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LUTEIN AND ZEAXANTHIN: CLINICAL INSIGHTS INTO THEIR ROLE IN EYE AND OVERALL HEALTH

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ABSTRACT: Lutein, a xanthophyll carotenoid found in most of the leafy greens and medicinal plants, promotes eye health by filtering blue light and reducing oxidative stress. It gathers in the macula, helping shield the eyes from conditions like age-related macular degeneration, cataracts, and diabetic retinopathy. This review compiles information from databases such as Google Scholar, PubMed, ScienceDirect, and ResearchGate. Studies indicate that lutein supplementation enhances contrast sensitivity, boosts macular pigment density, and supports retinal function, particularly in those with age-related macular degeneration. Beyond ocular benefits, lutein demonstrates neuroprotective, anti-inflammatory, and antioxidant properties, supporting cognitive function and skin health. Studies indicate that lutein is generally safe, even at higher doses, with no significant adverse effects reported. This review highlights lutein's broad health benefits and emphasizes the need for further research to determine optimal intake levels. Including lutein-rich foods or supplements in daily nutrition can support long-term health and wellness essential for body functioning.

INTRODUCTION: Optimal eye health is crucial for overall well-being, as clear vision is fundamental for daily functioning and a good quality of life. Progressive vision impairment can result from conditions such as cataracts, age-related macular degeneration (AMD), glaucoma, and diabetic retinopathy (DR) [1]. The WHO reports that approximately 2.2 billion people globally experience vision impairment, with cases being more common in low and middle-income countries due to limited healthcare access [2].

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Numerous studies indicate that consuming a carotenoid-rich diet may help lower the risk of age-related vision problems [3]. Carotenoids constitute a diverse class of naturally occurring phyto pigments that contribute to the yellow, orange, and red coloration in various fruits and vegetables. These bioactive compounds exhibit strong antioxidant properties, essential for safeguarding cells against oxidative stress and damage [4].

Humans cannot synthesize carotenoids on their own, so they must be acquired through dietary sources or supplements. Typically, about 30 to 50 different carotenoids are consumed through the diet, and approximately 20 to 40 of them are found in the human body [5]. Among the various carotenoids, lutein and zeaxanthin stand out for their important contribution to eye health and vision.

They accumulate in the macula of the retina, where they act as natural filters for blue light and help protect retinal cells against oxidative damage [6]. Lutein, a carotenoid pigment from the xanthophyll group, is naturally found in various plants, including flowers, grains, fruits, and leafy green vegetables like spinach, kale, and carrots [7].

Some medicinal plants, like the marigold flower (*Tagetes erecta* L.), possess a significantly higher lutein content [8]. Being one of the main carotenoids concentrated in the eye's macula, it plays a protective role against AMD and cataracts by filtering harmful blue light and reducing oxidative stress [9]. In addition to its role in eye health, lutein has also been linked to enhanced brain function and cognitive performance, reduced risk of cardiovascular diseases, and potential benefits for skin health due to its ability to manage oxidative stress and inflammatory processes [10]. Zeaxanthin is a carotenoid found in colourful fruits and dark green leafy vegetables, it is mainly concentrated in the retina and macula of the eye and acts as a natural filter by preventing the absorption of harmful rays which can damage ocular cells and tissues [11].

Studies have indicated that the consumption of zeaxanthin is directly associated with lower risk of age-related ocular disorders as it helps in increasing the macular density and also reduces the risk of light-induced damage [12]. In synergy with lutein, it helps in improving overall ocular health by protecting retinal cells from oxidative stress [13]. Graphical abstract has been illustrated in **Fig. 1.**

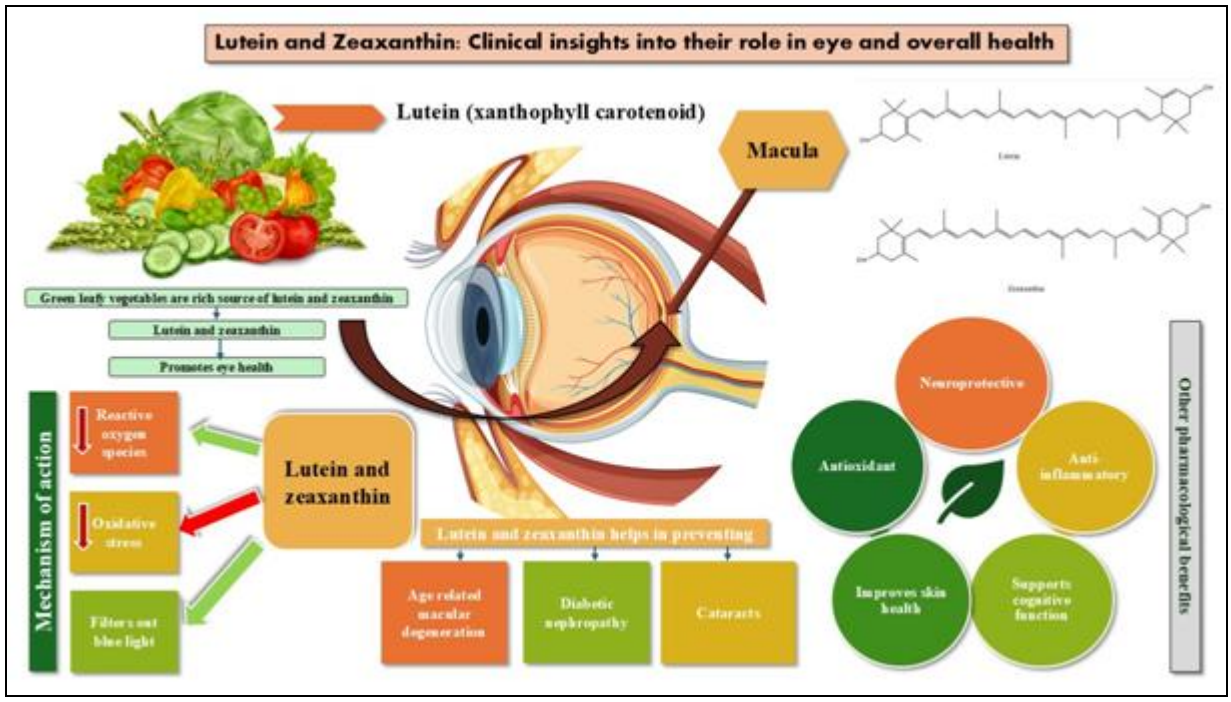

FIG. 1: GRAPHICAL ABSTRACT

Chemical Properties: Lutein and zeaxanthin possess a 40-carbon backbone with alternating single and double bonds, enabling their antioxidant properties.

Both molecules contain cyclic ionone rings, but Lutein contains hydroxyl groups at the 3 and 3' positions of its β-ionone rings, providing structural flexibility. Zeaxanthin differs by having two identical β-ionone rings, making it more symmetric. These structural variations affect their retinal distribution, with lutein being more abundant in peripheral areas and zeaxanthin primarily concentrated in the central fovea. Their conjugated double-bond systems enable light absorption, particularly in the blue wavelength range, protecting ocular tissues from oxidative damage.

Additionally, their lipophilic nature allows them to integrate into cellular membranes, enhancing stability and function [11, 12]. The structural formulas of lutein and zeaxanthin are shown in **Fig. 2.**

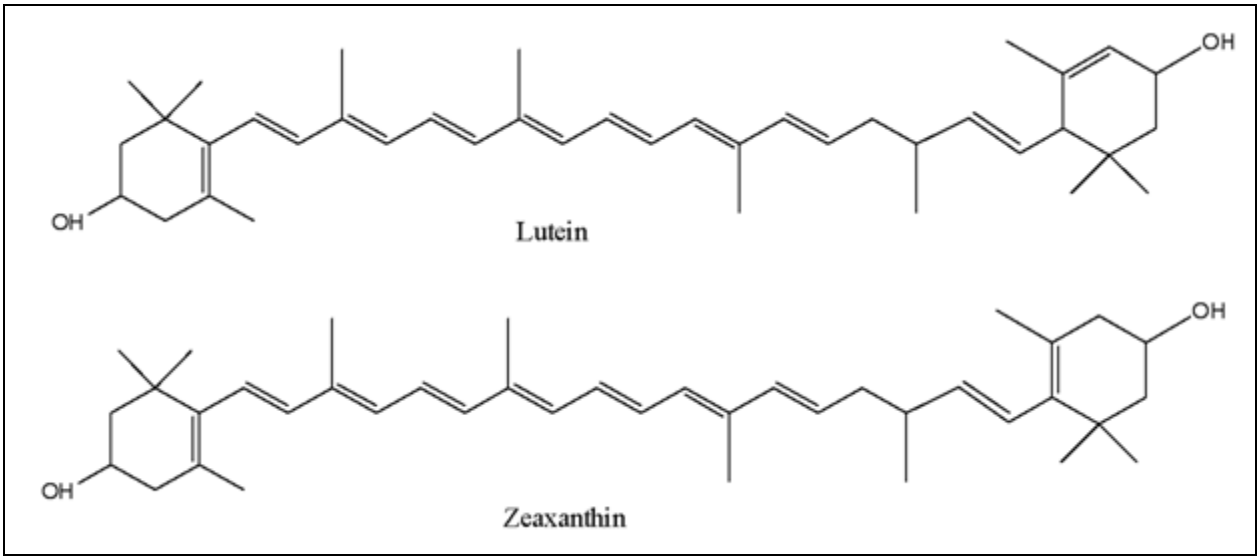

FIG. 2: STRUCTURE OF LUTEIN AND ZEAXANTHIN

Lutein and Zeaxanthin Role in Eye Protection: The macula lutea, located at the central part of the retina, is rich in photoreceptors essential for sharp vision. Its distinct yellow coloration is primarily due to the presence of lutein and zeaxanthin, which help protect the retina by filtering harmful blue light and safeguarding the retina. In older individuals, AMD is a primary cause of vision impairment, with two distinct forms: dry AMD, characterized by the buildup of drusen, and wet AMD, caused by the development of abnormal blood vessels. Several factors contribute to the risk of AMD, including aging, genetic predisposition, smoking, an unhealthy diet, and prolonged exposure to sunlight. Early AMD is often asymptomatic, while advanced stages can lead to central vision loss. Nutrients like zinc, omega-3s, vitamins C and E, and carotenoids like lutein and zeaxanthin have shown potential in slowing the progression. Research, including observational and clinical studies, has explored the benefits of dietary and supplemental lutein and zeaxanthin in AMD prevention [13, 14].

Diabetic retinopathy (DR), a serious complication of diabetes, develops progressively from the non-proliferative (NPDR) to proliferative (PDR) stages, causing retinal damage and vision loss. NPDR involves vessel damage and haemorrhages, while PDR is marked by abnormal vessel growth, leading to severe complications like retinal detachment. Diabetic macular edema, occurring in both stages, results from fluid accumulation in the macula, causing gradual vision impairment.

In a retrospective study involving individuals with type 2 diabetes, supplementation with lutein and zeaxanthin was shown to enhance retinal thickness and function. These improvements, assessed through optical coherence tomography (OCT) and multifocal electroretinography (mfERG), suggest a protective effect of these carotenoids against vision impairment associated with diabetes. Studies investigating lutein's impact on DR remain limited, primarily concentrating on its concentration in the retina and bloodstream. However, findings consistently suggest that higher plasma lutein levels or greater macular pigment optical density (MPOD) may be associated with a reduced risk of DR progression, underscoring its potential protective role in diabetic eye health [15].

Preclinical and Clinical and Safety Studies of Lutein - Zeaxanthin in Eye Health:

***In-vitro* Studies:** The present study explored the protective effect of Gleamax/Vividawn™ supplement containing lutein and zeaxanthin on retinal health, for this purpose, human ARPE-19 retinal cells were exposed to stress UV radiations. Researchers found that the supplement containing lutein and zeaxanthin helped in reducing levels of lipofuscin and A2E. This supplement was able to enhance cell proliferation and provided cytoprotection, thus promoting retinal health [1].

Ultraviolet radiations are responsible for increasing oxidative stress which further leads to damage of RPE and ultimately causes retinal degeneration. In this study, the effect of Lutemax containing

isomers of lutein and zeaxanthin was observed on RPE cells. Result indicated that the treatment was able to inhibit cholinesterase activity while enhanced the activity of catalase, SOD, and GPx activities which is an indicator towards improved antioxidant mechanisms. Treatment also showed down regulation of β-catenin and upregulation of specific G protein constituents responsible for neurophysiological processes involved in vision [2]. Another study revealed the anti-inflammatory activity on lutein and zeaxanthin on RPE cells by reducing the production of inflammatory cytokines [3]. Lutein has been found to show anti-inflammatory properties apart from antioxidant and antiapoptotic properties. Lutein acts on Muller cells responsible for retinal inflammation and shows anti-inflammatory activity. In this study, researchers have explored the effect of lutein on Muller cells with cobalt-chloride induced hypoxia. Results indicated that lutein was able to increase the viability of Muller cells and also significantly reduced the levels of inflammatory mediators except TNF-α [4].

Zeaxanthin has also been found to possess antioxidant effects as found in lutein. The main mechanism involved behind this is the reduction in the levels of lipofuscin, a marker responsible for retinal aging and degeneration. In the present study, effects of carotenoids such as zeaxanthin and lutein were observed on normobaric hypoxia-induced RPE of rabbit and bovine. The results indicated that lower amounts or levels of lipofuscin was seen in hypoxic RPE cells indicating improved retinal health [5]. In this study, the effect of lutein and zeaxanthin in preventing photo-oxidative damage and modulating the expression of inflammatory genes was observed. Results indicated that both carotenoids attenuate proteasome inactivation and help in normalizing expression of inflammatory genes [6].

Pre-clinical Studies: The study explored the ability of lutein to prevent the retina from damage triggered by blue LED light in rats. Six groups of animals were treated with different substances, including distilled water, corn oil, or varying doses of lutein (25, 50, and 100 mg/kg) in corn oil for 30 days. After treatment, all groups, apart from the normal control, were subjected to blue light exposure for 1.5 hours. Lutein treatment helped preserve retinal function by reducing the decline in electroretinogram a-wave and b-wave response amplitudes, indicating better retinal activity. It also helped preserve the thickness of the photoreceptor cell layer typically affected by cell loss and minimized oxidative stress and retinal inflammation. Additionally, lutein enhances the expression of BCO2, an enzyme that plays a key role in maintaining retinal health. The results suggest that lutein could help shield the retina against light-related damage by lowering levels of oxidative stress and inflammation [16].

The research examined the impact of lutein on endotoxin-induced uveitis (EIU) in rats, with lutein being administered before, during, or after lipopolysaccharide treatment, and its effects on inflammation were measured. Lutein lowered the concentrations of key inflammatory markers including nitric oxide, PGE2, MCP-1, TNF-α, IL-6, and MIP-2 within the aqueous humour. It also suppressed NF-κB activation in the iris-ciliary body and reduced iNOS and COX-2 expression in macrophage cells. The anti-inflammatory properties of lutein were comparable to dexamethasone at a dose of 100 mg/kg. These results suggest that lutein alleviates EIU by suppressing NF-κB signalling and decreasing proinflammatory mediators [17].

This study analysed the influence of lutein, a naturally occurring antioxidant, on ovarian injury induced by ischemia-reperfusion (I/R) in rats. (I/R) injury takes place when ovarian blood flow is temporarily blocked and then restored, causing damage due to reactive oxygen species and inflammation. The rats were divided into three groups: one with I/R injury, one with I/R injury plus lutein treatment, and a healthy control group. The findings revealed that I/R injury led to a rise in damaging compounds like malondialdehyde and cyclooxygenase-2(COX-2), alongside a reduction in protective elements such as glutathione and cyclooxygenase-1(COX-1). However, the group treated with lutein showed a reversal of these effects, as lutein alleviated oxidative stress and inflammation, leading to improved ovarian function. The study concluded that lutein helps safeguard the ovaries against I/R injury by exerting antioxidant and anti-inflammatory effects [18].

Clinical Studies: The study explored the effects of different lutein doses on eye function in those frequently exposed to computer screens. A total of 37 healthy participants, aged 22–were randomly assigned to one of three groups: Group L6 (6 mg lutein daily, n=12), Group L12 (12 mg lutein daily, n=13), and a placebo group receiving maltodextrin (n=12). After 12 weeks, serum lutein concentrations significantly increased in both supplementation groups, with Group L12 showing the highest levels. While there were no significant changes in uncorrected and optimally corrected visual acuity (VA), Group L12 exhibited a noticeable improvement trend.Contrast sensitivity improved in both lutein groups, with Group L12 showing significant enhancements across most visual angles, while glare sensitivity remained unaffected. These results indicate that lutein supplementation, particularly at higher doses, may contribute to better visual performance, especially in contrast sensitivity [19].

This study was to assess how lutein intake impacts VA, central visual field, and subjective visual disturbances in individuals with retinitis pigmentosa (RP) and other related retinal conditions. 16 individuals (13 with RP, three with other conditions) took lutein for 26 weeks (40 mg/day for 9 weeks, then 20 mg/day). Ten also took DHA, vitamin B complex, and digestive enzymes, while others continued vitamin A or beta-carotene. Visual function was self-tested weekly for 14 weeks, then bi-weekly. Results showed improvements in VA (0.7 dB) and visual-field area (0.35 dB), with benefits appearing within 2–4 weeks and stabilizing by 6–14 weeks. Blue-eyed participants saw greater acuity gains (1.2 dB) than dark-eyed ones (0.3 dB). Those with prior supplement use showed better central visual-field improvement. These findings suggest lutein may offer short-term visual benefits, especially for blue-eyed individuals and those already taking supplements [20].

This controlled clinical study, using a randomized and double-masked design, assessed the effects of L and Z (lutein and zeaxanthin) intake on ocular pigment density and vision in people with the initial phase of AMD. A total of 108 participants with early AMD were randomly allocated to receive either 10 mg/day or 20 mg/day of lutein, a combination of 10 mg/day lutein and 10 mg/day zeaxanthin, or a placebo for 48 weeks. MPOD and various visual function measures, such as best-corrected visual acuity (BCVA), contrast sensitivity (CS), and photo recovery time, were evaluated at the start of the study, as well as at 24 and 48 weeks. The findings revealed notable increases in MPOD in both the 20 mg lutein group and the lutein-zeaxanthin group, with improvements correlated negatively with baseline MPOD. At48 weeks, trends toward improved BCVA and significant improvements in CS at specific spatial frequencies were observed, particularly in the 20-mg lutein group. The findings suggest that L and Z supplementation increases macular pigment density, improves visual performance, and may contribute to slowing the advancement of AMD [21].

This placebo-controlled randomized trial explored how lutein intake influences visual performance in 120 healthy drivers exposed to extended periods of light. Individuals were randomly divided into an active group (20 mg lutein/day) or placebo group for 12 months, with assessments conducted at baseline and at 1, 3, 6, and 12 months. Assessments covered visual acuity, blood lutein concentrations, MPOD, and overall visual function, along with dietary lutein consumption and vision-related well-being. The findings revealed notable increases in blood Lutein levels and central macular pigment thickness in the group that received the supplement, while no changes were observed in the placebo group. Although improvements in best spectacle-corrected VA were not statistically significant, the supplemented group demonstrated significant enhancements in contrast sensitivity, glare tolerance under low-light conditions, and vision-related performance for driving. These findings suggest that lutein supplementation enhances MPOD and may improve vision during low-light tasks, such as night time driving [22].

This placebo-controlled, randomized study assessed the effect of L and Z on retinal performance in individuals with early AMD using multifocal electroretinograms. During a 48-week study, 108 patients with AMD were given either 10 mg or 20 mg of lutein, a combination of 10 mg lutein and 10 mg zeaxanthin, or a placebo. Additionally, 36 healthy individuals served as a control group for comparison.

Patients with AMD initially showed reduced N1P1 response densities in the central retina. However, following supplementation, notable improvements were observed in those receiving 20 mg of lutein and the lutein–zeaxanthin combination, which were associated with enhanced MPOD. No significant changes occurred in peripheral retinal responses. The study suggests L and Z enhance central retinal function in early AMD by increasing MPOD [23].

This multi-centre, open-label controlled trial examined the effects of nutritional enrichment on VA and overall ocular function in individuals with AMD. A group of 145 participants was randomly assigned to receive either a combination of lutein (10 mg), zeaxanthin (1 mg), astaxanthin (4 mg), along with an antioxidant and vitamin supplement, or no supplementation over a two-year period. The main outcome assessed was VA, while CS and scores from the National Eye Institute Visual Function Questionnaire (NEI VFQ-25) served as secondary evaluation measures. After 24 months, the supplemented group showed a significant stabilization of VA (81.4 ± 7.2) compared to the non-supplemented group (76.8 ± 8.9; p=0.003). Furthermore, the group receiving supplementation showed significant enhancements in CS ($p = 0.001$) and reported higher scores on the NEI VFQ-25 ($p < 0.001$). These results suggest that supplementation with lutein, zeaxanthin, astaxanthin, and additional nutrients may contribute to maintaining or improving VA, CS, and overall visual performance in individuals with AMD [24].

The LUTEGA trial, a randomized, double-blind, placebo-controlled study, assessed the 12-month effects of L, Z, and omega-3 fatty acids (O-3-LCPUFAs), and antioxidants on MPOD and visual acuity in 145 patients with non-exudative AMD. Participants were administered either a placebo or supplements once or twice daily. Results showed significant increases in all MPOD parameters ($p<0.001$) in both treatment groups, with decreases observed in the placebo group. Best-corrected visual acuity (BCVA) also improved significantly in the treatment arms ($p<0.001$). The study suggests that supplementation enhances MPOD, stabilizes BCVA, and may provide protective benefits for the macula in AMD patients [25]. A study involving 72 participants with early-stage AMD examined the effects of daily lutein intake (10 mg) on MPOD and VA over 12 months. In the lutein-treated group, MPOD significantly increases from 0.38 ± 0.19 to 0.53 ± 0.22 optical density units ($p < 0.001$), whereas the placebo group showed no notable change. VA remained unchanged in participants receiving lutein supplementation, while the placebo group showed significant deterioration ($p < 0.05$). Among participants with lower baseline VA, lutein supplementation notably improved VA ($p < 0.05$). The study concluded that lutein supplementation may enhance MPOD and slow disease progression in early AMD [26].

The study aimed to assess how lutein intake influences visual performance in individuals with non-proliferative diabetic retinopathy (NPDR). Over the course of 36 weeks, A double-blind, placebo-controlled, randomized trial was carried out with 31 participants, where they were randomly allocated to receive either 10 mg/day of lutein or a placebo. VA, CS, and glare sensitivity (GS) were evaluated at baseline, week 18, and week 36. The findings indicated a slight improvement in VA in the lutein group and a statistically significant rise in CS at low spatial frequencies (3 cycles/degree, p=0.02). No significant changes in GS were observed. The findings suggest lutein may enhance CS in NPDR patients, potentially serving as an adjunct therapy to prevent vision loss in diabetic patients [27].

The study evaluated how supplementation with L and Z affected MPOD and retinal function in people with early-stage AMD. A total of 112 participants were divided into four groups: 10 mg lutein, 20 mg lutein, a combination of 10 mg lutein and 10 mg zeaxanthin, or a placebo daily for two years. The findings revealed a notable rise in MPOD in all groups receiving active treatment ($p < 0.05$). Retinal sensitivity, measured by multifocal electroretinogram and microperimetry, improved in the treatment groups, particularly with 10 or 20 mg lutein, while the placebo group showed no noticeable improvements. These results indicate that supplementing with lutein and zeaxanthin may boost MPOD and retinal sensitivity in individuals with early-stage AMD [28].

Safety Studies: This study investigated the relationship between lutein supplementation and blood lutein concentrations in adults aged 60 and

above, including those with and without AMD. A total of 45 participants were randomly divided to receive daily doses of 2.5, 5, or 10 mg of lutein for six months, followed by a 6-month observation period without supplementation. Serum lutein concentrations rose significantly, with increases of 2-fold, 2.9-fold, and 4-fold in the 2.5 mg, 5 mg, and 10 mg groups, respectively ($p \leq 0.001$), regardless of the degree of AMD severity. No toxicity or adverse effects were noted, and there were no significant changes in VA or visual field measurements. Supplementation with up to 10 mg of lutein was both safe and effective in boosting serum lutein concentrations [29].

The study investigated the potential toxicity of lutein from *Tagetes erecta*in male mice with lutein deficiency. Acute toxicity tests revealed an LD_{50} exceeding 10,000 mg/kg body weight, with no mortality or adverse clinical signs observed. In a subacute study, mice were gavaged with 0, 100, and 1000 mg/kg/day of lutein for 4 weeks, the findings showed a dose-dependent rise in plasma lutein levels. Toxicity assessments revealed no adverse effects from the treatment in ophthalmic or gastrointestinal assessments, clinical observations, haematology, or histopathology. Yellow faces indicated unabsorbed lutein, attributed to its low bioavailability and hydrophobic nature. The NOAEL was determined to be 1000 mg/kg/day, with no significant toxicity even at the highest doses tested.

This study examined the safety profile of lutein-enriched purple sweet potato leaf (PSPL) extract in male Sprague Dawley rats. In the acute phase, rats received a 2,000 mg/kg dose for 14 days. The subacute phase involved doses of 50, 250, 500, or 1,000 mg/kg over a 28-day period, with a 14-day observation period following treatment. Body weight, blood biochemistry, haematology, organ weight, and tissue histology (heart, kidney, liver, pancreas, aorta, retina) showed no abnormalities in treated groups compared to controls. Results confirmed no toxicity at doses up to 2,000 mg/kg/day. PSPL extract appears safe within the tested dosage range [31]. The study assessed the safety profile of lutein diacetate by administering it sub-chronically for 90 days to Sprague Dawley rats. Oral doses of 2.1, 22.5, and 210 mg per kg of body weight per day were administered *via* gavage, followed by a 28-day recovery period for the control and high-dose groups. Minor changes, such as light brown faeces at the highest dose, resolved during the healing period. No treatment-related effects were observed in any monitored parameters across all doses. The findings suggest that Lutein diacetate is safe in rats at doses up to 210 mg/kg body weight/day [32].

This study investigated the short- and long-term toxic effects of lutein and its esterified form, extracted from marigold flowers (*Tagetes erecta*), in male and female young adult Wistar rats. Lutein and its esterified form were orally administered to rats at doses of 4, 40, and 400 mg/kg body weight. The short-term toxicity assessment lasted 4 weeks, whereas the sub-chronic study extended over 13 weeks. Throughout both study durations, no mortality was observed, and no substantial differences were observed in food intake, body mass, or organ weights. Additionally, liver and kidney functions were not impacted, and there were no alterations in the rats' hematological or lipid profile parameters. Histopathological examinations of organs also showed no signs of toxicity, indicating that both lutein and its esterified form were safe even at higher doses over extended periods [33].

The study investigated the effects of lutein intake in individuals diagnosed with cataracts and AMD. Participants took three capsules per week, providing a total of 18.3 mg of lutein and 3.3 mg of α-tocopherol. After an average of 13 to 26 months, serum lutein levels showed a significant rise, surpassing the 95th percentile of the reference group. Ophthalmological evaluations showed improvements in VA and glare sensitivity. No significant side effects were observed, indicating that lutein supplementation can enhance serum lutein levels and improve visual function [34].

The study examined the impact of high doses of L, and Z, or their combination on carotenoid levels in plasma and eye tissues of rhesus monkeys, while also evaluating any signs of ocular toxicity. For a duration of 12 months, the monkeys received daily supplementation with different doses of L, Z, or their combination. After supplementation, retinal levels of L and Z significantly increased, with no signs of ocular toxicity or kidney damage.

The supplementation resulted in higher carotenoid metabolite levels in both plasma and ocular tissues. The results suggest that high doses of lutein and zeaxanthin, either alone or together, safely boost carotenoid levels without inducing adverse effects [35]. The study concluded that a daily intake of up to 10 mg of lutein over a six-month period is safe for older individuals, regardless of whether they have AMD. No noticeable toxicity or adverse effects were detected throughout the supplementation period [36].

The study investigated the antimutagenic activity of lutein using the Ames test with various *Salmonella typhimurium* strains. Lutein significantly inhibited mutagenicity caused by both direct-acting mutagens and those requiring microsomal activation, such as tobacco extract, at very low concentrations (IC_{50}<50 μg/plate). The inhibition was linked to lutein's strong antioxidant properties and its ability to inhibit cytochrome P450 enzymes, which are involved in the activation of carcinogens. The results suggest that lutein effectively prevents mutagenicity, potentially due to its antioxidant activity and inhibition of carcinogen metabolism [37].

The study examined how dietary supplementation with meso-zeaxanthin (MZ), lutein (L), and zeaxanthin (Z) influenced serum concentrations and macular pigment optical density (MPOD) in healthy subjects. The findings revealed notable increases in serum L and Z levels, along with enhanced central MPOD in those who received the supplements. Clinical pathology analysis revealed no adverse effects, except for some baseline cholesterol and LDL levels outside the normal range before supplementation. The study showed that taking MZ, lutein, and zeaxanthin safely increased carotenoid levels in the blood and improved MPOD [38].

The study assessed the effects of L and Z supplementation on individuals aged 35 to 75 with elevated blood glucose levels. The findings revealed that the supplementation significantly improved HbA1c levels in comparison to the placebo group. No severe adverse effects were observed, with stable renal and liver function markers, such as creatinine, blood urea nitrogen (BUN), serum urea, and bilirubin remained within normal ranges. Moreover, bone health remained unaffected, and the supplements did not adversely influence kidney or liver function. The findings support the effectiveness and safety of lutein and zeaxanthin in regulating blood sugar levels. Overall, lutein supplementation proved beneficial for individuals with impaired glucose metabolism [39].

Benefits of Lutein and Zeaxanthin beyond Eye Health: Lutein, a powerful xanthophyll carotenoid, plays a vital role in both skin and brain health by providing oxidative protection and reducing inflammation. In the skin, it enhances hydration, elasticity, and UV protection while reducing oxidative stress and lipid Peroxidation [40]. In the brain, lutein accumulates in cognitive regions, where it supports neural function, reduces inflammation, and protects against oxidative damage. Its neuroprotective properties help maintain cognitive health and may lower the risk of neurodegenerative disorders [41].

This placebo-controlled, double-blind clinical study included a total of 60 children (ages 5–12 years) were given either 10 mg lutein and 2 mg zeaxanthin or a placebo for 180 days. The study measured MPOD, serum levels of L and Z, brain-derived neurotrophic factor (BDNF), eye strain, fatigue, sleep patterns, and cognitive performance. From day 42 onward, the LZ group showed notable increases in MPOD, serum LZ, and BDNF levels. Participants experienced a reduction in eye strain and fatigue, and showed improvements in focus, memory, and processing speed by days 90 and 180. The supplement group improved in visual processing speed and attention by day 180 compared to the placebo group. No safety concerns were observed, indicating that LZ supplementation was well-tolerated and effective [42].

This 4-month, double-blind trial investigated the cognitive benefits of DHA (800 mg/day) and lutein (12 mg/day) in 49 elderly women (60–80 years). Participants were randomized into DHA, lutein, combination, or placebo groups, and cognitive tests assessed processing speed, accuracy, verbal fluency, memory, and mood. Results showed significant improvements in verbal fluency for DHA, lutein, and combination groups, while memory and learning improved significantly in the combination group.

However, processing speed, accuracy, and mood remained unchanged. The results indicate that supplementing with DHA and lutein may help maintain cognitive function in older adults [43].

Researchers investigated how dietary intake of lutein and zeaxanthin (L + Z) influences cognitive performance, specifically immediate and delayed word recall (IWR and DWR). The analysis, based on the 2014 Health and Retirement Study, included 6390 adults aged 50+ years. The results indicated that Higher intake of L + Z was linked to improved IWR and DWR scores. Primary sources of lutein and zeaxanthin include leafy greens, cruciferous and yellow vegetables, seafood, legumes, eggs, and fruits. The research found that consuming a diet abundant in these foods is associated with increased L + Z levels and enhanced cognitive function in older adults [44].

Human participants received lutein and zeaxanthin either orally, topically, or in combination. The combined oral and topical administration provided the highest antioxidant protection, while both individual methods also showed significant benefits. Oral intake was more effective than topical application in reducing lipid peroxidation and enhancing photoprotection. The results suggest that lutein and zeaxanthin help protect the skin from UV-induced damage, making them valuable for skin health [45].

Mechanism of Action: Lutein and zeaxanthin contribute to visual development and performance through several mechanisms, primarily by protecting the retina and enhancing visual function. These carotenoids function as antioxidants, supporting retinal health by counteracting reactive oxygen species (ROS) produced through intense light exposure, elevated oxygen use, and mitochondrial processes. They quench singlet oxygen by absorbing its energy and returning to their ground state without permanent changes, making them reusable. Additionally, they neutralize free radicals by donating electrons from their polyene chains, preventing oxidation of cellular components like lipids, proteins, and DNA. L and Z also insert into the cell membrane, stabilizing the lipid bilayer and reducing oxidative damage. Moreover, they promote the activation of Nrf2 and HO-1, critical factors in phase II antioxidant protection. These effects support healthy neurophysiological function in the retina and brain, leading to better visual processing, improved contrast sensitivity, and reduced glare sensitivity. Adjusting the diet or using supplements can increase MPOD, which may enhance visual health and performance, emphasizing the benefits of lutein and zeaxanthin for vision support [46, 47].

Lutein has demonstrated significant anti-inflammatory effects, particularly on cytokines like TNF-α, IL-6, and IL-1β. Studies show that lutein can lower levels of these inflammatory agents and block inflammatory pathways, such as the NF-κB and PI3K/Akt pathways, through its strong antioxidant properties. It inhibits NF-κB activation by preventing IκBα degradation and also activates Nrf2 signalling, which further suppresses NF-κB activity. Lutein may also regulate inflammation by upregulating PPARα/RXRα and downregulating COX-2 and pro-inflammatory cytokines. Certain studies indicate that lutein may boost antioxidant defences and lower inflammation markers such as hs-CRP. Still, further clinical research is required to confirm its anti-inflammatory effects in humans [48].

CONCLUSION: Lutein is a vital carotenoid with significant benefits for eye health, particularly in preventing and managing AMD, cataracts, and diabetic retinopathy. Its antioxidant and blue light-filtering properties help protect retinal cells from oxidative stress and damage. Clinical studies confirm that lutein supplementation enhances MOPD, improves contrast sensitivity, and supports overall visual function. Beyond eye health, lutein contributes to cognitive function, cardiovascular protection, and skin health. Its anti-inflammatory effects further reinforce its role in disease prevention. Lutein is considered safe at recommended doses, with no reported toxicity. Regular dietary intake or supplementation can help maintain optimal lutein levels in the body. More studies are required to understand its wider health benefits and lasting effects. Including lutein in the daily diet may offer a natural and beneficial way to support eye health and overall well-being.

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