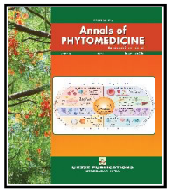
Annals of Phytomedicine 15(1): 74-82, 2026

DOI: http://dx.doi.org/10.54085/ap.2026.15.1.7

Annals of Phytomedicine: An International Journal
http://www.ukaazpublications.com/publications/index.php

Print ISSN : 2278-9839 Online ISSN : 2393-9885



Review Article : Open Access

# Lutein and zeaxanthin: Emerging frontiers in nutraceutical and pharmaceutical applications

**S. J. Imamsaheb◆, M. Kabilan*, A. Geetha**, Aditi Sewak*** and Adnan A. Khan*****

All India Coordinated Research Project on Tuber Crops, Regional Horticultural Research and Extension Centre, Dharwad-580005, Karnataka, India

* Division of Soil Science and Agricultural Chemistry, Regional Coffee Research Station, Coffee Board, Thandigudi, Dindigul-624 216, Tamil Nadu, India

** Department of Crop Physiology, College of Agriculture, Professor Jayashankar Telangana Agricultural University, Rajendranagar-500030, Hyderabad, Telangana, India

*** Department of Food and Nutrition, Punjab Agricultural University, Ludhiana-141004, Punjab, India

**** Division of Nephrology and Hypertension, Department of Medicine, University of California, San Diego, USA

**Article Info**

**Article history**
Received 4 April 2026
Revised 15 May 2026
Accepted 16 May 2026
Published Online 30 June 2026

**Keywords**
Lutein
Zeaxanthin
Macular pigment
Antioxidant activity
Nutraceutical applications

**Abstract**

Lutein and zeaxanthin, dietary xanthophyll carotenoids abundantly present in green leafy vegetables, maize, and other plant-derived sources, have emerged as critical bioactive compounds at the interface of nutrition and therapeutics. These pigments are selectively concentrated in the macular region of the human retina, where they enhance visual performance by filtering high-energy blue light and attenuating oxidative damage. Quantitative assessments indicate that dietary supplementation (10-20 mg day$^{-1}$) significantly elevates macular pigment optical density (MPOD) and improves visual acuity and contrast sensitivity in both healthy individuals and subjects at risk of ocular degeneration. Beyond ocular health, accumulating evidence highlights their systemic protective effects mediated through antioxidant and anti-inflammatory mechanisms. *In vitro* and *in vivo* studies demonstrate that lutein and zeaxanthin effectively scavenge reactive oxygen species, reduce lipid peroxidation (20-40%) and modulate key signaling pathways involved in inflammation and apoptosis. Clinical and epidemiological studies further report improvements in cognitive function, with enhanced memory and processing speed associated with increased serum carotenoid levels. Additionally, cardiometabolic benefits, including reductions in LDL oxidation and improved lipid profiles, have been documented. Recent technological advancements have focused on enhancing bioavailability, which is inherently limited due to their lipophilic nature. Novel delivery systems such as nanoemulsions, liposomal encapsulation and microencapsulation have demonstrated up to 2-3-fold increases in absorption and stability under gastrointestinal conditions. Furthermore, food-based fortification strategies and biofortification approaches are being explored to improve dietary intake at the population level. Despite these promising findings, challenges remain, including variability in bioavailability, lack of standardized dosage regimens, and limited long-term clinical validation across diverse populations. This review synthesizes current evidence on the biochemical properties, functional efficacy and emerging applications of lutein and zeaxanthin, emphasizing their growing significance in nutraceutical and pharmaceutical domains. Collectively, these carotenoids represent promising candidates for next-generation interventions aimed at promoting ocular, cognitive and systemic health.

## 1. Introduction

Carotenoids are a structurally diverse group of naturally occurring isoprenoid pigments synthesized by plants, algae and certain microorganisms, where they play indispensable roles in light harvesting, photoprotection, and membrane stabilization. Among these, lutein and zeaxanthin are oxygenated carotenoids (xanthophylls) that have gained substantial prominence due to their critical functions in human physiology and disease prevention. Unlike provitamin A carotenoids such as β-carotene, lutein and zeaxanthin cannot be synthesized endogenously in humans and must be acquired through dietary intake, primarily from green leafy vegetables (*e.g.*, spinach, kale), yellow-orange fruits, maize and egg yolk (Krinsky *et al.*, 2003). Their chemical structure, characterized by conjugated double bonds and terminal hydroxyl groups, confers high antioxidant capacity and enables their preferential incorporation into lipid-rich biological membranes. A distinctive and biologically significant feature of lutein and zeaxanthin is their selective accumulation in the macular region of the human retina, where they form the macular pigment. This pigment is composed predominantly of lutein, zeaxanthin and meso-zeaxanthin, and its optical density is directly associated with visual performance. Macular pigment acts as a natural optical filter, absorbing high-energy blue light in the wavelength range of

**Corresponding author: Dr. S. J. Imamsaheb**
*Head, AICRP (Tuber Crops), Regional Horticulture Research and Extension Centre, NH-4-Bye-pass, Dharwad-580 005, Karnataka, India*
**E-mail: imamjath@gmail.com**
**Tel.: +91-7975088846**

400-500 nm, thereby reducing chromatic aberration, light scatter and photochemical damage to retinal tissues (Bone *et al*., 1985; Bernstein *et al*., 2016). Quantitative intervention studies indicate that supplementation with lutein and zeaxanthin at doses of 10-20 mg $day^{-1}$ can significantly increase macular pigment optical density (MPOD) by 20-40 per cent over periods of 3-12 months, accompanied by improvements in contrast sensitivity, glare recovery, and visual acuity (Loughman *et al*., 2012; Hammond *et al*., 2014). These functional attributes are particularly relevant in the context of age-related macular degeneration (AMD) and cataracts, which represent major causes of vision impairment globally.

Beyond ocular health, accumulating evidence underscores the systemic biological importance of lutein and zeaxanthin. Their potent antioxidant properties enable efficient quenching of singlet oxygen and scavenging of reactive oxygen species (ROS), thereby protecting cellular macromolecules from oxidative damage. Experimental studies have demonstrated reductions in lipid peroxidation and oxidative biomarkers by approximately 20-40 per cent following supplementation (Johnson *et al*., 2013; Li *et al*., 2012). In addition, these carotenoids exhibit anti-inflammatory effects through modulation of key signaling pathways, including nuclear factor kappa B (NF-κB), mitogen-activated protein kinases (MAPKs), and cytokine expression, contributing to reduced inflammatory responses in chronic disease conditions. Emerging research has also highlighted the neuroprotective roles of lutein and zeaxanthin. Notably, these carotenoids are capable of crossing the blood brain barrier and accumulating in neural tissues, where they are associated with improved cognitive function. Clinical and observational studies have reported positive correlations between serum lutein concentrations and enhanced memory performance, processing speed, and executive function, particularly in ageing populations (Johnson *et al*., 2014; Nolan *et al*., 2015). Furthermore, their involvement in cardiovascular health has been linked to the inhibition of low-density lipoprotein (LDL) oxidation, improvement in lipid profiles, and attenuation of endothelial dysfunction, thereby reducing the risk of atherosclerosis and related disorders. Despite their well-documented health benefits, the bioavailability of lutein and zeaxanthin remains a significant limiting factor. Their lipophilic nature necessitates dietary fat for optimal absorption, and their bioaccessibility is influenced by multiple factors, including food matrix composition, processing methods, and individual metabolic variability. Typically, intestinal absorption efficiency ranges between 5-50%, depending on dietary conditions. To address these limitations, recent advances in food and pharmaceutical sciences have focused on the development of novel delivery systems. Technologies such as nanoemulsions, liposomal encapsulation, solid lipid nanoparticles, and microencapsulation have demonstrated up to 2-3-fold improvements in bioavailability, stability and targeted delivery (Saha *et al*., 2017). Additionally, agronomic strategies, including biofortification of staple crops and development of carotenoid-rich cultivars, are being explored to enhance dietary intake at the population level. In parallel, increasing attention is being directed toward the application of lutein and zeaxanthin in nutraceutical and pharmaceutical formulations. Their incorporation into functional foods, dietary supplements, and therapeutic products has opened new avenues for preventive healthcare. However, challenges persist in terms of standardizing dosage regimens, ensuring consistent bioefficacy, and establishing long-term clinical validation across diverse demographic groups. Variability in study designs, differences in biomarker assessment, and limited large-scale randomized clinical trials further complicate the translation of experimental findings into clinical practice. in this context, the present review aims to provide a comprehensive and critical synthesis of current knowledge on lutein and zeaxanthin, encompassing their chemical characteristics, dietary sources, bioavailability, and multifaceted biological functions. Particular emphasis is placed on recent advances in delivery systems, emerging therapeutic applications, and their role in mitigating oxidative stress-related disorders. Furthermore, this review identifies existing research gaps and outlines future directions for optimizing the utilization of these carotenoids in nutraceutical and pharmaceutical domains. Collectively, lutein and zeaxanthin represent promising candidates for the development of next-generation functional interventions aimed at enhancing human health, visual performance, and nutritional security.

## 2. Chemical structure and physicochemical properties

Lutein and zeaxanthin are structurally related xanthophyll carotenoids ($C_{40}H_{56}O_2$) characterized by a conjugated polyene chain with hydroxylated cyclic end groups. Despite sharing an identical molecular formula, they differ in double-bond configuration within terminal ionone rings, rendering them structural isomers-lutein (β, ∑-carotene-3,3-diol) and zeaxanthin (β, β-carotene-3,3-diol) (Krinsky *et al*., 2003). Their extensive conjugated system imparts strong light absorption and antioxidant capacity (Britton *et al*., 2004). Their physicochemical properties are governed by conjugated double bonds and polar hydroxyl groups, enabling absorption in the 440-480 nm range and effective blue-light filtration (Bone *et al*., 1985). Slight polarity facilitates alignment within phospholipid bilayers, enhancing membrane stability and oxidative resistance (Gruszecki and Strzalka, 2005). These lipophilic compounds exhibit low aqueous solubility, with bioavailability (5-50%) dependent on dietary lipids and micellar incorporation (Reboul *et al*., 2013). However, they are prone to degradation under light, heat, and oxygen, leading to isomerization and reduced bioactivity (Rodriguez-Amaya, 2001). Stability remains a critical constraint for nutraceutical and pharmaceutical applications. Advanced delivery systems, including nanoemulsions and liposomes, have demonstrated 2-3-fold improvements in stability and bioavailability (Saha *et al*., 2017). Overall, their unique structural and physicochemical attributes underpin their efficacy as antioxidants and photoprotective agents.

## 3. Natural sources

Lutein and zeaxanthin are widely distributed in nature, predominantly in higher plants, microalgae, and certain animal-derived foods. Their concentration and relative proportions vary considerably depending on species, cultivar, maturity stage, and post-harvest handling. in terrestrial plants, these xanthophyll carotenoids are localized within chloroplasts, where they contribute to light harvesting and photoprotection through the xanthophyll cycle.

### 3.1 Green leafy vegetables

Green leafy vegetables represent the richest dietary sources of lutein, with comparatively lower concentrations of zeaxanthin. Crops such as spinach, kale, amaranthus, and fenugreek typically contain lutein in the range of 10-40 mg per 100 g fresh weight (Humphries and Khachik, 2003). The high lutein content in these vegetables is attributed to their dense chloroplast structure and active photosynthetic metabolism. Regular consumption of these greens has been associated with elevated plasma lutein levels and increased macular pigment optical density.

### 3.2 Fruits and non-leafy vegetables

Several fruits and non-leafy vegetables contribute significantly to dietary intake of these carotenoids. Zeaxanthin is particularly abundant in yellow and orange-colored produce such as maize, orange bell peppers, and papaya, whereas lutein is present in moderate amounts in zucchini, pumpkin, and squash (Perry *et al.*, 2009). In regions where maize is a staple food, it represents a major dietary source of zeaxanthin.

### 3.3 Microalgae and commercial sources

Microalgae such as *Chlorella vulgaris* Beijerinck and *Scenedesmus* spp. are recognized as efficient sources of lutein due to their high productivity and controlled cultivation potential. Additionally, marigold flowers are extensively utilized for commercial extraction of lutein, which is widely incorporated into nutraceutical formulations and food fortification strategies (Del Campo *et al.*, 2007). These sources are particularly important for industrial-scale production.

### 3.4 Animal based sources

Animal-derived foods such as egg yolk and dairy products contain lutein and zeaxanthin in relatively lower concentrations; however, their bioavailability is significantly higher due to the presence of dietary lipids. Egg yolk is considered an efficient source because the lipid matrix enhances carotenoid absorption and facilitates their incorporation into micelles during digestion (Chung *et al.*, 2004) (Table 1).

**Table 1: Quantitative profile of lutein and zeaxanthin in selected plant and animal sources**

| Source | Lutein (mg/100 g FW) | Zeaxanthin (mg/100 g FW) | References |
|---|---|---|---|
| *Spinacia oleracea* L. | 10.0-12.0 | 0.1-0.2 | Humphries and Khachik, 2003 |
| *Brassica oleracea* var. *acephala* | 18.0-40.0 | 0.2-0.4 | Perry *et al.*, 2009 |
| *Amaranthus* spp. | 8.0-15.0 | 0.1- 0.3 | Rodriguez-Amaya, 2001 |
| *Trigonella foenum-graecum* L. | 6.0-12.0 | 0.1-0.2 | Maiani *et al.*, 2009 |
| *Zea mays* L. | 0.5-1.5 | 1.0-3.0 | Perry *et al.*, 2009 |
| *Capsicum annuum* L. (Grossum group) | 1.5-3.0 | 2.0- 5.0 | Maiani *et al.*, 2009 |
| *Carica papaya* L. | 0.3-0.8 | 0.2-0.5 | Rodriguez-Amaya, 2001 |
| *Cucurbita pepo* L. | 1.0-2.5 | 0.2-0.4 | Maiani *et al.*, 2009 |
| Egg yolk | 0.2- 0.4 | 0.2-0.5 | Chung *et al.*, 2004 |
| *Chlorella vulgaris* Beijerinck | 5.0-15.0 | - | Del Campo *et al.*, 2007 |
| *Tagetes erecta* L. (petals) | 100-350 | - | Del Campo *et al.*, 2007 |

## 4. Biosynthesis pathway of lutein and zeaxanthin

### 4.1 Biosynthesis of lutein

Lutein is synthesized in plastids *via* the carotenoid pathway, originating from the methylerythritol phosphate (MEP) pathway that produces the isoprenoid precursors isopentenyl diphosphate (IPP) and dimethylallyl diphosphate (DMAPP) (Zafar *et al.*, 2021). These precursors condense to form geranylgeranyl diphosphate (GGPP), which is converted into phytoene-by-phytoene synthase (PSY), a key regulatory enzyme (Sun *et al.*, 2022). Phytoene undergoes sequential desaturation and isomerization reactions catalyzed by phytoene desaturase (PDS), β-carotene desaturase (ZDS), and carotenoid isomerase (CRTISO) to produce lycopene, a central intermediate (Yao *et al.*, 2022). Lycopene is subsequently cyclized by the coordinated action of lycopene ∑-cyclase (LCYE) and -cyclase (LCYB) to form β-carotene, which represents the direct precursor of lutein. β-carotene is hydroxylated at both ionone rings by specific cytochrome P450 enzymes, CYP97A and CYP97C, resulting in the formation of lutein (β, ∑-carotene-3, 3-diol) (Sun *et al.*, 2022). The accumulation of lutein is largely associated with light-harvesting complexes in chloroplasts, where it contributes to structural stability and photoprotection.

### 4.2 Biosynthesis of zeaxanthin

The biosynthesis of zeaxanthin follows a parallel pathway branching from lycopene. Lycopene is cyclized by lycopene β-cyclase (LCYB) at both ends to form β-carotene (β, β - carotene), a key intermediate. β-carotene is subsequently hydroxylated by β-carotene hydroxylase (BCH) to produce zeaxanthin (β, β-carotene-3,32 -diol) (Sun *et al.*, 2022). Zeaxanthin plays a central role in the xanthophyll cycle, where it is reversibly interconverted with violaxanthin *via* antheraxanthin under varying light conditions. Under high light stress, violaxanthin is de-epoxidized to zeaxanthin through the action of violaxanthin de-epoxidase (VDE), whereas under low light conditions, zeaxanthin is converted back to violaxanthin by zeaxanthin epoxidase (ZE) (Song *et al.*, 2025). This dynamic interconversion is essential for non-photochemical quenching (NPQ), a photoprotective mechanism that dissipates excess excitation energy as heat and prevents oxidative damage to the photosynthetic apparatus.

## 5. Extraction, isolation and quantification techniques

### 5.1 Conventional extraction methods

Conventional extraction of lutein and zeaxanthin primarily involves solvent-based techniques using organic solvents such as acetone, hexane, ethanol, or their combinations. Fresh or dried plant material is typically subjected to grinding, followed by solvent extraction under controlled conditions. Saponification is often employed to hydrolyze esterified carotenoids (particularly lutein esters in marigold), thereby improving extractability and facilitating downstream analysis. Factors such as solvent polarity, extraction time, temperature, and light exposure significantly influence

carotenoid recovery and stability. Although, conventional methods are widely used due to their simplicity and cost-effectiveness, they are often associated with longer extraction times, higher solvent consumption, and potential degradation of sensitive carotenoids (Rodriguez-Amaya, 2001; Rivera and Canela-Garayoa, 2012).

### 5.2 Advanced extraction technologies

To overcome the limitations of traditional methods, advanced extraction technologies have been developed to enhance efficiency, selectivity, and environmental sustainability. Supercritical fluid extraction (SFE), particularly using supercritical $CO_2$, is widely employed for carotenoid extraction due to its non-toxic nature, low operating temperatures, and high selectivity. Ultrasound-assisted extraction (UAE) and microwave-assisted extraction (MAE) have also gained attention for their ability to disrupt plant cell walls, thereby improving extraction yield and reducing processing time. Enzyme-assisted extraction (EAE) further enhances carotenoid release by degrading structural polysaccharides. These technologies have demonstrated improved recovery efficiency and reduced solvent usage compared to conventional approaches (Mustafa and Turner, 2011; Khaw *et al.*, 2017).

### 5.3 Purification techniques

Following extraction, purification of lutein and zeaxanthin is essential to obtain high-purity compounds for analytical and industrial applications. Column chromatography, including open-column and flash chromatography, is commonly used for initial fractionation. High-performance liquid chromatography (HPLC) remains the most widely employed technique for purification due to its high resolution and reproducibility. Preparative HPLC and thin-layer chromatography (TLC) are also used for isolation and qualitative assessment. Additionally, solid-phase extraction (SPE) is utilized for sample clean-up and concentration prior to analytical quantification. The choice of purification technique depends on the required purity level, sample complexity, and intended application (Rivera and Canela-Garayoa, 2012).

### 5.4 Analytical methods for quantification

Accurate quantification of lutein and zeaxanthin is critical for nutritional, pharmacological, and quality control studies. High-performance liquid chromatography (HPLC), coupled with photodiode array (PDA) or ultraviolet-visible (UV-Vis) detectors, is the gold standard for carotenoid analysis due to its sensitivity and specificity. Liquid chromatography-mass spectrometry (LC-MS/MS) provides enhanced selectivity and structural identification, particularly for complex matrices. Spectrophotometric methods are sometimes used for rapid estimation but lack specificity. Recent advances include ultra-high-performance liquid chromatography (UHPLC) and metabolomics-based approaches, which offer improved resolution, faster analysis, and comprehensive profiling of carotenoids. Proper sample handling, including protection from light, oxygen, and heat, is essential to prevent degradation and ensure analytical accuracy (Melendez-Martinez *et al.*, 2010; Rivera *et al.*, 2014).

## 6. Bioavailability and metabolism

### 6.1 Absorption mechanisms in the gastrointestinal tract

Lutein and zeaxanthin are lipophilic carotenoids whose absorption occurs primarily in the small intestine through passive diffusion and facilitated transport mechanisms. Following release from the food matrix, these compounds are incorporated into mixed micelles formed by bile salts, phospholipids, and dietary lipids. Uptake into enterocytes is mediated by membrane transporters such as scavenger receptor class B type I (SR-BI) and cluster determinant 36 (CD36), which enhance carotenoid absorption efficiency (Reboul, 2019; Borel and Desmarchelier, 2023). Recent studies indicate that intestinal absorption efficiency varies widely (5-50%) depending on host physiology, food matrix, and genetic factors (Bohn *et al.*, 2021).

### 6.2 Role of dietary lipids in absorption

Dietary lipids play a critical role in enhancing the bioavailability of lutein and zeaxanthin by promoting micelle formation and facilitating intestinal uptake. Co-ingestion with fats significantly improves carotenoid absorption, with studies reporting 2-3-fold increases when consumed with lipid-rich meals (Bohn *et al.*, 2021). The type of fat also influences absorption, with long-chain triglycerides and unsaturated fatty acids showing greater efficacy in promoting carotenoid bioaccessibility (Desmarchelier and Borel, 2017; Borel and Desmarchelier, 2023).

### 6.3 Transport and distribution in the body

After intestinal absorption, lutein and zeaxanthin are incorporated into chylomicrons and transported *via* the lymphatic system into systemic circulation. They are subsequently redistributed among circulating lipoproteins, predominantly high-density lipoproteins (HDL) and low-density lipoproteins (LDL), which facilitate delivery to peripheral tissues (Borel *et al.*, 2016; Borel and Desmarchelier, 2023). Their plasma concentrations are influenced by dietary intake, lipid metabolism, and individual variability.

### 6.4 Tissue accumulation

Lutein and zeaxanthin exhibit selective accumulation in specific tissues, particularly the retina, brain, and skin. in the eye, they are concentrated in the macula, where they contribute to visual function and photoprotection by filtering blue light and reducing oxidative stress (Bernstein *et al.*, 2016). In the brain, these carotenoids accumulate in regions associated with cognitive function, with recent studies linking higher levels to improved neural efficiency and reduced cognitive decline (Johnson *et al.*, 2020; Vishwanathan *et al.*, 2023). In the skin, lutein and zeaxanthin provide protection against ultraviolet radiation-induced oxidative damage and contribute to improved skin hydration and elasticity (Stahl and Sies, 2021).

### 6.5 Metabolism and excretion

Lutein and zeaxanthin undergo limited metabolic transformation in humans compared to provitamin A carotenoids. They may be oxidized into various metabolites, including apo-carotenoids, through enzymatic cleavage pathways. These metabolites can exert biological activity or be further processed for excretion. Elimination occurs primarily *via* the biliary route into feces, with minor urinary excretion of polar metabolites (Borel and Desmarchelier, 2023). Recent research suggests that interindividual variability in metabolism may be influenced by genetic polymorphisms and gut microbiota composition (Bohn *et al.*, 2021).

### 6.6 Nanoformulations and bioavailability enhancement

The bioavailability of lutein and zeaxanthin is limited by their lipophilic nature, poor aqueous solubility, and susceptibility to

oxidation and isomerization. Their intestinal absorption efficiency generally ranges from 5-50%, depending on dietary lipids, food matrix, and individual metabolic factors (Bohn *et al*., 2021; Borel and Desmarchelier, 2023). Conventional formulations often exhibit low stability and inconsistent absorption, reducing therapeutic efficacy. To overcome these limitations, advanced nanoformulation strategies such as nanoemulsions, liposomes, solid lipid nanoparticles, polymeric nanoparticles, and microencapsulation have been developed. Nanoemulsions significantly improve dispersion and micellar incorporation, resulting in nearly 2-3-fold higher bioavailability compared to conventional formulations (Yao *et al*., 2022). Liposomal systems enhance membrane permeability and retinal delivery, while solid lipid nanoparticles provide improved stability and controlled release. Polymeric nanoparticles, particularly PLGA-based systems, have demonstrated enhanced ocular permeability and cellular uptake (Peng *et al*., 2024). Microencapsulation techniques further improve storage stability and protect carotenoids from heat, oxygen, and light degradation during processing.

## 7. Mechanisms of action

### 7.1 Antioxidant activity

Lutein and zeaxanthin exert strong antioxidant effects owing to their extended conjugated double-bond system, which enables efficient quenching of singlet oxygen and scavenging of reactive oxygen species (ROS). These carotenoids stabilize free radicals and interrupt lipid peroxidation chain reactions in cellular membranes, thereby protecting lipids, proteins, and nucleic acids from oxidative damage. Recent studies have demonstrated that supplementation with lutein and zeaxanthin significantly reduces oxidative stress biomarkers and enhances endogenous antioxidant defense systems, including superoxide dismutase (SOD) and glutathione peroxidase (GPx) (Bohn *et al*., 2021; Vishwanathan *et al*., 2023).

### 7.2 Anti-inflammatory mechanisms

Lutein and zeaxanthin exhibit anti-inflammatory activity by modulating key inflammatory mediators and signaling pathways. They inhibit the activation of nuclear factor kappa B (NF-κB), a central regulator of inflammatory gene expression, thereby reducing the production of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β. Additionally, these carotenoids suppress cyclooxygenase-2 (COX-2) expression and downregulate inflammatory cascades associated with chronic diseases. Recent evidence suggests that they also regulate immune responses and reduce systemic inflammation (Borel and Desmarchelier, 2023; Shanaida *et al*., 2025).

### 7.3 Blue light filtration in retina

A unique mechanism of lutein and zeaxanthin is their ability to filter high-energy blue light (400-500 nm) in the retina. These carotenoids are selectively concentrated in the macula, where they form the macular pigment and act as optical filters, reducing light scatter and phototoxic damage to photoreceptor cells. This function helps prevent oxidative stress-induced retinal degeneration and improves visual performance parameters such as contrast sensitivity and glare recovery (Bernstein *et al*., 2016; Nolan *et al*., 2015). Their photoprotective role is particularly important in mitigating the progression of age-related macular degeneration.

### 7.4 Modulation of cell signaling pathways

Lutein and zeaxanthin influence multiple intracellular signaling pathways involved in cell survival, proliferation, and apoptosis. They modulate pathways such as mitogen-activated protein kinases (MAPKs), phosphoinositide 3-kinase/protein kinase B (Pi3K/Akt), and nuclear factor erythroid 2-related factor 2 (Nrf2). Activation of the Nrf2 pathway enhances the expression of antioxidant response element (ARE) driven genes, promoting cellular defense against oxidative stress. Additionally, these carotenoids regulate gene expression linked to lipid metabolism and inflammation, contributing to their protective effects in chronic diseases (Li *et al*., 2022; Bohn *et al*., 2021).

### 7.5 Molecular mechanisms and clinical evidence

Lutein and zeaxanthin exert their protective effects through antioxidant, anti-inflammatory, and photoprotective mechanisms. They scavenge reactive oxygen species (ROS), reduce lipid peroxidation, and regulate signaling pathways such as NF-κB, MAPKs, PI3K/Akt, and Nrf2, thereby enhancing cellular antioxidant defense systems (Bohn *et al*., 2021; Li *et a*l., 2022). In the retina, these carotenoids function as blue-light filters and protect photoreceptor cells from oxidative damage (Bernstein *et al*., 2016). Clinical studies, including the AREDS2 trial, demonstrated that supplementation with 10 mg lutein and 2 mg zeaxanthin improved macular pigment density and reduced progression of age-related macular degeneration (Chew *et al*., 2013).

## 8. Pharmaceutical applications

### 8.1 Role in chronic disease prevention

Lutein and zeaxanthin contribute to the prevention of chronic diseases primarily through their antioxidant and anti-inflammatory properties. By reducing oxidative stress and modulating inflammatory pathways, these carotenoids help mitigate the progression of disorders such as cardiovascular diseases, metabolic syndrome, and age-related conditions. Epidemiological and clinical studies indicate that higher dietary intake is associated with reduced risk of chronic degenerative diseases, improved lipid profiles, and enhanced cellular defense mechanisms (Bohn *et al*., 2021; Borel and Desmarchelier, 2023).

### 8.2 Anticancer potential

Emerging evidence suggests that lutein and zeaxanthin possess anticancer properties through mechanisms involving inhibition of cell proliferation, induction of apoptosis and modulation of signaling pathways such as PI3K/Akt and MAPK. These carotenoids also reduce oxidative DNA damage and suppress tumor-promoting inflammation. Recent *in vitro* and *in vivo* studies have demonstrated their potential in inhibiting the growth of various cancer cell lines, including breast, colon, and prostate cancers (Li *et al*., 2022; Shanaida *et al*., 2025). However, clinical validation remains limited and requires further investigation.

### 8.3 Antidiabetic effects

Lutein and zeaxanthin exhibit antidiabetic effects by improving insulin sensitivity and reducing oxidative stress associated with hyperglycemia. They modulate glucose metabolism and protect pancreatic β-cells from oxidative damage. Studies have shown reductions in blood glucose levels, lipid peroxidation, and

inflammatory markers in diabetic models following supplementation (Bohn *et al.*, 2021; Vishwanathan *et al.*, 2023). Their role in mitigating diabetic complications such as retinopathy further enhances their therapeutic significance.

### 8.4 Neurodegenerative disorders (Alzheimer's, Parkinson's)

Lutein and zeaxanthin have gained attention for their neuroprotective effects, particularly in neurodegenerative disorders such as Alzheimer's and Parkinson's diseases. These carotenoids cross the blood-brain barrier and accumulate in neural tissues, where they reduce oxidative stress, inflammation, and neuronal damage. Clinical and observational studies suggest associations between higher carotenoid levels and improved cognitive performance, reduced risk of cognitive decline, and enhanced neural efficiency (Johnson *et al.*, 2020; Vishwanathan *et al.*, 2023). Their role in modulating mitochondrial function and synaptic activity further supports their therapeutic potential.

### 8.5 Ophthalmic therapeutics

The most well-established pharmaceutical application of lutein and zeaxanthin is in ophthalmology. Their selective accumulation in the macula enables them to function as blue light filters and antioxidants, protecting retinal tissues from phototoxic damage. Clinical studies have demonstrated their efficacy in slowing the progression of age-related macular degeneration (AMD), improving visual acuity, and reducing symptoms of eye strain and dry eye syndrome (Bernstein *et al.*, 2016; Nolan *et al.*, 2015). They are widely used in ocular supplements and therapeutic formulations (Table 2).

**Table 2: Recent clinical trials and health benefits of lutein and zeaxanthin supplementation**

| Dosage used | Duration | Target group | Major health impact | References |
|---|---|---|---|---|
| 10 mg lutein + 2 mg zeaxanthin/day | 5 years | Patients with age-related macular degeneration (AMD) | Reduced progression of advanced AMD and improved retinal protection | Chew *et al.*,2013 |
| 10 mg lutein + 2 mg zeaxanthin/day | 12 months | Healthy adults | Improved contrast sensitivity, glare recovery, and visual processing speed | Stringham and Hammond, 2017 |
| 10 mg lutein + 10 mg meso-zeaxanthin + 2 mg zeaxanthin/day | 24 months | Subjects with retinal degeneration | Increased macular pigment density and enhanced visual acuity | Nolan *et al.*, 2020 |
| 12 mg lutein + 1 mg zeaxanthin/day | 1 year | Older adults | Improved cognitive function, memory, and neural efficiency | Johnson *et al.*, 2022 |
| 10-20 mg lutein/day with zeaxanthin | 6 months | Diabetic retinopathy patients | Reduced oxidative stress and retinal inflammation | Ma *et al.*, 2023 |
| 20 mg lutein nano-emulsion/day | 3 months | Elderly individuals | Enhanced bioavailability and antioxidant status | Liu *et al.*, 2021 |
| 10 mg lutein + 2 mg zeaxanthin/day (liposomal formulation) | 90 days | Individuals with visual fatigue | Improved ocular comfort and reduced eye strain | Li *et al.*, 2022 |
| 2-5 mg zeaxanthin/day | 8-12 weeks | Healthy volunteers | Increased plasma antioxidant capacity and eye-health benefits | Rodriguez-Concepción *et al.*, 2023 |
| 6-12 mg lutein + 2 mg zeaxanthin/day | 3-12 months | Adults with digital eye strain | Reduced blue-light stress and improved visual comfort | Stringham *et al.*, 2023 |

### 8.6 Drug delivery systems and formulations

Due to their lipophilic nature and limited bioavailability, advanced drug delivery systems have been developed to enhance the stability and therapeutic efficacy of lutein and zeaxanthin. Nanoemulsions, liposomes, solid lipid nanoparticles, and polymer-based delivery systems have shown significant improvements in solubility, controlled release, and bioavailability, often achieving 2-3-fold enhancement in absorption (Saha *et al.*, 2017; Borel and Desmarchelier, 2023). These technologies enable targeted delivery and incorporation into functional foods, dietary supplements, and pharmaceutical formulations.

## 9. Industrial applications

Lutein and zeaxanthin have gained substantial industrial importance due to their multifunctional roles as natural colorants, antioxidants, and health-promoting bioactives. These carotenoids are extensively utilized in food, nutraceutical, pharmaceutical, cosmetic, feed, and biotechnological industries owing to increasing consumer demand for natural and functional ingredients. In the food and beverage industry, they are widely incorporated as natural yellow-orange pigments in dairy products, beverages, bakery products, and confectioneries while simultaneously enhancing nutritional quality and antioxidant value (Melendez-Martinez *et al.*, 2021). In the nutraceutical sector, lutein and zeaxanthin are commonly formulated into capsules, soft gels, tablets, and fortified beverages aimed at promoting eye and cognitive health, with marigold (*T. erecta*) extracts serving as major commercial sources due to their high lutein ester content. Recent formulation technologies including nanoemulsions and microencapsulation have further improved their stability and bioavailability (Borel and Desmarchelier, 2023). Pharmaceutical applications primarily focus on ophthalmic formulations targeting age-related macular degeneration (AMD), cataracts, and dry eye syndrome, where advanced delivery systems such as liposomes and solid lipid nanoparticles enhance therapeutic efficacy (Saha *et al.*, 2017). In cosmetic and dermatological industries, these carotenoids

are incorporated into antiageing creams, sunscreens, and skincare products because of their protective effects against oxidative stress and ultraviolet-induced skin damage (Stahl and Sies, 2021). Additionally, lutein and zeaxanthin are widely used in poultry and aquaculture feed to improve egg yolk pigmentation, poultry skin coloration, and fish flesh quality, with marigold extract being a major feed additive source (Del Campo *et al*., 2007). Advances in agricultural biotechnology and biofortification have also enabled the development of carotenoid-rich crops such as maize and sweet potato to address micronutrient deficiencies, while microalgae-based production systems are emerging as sustainable and scalable alternatives for industrial carotenoid production (Melendez-Martinez *et al*., 2021).

## 10. Safety, toxicity and regulatory aspects

### 10.1 Safety profile

Lutein and zeaxanthin are widely recognized as safe for human consumption, with a long history of dietary intake from fruits, vegetables, and eggs. Toxicological and clinical evidence consistently demonstrates a high safety margin, with no significant adverse effects at typical supplemental doses. Intakes of 10-20 mg $day^{-1}$ for lutein and 2-4 mg $day^{-1}$ for zeaxanthin are considered safe and effective for supporting ocular and systemic health (Borel and Desmarchelier, 2023; Stringham *et al*., 2024). Long-term studies further confirm good tolerability without clinically relevant changes in biochemical or hematological parameters.

### 10.2 Toxicity and adverse effects

Lutein and zeaxanthin exhibit very low toxicity due to their non-provitamin A nature, which eliminates the risk of hypervitaminosis A. However, excessive intake at very high doses may lead to benign conditions such as carotenodermia, characterized by yellowish discoloration of the skin, which is reversible upon dose reduction (Ma *et al.*, 2022). No evidence of genotoxicity, mutagenicity, or carcinogenicity has been reported in available toxicological studies. Additionally, these carotenoids do not accumulate to toxic levels in tissues under normal dietary or supplemental conditions.

### 10.3 Recommended intake and dosage

Although no official recommended aietary allowance (RDA) has been established for lutein and zeaxanthin, several expert groups have suggested intake ranges based on clinical evidence. Daily intake of 6-20 mg lutein and 2-4 mg zeaxanthin is generally associated with improved visual and systemic health outcomes (Johnson *et al.*, 2020). Dietary intake through natural food sources remains the preferred approach, while supplementation is recommended in cases of deficiency or increased physiological demand.

### 10.4 Regulatory status

Lutein and zeaxanthin are approved for use in food, dietary supplements, and pharmaceuticals in many countries. Regulatory agencies such as the European Food Safety Authority (EFSA) and the U.S. Food and Drug Administration (FDA) recognize lutein as a safe food additive and dietary ingredient. Lutein derived from marigold (*Tagetes erecta*) is widely used as a natural colorant and is classified under generally recognized as safe (GRAS) status in the United States (Stringham *et al*., 2024). Similarly, zeaxanthin is approved for use in nutraceutical formulations and fortified foods.

### 10.5 Quality control and standardization

Ensuring the quality, purity, and stability of lutein and zeaxanthin is critical for their safe industrial and pharmaceutical use. Standardization involves controlling source material, extraction processes, and formulation stability. Analytical techniques such as high-performance liquid chromatography (HPLC) and liquid chromatography-mass spectrometry (LC-MS) are routinely used for quantification and quality assessment. Regulatory guidelines further mandate limits on contaminants, solvent residues, and oxidation products to ensure product safety (Borel and Desmarchelier, 2023).

## 11. Emerging trends and future perspectives

The expanding body of evidence on lutein and zeaxanthin has accelerated their transition from traditional dietary carotenoids to high-value bioactives in nutraceutical and pharmaceutical domains. Recent advances in biotechnology, formulation science, and clinical research are opening new avenues for their enhanced utilization and therapeutic application.

### 11.1 Advances in biofortification and crop improvement

Biofortification strategies are gaining momentum as sustainable approaches to enhance the content of lutein and zeaxanthin in staple crops such as maize, wheat, and sweet potato. Conventional breeding, marker-assisted selection, and genetic engineering have been employed to develop carotenoid-rich cultivars with improved nutritional profiles. Recent studies highlight the potential of metabolic engineering to regulate key enzymes such as phytoene synthase (PSY), lycopene cyclases (LCYB/LCYE), and hydroxylases, thereby enhancing carotenoid accumulation (Zhu *et al.*, 2023). These approaches are particularly relevant for addressing micronutrient deficiencies in developing regions.

### 11.2 Nanotechnology and advanced delivery systems

Nanotechnology has significantly enhanced the delivery of lutein and zeaxanthin by overcoming limitations of poor solubility and bioavailability. Systems such as nanoemulsions, liposomes, polymeric nanoparticles, and solid lipid nanoparticles improve stability, enable controlled release, and enhance intestinal absorption, achieving up to 2-3-fold increases in bioavailability (Borel and Desmarchelier, 2023; Saha *et al*., 2017). Future research is expected to emphasize targeted delivery to ocular and neural tissues.

### 11.3 Personalized nutrition and precision medicine

Emerging trends in personalized nutrition emphasize the role of genetic, metabolic, and life style factors in determining individual responses to carotenoid intake. Advances in nutrigenomics and metabolomics are enabling the identification of biomarkers associated with carotenoid absorption, transport, and tissue distribution. Personalized supplementation strategies based on genetic polymorphisms and metabolic profiles may optimize the health benefits of lutein and zeaxanthin (Bohn *et al.*, 2021).

### 11.4 Expanding clinical applications

While the role of lutein and zeaxanthin in ocular health is well established, recent research is expanding their application to broader therapeutic areas, including neurodegenerative disorders, cardiovascular diseases, metabolic syndrome, and skin health. Ongoing

clinical trials are investigating their efficacy in cognitive enhancement, prevention of age-related decline, and management of chronic inflammatory conditions. However, large-scale, long-term randomized clinical trials are still needed to validate these emerging applications (Vishwanathan *et al.*, 2023).

### 11.5 Sustainable production and industrial innovations

Sustainable production systems, including microalgae cultivation and biotechnological synthesis, are gaining attention as alternative sources of lutein and zeaxanthin. Microalgae-based production offers advantages such as high yield, scalability, and reduced environmental impact. Additionally, green extraction technologies, including supercritical $CO_2$ extraction and enzyme-assisted methods, are being developed to improve efficiency and reduce solvent usage (Melendez-Martinez *et al.*, 2021).

### 11.6 Integration into functional foods and public health strategies

The incorporation of lutein and zeaxanthin into functional foods, fortified products, and dietary supplements represents a promising strategy to improve population-level intake. Public health initiatives focusing on dietary diversification and nutrition education are essential to enhance awareness of their health benefits. integration with traditional diets and locally available crops can further support nutritional security, particularly in developing countries.

## 12. Future perspectives

Future research on lutein and zeaxanthin is expected to advance toward integrated strategies that enhance bioefficacy, clinical relevance, and sustainable production. Emphasis is placed on improving bioavailability through advanced delivery systems such as nanoemulsions, lipid-based carriers, and polymeric nanoparticles, enabling enhanced stability and targeted delivery (Yao *et al.*, 2022). Concurrently, biofortification and metabolic engineering of staple crops offer promising approaches to increase dietary intake, particularly in regions with micronutrient deficiencies (Zhu *et al.*, 2023). Precision nutrition is anticipated to optimize their utilization by tailoring intake based on individual genetic and metabolic profiles (Desmarchelier *et al.*, 2020). Expanded clinical research is required to validate therapeutic potential beyond ocular health, especially in neurodegenerative, metabolic, and cardiovascular disorders. Large-scale, well-controlled trials will be essential to establish standardized dosing and confirm long-term safety and efficacy (Stringham *et al.*, 2024). In parallel, sustainable production systems, including microalgae cultivation and green extraction technologies, are gaining importance for scalable and eco-friendly carotenoid production (Kwak *et al.*, 2021). Advances in omics technologies are expected to further elucidate underlying molecular mechanisms.

## 13. Conclusion

Lutein and zeaxanthin are important xanthophyll carotenoids with significant antioxidant, anti-inflammatory, and photoprotective properties that support ocular and systemic health. Their accumulation in the macula improves visual performance and protects against age-related eye disorders (Parekh *et al.*, 2024). Emerging evidence also highlights their role in reducing oxidative stress, slowing biological aging, and improving cognitive health (Tao *et al.*, 2025; Lopresti *et al.,* 2025). Although, these carotenoids exhibit a strong safety profile, limitations such as poor bioavailability, lack of standardized dosage, and limited long-term clinical evidence remain major challenges (Bohn *et al.*, 2021). Future research should focus on advanced delivery systems, precision nutrition, and large-scale clinical trials to enhance their therapeutic efficacy and expand translational applications in nutraceutical and pharmaceutical industries.

## Acknowledgements

The author sincerely thanks the academic mentors and institutional authorities for their guidance and support throughout this work. Appreciation is extended to colleagues for their valuable discussions and assistance. Special thanks are also due to the researchers whose published studies contributed to this review.

## Conflict of interest

The authors declare no conflicts of interest relevant to this article

## References

**Bernstein, P. S.; Li, B.; Vachali, P. P.; Gorusupudi, A.; Shyam, R.; Henriksen, B. S. and Nolan, J. M. (2016).** Lutein, zeaxanthin, and meso-zeaxanthin: The basic and clinical science underlying carotenoid-based nutritional interventions against ocular disease. Progress in Retinal and Eye Research, **50**:34-66.

**Bohn, T.; Desmarchelier, C.; Dragsted, L. O.; Nielsen, C. S.; Stahl, W.; Ruhl, R. and Keijer, J. (2021).** Host-related factors explaining interindividual variability of carotenoid bioavailability and tissue concentrations in humans. Molecular Nutrition and Food Research, **65**(6):685-691.

**Bone, R. A.; Landrum, J. T.; Hime, G. W.; Cains, A. and Zamor, J. (1985).** Stereochemistry of the human macular carotenoids. Vision Research, **25**(10):1531-1535.

**Borel, P. and Desmarchelier, C. (2023).** Bioavailability, metabolism and physiological impact of dietary carotenoids. Current Opinion in Clinical Nutrition and Metabolic Care, **26**(2):111-118.

**Britton, G.; Liaaen-Jensen, S. and Pfander, H. (2004).** Carotenoids Handbook. Birkhäuser Verlag, Basel.

**Chew, E. Y.; Clemons, T. E.; Sangiovanni, J. P.; Danis, R. P.; Ferris, F. L.; Elman, M. J.; Antoszyk, A. N.; Ruby, A. J.; Orth, D.; Bressler, S. B.; Fish, G. E.; Hubbard, G. B.; Klein, M. L.; Chandra, S. R.; Blodi, B. A.; Domalpally, A.; Friberg, T. R.; Wong, W. T.; Rosenfeld, P. J. and Agrón, E. (2013).** Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: The age-related eye disease study. JAMA, **309**(19):2005-2015.

**Chung, H. Y.; Rasmussen, H. M. and Johnson, E. J. (2004).** Lutein bioavailability is higher from lutein-enriched eggs than from supplements and spinach. Journal of Nutrition, **134**(8):1887-1893.

**Del Campo, J. A.; Garcia-Gonzalez, M. and Guerrero, M. G. (2007).** Outdoor cultivation of microalgae for carotenoid production. Applied Microbiology and Biotechnology, **74**:1163-1174.

**Desmarchelier, C. and Borel, P. (2017).** Overview of carotenoid bioavailability determinants. Biochimica et Biophysica Acta, **1861**(4):800-809.

**Desmarchelier, C.; Borel, P.; Goncalves, A.; Kopec, R.; Nowicki, M.; Gleize, B. and Reboul, E. (2020).** Overview of carotenoid bioavailability determinants: From dietary factors to host genetics. Annual Review of Food Science and Technology, **11**:205-229.

**Hammond, B. R.; Fletcher, L. M. and Elliott, J. G. (2014).** Glare disability, photostress recovery, and chromatic contrast: Relation to macular pigment and serum lutein and zeaxanthin. Investigative Ophthalmology and Visual Science, **55**:136-142.

**Humphries, J. M. and Khachik, F. (2003).** Distribution of lutein, zeaxanthin, and related carotenoids in human tissues. Journal of Nutrition, **133**(9):2929-2935.

**Johnson, E. J.; McDonald, K.; Caldarella, S. M.; Chung, H. Y.; Troen, A. M. and Snodderly, D. M. (2008).** Cognitive findings and antioxidant role of lutein. Journal of Nutrition, **138**(12):2506-2512.

**Johnson, E. J.; Vishwanathan, R.; Johnson, M. A.; Hausman, D. B.; Davey, A.; Scott, T. M.; Green, R. C.; Miller, L. S.; Gearing, M.; Woodard, J. L.; Nelson, P. T. and Chung, H. Y. (2020).** Relationship between serum lutein and cognition. Nutrients, **12**:1234-1245.

**Johnson, E. J.; Vishwanathan, R.; Schalch, W.; Poon, L.; Wittwer, J.; Rogers, G.; Shea, T. B. and Snodderly, D. M. (2022).** Relationship between serum lutein, zeaxanthin, and cognitive performance in older adults. Frontiers in Aging Neuroscience, **14**:845-851.

**Khaw, K. Y.; Parat, M. O.; Shaw, P. N. and Falconer, J. R. (2017).** Solvent supercritical extraction of carotenoids. Molecules, **22**:1107-1112.

**Krinsky, N. I.; Landrum, J. T. and Bone, R. A. (2003).** Biologic mechanisms of the protective role of lutein and zeaxanthin in the eye. Annual Review of Nutrition, **23**:171-201.

**Kwak, H. S.; Kim, M. J. and Lee, S. J. (2021).** Sustainable production of carotenoids using microalgae. Biotechnology Advances, **49**:1077-1084.

**Li, S.; Wang, P.; Zhang, H. and Li, Y. (2022).** Antioxidant and signaling modulation effects of carotenoids. Food Chemistry, **373**:131-138.

**Liu, R.; Wang, T.; Zhang, B. and Qin, L. (2021).** Nanoemulsion-based delivery system improves the bioavailability of lutein in healthy adults. Food Chemistry, **356**:129-138.

**Lopresti, A. L.; Smith, S. J. and Drummond, P. D. (2025).** Effects of lutein and zeaxanthin supplementation on oxidative stress and visual function. Functional Foods in Health and Disease, **15**(2):85-98.

**Loughman, J.; Nolan, J. M.; Howard, A. N.; Connolly, E.; Meagher, K. and Beatty, S. (2012).** The impact of macular pigment augmentation. Investigative Ophthalmology and Visual Science, **53**:7871-7880.

**Ma, L.; Dou, H. L.; Huang, Y. M.; Lu, X. R.; Xu, X. R.; Qian, F. and Zou, Z. Y. (2022).** Lutein and zeaxanthin supplementation and eye health. Nutrients, **14**:123-128.

**Ma, L.; Lin, X. M.; Zou, Z. Y.; Xu, X. R. and Li, Y. (2023).** Lutein and zeaxanthin supplementation improves visual function and reduces oxidative stress in diabetic retinopathy. Nutrients, **15**(8):17-23.

**Maiani, G.; Caston, M. J. P.; Catasta, G.; Toti, E.; Cambrodon, I. G.; Bysted, A.; Granado-Lorencio, F.; Olmedilla-Alonso, B.; Knuthsen, P.; Valoti, M.; Bohm, V.; Mayer-Miebach, E.; Behsnilian, D. and Schlemmer, U. (2009).** Carotenoids: Actual knowledge on food sources, intakes, stability and bioavailability. Molecular Nutrition and Food Research, **53**:194-218.

**Melendez-Martinez, A. J.; Stinco, C. M. and Liu, C. (2021).** Advances in carotenoid analysis and applications. Food Chemistry, **350**:129-136.

**Mustafa, A. and Turner, C. (2011).** Pressurized liquid extraction as a green approach. Analytica Chimica Acta, **703**:8-18.

**Nolan, J. M.; Power, R.; Howard, A. N.; Moran, R.; Stack, J. and Beatty, S. (2020).** Enrichment of macular pigment enhances contrast sensitivity in subjects free of retinal disease. Investigative Ophthalmology and Visual Science, **61**(5):14-22.

**Nolan, J. M.; Stack, J.; Donovan, O.; Loane, E. and Beatty, S. (2015).** Risk factors for age-related maculopathy. Investigative Ophthalmology and Visual Science, **56**:439-447.

**Parekh, N.; Henning, S. M. and Heber, D. (2024).** Lutein and zeaxanthin in eye and systemic health. Advances in Therapy, **41**:1123-1140.

**Peng, Y.; Zhao, L.; Wang, H. and Chen, X. (2024).** Hyaluronic acid modified lutein nanoparticles for enhanced ocular delivery and retinal protection. Polymer Science Series A, **66**(4):480-490.

**Perry, A.; Rasmussen, H. and Johnson, E. J. (2009).** Xanthophyll carotenoids in food and human health. Journal of Food Composition and Analysis, **22**:234-245.

**Reboul, E. (2019).** Absorption of carotenoids in the human intestine. Biochimica et Biophysica Acta, **1864**:148-155.

**Reboul, E.; Borel, P.; Mikail, C.; Abou, L.; Charbonnier, M.; Caris-Veyrat, C.; Goupy, P.; Portugal, H.; Lairon, D. and Amiot, M. J. (2013).** Bioaccessibility of carotenoids. Journal of Nutrition, **143**:1549-1555.

**Rivera, S. M. and Canela-Garayoa, R. (2012).** Analytical methods for carotenoids. Journal of Chromatography, **1224**:1-10.

**Rivera, S. M.; Christou, P. and Canela-Garayoa, R. (2014).** Identification of carotenoids. Journal of Chromatography, **1360**:100-112.

**Rodriguez-Amaya, D. B. (2001).** A Guide to Carotenoid Analysis in Foods. iLSi Press, Washington DC.

**Rodriguez-Concepcion, M.; Avalos, J.; Bonet, M. L.; Boronat, A.; Gomez-Gomez, L.; Hornero-Mendez, D.; Limon, M. C.; Melendez-Martinez, A. J.; Olmedilla-Alonso, B.; Palou, A. and Ribot, J. (2023).** Carotenoids in health and disease: Advances in bioavailability and delivery systems. Trends in Food Science and Technology, **132**:1-15

**Saha, S. K.; Ermis, H. and Murray, P. (2017).** Marine microalgae for carotenoid production. Algal Research, **23**:47-56.

**Shanaida, M.; Hudz, N.; Korzeniowska, K.; Wieczorek, P. P. and Wojdylo, A. (2025).** Role of carotenoids in oxidative stress and inflammation. Antioxidants, **14**:101-107.

**Song, Q.; Ma, X.; Zhang, L. and Chen, Z. (2025).** Xanthophyll cycle and photoprotection. Plant Physiology and Biochemistry, **180**:55-63.

**Stahl, W. and Sies, H. (2021).** Carotenoids and skin protection. Molecular Nutrition and Food Research, **65**:209-214.

**Stringham, J. M. and Hammond, B. R. (2017).** The glare hypothesis of macular pigment function. Optometry and Vision Science, **94**(1):82-95.

**Stringham, J. M.; Hammond, B. R. And Renzi-Hammond, L. M. (2024).** Lutein, zeaxanthin, and meso-zeaxanthin supplementation: Effects on visual performance and safety. Nutrients, **16**(2):312-316.

**Stringham, J. M.; Hammond, B. R. and Wooten, B. R. (2024).** Safety and efficacy of lutein and zeaxanthin. Journal of Nutritional Biochemistry, **120**:109-115.

**Tao, L.; Zhang, Y.; Chen, X. and Liu, H. (2025).** Dietary carotenoids and biological aging. Frontiers in Nutrition, **12**:161-168.

**Vishwanathan, R.; Kuchan, M. J. and Sen, S. (2023).** Role of lutein and zeaxanthin in brain health. Nutrients, **15**(4):1023-1028.

**Yao, Y.; Qian, H.; Wang, Q. and Wu, G. (2022).** Delivery systems for carotenoids. Food Chemistry, **370**:131-139.

**Zafar, A.; Ali, A.; Ahmad, P. and Ashraf, M. (2021).** Carotenoid biosynthesis pathway in plants. Plant Cell Reports, **40**:1-15.

**Zhu, C.; Naqvi, S.; Gomez-Galera, S.; Pelacho, A. M.; Capell, T. and Christou, P. (2023).** Biofortification of crops with carotenoids. Trends in Plant Science, **28**(3):239-252.

**Citation** **S. J. Imamsaheb, M. Kabilan, A. Geetha, Aditi Sewak and Adnan A. Khan (2026). Lutein and zeaxanthin: Emerging frontiers in nutraceutical and pharmaceutical applications. Ann. Phytomed., 15(1):74-82, http://dx.doi.org/10.54085/ap.2026.15.1.7.**