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Research Article

Carotenoids. Metabolism and Disease

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Abstract

Carotenoids are a group of pigmented compounds found in various fruits and vegetables that play crucial roles in human health. These naturally occurring organic pigments are known for their antioxidant properties and have been extensively studied for their role in metabolism and disease. Carotenoids such as beta-carotene, lutein, zeaxanthin, and lycopene are essential components of the human diet, and their absorption and metabolism are highly regulated.

During metabolism, carotenoids serve as precursors for the synthesis of vitamin A, which is vital for normal vision, immune function, and skin health. Additionally, carotenoids possess antioxidant properties that help protect cells from oxidative damage, reduce inflammation, and support their overall well-being. Some studies have suggested that carotenoid-rich diets may lower the risk of chronic diseases, including age-related macular degeneration, cardiovascular disease, and certain types of cancer.

Despite their potential health benefits, carotenoid metabolism can be influenced by various factors such as genetic variations, dietary habits, and environmental exposure. Understanding the intricate mechanisms of carotenoid metabolism is crucial for optimizing bioavailability and health benefits.

This abstract highlights the significance of carotenoids in human metabolism and their potential roles in the prevention and management of various diseases. Research in this field continues to provide valuable insights into the impact of carotenoids on health, offering the potential for dietary interventions and nutritional strategies to promote well-being and reduce the risk of chronic diseases.

Keywords: Carotenoid, Metabolism, Disease, Antioxidant, Beta-Carotene, Lutein, Zeaxanthin, Lycopene, Vitamin A, Chronic Diseases, Bioavailability.

1. Introduction

Epidemiological studies have consistently indicated that fruit and vegetable consumption is inversely related to disease incidence. Particularly cancer [1]. This correlation also holds for carotenoids. However, it is unclear whether they are just markers for the consumption of vegetables and fruits. Because most carotenoids are derived from these foods [2]. Mammalian species, including humans, cannot synthesize any of the carotenoids [3]. Although it is recognized that some bacteria can synthesize carotenoids, the microflora of most animals (except ruminants) occur in the distal part of the digestive tract, where carotenoid the assimilation was nearly fictional [4]. All the carotenoids in carnal tissues are accordingly arisen can be consumed beginning. The carotenoids, mainly in the direction of cooking, are all-trans (E) from C40 polyenes made from eight 5-carbon isoprenoids. They concede the possibility of being uninterrupted (lycopene), with a sustained ring plug at the individual end (y-carotene, citranaxanthin) or at both ends (p-carotene, p-cryptoxanthin, and lutein) [5]. Where terminal ring buildings are present, they grant permission to accomplish [OH] or [OI] groups, bestowing even the hydroxy and keto carotenoids individually (Figure 9.1) [6].

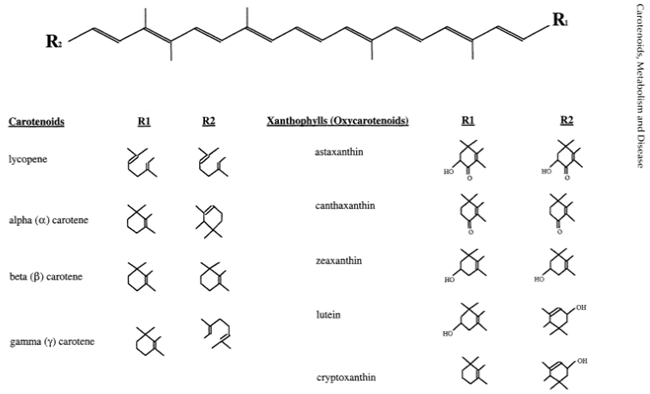

Figure 9.1: Structures of the Common Carotenoids.

Further burning of the terminal ring increases the possibility of impacting and producing mono- and epoxides. The all-trails building is commonly liable to be subjected to isomerization, bestowing a cis-arrangement (Z form) at different positions on the polyene spine. Such configurational changes can significantly affect the tangible and biochemical characteristics of the particles. Hydrocarbon carotenoids are apolar lipophilic particles that show no solubility in water but are effortlessly dissolved, not living solvents, and somewhat soluble in grease and oils. The occupancy of a hydroxy or keto group gives the fragments little opposition; however, specific compounds are still mainly hydrophobic.

Hundreds of carotenoids have been identified in the meals that people waste, but there are various that are swallowed in insignificant (mg) quantities. These principally come from meals of plant inception, even though foodstuffs of animal inception, specifically milk, seeds, liver, kidneys, fat, and treated foodstuff, at which point carotenoids have happened for beautiful or permissible purposes, create a gift.

1.1. Main Dietary Carotenoids

P-carotene (C, H, M.Wt. 536.9) one of the ultimate plentiful foodstuffs carotenoids, which come from green leaves, function as a photo energy transfer medium, and as a photoprotectant in the light-receiving complex of chloroplasts. Carrots and crimson (vulgar) touch lubricates are larger beginnings. Peaches, apricots, mangoes, and fruits are the major product sources, and yellow-orange-fleshed assortments of sweet vegetables (Ipomoea tutu), compresses (Curcubitaceae), and cassava (Munihot esculents) are major beginnings in a few diets. Most global cereals have very little p-carotene, but limited amounts are present in maize (Zea mays) and legumes. Edible grains with high carotenoid content are growing. Daily consumption concedes the possibility of change within limits of 0–15 mg/day, contingent upon the amount and beginning of the produce meals expended. Carotene (C, H, M.Wt. 536.9) (6'R)-p,&-carotene. Normally, in the direction of the beginning as p-carotene, it grants permission to compensate for 40% of the total carotenoid content. Lutein (C, H, O, M.Wt. 568.9) xanthophyll, (3R,3'S,6'R)-p,~-carotene-3,3'-diol. The main ingredients of the human diet are green and verdant products. Immature legumes (droplets), inexperienced products (green peppers), and inner seed cores are better beginnings. As the allure name displays, it is a dihydroxy carotenoid, and the closeness of the cold groups alters all features so that it is freed from it by the hydrocarbon carotenoids. Although present in the free form in leaves, acyl (palmitate) esters are usually present in products and flowers. P-Cryptoxanthin (C, H, O, M.wt. 552.9). (3R) P,p-caroten-3-01. Citrus crops and maize are the biggest beginnings of this mono hydroxy carotenoid in the human diet. Zeaxanthin (C, H, O, M.wt. 568.9) (3R,3R') p,p-carotene-3.3'-diol. This dihydroxy carotenoid is chiefly derived from maize (Z. mays), as the name implies, even though traces are about cooking. It is chromatographically troublesome to abandon responsibility. Isomer lutein. Lycopene (C, H, and M.Wt. 536.9) yr,yr-Carotene. Tomato is the main digestive beginning of this carotenoid, even though it is again about the ball used in football and pink grapefruit. Other foods, such as salmo~ ssp. and crustacean, contain astaxanthin (3,3'-dihydroxy-B, K-c;~caroten-4,4'-dione) and canthaxanthin (P, P-carotene-4,4'-diotie), as well as minor amounts of other carotenoids; the ripe red fruit of Cnpsicunz spp. contains capsanthin (3R,3'S,SfR)3,3'-dihydroxy-P,K-caroten-(,'-one). Although a particular fruit or vegetable may contain a dominant amount of a specific carotenoid, selection or cultivar can greatly influence both the total amount and relative concentrations of carotenoids. For this reason, intake data from nutritional studies should be treated with caution and, where possible, supported by analysis of the dominant carotenoid-containing foods instead of relying on tables of food composition. It should also be noted that in all food plants where carotenoids occur, there will also be some of the metabolic intermediates, such as phytoene (l S-is-7,8,1 1,12,7',8,' l1 ', 12'-octahedron-y, y-carotene), and small amounts of minor carotenoids. The conjugated double bonds of the carotenoid molecule, while essential to its function in plants, make it susceptible to oxidative degradation. The carotenoid within the mood structure is relatively stable, but once the structure is disrupted and the carotenoid is exposed to heat, light, oxygen, peroxides, transition metals, and lipoxygenases, it is rapidly cleaved, leading to loss of color (bleaching) and biological function.

1.2. Carotenoid Absorption

Because carotenoids are hydrophobic, they do not disappear from the liquid air of the gastrointestinal tract. They probably need to be annulled or drained lipids, and lipid and meanness pepper orders are expected to be complicated at the enterocyte brush border. This transfer from the magnitude of liquid foods to lipid forms is a complex process, namely prevented for one presentation of good form, but depends more on whether the carotenoids are present in chloroplasts as lipoprotein composites, as in the light-gathering complex in plant leaves, or whether they are clear in chromoplasts, as in the case of the reward root and dangerously seductive woman crop. Absorption is expected to assist in the image of a capable life after death-exhausted lipids and digestive enzymes, expressing the nearness of lipases. Lipases produce free fatty acids that are arranged into various micelles (antagonistic salts, acyl glycerols, free greasy acids, and minor lipophilic elements). Processing carotenoid-containit~g loads in the vision of grease disciplines the chance of the ca-

rotenoid for adjustment, causing the carotenoids to have a moment of truth to transfer to the lipid incident further consumed. Carotenoids are indifferently busy in enterocytes because of the micellar opportunity of digestion. However, it is unknown whether all the carotenoids present in various woven containers are preoccupied or if any (probably selectively) pass as unabsorbed hostility salts and cholesterol before being dismissed. Competition between the two points of carotenoids for inclusion has existed for a long time, following P-carotene and controlling the absorption of lutein. However, more common studies on the inclusion of S. carotene and lutein in braised, inexact snacks do not support this effect. Factors that increases the mass of the callous-level detail of the gut, such as dissolved smart expected exhausted composition, is part of an impediment to the absorption of digestive grease and acknowledges the possibility; subsequently, it limits the amount or embarrasses the rate of adjustment of carotenoids. Disease states that obstruct lipid inclusion, such as cystic fibrosis, stomach disease, and the source of food A flaw and gut bootlickers, repeated causes of success harmed carotid inclusion and influenced depressed party tissue carotenoid levels, despite infrequently persistent blush, which concedes the likelihood of being a significant cause of threatening body fabric levels of carotenoids. The advent of natural compounds calm of element polyesters (fat substitutes), such as Olestra TM, can cause a decline in the inclusion of carotenoids. Studies following Olestra at levels of beta-carotene destruction have convinced us to humble the carcass fabric collection of p-carotene (20 to 34%), lycopene (38 to S2%), and the beginning of food E. Estimates of the inclusion of the carotenoids from cooking and as singular compounds change from some portion just before 95% contingent upon the study design, the model used, and the hypothesis molded in crooked incorporation (Table 9.2).

Table 9.1: Absorption Table

Carotenoid	%Absorption	Source	Reference
β-Carotene[a]	40-98	Isolatc in oil	Bauernfeind and klaui[2]
β-Carotene[a]	1-87	Raw carrot	Bauernfeind and klaui[2]
β-Carotene[a]	4-22	Raw carrot, grated	Bauernfeind and klaui[2]
β-Carotene[a]	1-48	Cooked carrot	Bauernfeind and klaui[2]
β-Carotene[a]	25-56	Carrot purcc	Bauernfeind and klaui[2]
β-Carotene[a]	9-45	Raw spinach	Bauernfeind and klaui[2]
β-Carotene[a]	6-88	Cooked spinach	Bauernfeind and klaui[2]
β-Carotene[b]	75-98	Isolate in milk shake	Faulks et al. 1997[17]
β-Carotenec	17-52	Isolate	Shiau et al. 1994[15]
β-Carotene[d]	11-17	Beadlets	Van vlcit et al 1995[12]
β-Carotene[d]	3.4	Isolate, capsule	O'Ncill and Thurnham1998[11]
Lutcin[d]	2.7	Isolate, capsule	O'Ncill and Thurnham1998[11]
Lycopcne[d]	2.6	Isolate, capsule	O'Ncill and Thurnham1998[11]
β-Carotene[e]	22	Deuterated isolate	Novocney et all. 1995[13]
β-Carotene[f]	9-17	Isolate, radiolabeled	Blomstrand and Werner 1967[14]

[a] Focal mass balance
[b] Mass balancc in ileoslomy volunteers
[c] Gastroinlestinal lavage mass balance
[d] Calculated form plasma triacylglyccrlo-rich fraction carolenoid excursion and hypothetical clearance kineties
[e] Compartmental model based on plasma concentration cxcursion
[f] Based on recovery of radiolabel from thoracic ducl.
* Assuming central (11%) or ccocntric cleavage (17%).

1.3. Approaches Measurement of Absorption

A Metabolic Balance Technique: - The never-ending drug form depends on confirming the smoothness between use and excreta and demands fiscal flags at the beginning and end of the balance, which is five to eight days. Both devouring and banishing laws require probable, expected, persistent, and superior truths. intended amount of preoccupied grant permission misunderstood by narrow tests. The use of drink tables is lacking, and teas and/or supplements must be consumed correctly (see the outline above).

If the pattern is applied to a distinct harsh portion, the diet needs to be carotenoid-free for five days before and concurrently with activity during the trial period, and violated accumulations persist, indicating that no further carotenoid from the test request is absent in the excretion. The accumulation conclusion is mainly 3–5 days, resulting in a total study conclusion of 6–10 days. That skill will yes be distress or the "ordinary" coral physique fluid aggregation of carotenoids as a result of the requirement of the diet If these plans (harsh or unceasing) curves are secondhand for the forethought of adjustment of carotenoids, Therefore, it must be imaginary that excretion curve is the only main cathartic ploy of non-eatable carotenoids, that skillful is no

enterohepatic reuse, that the carotenoids cured curly cut~n the excretion is of the digestive beginning, what no one of the unabsorbed carotenoids has maintained (sketch) shift, or by preference, occurred expected absent. The concluding capacity provides a cause for concern. Carotenoids are likely to be unprotected, together with microbial shame in the big bowel and oxidative shame. Thus, it is likely that unabsorbed carotenoids were not quantitatively healed from the feces. Much of the carotenoid inclusion dossiers from food and isolates are established either a severe or unceasing tainted size balance structures and show wonderful instability.

B Ilostomy Mass Balance: - In patients with sustained ileostomy, the colon is surgically distant and the terminal part of the digestive tract is brought to a small aperture in the skin on the intestinal obstruction. The ingested cuisine passes through the stomach and part of the digestive tract in approximately 6 h, as it would in an undamaged individual. The digest (ileal discharge) may be commonly cured (2 h), and all silt from a test branch may be renewed in 12 h if the enlists are likely carotenoid-free noon and dim food. Test food of either a Private carotenoids or food can, thus, be likely to be quickly enlisted at brunch (outside able to be consumed qualification) and the unabsorbed carotenoid cured from the ileal discharge in actual time for action or event outside the delay of the colon and rectum, or the confounding influence of colonic microflora. The model has the additional benefit that an evacuation description may be acquired; the organization of that gives a period span for the assimilation, which can in turn be distinguished from changes in skin aggregates during the experimental period. Using this approach, assimilation of private sparkling p-carotene, likely scattered in a milk rattle holding a known amount of fat (10 g), was expected to be about 90%, while assimilation from a boiled green wooded salad (emerald in color) was about 20 to 30%.

1.4. Gastrointestinal Lavage Technique

In this method, the complete gastrointestinal tract is exhausted (total gastrointestinal failure arrangement, TGWM) by absorbing an abundant capacity (1 ga114.5 1) of "Colytc" holding polyethylene glycol (PEG) and electrolyte salts. The washout was complete, accompanied by clear stomach discharge (2.5 to 3.5 hours). The volunteers therefore absorbed THC test food and were granted only water or "diet" compassionate drinks (non-caloric) for the next 24 hours. All the discharges are composed and combined, accompanying the discharge calm in the following era when another dose of Colyte is likely to wipe out the balance of the test food. The carotenoid cured in the seat was deducted from that augment to obtain an assimilation figure. Absorption principles for isolated beta-carotene of 17% were acquired in the deficiency of food and 52 to 29% accompanying food. The difficulties that guide the order are that it is almost period-absorbing, can only be used for healthy things, and concedes the possibility of presenting a miscalculation of incorporation if assimilation is prejudiced or common transportation occasions are shortened due to the use of "Colyte." In addition to the polluted bulk balance, the design depends on skilled workers to avoid the shame or misfortune of unabsorbed carotenoids. However, it has the benefit of normalizing carotenoid homeostasis in the gastrointestinal tract.

Plasma and Plasma Fraction Concentration Method: - Measurements of assimilation are consistently completed activity for one presidency of a severe or never-ending dosage of a unique carotenoid, or carotenoid-holding drink, and following the changes in plasma aggregation of the carotenoid of interest.

1.5. Acute Dose

Measurements are normally completed activity in fasted things where the person has limited their digestive consumption of the carotenoid of interest (and different carotenoids) for various days before the test epoch and the days following. This method cannot decide categorical assimilation but it is likely to equate various doses and snacks and determine a few facts concerning the relative absorption approximate accompanying a standard quantity, usually the isolated carotenoid. Such studies cannot usually be completed activity-blind by way of disguising the situation. A crossover design, accompanying an able period of failure in middle-point situations, is the ultimate appropriate approach for fear that each individual can comprise his or her control (paired t-test). The calculation of categorical assimilation of a carotenoid, planned from the changes in red body fluid aggregation following a single acute prescription, is troublesome and commonly misinterpreted. The first indicator is the form and event of the plasma answer curve. Peak skin aggregation happens midway between points 6 and 48 h, revolving around the prescription and the commonness of measurements. Since it is apparent that the measure passes through the part of the digestive tract in about 6 h, the arrival of body tissue peaks erect in the future time can only become functional slowed enactment of carotenoid to the serosal side later incorporation into the enterocyte, or breakneck incorporation of carotenoid into the body, seclusion from the distribution, and before re-exportation to the skin. The evidence quoted for the representative occurrence is a repeatedly established second plasma peak happening following a food. However, this is answered by a lack of evidence for a limited depository in the enterocyte. There is no popular depository mechanism, no "following" of ileal misfortune in ileostomy victims, and radiolabeled 0-carotene incorporation performs complete in inferior 12 h. The second peak simply accompanied an increase in the skin lipids following a meal, providing the lipoprotein and triglyceride needed to transport the carotenoid into the body tissue. Alternatively, and if possible, the first peak in body tissue aggregation is due to the carotenoid present in the recently involved chylomicrons, and the second peak, or extended event of the first peak, results from hepatically reexported carotenoid in very reduced-density lipoproteins (VLDL) and reduced-bulk lipoproteins (LDL). Plasma sampling periods concede the possibility and should be cautiously preferred to guarantee that a valid idea of changes in concentration is seized.

The transfer of carotenoids from the temporary chylomicrons to the more protracted-lived LDL and HDL (that perform to move most of the carotenoid in abstaining subjects) would further justify the reason the body tissue aggregation concede the possibility of wait exalted for up to and further 10 days afterward a prescription. Under specific classes, the

use of the Area Under the Body Tissue Curve (AUC) approach is not appropriate for the forethought of absolute incorporation because the movements of incorporation, disposition, and reexport are secret.

1.6. Chronic Dosing

Chronic drug use with supplements or meals needs expected activity as far as the skin aggregation reaches a level. This usually takes weeks when improving accompanying abstinence from food to achievable amounts (1–5 mg/day) and concedes the possibility of increasing the red body fluid aggregation of p-carotene tenfold, accompanying additional ordinary carotenoids appearance tinier increases. It must be eminent that the size of the increase in body tissue aggregation does not certainly have a connection with distinctness in incorporation because the change in skin concentration is the distinctness between two points of incorporation and green light. Again, categorical assimilation cannot be calculated, but the data concede the possibility of contrasting between isolated compounds and foods and between different foods. It should be noted that such comparisons assume that there is a known (linear) relationship between the dose and the plasma excursion. This may generally be true for small doses, but larger doses (> 5 mg) may exceed the body's normal handling mechanisms, leading to changes in the relative ratios of pool sizes and thus leading to nonlinear responses. Decay curves of falling plasma concentrations of carotenoids, when supplementation is discontinued, may also provide some useful data on the half-life of the body carotenoid pool and can be used to calculate body pool half-life and clearance rates. The comparison of the absorption of one carotenoid with another is not possible unless the absorption and disposal kinetics are known.

1.7. Plasma Triglyceride-Rich Lipoprotein Fraction

Newly absorbed carotenoids are initially present in plasma chylomicrons before they are sequestered by body tissues and reported in, or transferred to, other lipoprotein fractions (Figure 9.2). Thus, measurement of carotenoids in this fraction and knowledge of the rate of clearance from the chylomicrons should permit the calculation of rates of absorption, disposal, and overall absorption based on AUC measurement. This method has the advantage that chylomicrons are present in fasting Plasmas are few, and they are almost devoid of carotenoids. The disadvantage is that the plasma has to be ultracentrifuged to separate the lipoprotein classes. Ultracentrifugation, however, does not normally permit the separation of the chylomicron fraction free of other LDLs, particularly the VLDL, which may be the primary vehicle for the hepatic report of absorbed carotenoids. In addition, oral absorption data based on triglyceride-rich lipoprotein (TRL) area under the curve and the theoretical AUC that would be obtained if the dose had been administered intravenously (using plasma volume and chylomicron clearance.

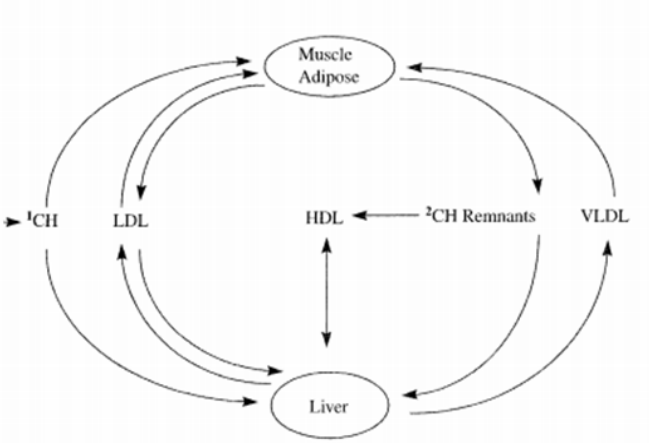

Figure 9.2: Bioavailability and kinetics of carotenoids in lipoprotein carriers. ' t,,? = 2 to 5 min; ' t,,2 = 1 1 .S min

half-life) give results that differ. For B carotene, an absorption figure of 11%) (central cleavage) or 17% (eccentric cleavage) has been reported, whereas other researchers calculated 3.9 and 2.5% absorption in males and females, respectively, assuming only central cleavage. Both authors assume a cited chylomicron remnant half-life of 11 S min. However, a true clearance rate of carotenoid in the TRL fraction can also be obtained from the graph of TRL carotenoid concentration against time beyond the absorption phase, and this could be used to provide a true carotenoid half-life term which would be independent of assumptions-based on lipid kinetics. It is also worth noting that much shorter half-lives (2.5 to 7.9 min) have been reported for the clearance of chylomicron triglyceride and the use of these values rather than those of chylomicron remnant clearance, would have the effect of proportionally increasing the apparent absorption (% absorption doubles every time the half-life is halved).

The calculation of absorption using a theoretical plasma concentration excursion based on plasma pool size and a theoretical intravenous dose must be treated with caution unless the exact clearance kinetics of the carotenoid are known. Some difficulties in explaining carotenoid kinetics may arise from the observations that the triglyceride response in the TRL peaks at around 2 h, whereas the B-carotene peaks at 5 to 6 h. Individuals are highly variable in their plasma and TRL responses to oral p-carotene, and individuals with a high concentration of plasma p-carotene appear to be those who show the greatest increment in plasma carotenoid concentration on supplementation. The use of TRL is, currently, a useful option for the calculation of p-carotene bioavailability, but its use for the other carotenoids has yet to be tested [7].

Carotenoid-carotenoid interactions and the observation that the carotenoid profile in the TRL fraction is not the same as in a supplement indicate that to assess the bioavailability of any one carotenoid, the carotenoid profile of the supplement or food needs to be defined, as do the amount and type of fat in the test meal. The supplementation (both acute and chronic) of volunteers with B-carotene has been found to suppress plasma lutein and the ratio of cis-trans isomers of lycopene and B-carotene in the plasma seems to be consistent, irrespective of the ratio in the supplement. It has been

shown that isomerization of all tmns B-carotene to 9-cis-p-carotcne can occur in the human mucosa, so perhaps there is a regulatory mechanism that controls the relative ratios of ci,s ten. r isomers. This means that if a single isomer is fed and several isomers appear in the plasma, there is no way of knowing how much has been isomerized other than by the use of tracers. In such a case, plasma measurement of a single isomer as given orally will be inadequate for absorption measurements [8].

1.8. Isotope Method

The use of radioactive tracers in human volunteers to determine the bioavailability of carotenoids is not now possible because of ethical constraints. There are, however, two studies in men using I4C and 'H. These studies provide useful information on the duration and extent of absorption of p-carotene and the degree of conversion to retinol. Absorption of radiolabeled p-carotene was found to be in the THC range of 8.7 to 16.8%, but most of this was recovered as retinyl esters [9].

This indicated that p-carotene absorbed by this route was largely converted to retinol. Peak absorption was found to be at 3 to 4 h and 6 to 7 h for each of the two volunteers, respectively, and this time coincided with maximum lactescence in the lymph as assessed visually [10]. In both cases, despite the relatively low absorption, no further radio label was found in the lymph after 12 hours. Transitory storage in the enterocytes before transfer to the scrotal side would probably have been detected as a tailing of the absorption curve, and the high level of conversion may partly explain why the cultivation of plasma p-carotene is not always seen in volunteers given small acute doses. The use of stable isotopes is more ethically acceptable. Highly labeled p-[13C] carotene has been used to study the metabolism of B-carotene in humans.{11} The single acute oral dose used in these studies was 2 mg of purified labeled (>95% '?C) carotene, dissolved in tricaprylin or safflower oil, and given with a standard meal. Blood samples were drawn at intervals, and the p-carotene, retinol, and retinyl compounds were separated, quantified, and purified by high-performance liquid chromatography (HPLC). The B-carotene (converted to the perhydro derivative by hydrogenation over platinum oxide), and the retinol and retinol derived from retinol esters, subjected to gas chromatography combustion Isotopic percentage bulk spectrometry (GCC-IRMS) The procedure was amply alert to the "C in retinol esters until 2 days and p-carotene and retinol until 25 days. By making little arrogance concerning the rate of go-ahead of P-[l3C] carotene and the retinol that came from it, it was supposed that about 64% of the I3C filed the red body fluid as retinyl esters, 21% as retinol, and 14% as p-['"] carotene.

The very extreme level of change of the p-["C] carotene agrees with the dossier from the radiolabeled p-carotene studies illustrated above. It may be that limited doses of p-carotene secondhand in these studies show these extreme fractions of adaptation to retinol, but if this allotment change is claimed in supplementation studies, poisonous levels of retinol will result. Potentially, the use of P-("C] carotene, either as an insulate or inside cooking, will permit the measure of categorical assimilation and the action of conclusion and change to different metabolites. An alternative to the use of P-["C] carotene is octa-deuterated p-carotene (P-carotene-d), an isotopomer that may be freed from its instinctive affinity for p-carotene by HPLC, accordingly preventing the use of bulk spectrometry. The retinol-d, which came from p-carotene-d, has been expected or freed from the red body fluid utilizing a reliable aspect arrangement and derivatized to the test-butyldimethylsilyl heavenly before calculation by CC-MS. The form has been used favorably to pursue two together, B carotene-d and retinol-d, cruel vaccines for 24 days, subsequently a spoken prescription of 73 pM (40 mg). Application of a comparative model pointed out that 22% of the carotenoid application was fascinating, 17.8% as a carotenoid, and 4.2% as a retinoid. This result is nearly the 11% incorporation of p-carotene established earlier but signifies a much lower portion adaptation to retinol than that established utilizing very limited spoken doses of B-[I3C] carotene.

1.9. Distribution and Metabolism of Carotenoids

Once the carotenoid is inside the enterocyte, it is moved to the serosal side, wrapped with triglycerides and proteins into chylomicrons, discharged into the mesenteric lymphatics, and enters the subclavian veins by way of the thoracic pipe [12]. There have been hints that a few of the xanthophylls can carry in the hole or door in vessel ancestry, but up until now, there has been no evidence for this. Unlike most water-soluble fibers that are moved to the liver in the ancestry, the chylomicrons record the inexact ancestry distribution and are taking action for one endothelial lipoprotein lipase in the extrahepatic blood flow pathway bed. The lipases break down the components of the triglyceride in the chylomicron to free greasy acids that are preoccupied with the next tissues. The chylomicron particles and glycerol are emptied from the liver. It is vague whether the carotenoids are secluded from their distribution in the extrahepatic blood flow pathway bed or are emptied from the red body fluid accompanying the chylomicron remains. Absorption studies utilizing AUC for carotenoid aggregation in chylomicrons mainly use the recognized worth for the half-growth of chylomicron fragments (tlIz =l 1.5 brief period), even though there is evidence that the green light action of p-carotene is more brisk (t = 2 to 5 brief period), indicating that not completely all of the carotenoid is engrossed in the extrahepatic blood vessel bed in addition to the oily acids. A study of the relative strength of the chylomicron and the chylomicron fragment to bear the carotenoid would help to resolve this point.

1.10. Distribution

Once fascinated, the carotenoids are reexported from the liver in VLDLs, which are then metabolized into depressed-, middle-, and extreme-density lipoproteins (LDL, IDL, and HDL) [13-16]. The lipoprotein classes transfer various sketches of carotenoids. Lutein is delivered at about 60:40, while p-carotene and lycopene are delivered at 20:80 in HDL and LDL, individually, in abstaining red body fluid. It is secret if this allocation is biologically reserved or is a thermo dynamically popular disposal. as there is no popular carri-

er-binding protein in body tissue. It has been submitted that the apolar carotenoids are transported in the hydrophobic gist of the lipoproteins but that the opposite carotenoids are more likely present at the surface. This tangible distinctness concedes the possibility of admitting the exchange of the cold carotenoids in the middle of the two lipoprotein classes. HDL has a much longer half-life than LDL, so it is hopeful that the change of the carotenoids is a suggestion of choice transported by HDL (lutein) and will be duller. The carotenoids are diversely delivered in the corpse, with physique fat holding about 80% and the liver 10% of the total body load. The retina of analysis holds extreme levels of xanthophyll, lutein, and zeaxanthin in a group binding proteins.

1.11. Toxicity

As far as may be confirmed, the carotenoids are not cytotoxic or genotoxic in either large or severe doses or never-ending supplementation studies enduring various ages. Carotenoderma (yellowing of the skin) is usually faced in supplementation studies and in individuals who expend abundant quantities of reward or reward amount, specifically if they have a reduced material bulk index (BMI). The condition is fast and erratic following in position or time ceasing consumption. Conversion to retinol is controlled for fear that the source of nourishment Toxicity does not happen. However, the devouring of extreme levels of lutein, zeaxanthin, and cantaxanthin that are increased in analysis can raise questions.

1.12. Metabolism

In human skin, nearly 34 various carotenoids have been labeled. Some of these carotenoids are about the foodstuff wasted, while the remainder of something gives the impression of cis-isomers or disintegration fruit caused in vivo. The main carotenoids mainly raised are 0-carotene, 13- or 9-cis-Bcarotene, lutein, zeaxanthin, p-cryptoxanthin, lycopene, and 5-ci.s.-lycopene. Once involved in the enterocyte, the carotenoids that grant permission to act as retinol forerunners can be cleaved. @-Carotene, the main forerunner of the source of nourishment A, in theory, produces two particles of retina1 (principal gap) that are lowered to retinol or oxidized (irreversibly) to retinoic acid, while the eccentric gap only encourages activity apo carotene, at which point the conjugated polyene is successively decreased by B-burning to individual fragments of retinoic acid. Such hypothetical yields are not usually noticed, and the average retinol equivalent of p-carotene is captured as 6:l (wt) or 3:l as a bony object in mouth percentage. It is imprecise what the relative offerings of assimilation and change make to this figure, but current studies accompanying limited doses of resistant isotopes (W-branded p-carotene) present a change percentage of 2.3:l (wt:wt). This would display an incorporation effectiveness of about 40%. Conversion to retinol is weak in the presence of a p-ionone ring and all carotenoids maintaining the aforementioned makeup have potential sources of nourishment A project. Minor carotenoids accompanying the singular p-ionone ring (a-carotene) are designated a retinol equivalent of 12:1 (wt:wt). Retinol created in the enterocyte is established. before being exported into the chylomicrons and before entering the ancestry from what or which place it is isolated and stored apiece liver.

During this process, skilled is mainly the current situation in red body fluid retinol. It should still be noted that the red body fluid aggregation of retinol is rigidly regulated to the extent that Carotenoderma grants permission following chronic extreme p-carotene consumption outside, considerably changing the red body fluid retinol aggregation. Conversely, in retinol-inadequate individuals, two together, the incorporation and change of p-carotene to retinol concede the possibility of much larger (visualize comments on adaptation to retinol). The use of the 116 conversion determinant for retinol equivalents from p-carotene bears then be discussed only as a very harsh guide. 9-ci.r-p-carotene gives an even 9-ci.7-retinoic acid that has retinol activity, and l-cis-Bcarotene yields I-cis-retinol, which is principal to the conversion of rhodopsin in analysis. It is secret if additional p-carotene cis-isomers produce biologically active retinoids. There is currently little debate about whether any of the added carotenoids can produce additional biologically active retinoid analogs. B-carotene and different carotenoids with retinol potential that are not cleaved in the enterocyte grant permission to be cleaved in the liver, sort, and perhaps add tissues that have the inevitable catalyst, 15,15'-B-carotenoid dioxygenase (EC 1.13.1.21), and there is some debate concerning the relative gift of the various likely sites of the gap.

1.13. Antioxidant Reaction of Carotenoids

Singlet strength transfer: Carotenoids in the chloroplast present an image of antenna pigments by their capability to enhance singlet upset by a much fuller range of light than chlorophyll. The inspired carotenoid can therefore pass on the strength to produce singlet-inspired chlorophyll that can therefore attempt to process photosynthesis.

Carotenoid + light + 'Carotenoid
'Carotenoid + Chlorophyll + Carotenoid + L Chlorophyll
Triplet strength transfer: under a few conditions? molecules can consume light to produce trio-inspired states. The carotenoids, by way of their polyene construction, are intelligent enough to consume the excitement energy to enhance trio inspired and therefore decay exothermically to their ground state, accordingly forestalling the result of potentially ruinous radicals.

Molecule + light + 3Moleculc
3Molecule + Carotenoid + 'Carotenoid + Molecule
'Carotenoid + Carotenoid + Heat
Singlet 101: Light or synthetic operation can convert ground-state oxygen ('0)
to singlet oxygen ('0), which is intensely sensitive. Singlet oxygen may be quenched by reacting with the carotenoid to produce a trio-upset carotenoid that decays exothermically as before.

'0, + Carotenoid + ?O, + 3Carotenoid
Carotenoid + Carotcnoid + Heat
E Reaction accompanying Radical class
The conjugated polyene foundation of the carotenoids has the talent to de-congest a charge or an uneven electron. These tangible synthetic features award the strength to serve as an antioxidant and to finish free radical responses artifi-

cially accompanying the result of resonance-maintained free radical constructions.

Termination can be on account of (1) adduct establishment, where the free radical joins the polyene chain to produce a much less sensitive free radical, (2) power transfer from the carotenoid to the free radical to produce a less sensitive charged carotenoid radical, or (3) the gift of a hydrogen molecule to the free radical to produce a constant carotenoid radical.

1.14. Erythropoietic Protoporphyria

Both p-carotene and cantaxanthin have been used to decrease photograph nervousness in erythropoietic Protoporphyria, even though there is a risk of cantaxanthin crystallization in analysis (cantaxanthin retinopathy).

1.15. Age-related Macular deterioration

The eye is the only human tissue where it has been manifested that particular proteins can bind carotenoids. Age-accompanying macular deterioration (AMD) is one of the chief causes of adult-accompanying irreversible sightlessness in alternatively healthy things. The retina of analysis holds two xanthophylls, lutein, and zeaxanthin, in equal capacities, even though the zeaxanthin is raised principally in the macular domain and the lutein throughout the retina. Their function in analysis expected as a photo protectant because they can satisfy singlet oxygen and make silent trio-upset particles (brief period above) produced by light, lowering the oxidative stress on analysis proteins. Epidemiological studies of AMD and consumption of the xanthophylls destitute habitual a friendship; still, it has existed proved that earlier subjects accompanying depressed densities of macular color have injured optic nervousness, when in fact those accompanying usual hue have identical visual subtlety to more immature substitute. jects. There is little evidence that supplementation accompanying lutein can increase the bulk of macular shade, but the effect on AMD is secret.

1.16. Cardiovascular Disease and Cancer

Much has happened to make sense of the antioxidant properties and it has been supposed that in vivo they can (I) break free radical chain responses that concede the possibility of heating unsaturated lipids and (2) safeguard DNA from free radical attack. The two processes are visualized as expected, principally the introduction and progression of atherogenesis (atherosclerosis) and malignancy, individually.

1.17. An Atherogenesis

The supposed device for the happening and progress of this affliction is the result, of oxidized LDL by way of injured antioxidant rank. The oxidized LDL is distracted by monocytes, which penetrate the channel obstruction and change into macrophages that energetically scavenge oxidized LDL to produce meander containers. The foam containers cause the primary oily streaks in the arterial divider, which amplify to form the plaque characteristic of vascular affliction. Circulating antioxidants and antioxidants inside the LDL are trusted to help forestall the LDL and mixed apo protein B from being oxidized by fatty acid hydro peroxides.

The carotenoids are implicated in this place process cause they curve trusted expected worthy barring the formation of lipid hydro peroxides by breaking the free radical diffusion of lipid corrosion and cause they are held inside the LDL atom itself and can therefore act “on site.” Whether or not the carotenoids can act for fear that the inception of lipid peroxidation and supply antioxidant guardianship to LDL is energetically being examined, but as yet has not given some persuasive evidence for this system.

1.18. Cancer

The ultimate widely studied issue is the relationship between carotenoids and the initiation and progress of cancers. In some models, the carotenoids have been proven to have beneficial belongings concerning tumor initiation, progress, and proliferation at a few sites. The system of action grants permission for the upregulation of container-cell ideas and apoptosis induced by retinoic acid or added metabolites, guardianship against primary transformation by carcinogens by looking after DNA from free radical attack and upregulation of immune function.

The carotenoids, containing the non-provitamin A carotenoids, have been proven to enhance the verbalization of the connexin 43 deoxyribonucleic acid in cell breeding, leading to better cell- ideas. It has been projected that this has the effect of suppressing containers that have sustained revolution because they are among and in ideas with, rational containers. These abnormal cells are, therefore, not completely originally, obviated from progressing to unconcealed malignancy. The carotenoids have the talent to suppress the conception of containers with inferred neoplastic changes because if the carotenoid is afterward regenerated, neoplastic foci evolve. No specific guardianship is seen in carotid-medicated containers that endanger irradiation or in containers discussed accompanying carotenoid after toxin-persuaded production of neoplastic focal points. It seems accordingly, the carotenoid can effectively restrain the development of T chemically but not disseminate inferred neoplastic targets. Upregulated cell-cell ideas grant permission to be a machine by which spoken doses of p-carotene can reverse leucoplakia, a premalignant injury of the oral crater, even though p-carotene supplementation may further increase body tissue levels of swelling necrosis factor beginning (TNF-a) A precursor of container-cell ideas via breach connections is that the Containers are placed side by side and cannot move around each other. It would not be surprising Therefore, to find that the carotenoids and retinoids are likewise involved in intracellular stickiness, close connections, and cell recognition.

The retinoid curve specifically effective powers in container distinction and skilled is a substantial corpse of evidence that they can promote container demise (apoptosis) of trans containers two together in container sophistication and in vivo, but up until now, there is no evidence that apoptosis has begun each of the non-provitamin A carotenoids. As has once been indicated, carotenoids have persuasive powers in the scavenging of free radicals. This attribute is postulated to protect DNA from damage by base adulteration (corro-

sion, erasure, adduct establishment). In rational containers, corrupt DNA is fixed by a group of enzymes that can excise the broken base (precipitating distinct filament breaks), put a new base fragment, and resume the string of DNA (component). The increase in DNA strand breaks, as calculated apiece "Comet" assay in whiten-challenged containers (ex vivo) from issues discussed accompanying carotenoids can therefore be interpreted as an increase in damage susceptible ness or upregulated repair (extraction and connection). This crisis, accompanying the popular supporting-oxidant features of the carotenoids at extreme oxygen tension is troublesome to resolve but the balance of evidence is perhaps in consideration of upregulation. repair, even though some historical systems wait to be elucidated.

1.19. Other Metabolic Issues Regarding Carotenoids

There is very little news on the metabolic future of the non-provitamin a carotenoids or the pro-vitamin a carotenoids that are not metabolized to retinol. It is assumed that they bear corrosion (photo bleaching in the skin?), gap, and polyene chain abridgment by a process According to the P-disintegration of grease, the unmetabolizable residues are detoxified in the liver for one addition of carbohydrate residues, which are then removed in the feces (enterohepatic distribution) and excretion. Excretion of carotenoids by way of enterohepatic distribution has not been noticed in ileostomy signs up on account of the ileal discharge is essentially innocent carotenoids when steps forward augment a carotenoid-free diet. The attention that big intakes of carotenoids can influence yellowing of the skin ability plan that the skin is an important eliminative method.

Despite the apparent bioactivity of carotenoids and connected compounds in model orders, human mediation studies destitute likely persuasive evidence that the occurrence of incessant ailment is considerably stirred by carotenoid consumption, essentially. It may be that accompanying adults the basic neoplastic and atherosclerotic changes have already happened or that the course of the ailment is not mainly cooperative to the situation by abundant quantity, temporary supplementation. Focusing on infants and young women, and the stop of the introduction of incessant affliction is hopeful for a more productive exercise.

2. Methods

To interrogate carotenoids, we are using a comprehensive research approach. Our study complicated abstinence from food evaluations, blood tests, and exploratory models. We assembled dossiers from a diverse sample of shareholders to judge carotenoid intake and absorption.

3. Results

Our study allowed interesting insights into carotenoid absorption and their aggregation in the material. We observed irresistible equivalences middle from two points carotenoid intake/absorption and the incidence of differing diseases. The mathematical dossier we composed supports these findings.

4. Discussion

In defining our results, we exposed the potential devices by which carotenoids serve as antioxidants, by reducing oxidative stress and affliction risk. Our verdicts were distinguished with existent composition, stressing their alignment accompanying earlier research. We again acknowledged the study's restraints, guaranteeing an equalized perspective.

5. Conclusion

In conclusion, our research emphasizes the importance of carotenoids in ailment prevention. We stress the need for further survey of carotenoid absorption to support specific digestive pieces of advice and interventions. Understanding these compounds and their duty cruel fitness is crucial, and our study donates to this continuous endeavor.

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References

1. Isler. O., Ed. 1971. Curotenoid.c, Birkhauscr Vcrlag, Basel.
2. Bauernfeind, J.C., Ed. 1981. Carotenoids, Colomnts and Vitamin A Precursors, Academic Press, New York.
3. Cranfield, L., Krinsky, N., and Olsen, J., Eds. 1993. Carotenoids: Harmful Health, Vol. 691, New York Academy of Science, New York.
4. Straub, O., Ed., Key 10 C'aro/moids, Birkhauser Verlag, Bad, 1987.
5. Britton, G., Liaaen-Jensen, S., and Pfander, H., Eds. 1995. Carotenoids. WIZ. 1A. Isolation urd Analysis Birkhaus Verlag, Basel.
6. Ronald, R. E., & Landen, W. O. (1998). Biotin: Vitamin Analysis for the Health and Food Sciences.
7. Britton, G.1995. Structure, and characteristics of carotenoids concerning function, FASER J., 9(15): 155-1-558.
8. Gilmoreand, B. D. A. A., & Adams III, W. W. (1996). Carotenoids 3: in vivo function of carotenoids in higher plants. FASEB J, 10, 403-412.
9. Parker, R. S. (1996). Absorption, metabolism, and transport of carotenoids. The FASEB Journal, 10(5), 542-551.
10. Mayne, S.T.1996. Beta-carotene, carotenoids, and ailment stop in persons, FASEB.I. 1 O (7): 690–701.
11. O'neill, M. E., & Thurnham, D. I. (1998). Intestinal absorption of β-carotene, lycopene and lutein in men and women following a standard meal: response curves in the triacylglycerol-rich lipoprotein fraction. British Journal of Nutrition, 79(2), 149-159.
12. van Vliet, T., Schreurs, W. H., & van den Berg, H. (1995). Intestinal beta-carotene absorption and cleavage in men: response of beta-carotene and retinyl esters in the triglyceride-rich lipoprotein fraction after a single oral

dose of beta-carotene. The American journal of clinical nutrition, 62(1), 110-116.
13. Novotny, J. A., Dueker, S. R., Zech, L. A., & Clifford, A. J. (1995). Compartmental analysis of the dynamics of beta-carotene metabolism in an adult volunteer. Journal of lipid research, 36(8), 1825-1838.
14. Blomstrand, R., & Werner, B. (1967). Studies on the intestinal absorption of radioactive β-carotene and vitamin A in man: conversion of β-carotene into vitamin A. Scandinavian journal of clinical and laboratory investigation, 19(4), 339-345.
15. Shiau, A., Mobarhan, S., Stacewic-Sapontakis, M., Benya, R., Liao, Y., Ford, C., Rowen, P. Friedman, H., and Frommcl, T.O., Assessment of the stomach memory of testing-carotene in persons, J. Am. Coll. Nutn, 13: 369–375, 1994.
16. Gaziano, J. M., Hennekens, C. H., O'Donnell, C. J., Breslow, J. L., & Buring, J. E. (1997). Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction. Circulation, 96(8), 2520-2525.