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A REVIEW ON THE β-CAROTENE: PRODUCTION, EXTRACTION, SYNTHESIS AND BIOLOGICAL PROPERTIES

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ABSTRACT:
The presence of double bonds gives β-carotene its distinctive hue, making it an oxygen-deficient isoprene-containing molecule. There are cyclic rings at both ends of the molecule. The present review was based on the production, extraction, synthesis and biological properties of β-carotene. Mammals can't produce carotenoids from scratch; therefore, they must get them from somewhere else. Algae, higher plants (in fruits and flowers as esters), fungi, and animals all have these yellow, red, and orange pigments in their natural forms. Carotenoids are found in human breast milk and can be modified through the mother's diet. Hexane, tetrahydrofuran, and acetone are examples of aprotic organic solvents that can be used for solvent-based extraction of -carotene from algae after and before they have been treated. The -carotene in algae, fungi, and plants can be extracted with the help of these solvents. The extraction process for -carotene is sped up and improved by the use of supercritical fluids. Increasing beta-carotene production can be accomplished by tailoring a number of environmental factors, including the type of organism used in the cultivation process, the amount of light available, the amount of salt present, the pH level, and the type and availability of carbon sources. Microalgae, plants, and fungus have all been optimised to increase their beta-carotene synthesis. It concluded that when administered in different doses, it has been shown to have effects like antioxidant and anti-inflammatory. it is also effective against cancer, cardiovascular diseases, Covid-19 and various other diseases.

Keywords: B-Carotene, Production, Extraction, Synthesis, Biological Properties.

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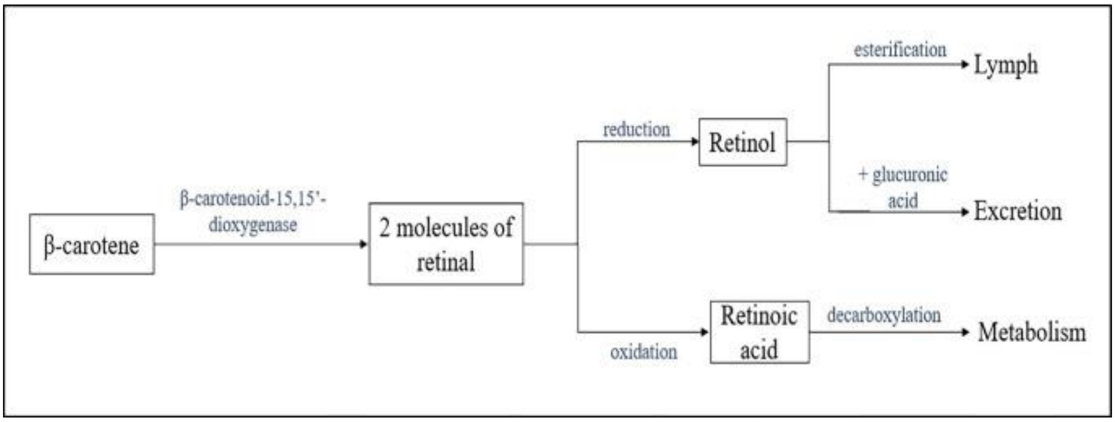
INTRODUCTION

The presence of double bonds gives β-carotene its distinctive hue, making it an oxygen-deficient isoprene-containing molecule. There are cyclic rings at both ends of the molecule. Although carotenoids tend to exist as their cis-isomers when isolated, this is easily converted to their trans-isomers when exposed to polar conditions [1]. Beta-carotene is a useful component of diet because of the many health benefits it provides. Inadequate retinol availability is countered by beta-carotene consumption in several regions of the world. Vegans and vegetarians have the greatest intakes of provitamin A. The corresponding beta-carotene intake is depicted in case RE is used with a conversion ratio of 6:1 [2][3].



Sources and Production

Mammals can't produce carotenoids from scratch, therefore they must get them from somewhere else. Algae, higher plants (in fruits and flowers as esters), fungi, and animals all have these yellow, red, and orange pigments in their natural forms. Carotenoids are found in human breast milk and can be modified through the mother's diet [4]. The serum levels of these -carotenoids are an indicator of various health indices. Once upon a time, the bio-pharmaceutical business would have revolved around a natural pigment with so much potential. But that's not the case. Only 3% of commercially available -carotenoids are of the bio-synthesized variety; the remainder are synthetic. There is no fundamental distinction between the natural and synthetic versions of the same function. In contrast, the latter has a higher price tag. Extracting beta-carotene from microalgae makes practical and scientific sense. In order to maximise pigment yields while minimising costs, scientists have studied a wide range of species and developed novel extraction methods [5][6].

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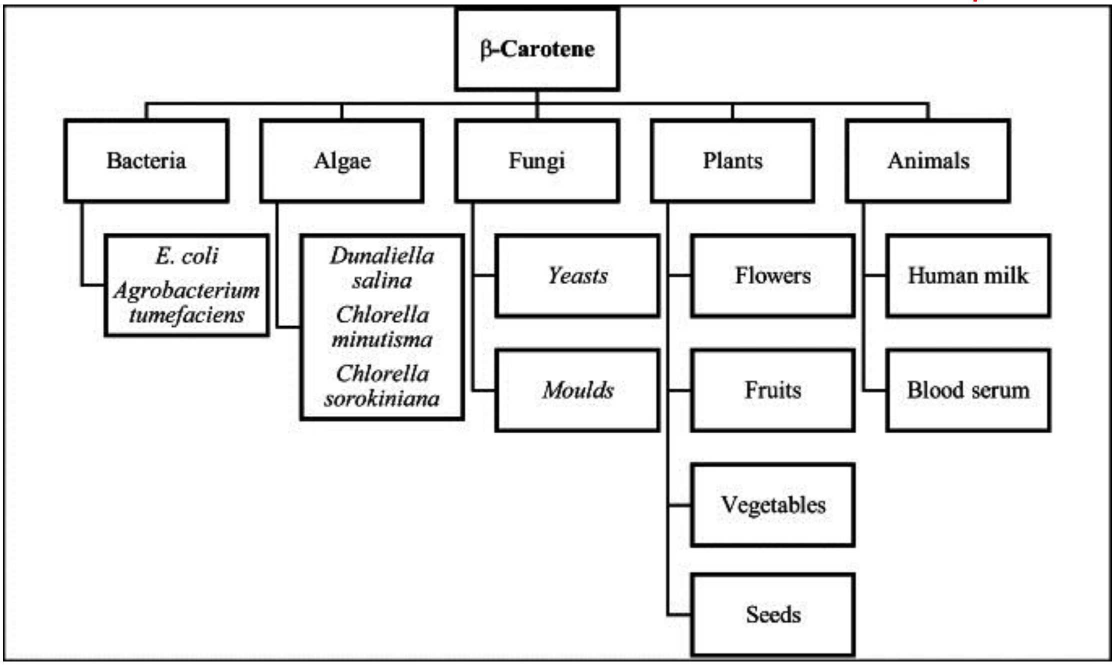

Fig 1. Natural sources of Beta-carotene

Depending on the chosen source, many methods of beta-carotene extraction might be used. Optimisation of pigment production and extraction requires a significant amount of study. Extraction techniques can be broadly classified as either organic solvent-based, enzymatic, or mechanical. There are also collaborative extraction strategies that combine existing methods with new ones [7].

Extraction

Hexane, tetrahydrofuran, and acetone are examples of aprotic organic solvents that can be used for solvent-based extraction of -carotene from algae after and before they have been treated. The -carotene in algae, fungi, and plants can be extracted with the help of these solvents. The extraction process for -carotene is sped up and improved by the use of supercritical fluids. Maceration aids atmospheric liquid extraction, which can be performed with minimal effort and requires no specialised equipment. Carotenoids like -carotene are often extracted using the far less complicated and more popular Soxhlet extraction method. The recovery rates are extremely high and simple tools are all that are needed for this technique. The high cost of the extraction process is a direct result of the method's need on a substantial quantity of solvents in addition to the beginning material [8]. The extraction of -carotene from plants and algae is accomplished with the aid of supercritical fluids. Ultrasonic waves, microwave-assisted extraction, pressurised liquid extraction, bead milling, and high-

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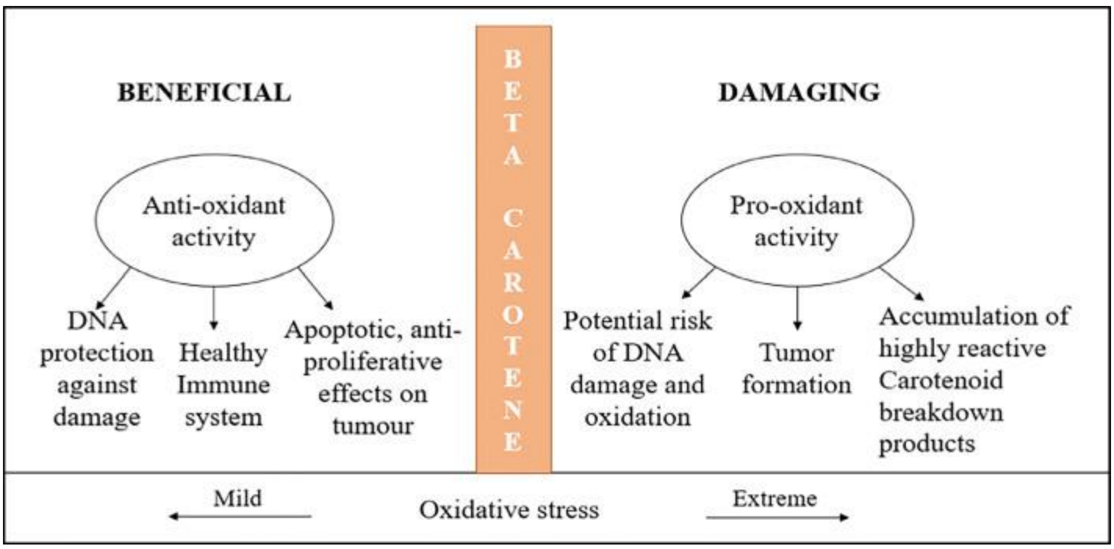
pressure homogenization are only a few of the physical methods employed for -carotene extraction. These techniques shield pigment from both heat and chemicals. Beta-carotene is isolated in this way from various organisms like algae and yeast as well as plants. Cell disruption and beta-carotene extraction can be achieved via a number of different extraction procedures, some of which involve the use of enzymes. Carrots, bagasse, apples, and any other residue from juice extraction can all be employed in these processes to isolate beta-carotene. Effectiveness and intended use are key considerations when settling on a beta-carotene extraction strategy [9][10].

Synthesis

By inserting functional genes like crtI, crtE, crtY, and crtYB, scientists are able to increase beta-carotene production and suppress the expression of repressor genes like crgA, which inhibits the synthesis of beta-carotene. So far, these methods have only been used on red yeast and fungi [11]. Increasing beta-carotene production can be accomplished by tailoring a number of environmental factors, including the type of organism used in the cultivation process, the amount of light available, the amount of salt present, the pH level, and the type and availability of carbon sources. Microalgae, plants, and fungus have all been optimised to increase their beta-carotene synthesis. The construction of polyene chains via Wittig's reaction, such as two 15-carbon-containing phosphonium salt molecules and one 10-carbon-containing dialdehyde molecule, and via Grignard's reaction involving two molecules of methanol and diketone, is one of the key methods for increased production of -carotene [12][13].

According to the Institute of Medicine's (IOM) dietary reference intake report, a vegetarian can meet his or her vitamin A needs by consuming a diet rich in -carotene.



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The NVS (1985-1988) on food and nutrient intake measured the average daily intake of vitamin A and carotenoids in Germany. These numbers show that 15 percent of people between the ages of 10 and 25 do not consume enough vitamin A as a whole. The importance of provitamin A in ensuring adequate vitamin A intake is highlighted by the fact that only about 25% of the population (depending on age group) will meet recommended vitamin A intake levels by consuming preformed vitamin A alone. When the daily consumption of beta-carotene is below the recommended amount, vitamin A levels in children and teenagers become dangerously low. Different findings emerged from the second iteration of Germany's National Nutrition Survey. According to the NVS, preformed retinol (meat, meat products, dairy, fat) provides 33% of vitamin A, -carotene (vegetables, vegetable soups, and nonalcoholic beverages) provide 48%, and combined carotenoids provide 19%. There is a median of 1.7 mg/d RE from these origins. Using the RE to -carotene conversion factor (6:1) from the NVS II, we can estimate that the average daily intake of -carotene is 4.5 mg/d, which is significantly higher than the average intake of -carotene reported in other studies from Germany and Europe, which range from 1.5 to 1.8 mg/d. If the numbers presented here are accurate, almost 15% of the women who participated in the study and 10.3% of the males do not consume enough vitamin A on a daily basis. Intake of beta-carotene from vegetables and fruits in Germany is not significantly higher than that in other countries such as Austria (0.8-2.1 mg/d), Ireland (0.5 mg/d), or Spain (0.3 mg/d) [14][15].

The researchers in Spain used a 24-hour memory questionnaire with photographic food models to estimate serving sizes. Inadequate vitamin A intake [less than two-thirds the RDI of vitamin A based on RE] was 60.5% in men and 48.5% in women in this sample of people aged 25-60 years old. The unusually low intake of preformed vitamin A (mean levels of 293 g/d in males and 276 g/d in women) appears to be the primary cause of these results [16]. Men consumed an average of 1.7 mg of beta-carotene per day, whereas women consumed 2 mg. Vitamin A intakes below the lower reference nutrient intake (LRNI) were found in 16% of males and 30% of women between the ages of 19 and 34 in a nutrition survey in the United Kingdom based on a 7-d weighted intake food record of 1724 respondents. A nutrient's LRNI is defined as the quantity at which 2.5% of the population can thrive. As a result, the needs of the vast majority of people are considerably more stringent. Importantly, the aforementioned survey found that 30 percent of women of childbearing age do not get enough vitamin A, which can have negative effects on foetal development [17].

The ability of beta-carotene to serve as a provitamin A is probably affected by a person's genetic makeup. Previously, we established that variations in the BCMO1 gene, specifically single nucleotide polymorphisms (SNPs), may influence the efficiency with which beta-carotene is converted into vitamin A. One patient with hypercarotenemia was found to have a point mutation (T170M) in the BCMO1 gene, which is extremely uncommon. The mutant

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BCMO1 protein showed only 10% of the biochemical activity of wild-type BCMO1 when produced in vitro. Two recently identified polymorphisms (R267S and A379V) in the human BCMO1 gene have been linked to greater fasting -carotene concentrations and a reduced intestinal conversion of a large dose of -carotene [18]. Indirect effects of variations in other genes involved in lipid and lipoprotein metabolism on beta-carotene metabolism have been suggested, as reviewed by Tourniaire et al. Some polymorphisms in hepatic lipase, lipoprotein lipase, and scavenger receptor-B1 have been linked to high- or low-plasma -carotene concentrations, suggesting that they contribute to the observed variation in the efficiency with which beta-carotene is converted to vitamin A. Large-scale population genetic studies are required to characterise the prevalence of BCMO1 genotypes and other polymorphisms in other genes that may alter carotenoid metabolism [19].

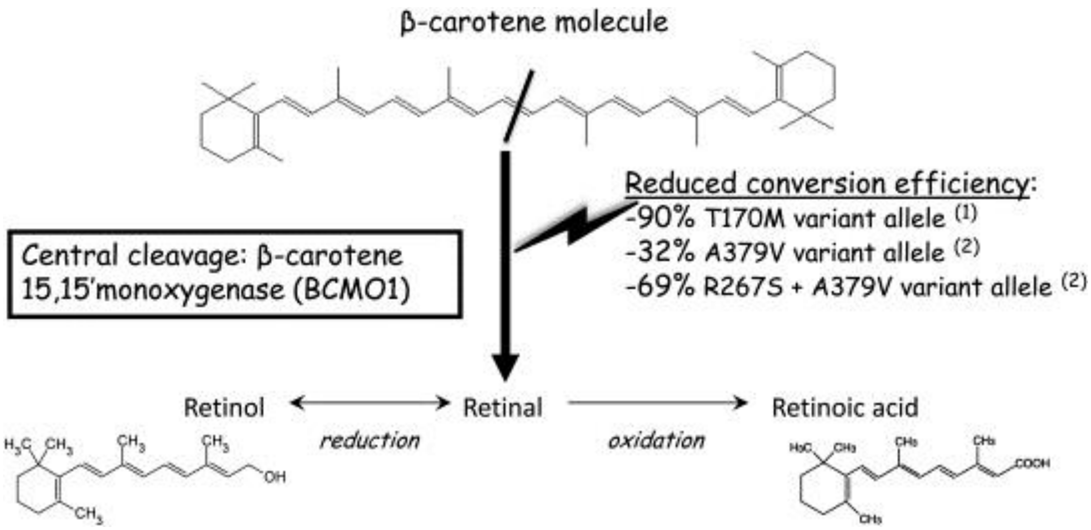


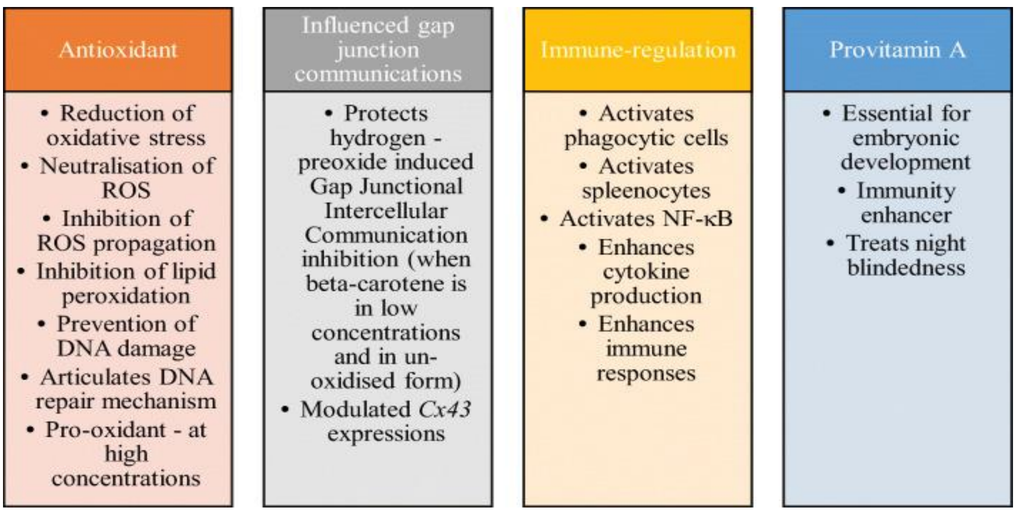
Fig 2. Metabolism of β-Carotene

Disease Prevention and Treatment

- The prognosis for many diseases is enhanced by treatment with or prevention of exposure to beta-carotene. When administered in different doses, it has been shown to have effects like antioxidant and anti-inflammatory [20].
- Subjects who consumed 12-25mg of -carotene per day showed a decrease in Cu-induced LDL oxidation and DNA strand breaking in research. Vitamins C and E were added as a supplement later on.
- CuZn-superoxide dismutase activity was observed to be boosted at a dose of 10 mg/day.
- Lipid peroxidation was reduced in a dose-dependent manner after administration of beta-carotene in participants with elevated oxidative stress, including smokers and people with

cystic fibrosis. When -carotene doses were higher than 25 mg/day, there was a lack of consistency in the responses of the biological markers.

- Activation of cellular communication via gap junctions has been shown in in vitro investigations. Positive effects of beta-carotene on intercellular connections in rats were found in a recent study.
- Vitamin A deficiency is frequent in youngsters, and whether or not they can be treated depends on how well their bodies convert the provitamin A carotenes they eat into retinol. This is because a lack of vitamin A can cause night blindness, a weakened immune system, and other symptoms. Beta-carotene boosted natural killer cell function in elderly males.
- Carotenoid-derived metabolites have been found to participate in gene alterations through interactions with nuclear and retinoic acid receptors, and there is an inverse association between serum pigment levels and systemic inflammation markers like neutrophil to lymphocyte ratio and insulin resistance and dysfunctional beta cells.
- Several studies have been conducted to determine the effects of beta-carotene consumption; the CARET research investigated the use of beta-carotene and retinol in the prevention of lung cancer. Daily use of 30 mg of -carotene and retinol supplementation was found to have no effect on reducing the risk of lung cancer. To determine the death and cancer rates of male smokers, researchers used beta-carotene and beta-tocopherol in a study titled ATBC (alpha-tocopherol, beta-carotene cancer prevention). According to the results, these chemicals have "chemo-preventive" potential against lung cancer [21].



- The actions can be helpful or harmful depending on the level of oxidative stress present in the environment to which the pigment is exposed. Pro-oxidation is aided by the buildup of highly reactive byproducts of carotenoid degradation. Aldehydes and other highly reactive organic molecules are created in this process. Carotene breakdown products (CBPs) are the name for

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these byproducts. An illustration of the significance of beta-carotene's antioxidant balance. To sum up, the pigment has multiple therapeutic effects in its role as a provitamin A, including antioxidants that neutralise reactive oxygen species (ROS), regulation of connexin expression that improves gap junction communication, activation of macrophages, and stimulation of an immunological response. a-carotene has a wide range of medicinal applications. It is believed that scavenging oxidative radicals created owing to trauma is how magnesium and vitamins with antioxidant capabilities have been employed to treat noise-induced hearing loss (NIHL) in animals [22].

Cancer

Epidemiological studies have confirmed the cancer-fighting effects of carotenoid-rich fruits and vegetables. The data showed that people preferred to eat pigment-rich foods before taking supplements. Metabolisms such as singlet-oxygen quenchers, immune augmentation, intracellular communications via gap junctions, and inhibition of cell division all contribute to carotene's anti-cancer effects [23].

Cells that are able to talk to one another in a controlled manner proliferate and divide in unison. Because of the breakdown in communication, abnormal cell development and eventually cancer could result. Therefore, beta-carotene's anti-cancer capabilities can also be attained through the modulation of cell-signaling pathways. For example, high-incidence malignancies at specific sites may benefit from beta-carotene supplementation. Many researchers have been studying the effects of this natural pigment on cancers with complicated origins like stomach cancer. Epidemiological and cohort studies on people with stomach cancer have employed various approaches and topics. In recent years, researchers have uncovered a number of molecular mechanisms of the pigment that likely contribute to the outcome of treatment for such patients. It also has anti-proliferative and apoptotic effects on cancer cells [24][25].

Cardiovascular Diseases

Studies have shown that eating a diet high in beta-carotene can reduce the risk of cardiovascular disease. Low-density lipoproteins (LDL) are the primary carriers because the pigment is fat-soluble. This interaction prevents LDL oxidation, which could lead to atherogenesis in the absence of protection. Reductions in intima-media thickness and serum total carotenoid concentration both correlate with reduced atherosclerosis risk. Because of beta-carotene's antioxidant properties, which alter the LDL oxidation and peroxidation mechanism, the risk of cardiovascular disease and its associated mortalities is reduced [26].

Bioavailability of NO and cyclic guanosine monophosphate (cGMP) are both increased by the presence of -carotene in the plasma. The adhesion molecules that are dependent on nuclear factor kappa B in endothelial cells decrease as a result. Additionally, the pigment can improve drug activity and serve to downregulate genes involved in cholesterol metabolism. Therefore, the risk of atherogenesis and other heart problems is diminished.

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COVID-19

Vitamin A deficiency is linked to respiratory tract infections, according to medical experts. On the other hand, seasonal influenza epidemics have been linked to vitamin D insufficiency because of less sun exposure throughout the winter. Vitamin insufficiency in patients and their connection to the COVID-19 practise of quarantine. Patients infected with the Corona virus were advised to adhere to stringent dietary regimens that included plenty of vegetables and fruits rich in beta-carotene, vitamin C, and other minerals. However, beta-carotene's antioxidant properties boost immunity in general by increasing lymphocyte responses, interleukin synthesis, and natural killer cell activity [27].

Other Diseases

Cystic fibrosis (CF) and non-CF-associated bronchiectasis patients had decreased levels of plasma -carotene and vitamin E compared to the general population. They are vulnerable to oxidative damage, which beta-carotene supplementation helps protect against. Cancer, cardiovascular disease, COVID-19, cystic fibrosis, and bronchiectasis are only few of the diseases that benefit from -carotene's multifaceted therapeutic effects. Beta-carotene has been shown to have antioxidant and anti-inflammatory effects, boost immunity, and improve intracellular signalling in cancer. Not only does beta-carotene have these results, but it also inhibits the growth and spread of tumours. The antioxidative effects of beta-carotene and its ability to boost medication activity in the treatment of cardiovascular disorders are well established. Antioxidant effects apart, beta-carotene also aids in lowering tumour necrosis factor (TNF-) and increasing vitamin E levels in people with cystic fibrosis. It has been shown that beta-carotene acts as an antioxidant and decreases malondialdehyde levels in bronchiectasis. Beta-carotene has been shown to have antioxidant and immune-stimulating effects in COVID-19 illness [28].

Bioavailability and Absorption

The mammalian small intestine is responsible for the absorption of lipophilic -carotene, which is then transported to the body's peripheral tissues. About half of the uncleaved -carotene enters the circulatory system, despite the presence of -carotene-cleaving enzymes in the small intestine. The concentration of intact plasma--carotene can be used as a proxy for the amount of bioavailable provitamin A absorbed by human intestinal epithelia. Factors such as pigment-cleaving gene polymorphisms and mutations, the type and lipid content of the food and its matrix, its digestibility and interactions, and subjective variations referring to individuals' endogenous digestive enzymes are additional factors affecting the bioavailability of -carotene.

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The non-polar -carotenes are easier to transport and distribute throughout the body thanks to lipoproteins and cholesterols. The hydrophobic centres of organic molecules, such as the different lipoprotein subtypes and cholesteryl-esters, include these groups. Tissues can absorb the beta-carotene in the blood for either storage or metabolism. The liver is the body's most concentrated store of beta-carotene, followed by the musculature, the kidneys, the skin, and finally the glands (such as the adrenal and mammary). The placenta and the yolk sac have also been shown to contain it. Therefore, unlike other types of carotenoids, it is found in relatively high quantities throughout the body. Humans are a useful model for studying the cleavage, transport, and distribution of -carotene because they are similar to those of ruminants [29].

CONCLUSION

Since beta-carotene does not dissolve in water, it has a very limited bioavailability when ingested. It needs to be transported in a secure manner because it is susceptible to physiochemical degradation during production, storage, and after consumption. When it comes to solubility, storage, target delivery, encapsulated protective stability, and dispersion, beta-carotene benefits greatly from nanotechnology. These nano-engineered forms of -carotene include, but are not limited to, microemulsions, nano-spheres, capsules, and nanostructure- or solid-lipid-carriers. The most widely used methods for administering beta-carotene are those based on polymers and lipids, respectively. For these nano-engineered pigments to be absorbed by the enterocytes and used in the body, they must first be directed to the fluid of the digestive system. Micelles and niosomes have been extensively used for this goal. However, before include these nano-pigments in functional foods, careful investigation into their interaction with the cells and environment of the gastrointestinal system is necessary.

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CONFLICT OF INTEREST

Authors declared for none conflict of interest.

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