomerization and oxidation of carotenoids. These structural changes decrease the vitamin A value of provitamin A carotenoids and perhaps alter the biological properties of carotenoids.

Incorporation into mixed micelles

Carotenoids released from the food matrix migrate and solubilize into lipid globules of varying sizes in the stomach, where they are eventually transformed into smaller lipid emulsion particles by normal digestive motility. Solubilization of individual carotenoid molecules into lipid emulsions is thought to be a selective process related to the specific polarity of each molecule. Non-polar carotenes most likely migrate to the triacylglycerol-rich core of the particle, while the more polar xanthophylls orient at the surface monolayer along with proteins, phospholipids, and partially ionized fatty acids. Borel *et al.* [31] reported this selective orientation of carotenoids in phospholipid-triacylglycerol droplets using an *in vitro* biological emulsion model. β-Carotene, a non-polar carotene, solubilized in the core of droplets, while zeaxanthin, a more polar xanthophyll, accumulated at the surface. Selective orientation of carotenoids in membranes, micelles, and lipoproteins is most likely similar to that of other lipid molecules and is based upon the polarity, length, and structure of the molecule [11,17,32]. Figure 1 illustrates these differences. Some carotenoids, such as all-*trans*-β-carotene and zeaxanthin or α-carotene and lutein, differ only in polarity due to the presence of hydroxyl groups substituted on the β-ionone ring. Other carotenoids, such as all-*trans*-β-carotene and 9-*cis*-β-carotene, are geometrical isomers that differ in length.

Carotenoids solubilized in lipid emulsion particles are transported from the stomach to the duodenum of the small intestine. The presence of dietary fat in the duodenum triggers the release of bile acids from the gall bladder and regulates levels of pancreatic lipase, the enzyme that hydrolyzes dietary

triacylglycerols into free fatty acids and monoglycerides. Bile acids aid in the reduction of lipid particle size and stabilization into mixed micelles. Carotenoids are solubilized into mixed micelles along with dietary triacylglycerols, their hydrolysis products, phospholipids, cholesterol esters, and bile acids. Since carotenoids are lipophilic molecules, it is reasonable to assume that dietary fat enhances their absorption [33,34].

Serum β-carotene increases in response to high dietary fat intake [35–37], but the addition of even a small amount of fat to the diet was reported to improve the bioavailability of carotenoids from vegetables [38]. However, optimal absorption of carotenoids may require an intake of as little as 5 g of fat per meal [39]. These studies suggest that the amount of fat present in a meal enhances carotenoid solubilization into micelles, although solubilization was not directly measured.

The extent of carotenoid solubilization into micelles may be affected by structural features of the carotenoid and/or micellar fatty acid composition and extent of saturation [31]. Boileau *et al.* [17] reported greater incorporation of *cis*-lycopene than *trans*-lycopene into bile acid micelles. Results from rat perfusion studies reported lower β-carotene absorption from polyunsaturated fatty acids than from monounsaturated fatty acids [40]. Medium-chain triacylglycerols (MCT) are reported to dramatically decrease chylomicron β-carotene response in humans compared to that of long-chain triacylglycerols [41]. This observation is most likely not explained by reduced solubilization of β-carotene into micelles, but rather by the lack of secretion of chylomicrons in response to MCT, or higher transport of β-carotene or its metabolites in the portal blood.

Other components within a food/meal can disrupt micelle formation and/or bind carotenoids, thereby inhibiting mucosal uptake of carotenoids. Soluble fiber, in particular citrus pectin, has been reported to reduce β-carotene absorption and liver vitamin A stores in animals [42] and plasma β-carotene levels in humans [43]. Results from a recent study reported that oat β-glucan, a different type of soluble fiber, did not have the same deleterious effect as citrus pectin [44]. Soluble fibers are viscous polysaccharides that can solubilize in the gastric contents of the intestinal lumen. Partitioning of bile acids into the gel phase of gastric contents could hinder micelle formation, resulting in increased fat and bile acid excretion in the feces. A decrease in cholesterol levels in serum and liver have resulted from soluble fiber consumption in humans and animals [45]. The cholesterol-lowering effect of some dietary phytosterols may similarly explain their effect on the inhibition of carotenoid uptake in humans [46,47]. Dietary fat analogs, such as sucrose polyesters, have also resulted in lipid malabsorption and inhibition of carotenoid uptake [48,49]. Notably the reduction in serum carotenoids in humans consuming a relatively high dose of 18 g of the sucrose polyester, olestra, was similar to that reported for high fiber diets [50]. Ingestion of orlistat, a novel lipase inhibitor used in the treatment of obesity, also inhibits dietary fat absorption by inhibiting triacylglycerol hydrolysis, resulting in reduced plasma concentrations of β-carotene and fat-soluble vitamins in humans [51,52].

Carotenoids have been shown to compete with each other for uptake and absorption in humans and animals. There may be competition for the incorporation into micelles, which could inhibit cleavage of β-carotene. Carotenoid interactions may also occur during exchange between lipoproteins during the post-prandial state. Overall, carotenoid interactions appear to exist between β-carotene and oxygen-containing xanthophylls, and between β-carotene and lycopene. Extensive details can be found in an excellent review of carotenoid interactions by van den Berg [53].

Uptake into intestinal mucosa

Uptake of carotenoids into the intestinal mucosa follows a similar path to other lipid components within the mixed micelle. Absorption is thought to occur by passive diffusion [40,54]. The process requires solubilization of the mixed micelle in the unstirred water layer surrounding the microvillus cell membrane of the enterocyte. The mixed micelles collide and diffuse into the membrane releasing carotenoids and other lipid components into the cytosol of the cell. Parker [7] suggests that a concentration gradient between the micelle and the cell membrane most likely determines the rate of diffusion. He further explains that high doses of carotenoid may saturate uptake, leading to insufficient removal from the plasma membrane, thereby reducing this concentration gradient.

Once uptake into the enterocyte is complete, some of the absorbed β-carotene and other provitamin A

carotenoids are converted to vitamin A after cleavage by the enzyme, β-carotene-15,15′-dioxygenase (βC-15,15′-DIOX). Dietary polyunsaturated fatty acids have been reported to increase the activity of βC-15,15′-DIOX and cellular retinol-binding protein type II (CRBP II) in rat intestinal mucosa [55,56]. Between 20% and 75% of β-carotene is estimated to be cleaved within the mucosal cell. The cleavage rate is dose dependent and influenced by vitamin A status [57] and varies among mammalian species. Humans absorb some β-carotene intact and presumably can selectively convert β-carotene to vitamin A in other tissues. Other species, such as rats, rabbits, chickens, and pigs, do not readily absorb carotenoids and must depend upon the intestinal mucosa to convert β-carotene to vitamin A [6].

Carotenoid uptake into the enterocyte does not ensure that carotenoids will be metabolized or absorbed into the body. Carotenoids in the enterocyte may be lost in the lumen of the gastrointestinal tract due to normal physiological turnover of the mucosal cells [5]. Moreover, initial uptake of carotenoids may or may not be selective based on the maturity of the enterocyte or morphology of the mucosa.

Incorporation into chylomicrons and release into lymphatics

Carotenoids and other lipid molecules are assembled into nascent chylomicrons in the Golgi apparatus of the enterocyte and released into the lymphatics. The mechanism of carotenoid translocation within the enterocyte is not known. It is not unreasonable to speculate that carotenoids would have an intracellular binding protein, since one exists for retinol and for long-chain fatty acids, or that these lipid transfer proteins may also transport carotenoids. However, carotenoid transport by proteins has not been reported in the literature.

Selective surface orientation of more polar xanthophylls into micelles suggests that their uptake into the enterocyte and incorporation into chylomicrons may occur before that of non-polar carotenes. Gartner *et al.* [58] reported the preferential uptake of lutein and zeaxanthin from the intestinal lumen into chylomicrons in humans, even in the presence of high amounts of β-carotene. In a more recent study, lutein appeared in human chylomicrons after 2 h and β-carotene and lycopene appeared after 4–5 h following a dose of all three carotenoids [59]. A similar preferential uptake has been reported in the preruminant calf [19]. Interestingly, while most xanthophylls are present in fruits as esters [60], only free xanthophylls have been found in the chylomicrons and serum of humans [61], suggesting a requirement for hydrolysis of carotenoid esters prior to uptake and incorporation into chylomicrons.

Distribution, metabolism and recycling among tissues

Chylomicrons are secreted from the enterocyte into the lymphatic circulation for transport to the liver. Prior to hepatic uptake, chylomicrons in the bloodstream are rapidly degraded by lipoprotein lipase associated with tissue endothelium and transformed into chlylomicron remnants. During this process, some carotenoids may be taken up by extrahepatic tissues. However, most chylomicron remnants deliver carotenoids to the liver where they are stored or resecreted into the bloodstream in very low density lipoproteins (VLDL) [62]. Circulating VLDL are subsequently delipidated to low density lipoproteins (LDL). Similar to other non-polar lipids, hydrocarbon carotenes, such as β-carotene and lycopene, are thought to migrate to the hydrophobic core of lipoproteins, while the more polar xanthophylls reside closer to the surface where the likelihood of exchange among lipoproteins is enhanced [63]. The lipid composition of lipoproteins varies, so that it is not surprising that the carotenoid content of individual lipoprotein classes varies as well. In the fasted state, LDL are the main carriers of non-polar carotenoids, β-carotene, α-carotene, and lycopene, in human serum [26]. The more polar xanthophylls are evenly distributed between high density lipoproteins (HDL) and LDL, and to a lesser extent VLDL. Carotenoids released from lipoproteins, especially LDL, are taken up by extrahepatic tissues. Factors controlling tissue uptake, recycling back to the liver, and excretion are not fully understood.

Carotenoids are ubiquitous in mammalian tissues and the accumulation of carotenoids among animals is species specific and highly variable [64]. These differences could be explained by dietary intake and/or species differences in absorption and metabolism, such as gut motility or handling of lipoproteins by the body. Goodwin [65] classified groups of animals into carotenoid accumulators, non-accumulators, and intermediates. Primates, similarly to humans, accumulate a wide range of carotenoids in high concentrations, while other mammalian species accumulate only one specific carotenoid/class of

carotenoid or no carotenoids at all. Birds preferentially accumulate xanthophylls in most tissues [64]. Contrary to past studies, Chew *et al.* [66] recently reported that the domestic cat absorbs significant amounts of β-carotene from dietary sources. Rats, gerbils, ferrets, and preruminant calves absorb and/or accumulate carotenoids in tissues to varying degrees and thus are animal models used to study absorption and metabolism [67,68].

In humans, dietary carotenoids accumulate in many tissues including the liver, adipose, serum, breast milk, adrenal, prostate, macula, kidney, lung, brain, and skin. Some tissues exhibit specific patterns of carotenoid accumulation, but factors controlling tissue uptake, metabolism, and excretion are not well studied. The extent to which plasma and serum concentrations of carotenoids reflect those of organ tissues may or may not be of importance to status or function of carotenoids [64]. Alternatively, tissue-specific patterns could suggest that certain carotenoids may exert a biological effect in one tissue over another. The focus of current research is to determine whether these particular carotenoids are simply present and serve as biomarkers of fruit and vegetable intake or function as specific modulators of disease in these tissues.

Tissue-specific accumulation of lycopene in the human prostate could suggest a biological effect related to cancer [69]. In 1995, an epidemiological study reported an inverse relationship between the consumption of lycopene-rich foods (i.e. tomatoes, tomato paste, and pizza) and reduced risk of prostate cancer [70]. A more recent meta-analysis of many epidemiological studies reported inverse relationships between tomato intake or serum lycopene and many cancers, including esophageal, stomach, pancreatic, lung, prostate, and colorectal [71]. The predominant form of lycopene in human tissues is the *cis* configuration, even though all-*trans*-lycopene is the primary form found in foods [69]. The significance of this observation may be related to the function of lycopene in specific tissues [72].

Other carotenoids are hypothesized to exert antioxidant effects in tissues. The polar xanthophylls, lutein and zeaxanthin, preferentially accumulate in the macular pigment of the human eye [4]. Increased levels of lutein and zeaxanthin in the macula of the eye have been associated with decreased risk of age-related macular degeneration (AMD), which is the leading cause of blindness in the elderly [73]. The potential role of lutein and zeaxanthin in the reduced risk of AMD could be to reduce photo-oxidative stress.

Dermal accumulation of carotenoids is another emerging area of research related to the ability of carotenoids to act as scavengers of singlet oxygen and peroxyl radicals and thus potentially provide protection from UV radiation. β-Carotene and lycopene are potential candidates for investigation. No data are available on dermal accumulation or distribution of carotenoids, but correlations between serum carotenoids and skin carotenoids after long-term supplementation appear to be suitable indicators for carotenoid accumulation in specific areas of the skin [74,75].

METHODS OF ASSESSMENT

The lack of a functional biomarker for the biological activity of carotenoids in mammals has resulted in defining carotenoid bioavailability as the ability or capacity to accumulate a defined body pool [76]. These pools can be characterized as dynamic pools, such as those found in post-prandial plasma chylomicrons, or more static pools, such as those found in adipose tissue or the macular pigment of the eye.

Humans

No standard methods are validated for the quantitative assessment of the bioavailability of carotenoids from food sources or synthetic preparations in humans [77]. Most research in humans has been restricted to determining serum or plasma concentrations of carotenoids. The results of these studies attempt to estimate the absorption of carotenoids by measuring the change in baseline levels after a dose or ingestion from a meal. These studies are often difficult to interpret because of the large variation within and between subjects and the existence of non-responders [9]. Whole plasma pharmacokinetics may not be the most practical way to measure carotenoid status because plasma concentrations are not only a measure of the absorption of carotenoids from the diet, but also a measure of exchange from tissue storage, bioconversion, and excretion [78]. One complication in comparative studies using serum or plasma

response with provitamin A carotenoids is the inability to account for cleavage of these carotenoids, which then underestimates their absorption [53].

The determination of carotenoid levels in chylomicrons following a meal is a technique used to study the uptake and metabolism of β-carotene [79] and, more recently, lycopene and lutein [25,80]. The triacylglycerol-rich, chylomicron fraction of plasma is considered to be more indicative of carotenoid uptake than serum/plasma levels because newly absorbed carotenoids are found primarily in chylomicrons. Nevertheless, carotenoids in chylomicrons clearly represent only a small fraction of total plasma carotenoids due to the rapid rate of catabolism of chylomicrons and uptake by the liver. The use of stable isotopes, such as tetradeuterated vitamin A [81] and ^{13}C-β-carotene [82–85], appears to hold the most promise for discerning carotenoid absorption and metabolism in humans. ^{13}C- and ^{2}H-labeled β-carotene have been used to investigate the kinetics of carotene uptake and removal from whole plasma [82,83]. You *et al.* [85] used ^{13}C-β-carotene to demonstrate that significant isomerization of 9-*cis*-β-carotene to all-*trans*-β-carotene occurs during absorption in humans. More recently, an extrinsically labeled, preformed vitamin A, $^{2}H_4$-labeled retinyl acetate, is being employed to study the absorption and vitamin A yield of foods containing pro-vitamin A carotenoids, such as carrots and spinach [76]. Food products, such as fruits and vegetables, can also be intrinsically labeled with ^{2}H by growing with $^{2}H_2O$ [76].

In vitro and animal models

Food matrix effects and lumenal events in the gastrointestinal tract are difficult to study in humans. Therefore, the use of *in vitro* digestion models, such as biological emulsions [31] and brush-border-membrane vesicles [86], and appropriate application of animal models, such as the lymph-cannulated ferret [17,87], have improved our understanding of the early pathway of absorption of carotenoids. The lymph-cannulated rat also demonstrates usefulness to study absorption of non-provitamin A carotenoids [88].

Clearly, there is no ideal animal model that totally parallels carotenoid absorption and metabolism in humans. The selection of an appropriate animal model depends on the desired endpoints of bioavailability [68]. The use of animal models is especially advantageous to determine the bioavailability of provitamin A carotenoids by measuring liver vitamin A, the most sensitive physiological endpoint of vitamin A status. The ferret and gerbil are animal models used to study β-carotene absorption and bioconversion because they appear to mimic observations in humans [87,89,90]. The ferret has also recently been used to study the hazardous association between β-carotene supplementation and tobacco smoke [91].

CONCLUSIONS

The interest in the potential function of carotenoids in the biology and health of mammalian species continues to drive research focused on carotenoids. Our approach/strategy for this paper has been to discuss the current knowledge related to the fundamental pathways of carotenoid absorption and metabolism in mammalian species, in particular humans. Continued improvement in assessment methodologies and techniques will provide the necessary tools to advance our understanding of carotenoids.

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