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Exploring the Role of Carotenoids in Human Health: Therapeutic Applications and Mechanistic Insights

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***Abstract*:** Tetraterpene pigments, known as carotenoids, are found in several organisms, including some types of algae, plants, mammals, and some species of archaea and fungi. Until 2018, 850 naturally occurring carotenoids had been reported. Photosynthetic bacteria, fungi, algae, and plants can make carotenoids. Levels of carotenoids in the human body have been strongly associated with preventing and treating numerous diseases because of their protective characteristics. A substantial body of research has been amassed about the possible health benefits of carotenoids, which have long been known for their antioxidant capabilities. Due to their antioxidant properties, the primary carotenoids such as carotene, lycopene, lutein, zeaxanthin, crocin (crocetin), and curcumin are responsible for the positive health benefits of carotenoid-rich vegetables and fruits and for lowering the risk of certain diseases. Neurodegenerative processes might be stopped or delayed by strategies, such as consuming carotenoid-rich food that disrupts apoptotic pathways. Also, it explores the novelty of green technology separation techniques for isolating carotenoids. This review briefly discusses the chemistry, classification, biological functions, potential mechanisms, and environmental and commercial outcomes of some important carotenoids used to treat various disorders.

***Keywords*:** Carotenoids, Pigments, Antioxidants, Ageing, Green technology, Neurodegeneration

Colourful liposoluble pigments, called carotenoids, are found in various foods, such as fruits, vegetables, plants, fish, fungi, bacteria, and algae. More than 600 different carotenoids, broken down into carotenes, xanthophylls, and lycopene, have natural structural variations. Approximately 20 carotenoids have been found in human blood and tissues, and 40 are in a typical human diet (Milani et al., 2017). A proton is lost during the creation of the tetraterpene skeleton (phytoene), which leads to the establishment of a double bond in the middle of the molecule. Cooking and chopping carotenoid-rich foods increases the potency of their nutrients when they enter the bloodstream, unlike other protein-rich foods and vegetables. Xanthophylls and carotenes are the two main types of carotenoids. Plants, fungi, and bacteria produce carotenoids that are terpenoid colours made up of eight isoprene units. Carotenoids of both types have antioxidant effects (Engelmann et al., 2011). Furthermore, some carotenoids are converted into vitamin A, which is necessary for human health and growth. The role of carotenoids in human health is being extensively studied due to epidemiological research suggesting that those who consume more carotenoid-rich food have a lower chance of developing various chronic diseases. Vitamin A insufficiency and various degenerative disorders, such as cardiovascular disease, cognitive deficits, and age-related macular degeneration, are linked to low levels of total plasma carotenoids and individual carotenoids (Meléndez-Martnez et al., 2019). Alpha-carotene, beta-carotene, and beta-cryptoxanthin are examples of provitamin A carotenoids, and lutein, zeaxanthin, and lycopene are non-provitamin A carotenoids.

Until 2018, the number of xanthophyll species reported in nature was around 850. The human body may be able to absorb, transport, distribute to tissues, metabolize, and utilize roughly 50 of them (Maoka, 2020). In order to ascertain the physiological significance of red and colourless tomato carotenoids, recent developments in our knowledge of their bioavailability (the percentage of intact carotenoid consumed that appears in the circulation), bioaccumulation (the amount of intact carotenoid consumed found in tissues), metabolism (the chemical modifications to a carotenoid for utilization as a participant in biological processes, or clearance), and bioactivity have been made (Milani et al., 2017).

Classification and Types of Carotenoids

Carotenoids are divided into two categories: carotenes, which include phytofluene, phytoene, lycopene and β-carotene, and xanthophylls, such as lutein, zeaxanthin, astaxanthin, fucoxanthin, and violaxanthin (von Lintig et al., 2020) (Fig. 1). Another carotenoid frequently found in food, beta-carotene, contains provitamin A activity. According to its structure, following central cleavage, it is transformed into one molecule of physiologically active retinol, and twice the molar amount is equivalent to beta-carotene. It contains antioxidant, anti-carcinogenic, and possibly immuneboosting characteristics like other carotenoids. Some epidemiological studies, although not all of them, found that eating more beta-carotene was linked to a lower risk of developing cancer and cardiovascular disease. There have not been any human clinical trials to investigate the effects of β-carotene yet, likely due to the difficulty in identifying β-carotene and the fact that it is frequently combined with significant amounts of β-carotene in fruits and vegetables.

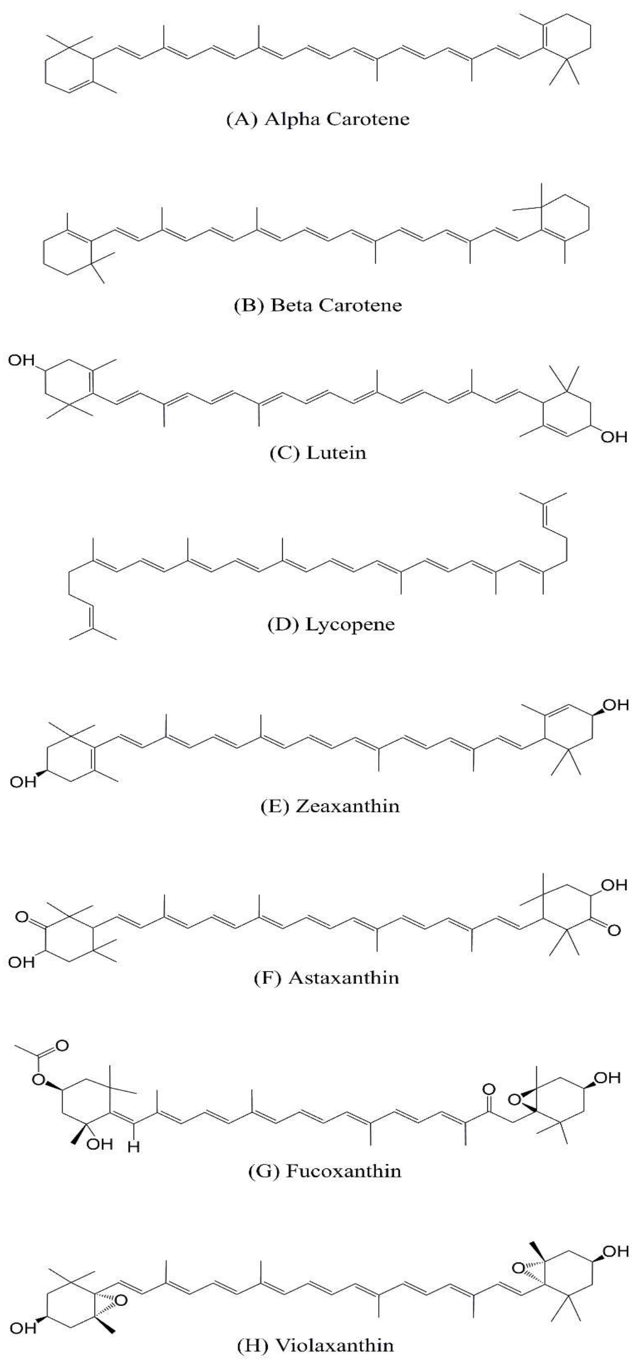

Fig. 1. The chemical structures of the most common carotenoids

The concentration of β-carotene is exceptionally high (Milani et al., 2017). Phytoene and phytofluene are colourless carotenoids found naturally in tomatoes and other crops. These are carotenoid precursors frequently discovered before the final carotenoid products in plants (Engelmann et al., 2011). These are also available in human fluids and tissues in respective concentrations of 0-2 mol/L (plasma) and 0-1 nmol/g (tissues). Regarding geometrical isomerisation, 15Z is the actual isomer for phytoene and phytofluene. They have anti-inflammatory, biomolecule stabilisation, augmentation, and protective properties and are effective against skin pigmentation (Maoka 2020).

Canthaxanthin, a red keto-carotenoid and one of the primary dietary carotenoids permitted as a food additive in many countries, has shown promise in treating erythropoietic protoporphyria, despite concerns regarding its accumulation in the retina with long-term use (Rebelo et al., 2020). It is naturally present in bacteria, algae, and some fungi. Since it is a ketocarotenoid, canthaxanthin has more potent anti-inflammatory and free radical-scavenging abilities than other carotenes and xanthophylls. Also, it is currently utilized widely as a natural skin-tanning ingredient in cosmetics and enhances the nutritional value of foods obtained from animals, as well as the health of both humans and animals who consume them (Coelho et al., 2023). Lutein is a dietary carotenoid found in many foods, including green vegetables, fruits, and egg yolk (Wackerbarth et al., 2009). A recent placebo-controlled, double-blinded, randomized, crossover study found that taking lutein capsules containing free lutein stabilized by 10% carnosic acid can protect against photodamage by lowering the expression of UVR-modulated genes like heme-oxygenase 1, intercellular adhesion molecule 1, and matrix metallopeptidase 1 (Wang et al., 2018). The distribution of lutein in different human tissues is inconsistent, with the macula having the highest concentration. Because of its high concentration of photoreceptor cells, the macula is responsible for visual acuity and central vision. It is located in the central retina, the posterior region of the eye. Zeaxanthin (a stereoisomer of lutein received from the diet) and meso-zeaxanthin (a lutein metabolite generated at the macula via metabolic transformation) are two different forms of carotenoids found in the macula (Li et al., 2020). Lycopene is an acyclic carotenoid in various foods, including tomato, watermelon, guava, papaya, apricot, and grapefruit (Mumu et al., 2022). As a dietary supplement, lycopene is a natural material that may be used in high doses without endangering the health or physiology of people. Numerous in vitro, ex vivo, and in vivo studies have shown an inverse relationship between lycopene-rich diets and heart diseases and cancer (Wang et al., 2018); several studies indicate that lycopene may provide photoprotection (Demmig-Adams et al., 2020). Zeaxanthin is a moderately polar carotenoid pigment abundant in parsley, spinach, kale, egg yolk, and meals enriched with lutein. Due to its capacity to connect with physiological proteins in people and as a scavenger for reactive oxygen species has exhibited several positive health impacts (TujJohra et al., 2020). The prevalence of AMD is inversely correlated with the amount of macular pigment (TujJohra et al., 2020). This is 1000 times more powerful than vitamin E and has the most significant ability for absorbing oxygen free radicals. It also has much more potent antioxidant activity than carotene. It has the chemical formula $C_{40}H_{52}O_4$ and is soluble in fatty acids and most organic solvents but insoluble in water. The conjugated double bond structure of astaxanthin, which also contributes to its reddish-orange hue by providing electrons for free radical reactions that produce more stable compounds, is a crucial defense mechanism against the free extreme chain reaction. Astaxanthin has garnered a lot of attention because of its possible pharmacological effects, which include a strong antioxidant property, DNA repair, stress tolerance, cell regeneration, neuroprotective, antiproliferative, anti-inflammatory, antiapoptotic, antidiabetic, anticancer, and skin-protective effects (Sluijs et al., 2015). Marine brown seaweeds, macroalgae, and diatoms, microalgae contain the marine carotenoid fucoxanthin, which is notable biologically. Numerous research studies have demonstrated fucoxanthin's significant potential and promising applications in human health. Fucoxanthin, a powerful carotenoid found in the chloroplasts of brown algae, accounts for more than 10% of the estimated total natural production of carotenoids, making it the most prevalent of all carotenoids (Yang et al., 2019).

Violaxanthin and other carotenoids are available in abundance in red, yellow and orange-coloured fruits, for example, Capsicum 5,6,50,60 -diepoxy-5,6,50,60 - tetrahydro-β, β-carotene-3,30 -diol, also called violaxanthin, is a natural orange xanthophyll, which may enzymatically be transformed into zeaxanthin when the light energy absorbed by plants exceeds the photosynthesis capacity. When exposed to low light or darkness, zeaxanthin is transformed into violaxanthin by zeaxanthin epoxidase; when exposed to intense sunlight, violaxanthin is de-epoxidized back to zeaxanthin by violaxanthin de epoxidase (Mumu et al., 2022).

Other Sources of Carotenoids

Pepper is a non-leafy vegetable that is high in carotenoids. In particular, β-carotene, β-cryptoxanthin, zeaxanthin, and capsorubin of *C. annuum* are the primary mixed carotenoids found in paprika and its oleoresin. Both are non-carcinogenic, have known biological functions linked to disease prevention, and are natural colours with fewer side effects. Also, they are secure substitutes for synthetic colouring compounds that give pharmaceutical, cosmeceutical, and nutraceutical goods their red colour. As a significant source of carotenoids, capsicum is also studied in terms of its main domesticated species, biosynthesis, carotenoid profile, antioxidant action, and safety (Imran et al., 2020).

Carotenogenesis

Cyanobacteria, mammals, plants, and microalgae produce isoprenoids called carotenoids. Carotenoids are pigments that absorb visible light during photosynthesis in photosynthetic systems. They also serve additional functions, such as signalling fruit development and luring insect pollinators, in addition to shielding photosynthetic bacteria, microalgae, and plants from light-induced cell damage. Carotenoids are found in many different types of food and are known to include over 1100 different types. Efficient mechanisms that regulate the rate of carotenoid synthesis in response to environmental stimuli are responsible for the diversity of carotenoid structures and biosynthetic pathways. Environmental factors that impact the carotenoid pathway's regulation include pH, temperature, salinity, dissolved O2, and light. Changes in the surrounding environment are known to initiate carotenogenesis, which in turn influences the accessibility and bioavailability of the pigments. Nowadays, only a small percentage of commercially sold carotenoids are extracted using microorganisms; the majority are either chemically synthesised or extracted from vegetables. According to reports, 80–90% of carotenoids are made artificially using chemicals. Toxic waste is produced when carotenoids are synthesised chemically. This prompt worries about the synthesis process' unintended consequences for human health. Carotenoids are the products of dimethylallyl pyrophosphate (DMAPP) and isopentenyl pyrophosphate (IPP), the universal C5 precursors. created through the cloning of genes that produce carotenoids.

Carotenoid Production Using Microorganisms

Bacteria: The production of carotenoids has great promise for bacteria. Heterotrophic bacteria create carotenoids as secondary metabolites, which are essential for a cell's capacity to adapt to its surroundings. It is well known that they shield cells from UV radiation. They are also thought to be responsible for the fluidity of cell membranes. Several common bacterial species have been linked to the production of carotenoids (Carlos et al., 2021).

Yeast and fungus: Different types of fungus are scattered based on their ecological roles. It is found that filamentous fungi produce colourful wide range of pigments including β-carotene, melanin, quinones, flavins, Anka Flavin. These fungal pigments have some useful roles such as, antioxidant, anticancer, cytotoxic activities enlarge the scope of their practical use. Based on the phylogenetics studies it is said some fungi can be considered as role model in the human system. Currently, industrial production of β-carotene is based on the use of heterothallic fungus *Blakeslea trispora*. The market value of carotenoid produced by *B. trispora* is expected to reach $2.0 billion in 2026. It is found that *B. trispora* is highly potentially active in for carotenoid production in industry. In case of Yeast, a big picture is basidiomycetes are a high source of microbial carotenoids. Also other yeast genera like Rhodotorula, Sporobolomyces produces highly antimicrobial carotenoids (Saubenova et al., 2024).

Green Technologies for the Separation of Carotenoids

As a possible replacement for synthetic carotenoids, the extraction of carotenoids from wastes and agro-industrial byproducts has attracted a lot of attention lately. Additionally, as consumers seek for more natural products with biological qualities and health advantages, the extraction of bioactive components is becoming more and more crucial. It has been shown that using natural monoterpenes instead of conventional solvents to extract carotenoids is more environmentally friendly. To extract lutein and xanthophylls from green Japanese knotweed leaves and avocado peels, βpinene was utilised. Furthermore, xanthophyll esters were synthesised using it as a bio-solvent (Papapostolou et al., 2023). Conversely, green extraction entails identifying and developing techniques that minimise energy consumption, facilitate the use of renewable natural resources and substitute solvents, and ensure the extraction of safe and high-quality products. The concepts of green extraction highlight the utilisation of numerous and sustainable plant varieties, innovation in variety selection, and the utilisation of renewable plant resources. Green extraction encourages using bio-based and substitute solvents, such as water or agro-solvents, instead of toxic and dangerous solvents like benzene or chlorinated solvents (Ferrando et al., 2024).

Technology Suitable for Green Extraction

Ultrasounds: A sound wave known as ultrasound has a frequency higher than what humans normally perceive as audible, usually exceeding 20 kHz. There are two types of ultrasound: low-frequency and high-frequency. High-frequency ultrasound is utilised in imaging, diagnostic, and therapeutic applications in medicine. It usually operates at frequencies higher than 1 MHz. The rapid formation and implosion of tiny bubbles in a liquid, known as "cavitation," is a phenomenon brought on by low-frequency ultrasound. This process can disrupt cellular structures and make it easier for compounds to be released from the sample, improving the extraction efficiency of compounds from solid matrices. Ultrasound-assisted extraction (UAE) raises the extracted yield while decreasing extraction time and energy in comparison to traditional extraction methods (maceration, Soxhlet, etc.). The most often used ultrasound devices in the food business are the bath and probe models. The probe ultrasound method uses a handheld probe that is submerged in the sample, whereas the bath approach immerses the sample in a liquid through which the ultrasound is applied. Both techniques have the potential to be successful in producing cavitation and breaking down cell walls to release bioactive substances; however, in order to maximise extraction efficiency and minimise any negative effects, it is important to optimise the choice of an appropriate solvent and other factors (Joshi et al., 2023).

Microwave-Assisted Extraction (MAE): Another documented green technique is the use of microwaves to extract carotenoids from microbes. Similar to sonication, this method breaks down the microbial cell wall by using the energy of microwave radiation in an effort to extract solvents more effectively. A rise in both temperature and pressure happens during microwave extraction, which causes the cell membrane to burst. Carotenoids are then liberated into the solvent, which is then diluted throughout the cell matrix. The foundation of this technique is the quick heating of the intracellular constituents, which puts a lot of strain on the cell wall. Either ionic conductivity or the use of a polarisation dipole are used to transfer the energy of the microwave radiation to the components. Because of the tremendous complexity and robust cell wall construction of microalgae, MAE may be very useful in this situation (Viñas et al., 2023). MAE's low cost and versatility in a range of matrices are further benefits. The technique's drawback is the possibility of damaging thermolabile substances and cis-trans isomerisation of carotenoids. Because of this, studies using sporadic radiation for three minutes were conducted, and the results demonstrated the effectiveness of this approach in recovering carotenoids. ADD a specific section on Green extraction technologies for carotene from plants, and microbial sources.

Biological roles and applications of carotenoids: Carotenoids have different kinds of biological roles and activities in photosynthetic organisms, including plants and microalgae, as well as humans, including Antioxidant, Anti-inflammatory, Anticancer, Anti−hyperglycemia, etc. (Fig. 3 and Table 1). Carotenoids' most critical biological roles in humans are tied to their antioxidant qualities, which are directly derived from their chemical structure (Vílchez et al., 2011).

Anti-oxidation: Free radicals are responsible for cancer, cardiovascular, ophthalmic, and neurological diseases (Meléndez-Martínez et al., 2015). Carotenoids can scavenge free oxygen radicals from the body, which aids in treating cancer and preventing tumor growth in cancer patients. Furthermore, specific carotenoids have been discovered to trigger antioxidant gene expression via the transcriptional factor Nuclear factor erythroid two related factor 2 (Nrf2), which aids in reducing neurological disorders and diabetes (Basu and Imrhan 2007). Astaxanthin has shown that it has

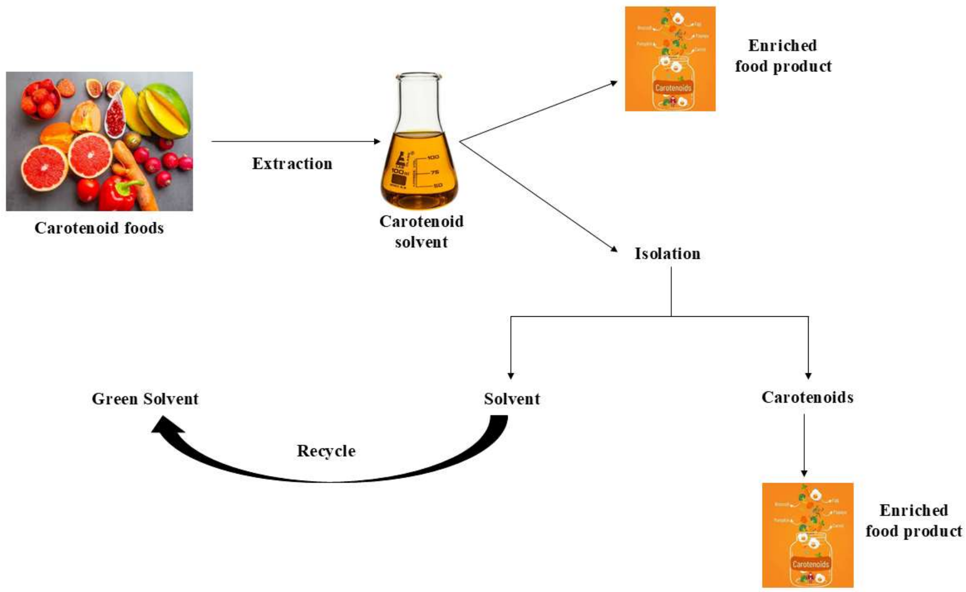

Fig. 2. Green solvents are used in the process to create a food product that is enhanced with carotenoids

Table 1. Source, biological functions and applications of carotenoids

Carotenoids	Pharmacological activity	Biological source	References
Astaxanthin	Antioxidant activity, anti-inflammatory properties, effects on skin damage, effects on DNA repair, and treatment of Colon cancer.	Soyabean, corn, olive, grape seed.	Yang et al. 2013
		Green sulfur bacteria *Xanthophyll omycesdendrorhous, Phaffia rhodozyma.*	Mapelli-Brahm et al. 2023
Canthaxanthin	1. Antioxidant activity 2. Anti-inflammatory effects 3. Food coloring agent 4. Effects on photosensitive disorders	Mushrooms, .eggs and fish.	Rebelo et al. 2020
Beta-Carotene	1. Antioxidant 2. Anticancer properties 3. Responsible for vision 4.Provides a strong immune system 5. Effects on healthy skin and mucous membrane	1. Carrots 2. Spinach 3. Lettuce 4. Tomatoes 5. Broccoli. *Rhodosporidium kratochvilovae*	Milani et al. 2017
Lutein	1.Anti-inflammatory effects 2.Responsiblefor eye health 3. Effects against age-related macular diseases.	1. Spinach 2. Broccoli 3. Peas 4. Egg yolks. *Chlorella saccharophila*	Abdel-Aal et al. 2013
Lycopene	1. Antihypertensive 2. Anticancer properties 3. Antioxidant 4. Anti-inflammatory effects 5. Cardiovascular effects 6. Neurobiological effects	1. Tomatoes 2. Apricots 3. Watermelons 4. Papaya 5. Grapes 6. Cranberries	Khan et al. 2021
Zeaxanthin	1. Anti-inflammatory effects 2. Effects on eye health 3. Antioxidant	Grapes,Oranges, Corns Mango ,*Chlorella zofingiensis*	Abdel-Aal et al. 2013
Fucoxanthine	1. Antioxidant 2. Anti neuroinflammation	Brown seaweeds	Mumu et al. 2022

antioxidant properties, such as the ability to quench singlet oxygen, effectively scavenge superoxide, hydrogen peroxide, and hydroxyl radicals, and inhibit lipid peroxidation, owing to its unique molecular structure-based chemical characteristics. Each ionone ring's hydroxyl and keto moieties are responsible for its enhanced antioxidant activity. Radicals are captured by astaxanthin both at the conjugated polyene chain and in the terminal ring moiety (Ambati et al., 2014). Fucoxanthin also successfully suppress the development of intracellular reactive oxygen species, DNA damage and apoptosis brought on by H_2O_2 (Epplein et al., 2011, Fiedor et al., 2014). It is possible to use violaxanthin as a natural antioxidant for medicinal or functional adjuvant purposes because it is highly effective at scavenging DPPH and ABTS+ radicals (Mumu et al., 2022).

Anti-inflammatory: Fucoxanthin and astaxanthin, two carotenoids with oxygen in their structure, have been shown to decrease the expression of the cytokines IL-6, TNF-α, and IL-1β and serve as pro and anti-inflammatory chemicals (von Lintig et al., 2020). Carotenoids strengthened the anti-inflammatory response by decreasing TNF-α and IL-1β gene expression in vascular cells. (Aust et al., 2005). Carotenoids inhibited inflammation by lowering NF-κB and IL-1β levels. Furthermore, in individuals with stable angina, this drug inhibited LPS-induced TNF-α, IL-6, and IL-1β production in peripheral blood mononuclear cells. Additionally, β-carotene supplementation reduced IL-1, IL-6, and IL-12 p40 cytokine transcription. Due to its capacity to decrease cytokine expression in Suid herpes virus-induced inflammation via NF-κB inactivation, it could be thought of as a possible anti-inflammatory agent for DNA-virus infections and, precisely, for the human herpes simplex virus (Milani et al., 2017). Finally, decreased levels of β-carotene have been found in individuals with inflammatory illnesses such as nonalcoholic fatty liver disease (Si and Zhu, 2022), chronic obstructive pulmonary disease (Kumar et al., 2020), acute myocardial infarction (Mohana et al., 2013), *H. pylori* infection (Fiedor and Burda 2014), and advanced coronary artery disease (Wojtasiewicz and Stoń-Egiert 2016). These findings support the theory thatβ-carotene protects the body by inhibiting inflammatory processes. Similarly, fucoxanthin plays a significant role in suppressing colitis caused by dextran sulphate sodium. It can manage the inflammatory bowel illness ulcerative colitis (UC) (Demmig-Adams et al., 2020). Astaxanthin efficiently warded off UV-induced inflammation in human keratinocytes by lowering iNOS and COX-2 mRNA and protein levels(Freitas et al., 2014).

Anticancer: Carotenoids have been shown to have anticancer properties in several studies. In most cases, carotenoids are known to stop the cell cycle, related to decreased expression of cyclin D1, cyclin D2, CDK4, and CDK6. As a result, it upregulates GADD45, which prevents the cell from entering the S phase (Grether-Beck et al., 2017). Furthermore, chemicals isolated from saffron, such as crocin and crocetin in combination, displayed anti-metastasis activities on the 4T1 cell line in breast cancer, including anti-

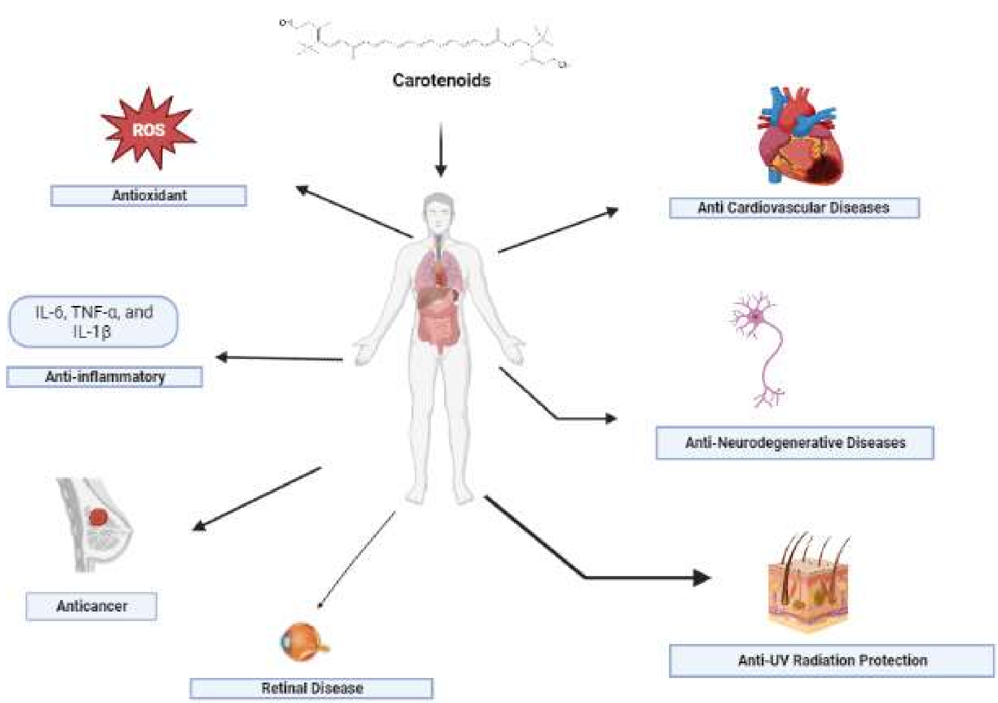

Fig. 3. Overview of carotenoids related to their biological roles for human health

migration, anti-invasive, and anti-nonadhesive effects (Biehler et al., 2012). Carotenoids such as β-cryptoxanthin and lycopene have been shown to decrease the NF-κB, which is effective in treating lung and prostate cancer (Abdel-Aal et al., 2013b). β-carotene has been discovered to have anti-angiogenic activity, which means it helps to prevent the formation of blood vessels. Zeaxanthin is inversely linked in the blood related to increasing the risk of pancreatic (Relevy et al., 2015) and ovarian cancer (Wang et al., 2019). In human epidemiological research, the benefits of dietary lutein and zeaxanthin in the prevention of cancer were discovered, with consumption of these carotenoids lowering the risk of various malignancies such as bladder cancer (Chambaneau et al., 2016), breast cancer (Epplein et al., 2011), and prostate cancer (Mužáková et al., 2010), Non-Hodgkin lymphoma (Shih et al., 2021), renal cell carcinoma (Freitas et al., 2014), head and neck cancer (Freitas et al., 2014). Similarly, intake of lutein and zeaxanthin was found to be inversely related to a lower incidence of gastrointestinal malignancies, such as oral, pharyngeal, oesophagus (Mužáková et al., 2010), colon (Shih et al., 2021) and pancreatic cancers (Shokri-Mashhad et al., 2021).

Anti Cardiovascular Diseases (CVD): Clinical and epidemiological research has demonstrated a negative relationship between eating fruits and vegetables and the likelihood of developing chronic conditions like cardiovascular illnesses (CVDs). One of the significant risk factors for stroke, heart attacks, renal failure and many other consequences is high blood pressure. Because carotenoids have such strong antioxidant qualities, eating a diet high in them significantly reduces the risk of developing the disease (Jansen et al., 2013). Astaxanthin has been shown to positively benefit the heart by lowering atherosclerosis-related inflammation and altering LDL- and HDL-C levels in the blood. Compared to healthy individuals, patients with coronary artery disease had lower plasma levels of lutein, zeaxanthin, β -cryptoxanthin, β -carotene and lycopene. Furthermore, the lower plasma levels of lutein, zeaxanthin, and β -cryptoxanthin were linked to smoking, a high body mass index, and low levels of high-density lipoprotein cholesterol (HDL-C) (Broekmans et al., 2002). In addition, it can also be utilised as a food supplement to help prevent obesity-related heart dysfunction. However, further studies are necessary, particularly *in vivo* experimental approaches for cardiovascular protection (Ciccone et al., 2013)

Anti-neurodegenerative diseases: Neurodegenerative diseases such as Alzheimer's, Huntington's, Parkinson's, and amyotrophic lateral sclerosis (ALS) are brought on by increased oxidative stress in the nervous system. Proper dietary carotenoids can decrease dysfunction caused by improper signalling. Carotenoids, including astaxanthin, carotene, and lycopene, are implicated in Ca2+ ion transportation in the brain (Bhatt and Patel 2020). The antioxidant qualities, blood-brain barrier-crossing ability, and cell mitochondrial membrane integrity of carotenoid astaxanthin may all help reduce the risk of diseases of the nervous system (neurodegenerative). Astaxanthin also has antiapoptotic properties and lowers free radical damage, glutamate release, and cerebral infarction.(Aziz et al., 2020). Lycopene has also been shown to make the blood-brain barrier permeable, lessening certain disorders' severity (Fiedor and Burda 2014). ROS increases caspase activation and Akt/GSK-3β signaling in Alzheimer's disease. Carotenoids aid in restoring normal signaling and reduce caspase activation. Another well-known xanthophyll, fucoxanthin, has also shown neuroprotective properties by triggering Nrf2/HO-1 signaling and causing Nrf2 nuclear translocation to protect against brain ischemic/reperfusion injury (Almeida et al., 2019).

Anti−hyperglycemia: According to statistical analysis and assessment conducted by the European Prospective Investigation into Cancer and Nutrition-Netherlands, human use of carotenoids in their diet can reduce the incidence of type 2 diabetes. Despite this, after incorporating a few criteria such as age, sexual orientation, risk factors, and nutrition, the Hazard percentage for β-carotene was determined to be 0.78, while for α-carotene, it was 0.85. Furthermore, research shows that using carotenoids can reduce the incidence of type 2 diabetes in healthy women and men (Arzi et al., 2020). The leading cause of hyperglycemia is a person's lifestyle and eating habits. Hypertension causes oxidative stress linked to obesity, diabetes, dyslipidemia, and hyper homocysteinemia. Fatty acid radicals and ROS are crucial in raising GR, GPx and other hormones. By scavenging this fatty acid radical and ROS, carotenoids restore regulatory signals and lower illnesses by 40 to 79 per cent (Bhatt and Patel 2020).

Anti-tuberculosis: The fatty acids-carotenoid complex (FACC) has anti-TB properties that can affect MDR strains of M. tuberculosis. A promising anti-TB medication was created by using the sole biomass of the marine microalgae Chlorella vulgaris to produce CGF, lipid, lutein, and its geometric isomers. (Wojtasiewicz and Stoń-Egiert 2016).

Anti-UV Radiation Protection: The efficacy of UV-C protective activity of carotenoid pigments isolated from *M. roseus* and *M. luteus* on the growth of *S. faecalis* proved that 21 colonies out of 31 colonies were stable and resistant against UV exposure with approximately 70 to 95 percentage of coefficient of variation at 120 min. β-carotene and canthaxanthin are two carotenoids that have photoprotective characteristics. Patients with erythropoietic protoporphyria have lower serum levels of carotene, so they must take it as a dietary supplement. Furthermore, lycopene and β-carotene have been found to lessen skin redness and damage from UV radiation. This acts as a calming agent when exposed to UV radiation from the sun (Galasso et al., 2017).

Antiaging: Age-related macular degeneration (AMD), the leading cause of blindness in developed nations, is one of the most severe age-related diseases. Due to its antioxidant characteristics, GSH, a reducing molecule found in high concentrations in the lens, is crucial for maintaining tissue transparency. In ageing lenses, this substance diminishes, resulting in oxidative and degenerative processes. Zeaxanthin and lutein play essential roles in preventing AMD because their consumption is linked to an increase in macular pigment density, which affects intracellular GSH levels (Mrowicka et al., 2022).

Retinal disease: Notably, identified AMD risk factors also entail biological mechanisms that significantly lower the bioavailability of lutein and zeaxanthin. The cumulative impact of diminished antioxidant capacity due to protracted oxidative injury is believed to create a toxic, neurodegenerative environment. The proliferation of early cellular senescence in the retinal pigment epithelium (RPE), which in turn sets off the pathogenic chain of events that leads to AMD development, is known to be triggered by mitochondrial malfunction and photo-oxidation (Olufunmilayo et al., 2023). Furthermore, it has been demonstrated that the metabolic syndrome's root causes seriously impair the digestion and transport of dietary carotenoids in diabetic retinopathy. Obesity, insulin resistance, and chronic hyperglycemia lead to atherogenic metabolic imbalance, furthering the loss of macular pigment. Therefore, low macular pigment optical density (MPOD) levels probably play a crucial role in AMD development (de Carvalho and Caramujo 2017).

Miscellaneous applications: Carotenoids are used in vegetable oils as a solution or suspension in margarine coloring, baked goods, and some prepared foods as emulsions or microencapsulated beadles. It is also used in drinks like orange juice, confectionery, and other ready-to-eat meals (Epplein et al., 2011). Carotenoids were first coupled to bovine serum albumin (BSA) in a new way, and then this carotenoid-protein combination was employed to make fortified food emulsions (Terlikowska et al., 2021).

The global market for carotenoids was assessed to be close to USD 1.5 billion in 2017, and it is anticipated to increase to $2.0 billion in 2022, with a compound annual growth rate (CAGR) of 5.7% from 2017 to 2022. The following compounds account for over 90% of the market's value: capsanthin, astaxanthin, β-carotene, lutein, annatto, lycopene and canthaxanthin. By itself, capsanthin made up USD 300 million in 2017 (20% of the market). Similarly, the astaxanthin market contributed USD 288.7 million (Leoncini et al., 2015). Astaxanthin leads the carotenoids market for the anticipated period, followed by β-carotene and lutein. Because of their well-established applications, carotene, lycopene, astaxanthin, zeaxanthin, and lutein are the most critical current carotenoids. However, the colorless carotenoid precursor phytoene, fucoxanthin, and canthaxanthin are approaching the market with the potential to be economically significant (Wackerbarth et al., 2009). Recent developments in systems biology, genetic engineering, and ways to profit from biomass leftover fractions present new scenarios for making microalgae-based biofuel production financially viable in around 15 years. Combining the production of microalgae-based biodiesel and other bioproducts can increase efficiency and profitability (Vílchez et al, 2011).

CONCLUSION

Microalgae have garnered the attention of scientists owing to their rich supply of bioactive compounds. Their straightforward and economical development needs render them attractive for widespread employment in the pharmaceutical, culinary, and cosmetic sectors to enhance health. Carotenoids are one of the most frequent components of microalgae, and research has demonstrated significant health advantages. Microalgal carotenoids have demonstrated anti-inflammatory, antioxidant, and anticancer activities in various in vitro studies, animal tests, and human trials. In this regard, they have been reported to be useful in treating several inflammatory conditions including colitis and nonalcoholic fatty liver disease. Owing to the increasing demand for natural products, the identification of novel carotenoids, advancements in upstream and downstream methodologies, and broadening market opportunities, the microalgal carotenoid market is anticipated to persist in its growth.Microalgal-derived carotenoids are utilized in the food, feed, nutraceutical, and cosmetics sectors; nevertheless, legal and regulatory frameworks are lagging behind scientific progress. This study examined the possibility of several green solvents and innovative techniques for extracting carotenoids from fruit and vegetable by-products. Due to their attributes and low toxicity, green solvents are really a superior alternative to organic solvents. Cost-effective techniques for the production of microbial pigments are required to substitute synthetic alternatives.

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