Journal of Ocular Sciences and Ophthalmology
ISSN: 2998-1476

Academic Strive
Researcher's perception is our reality

Review Article *Volume 6 Issue 1*

Exploring the Impact of Dietary Factors on Glaucoma Outcomes

Hosseini Imeni SM[1]*, Zare M[1], Shajirat N[2], Ghasemi A[1] and Taleb MK[1]

[1]Department of Ophthalmology, Shahid Beheshti University of Medical Sciences, Iran

[2]Department of Internal Medicine, Tehran University of Medical Sciences, Iran

***Corresponding author:** Seyyed Morteza Hosseini Imeni, Department of Ophthalmology, Torfeh Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran, Tel: +989120729467; Email: Mortezahosseinimd@gmail.com

Received Date: December 10, 2024; **Published Date:** January 03, 2025

Abstract

Glaucoma, a leading cause of irreversible blindness, is a multifactorial neurodegenerative disease primarily characterized by elevated intraocular pressure (IOP), vascular dysregulation, and the degeneration of retinal ganglion cells. Although IOP-lowering therapies are established as effective treatments for managing glaucoma, many patients still experience disease progression. This highlights the need for additional adjunctive therapies. Recent research has explored the potential role of nutrition in managing glaucoma, focusing on dietary factors that may affect oxidative stress, inflammation, blood flow, and neuroprotection. This systematic review evaluates the impact of various nutrients-such as antioxidants (vitamins C and E, and selenium), B vitamins (folate, B6, and B12), omega-3 fatty acids, and minerals like zinc, magnesium, and calcium-on disease progression and visual outcomes in all glaucoma (POAG). Our findings suggest that certain dietary factors, including omega-3 fatty acids, vitamin E, and flavonoids, may provide protective effects. Conversely, excessive calcium and magnesium intake might pose risks. However, the evidence remains conflicting, and further research with standardized protocols is needed to establish definitive recommendations. This review emphasizes the importance of incorporating nutritional assessments into glaucoma management and suggests the need for personalized dietary interventions that complement conventional treatments in order to preserve vision. Future studies should aim to clarify the specific mechanisms by which nutrition impacts glaucoma progression, and randomized controlled trials are essential to confirm the efficacy of nutritional supplements in clinical practice.

Keywords: Glaucoma, Nutrition; Intraocular Pressure; Vitamin; Trace Elements; Visual Field; Dietary Interventions; Oxidative Stress

Abbreviations

POAG: Primary Open-Angle Glaucoma; IOP; Intraocular Pressure; VF: Visual Field; OCT: Optical Coherence Tomography; RNFL: Retinal Nerve Fiber Layer; GCC: Ganglion Cell Complex; RCT: Randomized Controlled Trial.

Introduction

Glaucoma is a neurodegenerative disease and a leading cause of irreversible blindness, affecting millions of people worldwide. It is projected that over 110 million individuals will have glaucoma by 2040 [1,2]. The burden of this disease is significant; the Global Burden of Disease Study reported an increase in Disability-Adjusted Life Years (DALY) attributed to glaucoma, rising from 442,182 in 1990 to 748,308 in 2019 [3]. Alarmingly, glaucoma can consume over 2.5% of the median household income in various countries, underscoring its economic impact on affected individuals and families [4]. Glaucoma is a multifactorial disease characterized by a complex interplay of factors, including elevated IOP, genetic predisposition, and vascular dysregulation. It is primarily categorized into two main types: open-angle glaucoma (OAG), which features an open anterior chamber angle, and angle-closure glaucoma (ACG), where the angle is closed or narrowed. While treatments primarily aim to lower IOP-one of the key modifiable risk factors-many patients continue to experience progression, indicating the importance of exploring IOP-independent therapies [5,6]. Current interventions primarily focus on lowering intraocular pressure (IOP), but many patients experience disease progression despite adequate IOP control, emphasizing the need for additional therapies. Recent research has highlighted the potential of dietary interventions to influence key pathways in the pathogenesis of glaucoma, such as oxidative stress, inflammation, and vascular dysregulation7. Emerging research suggests that nutrition may play a critical role in glaucoma management by influencing factors such as blood flow, neuroprotection, and oxidative stress [7].

This review will evaluate the evidence surrounding specific nutrients, dietary patterns, and nutritional supplements in the management of glaucoma, particularly primary open-angle glaucoma (POAG). We will analyse the impact of various nutritional components-including antioxidants (vitamins C, E, and selenium), B vitamins (folate, B6, B12), omega-3 fatty acids, and minerals like zinc, magnesium, and iron-as well as dietary nitrates and meat consumption-on disease progression and visual field outcomes in POAG. Ultimately, we aim to provide evidence-based nutritional recommendations for POAG patients. Through this examination of dietary factors, we seek to identify potential adjunctive treatments to help preserve vision in those affected by this condition.

Methods

Search Strategy

A systematic literature search was conducted in PubMed and Google Scholar to identify relevant studies examining the relationship between nutrition and glaucoma. The following search terms were used in PubMed: ("Nutrition"[Mesh] OR "Diet"[Mesh] OR "Dietary Supplements"[Mesh]) AND "Glaucoma"[Mesh]. In Google Scholar, the following searches were conducted separately: "nutrition AND glaucoma," "diet AND glaucoma", and "supplement AND glaucoma." The searches were limited to studies published in English from 1990 to 2024. Additionally, the reference lists of the included articles and relevant reviews were manually screened to identify any potentially missed studies.

Inclusion and Exclusion Criteria

Studies were included if they met the following criteria:
Population: Included adults with glaucoma.
Intervention/Exposure: Examined the impact of dietary factors, including specific nutrients (vitamins, minerals), dietary patterns, or nutritional supplements.
Outcomes: Reported on clinically relevant outcomes such as IOP, visual field progression, or glaucoma incidence.
Language: Published in English.
Studies were excluded if they: Non-English literatures were not original research articles (e.g., editorials, letters to the editor).

Study Selection

Two reviewers independently screened the titles and abstracts of the identified studies. They retrieved full-text articles for potentially relevant studies, and those meeting the inclusion criteria were included in the review. Any discrepancies between reviewers were resolved through discussion and consensus.

Data Extraction

Data from the included studies were extracted using a standardized form. The extracted information included:
Study characteristics (author, year, study design, sample size)
Participant characteristics (age, sex, glaucoma severity)
Intervention/exposure (specific nutrient, dietary pattern, supplement)
Comparator/control group (if applicable)
Outcomes (IOP, visual field, glaucoma incidence)
Key findings (including effect sizes and statistical significance, if reported)

Data Synthesis

A narrative synthesis of the findings was conducted. Studies were grouped by the specific nutrient their mechanism in general and in the plus the effect of each nutrient on the glaucoma outcome.

Results

Carbohydrates

Carbohydrates serve as a primary energy source for the body. Evidence suggests that they may contribute to oxidative stress, with low carbohydrate intake potentially offering protective effects for retinal ganglion cells (RGCs) [8]. A study by Hanyuda A, et al. [9] found that reduced carbohydrate intake was not linked to an increased risk of primary open-angle glaucoma (POAG). Furthermore, replacing carbohydrates with vegetable fats and proteins correlated with a decreased risk of POAG in cases of initial central visual field loss. In contrast, the SUN cohort study conducted by Moreno-Montañés J, et al. [10] indicated a positive association between higher carbohydrate consumption and increased glaucoma incidence. These findings suggest that moderating carbohydrate intake in glaucoma patients may be advisable.

Proteins

Proteins are vital for the structural integrity and functional maintenance of ocular tissues. Adequate intake is critical for preserving optic nerve health and supporting RGCs, primary targets in glaucoma pathology. While rich in protein and iron, meat can enhance oxidative stress and provide carnosine, an enzyme with antioxidant and mitochondrial protective roles [11]. A study by Kinouchi R, et al. [12] demonstrated a protective association between high meat consumption and open-angle glaucoma in a Japanese cohort. Conversely, Lee JY, et al. [13] study noted that lower protein consumption was significantly associated with POAG risk in females with low to medium BMI and males with medium BMI POAG, while Mylona I, et al. [14] found that reduced meat consumption was linked to increased disease incidence. Contrarily, Braakhuis A, et al. [15] reported that higher meat consumption correlated with an elevated risk of eye diseases, including glaucoma. Overall, adequate protein intake appears to confer a protective effect, particularly against POAG.

Fats

Fats are crucial components of cellular membranes and play significant roles in physiological processes such as inflammation and oxidative stress regulation. They also influence endogenous prostaglandin F2α production. Omega-3 fatty acids are well-regarded for their anti-inflammatory and neuroprotective properties. By improving blood flow, omega-3 supplementation has been explored as a potential adjunct therapy for glaucoma, with some studies indicating that it may reduce inflammation in the optic nerve and protect RGCs from inflammatory damage. A randomized placebo-controlled trial by Downie LE, et al. [16] demonstrated a statistically significant reduction in intraocular pressure (IOP) in patients receiving an oral omega-3 supplementation regimen (approximately 1000 mg/day of eicosapentaenoic acid with 500 mg/day of docosahexaenoic acid ± 900 mg/day of α-linolenic acid) compared to controls. An open-label randomized controlled trial by Romeo VS, et al. [17] further supported these findings, revealing significant IOP reductions, decreased IL-6 levels, and improved plasma antioxidant capacity in the DHA group (1g).

Kang JH, et al. [18] observed that a higher ratio of omega-3 to omega-6 polyunsaturated fats positively influenced the risk of POAG, particularly in patients with elevated IOP. Similarly, Wang YE, et al. [19] reported that elevated intake of DHA and EPA, coupled with lower PUFA consumption, was associated with reduced glaucoma risk in a cross-sectional study. However, the Rotterdam Study conducted by Ramdas WD, et al. [20] found no significant association between total fat, saturated fat, or monounsaturated fat intake and POAG risk. Lastly, Garcia-Medina JJ, et al. [21] conducted an open-label randomized controlled trial assessing antioxidant supplementation with or without omega-3 fatty acids, finding no discernible differences in visual field and OCT metrics between the two groups. Micronutrients and Their Implications in Glaucoma.

Vitamin A (Retinol)

Vitamin A plays a crucial role as an antioxidant and is vital for the visual cycle and the health of retinal cells. Lee JY, et al. [22] demonstrated that lower levels of vitamin A, thiamine, riboflavin, and vitamin C were significant in females with primary open-angle glaucoma (POAG), particularly among those with low and medium BMIs. Furthermore, the Rotterdam study by Ramdas WD, et al. [20] indicated that lower retinol equivalent intake correlates with an increased risk of open-angle glaucoma (OAG). This suggests that assessing dietary vitamin A deficiency could be a beneficial adjunctive strategy in glaucoma management.

Vitamin B1 (Thiamine)

Thiamine is pivotal for nerve function and energy metabolism. Lee JY, et al. [13] also found that higher thiamine intake was associated with lower risk of POAG. The Rotterdam study indicated a relationship between low thiamine intake and OAG [20], though the literature on vitamin B1's specific role in glaucoma is limited and warrants further investigation.

Vitamin B3 (Niacin)

Niacin contributes to mitochondrial energy metabolism and may have a protective effect on retinal ganglion cells by enhancing nitric oxide production, thereby improving optic nerve and retinal blood flow.

Lee SY, et al. [23] found that increased niacin intake was associated with a reduced odds ratio for glaucoma, particularly in women. This finding aligns with Taechameekietichai T, et al. [24] who reported lower glaucoma incidence with higher niacin intake. Nonetheless, a case report by Tittler EH, et al. [25] identified an increase in intraocular pressure (IOP) following oral niacin administration, suggesting that while niacin supplementation might be beneficial in glaucoma treatment, monitoring for potential IOP elevation is essential.

Vitamins B6, B9 (Folate), and B12

These vitamins are involved in homocysteine metabolism and may contribute to glaucoma through oxidative stress pathways. Turgut B, et al. [26] reported elevated plasma B6 levels in normal-tension glaucoma (NTG) and POAG patients but found no differences in B6 and B12 levels across study groups. Kang JH, et al. [27] noted a suggestive lower risk of exfoliative glaucoma with higher folate intake. Atalay K, et al. [28] found no clear association between these vitamins and POAG. Conversely, Türkcü FM, et al. [29] reported lower serum folate and B12 levels in pseudoexfoliative glaucoma (PEX) and NTG, indicating that more robust evidence is needed to establish the relationship of these vitamins with glaucoma.

Vitamin C

Vitamin C's antioxidant properties have potential implications in protecting cells from oxidative stress, with conflicting evidence regarding its role in glaucoma. Wang SY, et al. [30] found that both low and high-dose vitamin C supplementation reduced the odds of glaucoma but saw no association between serum vitamin C levels and glaucoma prevalence. These findings align with Lee JY, et al. [22] study. In contrast, Yuki K, et al. [31] observed reduced plasma vitamin C levels in NTG patients. Overall, the existing evidence for vitamin C's role and efficacy in glaucoma remains inconclusive.

Vitamin D

Vitamin D is hypothesized to possess antioxidant and neuroprotective properties. Krefting EA, et al. [32] found no significant effect of serum vitamin D levels or supplementation on IOP. However, lower serum vitamin D levels were reported in glaucoma patients by Vuković AZ, et al. [33] and corroborated by Kim HT, et al. [34] in glaucomatous women. Yoo TK, et al. [35] identified associations between vitamin D levels and OAG, yet Li S, et al. [36] found no correlation between serum vitamin D levels and glaucoma. Additionally, Lee T, et al. [37] did not observe associations between vitamin D levels and progressive visual field loss or retinal nerve fiber layer (RNFL) thinning in glaucomatous patients. Several studies, including Dikci S, et al. [38], emphasized the need for further investigation to clarify the relationship between vitamin D deficiency and glaucoma development and the unclear effects of vitamin D supplementation on glaucoma progression.

Vitamin E

Vitamin E is recognized for its antioxidant properties and plays significant roles in extracellular remodeling and apoptosis, particularly influencing TGFβ2-mediated alterations in the trabecular meshwork [39]. Studies have shown that vitamin E deficiency in rodent models leads to increased retinal ganglion cell (RGC) death under elevated intraocular pressure (IOP) conditions [40]. The SUN Project findings indicate no significant correlation between the isolated intake of vitamins A, C, and E and glaucoma; however, a combined intake of these vitamins appears to be linked to a reduced risk of developing the disease [10]. Research by Marino PF, et al. [41] has demonstrated that a daily regimen of citicoline, homotaurine, and vitamin E enhances contrast sensitivity and overall quality of life for glaucoma patients. In another study by Parisi V, et al. [42] the administration of coenzyme Q10 alongside vitamin E yielded beneficial effects on Pattern Electroretinogram (PERG) and visually evoked Potential (VEP) measurements in patients with open-angle glaucoma (OAG). Wang SY, et al. [30] reported no noteworthy association between serum concentrations or supplementation of vitamin E and glaucoma. Similarly, Xiong K, et al. [43] did not observe any significant improvements in macular retinal nerve fiber layer (RNFL) thickness, macular ganglion cell-inner plexiform layer (GCIPL) measurements, or cup-to-disc ratios following vitamin E intervention.

Additionally, Goldblum D, et al. [44] found no correlation between vitamin E supplementation and outcomes in trabeculectomy or phaco trabeculectomy surgeries. Engin KN, et al. [45] investigated the impact of alpha-tocopherol supplementation in glaucoma patients. They observed improvements in pulsatility indexes (PI) and resistivity indexes (RI) of the ophthalmic artery and a reduction in mean deviation in visual fields. These findings underscore the importance of assessing vitamin E status and considering supplementation as a potential adjunctive strategy in the management of glaucoma.

Calcium

Calcium plays a crucial role in cellular signaling, vascular regulation, and the modulation of oxidative stress. A study by Zhang Y, et al. [46] highlighted that sufficient dietary intake of calcium, magnesium, and potassium correlates with a diminished risk of glaucoma. In contrast, findings from Wang SY, et al. [47] suggest that excessive supplementation of iron and calcium may be associated with an elevated risk of developing glaucoma. These data advocate for the careful evaluation of calcium intake in patients with glaucoma while also emphasizing the necessity for clinicians to remain vigilant regarding the potential adverse effects associated with excessive calcium consumption.

Flavonoids

Flavonoids are a diverse group of phytonutrients prevalent in fruits, vegetables, tea, and chocolate, recognized for their antioxidant and anti-inflammatory properties. These compounds may confer protective effects on retinal ganglion cells, and some epidemiological studies suggest an association between flavonoid intake and a reduced risk of glaucoma or a slower disease progression. However, Kang JH, et al. [48] found no significant correlation between overall flavonoid consumption and the risk of primary open-angle glaucoma (POAG) in the Nurses' Health Study. However, flavonols was reported to be associated with lower risk of POAG progression. It showed that drinking 2 cups of tea per day decreased POAG risk by 18%. Conversely, Colman AC, et al. [49] and Giaconi JA, et al. [50] reported an inverse relationship between higher consumption of fruits and vegetables and glaucoma risk.

In the context of Ginkgo biloba extract, Chung JW, et al. [51] demonstrated a statistically significant increase in retinal blood flow and volume among normal-tension glaucoma (NTG) patients. Supporting this, Quaranta L, et al. [52] noted improvements in preexisting visual field defects with Ginkgo biloba supplementation. On the other hand, Guo X, et al. [53] reported no changes in mean deviation or contrast sensitivity in NTG patients following similar interventions. Further investigations by Shim SH, et al. [54] indicated that Ginkgo biloba supplementation enhances mean deviation in visual fields, while bilberry anthocyanins positively impact both best-corrected visual acuity (BCVA) and mean deviation. Ohguro H, et al. [55,56] found statistically significant improvements in visual field mean deviation with black currant anthocyanin consumption and noted IOP-lowering benefits in both normal and glaucomatous patients.

Contrarily, Terai N, et al. [57] observed that the consumption of dark chocolate did not exhibit the venous dilation response observed in normal subjects among glaucoma patients. Wu CM, et al. [58] identified a significant inverse relationship between tea consumption and glaucoma risk; however, this study did not demonstrate any correlation between coffee intake and glaucoma. In contrast, Bae JH, et al. [59] linked a higher prevalence of open-angle glaucoma (OAG) to coffee consumption without finding an effect of tea drinking on glaucoma. The Blue Mountains Eye Study corroborated these findings by observing increased intraocular pressure associated with coffee consumption [60]. Similarly, Kang JH, et al. [61] indicated an elevated risk of high-tension POAG among coffee drinkers with a familial predisposition to glaucoma. Also drinking one cup of coffee in glaucoma and nonglaucomatous subjects is associated with a transient 1-2mmHg increase in IOP lasting about 2 hours [62]. Although there is a report on increased risk of developing pseudoexfoliation glaucoma in patients who drink ≥ 3 cups of coffee per day [63]. Current evidence supports the beneficial role of fruits and vegetables in glaucoma management, while the impacts of chocolate, tea, and caffeinated beverages remain inconclusive.

Lutein and Zeaxanthin

Lutein and zeaxanthin are carotenoids that accumulate in high concentrations within the macula. They function as antioxidants and provide protection against oxidative stress in retinal cells. However, the investigation by Kang JH, et al. [64] did not establish a significant association between lutein and zeaxanthin intake and glaucoma incidence.

Magnesium

Magnesium functions as a calcium channel blocker and may enhance ocular blood flow, potentially addressing perfusion abnormalities linked to glaucomatous optic nerve damage. Several studies have noted an association between decreased serum magnesium levels and the incidence of glaucoma. For instance, a study by Aydin B, et al. [65] did not establish a correlation between Doppler imaging parameters of orbital vessels and magnesium supplementation in glaucomatous patients. However, magnesium supplementation in this cohort was associated with significant improvement in pattern standard deviation and mean deviation in visual fields. Contrarily, the Rotterdam study identified a correlation where higher magnesium intake corresponded with an increased risk of open-angle glaucoma (OAG) [20]. These findings suggest a nuanced role of magnesium status and supplementation in glaucoma, highlighting the need for further research to elucidate these associations.

Zinc, Copper, and Selenium

Trace elements play crucial roles in enzymatic processes and possess antioxidant capabilities. Akyol N, et al. [66] proposed an elevated copper-to-zinc ratio in the aqueous humor of glaucoma patients, while Hohberger B, et al. [67] reported higher zinc levels and lower iron concentrations in the aqueous humor of individuals with glaucoma. Moreover, the study by Bruhn RL, et al. [68] indicated a significant association between glaucoma risk and the highest tertile of plasma selenium, along with the middle tertile of selenium in the aqueous humor. Zhao R, et al. [69] demonstrated a linear relationship between daily selenium intake and glaucoma risk, and Zawadzka I, et al. [70] reported diminished serum concentrations of zinc and selenium in glaucomatous patients. Current data suggests a relevant role for these trace elements in the pathogenesis of glaucoma; however, their specific mechanisms and implications for management require further investigation.

Pyruvate

Pyruvate is final product of glycolysis and functions as energy source in many cells like neurons. Various studies showed its neuroprotective impact on neurodegenerative diseases like Parkinson disease and brain ischemic injury [71]. A recent study showed increased IOP is associated with decreased level of pyruvate in RGCs in DBA/2J mice probably as a result of transcriptional dysregulation and pyruvate metabolism [72]. Currently a clinical trial is performing on neuroprotective impact of pyruvate in glaucoma. (NCT03797469).

Ethanol

Ethanol has a transient reduction effect on IOP lasting about 60 minutes [73]. Farmingham Eye Study found an association between ethanol consumption and glaucoma but newer studies didn`t find any association [74-76].

Saffron

Studies exploring the effect of saffron in POAG are scarce. There was a pilot study that claimed oral saffron daily intake decreases IOP in POAG patients in a period of 3 weeks. The study assumed it was due to antioxidative effect on trabecular meshwork dysfuction [77]. Large clinical trials with longer follow ups are needed before any conclusion.

Discussion

The reviewed studies underscore the critical role of nutritional evaluation and interventions in the context of glaucoma (Figure 1 & Table 1). Carbohydrates, a staple in global diets, remain ambiguously related to the pathogenesis and management of glaucoma. While some evidence indicates that excessive carbohydrate consumption may elevate glaucoma risk, other studies suggest a neutral or even protective effect.

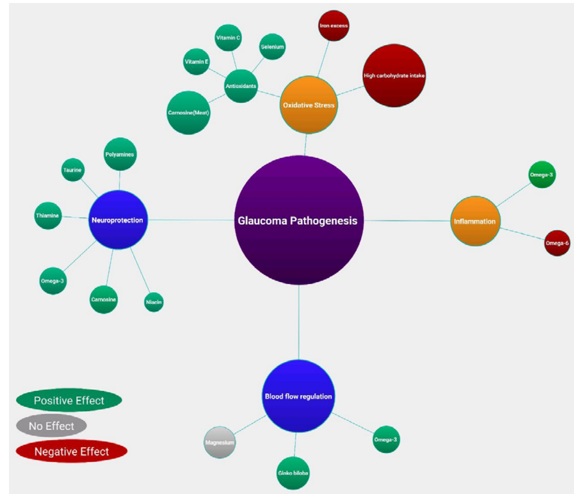

Figure1: (result section) Positive and negative effects of nutrient groups on glaucoma pathogenesis, Green: Positive effect, Grey: No effect, Red: Negative effect.

Outcome	Nutrient/Dietary Pattern	Effect	Type of Glaucoma	Related Articles
IOP	Omega-3 Fatty Acids	↓ (may reduce)	PEX glaucoma, Normotensive adults	Downie LE, et al. [16], Villadóniga, et al.
	Ginkgo Biloba Extract	No effect on IOP	-	Chung WS, et al. [51]
	Niacin	No effect from high-dose nicotinamide	POAG	Tittler EH, et al. [25]
	Vitamin D	No effect from supplementation	POAG	Gramer, et al.
	Ethanol	↓Transient reduction		Buckingham T, et al. [73]
Visual Field	Ginkgo Biloba Extract	↑ (improves in NTG)	NTG	Quaranta L, et al. [52] Shim SH, et al. [54]
	Anthocyanins	↑ (improves in NTG)	NTG	Ohguro H, et al. [55] Shim SH, et al. [56]
	Magnesium	↑ (improves in NTG)	NTG	Aydin B, et al. [65]
OCT Parameters	Omega-3 Fatty Acids	No significant association	POAG	Garcia-Medina JJ, et al. [21]
	Vitamin E	No effect		Lee JY, et al. [13] Xiong K, et al. [43]
VEP	Vitamin E	May improve PERG and VEP	OAG	Parisi V, et al. [42]
Ocular Blood Flow	Ginkgo Biloba Extract	↑ (improves)	-	Chung WS, et al. [51]

	Omega-3 Fatty Acids	↑ (improves)	-	Downie LE, et al. [16]
	Magnesium	No effect from supplementation	NTG	Bahri et al.
Glaucoma Prevalence/ Incidence	Meat Consumption	Conflicting findings	POAG	Kinouchi R, et al. [12], Braakhuis A, et al. [15], Mylona I, et al. [14]
	Vitamin A	↓ (lower levels associated with increased risk)	NTG, POAG	Lee JY, et al. [13], Ramdas WD, et al. [7]
	Vitamin B1 (Thiamine)	↓ (lower intake may be associated with increased risk)	OAG	Ramdas WD, et al. [20]
	Vitamin B3 (Niacin)	↓ (lower intake associated with lower risk)	-	Lee JY, et al. [13], Taechameekietichai T, et al. [24]
	Vitamin B6, B9, B12	Inconclusive	PXG, NTG, POAG	Turgut B, et al. [26], Kang JH, et al. [27], Atalay K, et al. [28], Türkcü FM, et al. [29]
	Vitamin C	Inconclusive	-	Wang SY, et al. [30], Yuki K, et al. [31]
	Vitamin D	↓ (lower levels associated with glaucoma, but supplementation role unclear)	POAG	Krefting EA, et al. [32], Vukovic AZ, et al. [33], Kim HT, et al. [34], Li S, et al. [36], Atalay K, et al. [28]
	Vitamin E	May have beneficial effects, but more research needed	-	Wang SY, et al. [30], Xiong K, et al. [43], Goldblum D, et al. [44]
	Calcium	↑ (supplementation may increase risk)	-	Wang SY, et al. [47]
	Flavonoids	↓ (higher intake may be associated with lower risk)	POAG, NTG	Kang JH, et al. [48], Keech AC, et al. [49], Giaconi JA, et al. [50], Park JW, et al. [51], Quaranta L, et al. [52], Ohguro H, et al. [55]
	Magnesium	↑ (supplementation may be beneficial, but higher dietary intake may increase risk)	OAG	Bahri, et al., Ramdas WD, et al. [20]
	Zinc, Copper, and Selenium	May play a role in pathogenesis, but specific mechanisms and management need further research	PEX, NTG	Akyol N, et al. [66], Hohberger B, et al. [67], Bruhn RL, et al. [68], Zawadzka I, et al. [70]
	Ethanol	Mixed results	POAG	Farmingham study, Xu L, et al. [75], Kang JH, et al. [76]

Table 1: Role of nutritional evaluation and interventions in the context of glaucoma.

In contrast, the roles of proteins and fats are more thoroughly examined, with evidence pointing to a protective influence of specific proteins and omega-3 fatty acids against the development of glaucoma. Conversely, polyunsaturated fatty acids (PUFAs) and omega-6 fatty acids are implicated in potential adverse outcomes for patients with glaucoma [16,18].

Vitamins and micronutrients also warrant attention, yet their impacts are variably documented. Specific vitamins, such as A and E, are highlighted for their protective roles, while the evidence surrounding iron, calcium, and trace elements suggests that clinicians should be cautious of over-supplementation and should conduct critical assessments of dietary habits to address possible deficiencies or excesses [11].

A focal point in examining nutritional influences on glaucoma is intraocular pressure (IOP). Omega-3 fatty acids have been proposed to facilitate IOP reduction; however, studies examining vitamin D and ginkgo biloba did not confirm any significant effects. Notably, a report by Tittler EH, et al. [25] highlighted the potential impact of oral niacin supplementation on IOP-elevating potential.

In terms of nutritional impacts on imaging metrics, such as Optical Coherence Tomography (OCT) and visual field parameters, vitamin E supplementation has been associated with improvements in retinal functions. Improvements in visual field metrics, including mean deviation (MD) and pattern standard deviation (PSD), were noted in cases treated with ginkgo biloba extract, anthocyanins, and magnesium. However, the latter was predominantly studied in normal-tension glaucoma (NTG) patients. These findings suggest the promise of intervention strategies, but standardized designs, along with careful consideration of dosage and duration, are essential in the future.

Additionally, blood flow enhancements have been associated with supplementation of omega-3 fatty acids and ginkgo biloba extract; however, studies exploring magnesium did not yield significant results. The limited number of studies and the absence of uniform protocols highlight a pressing need for future research.

Overall, various nutrients such as green leafy vegetables, flavonoids, proteins (including red meat studies), vitamins A, B1, B3, D, E, and magnesium correlate with a lower prevalence of glaucoma. Conversely, conflicting evidence exists regarding vitamins B6, B9, B12, and trace elements. Notably, elevated calcium and magnesium intakes have demonstrated negative associations, emphasizing the necessity for well-structured and balanced dietary protocols (Table 2).

Nutrition and Glaucoma		
Vitamins	A	leafy Green vegetables
		Carrots
		Sweet potatoes
	Vitamin B1 (Thyamine)	Whole grain
		Legume
		Nuts
		Seeds
	Vitamin B3 (Niacin)	Meat
		Poultry
		Fish
		Nuts
		Legumee
		Seeds

	Vitamin B6,B9,B12	Leafy green vegetables
		Legumes
		Nuts
		Seeds
		Meat
		Poultry
		Fish
		Eggs
		Dairy
	Vitamin C	Citrus fruits
		Berries
		Tomatoes
		Peppers
	Vitamin D	Fatty fish
		Eggs
		Fortified foods
	Vitamin E	Nuts
		Seeds
		Vegetable oil
		Leafy green vegetables
Minerals	Iron	Red meat
		Poultry
		Fish
		Beans
		Lentils
		Fortified cereals
	Calcium	Dairy products
		Leafy green vegetables
		Fortified foods
	Magnesium	Leafy green vegetables
		Nuts
		Seeds
		Whole grain
		Legumes
	Zinc	Meat
		Poultry
		Seafood
		Beans
		Nuts
		Whole grain

	Copper	Seafood
		Nuts
		Seeds
		Legumes
		Organ meats
	Selenium	Seafood
		Brazil nuts
		Meat
		Poultry
		Egg
Proteins	Animal based	Red meat
		Poultry
		Fish
	Vegetable based	Tofu
		Quinoa
		Beans
		Lentils
		Nuts
		Seeds
Carbohydrates	Grains	Pasta
		Bread
		Rice
	Fruits	
	Legumes	
	Dairy	
Fatty acid	Omega-3	Fatty fish
		Flaxseed
		Chia seed
		Walnuts
	Omega-6	Vegetable oil
		Nuts
		Seeds

Table 2: Nutrition and Glaucoma.

Conclusion

In conclusion, our analysis reveals the intriguing potential of nutritional interventions and the imperative for further high-quality studies. It also addresses concerns regarding malnutrition in glaucoma patients and the importance of careful evaluation to prevent over-supplementation. Limitations of this review include the retrospective nature and reliance on self-reported outcomes in many studies, along with the scarcity of standardized interventions targeting glaucoma-related outcomes with comprehensive evaluations.

Future Directions

The existing data is insufficient in terms of well-designed randomized controlled trials (RCTs) and longitudinal studies. Considering this, incorporating such data into practice requires standardized protocols and uniform treatment approaches. Additionally, information involving advanced ocular imaging is relatively limited in this field, illustrating an important area for future research.

Acknowledgements

We thank the participants and investigators of the studies included in this article.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Kingman S (2004) Glaucoma is second leading cause of blindness globally. Bull World Health Organ 82(11): 887-888.
2. Tham YC, Li X, Wong TY, Quigley HA, Aung T, et al. (2014) Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology 121(11): 2081-2090.
3. Lin Y, Jiang B, Cai Y, Luo W, Zhu X, et al. (2023) The Global Burden of Glaucoma: Findings from the Global Burden of Disease 2019 Study and Predictions by Bayesian Age-Period-Cohort Analysis. J Clin Med 12(5): 1828.
4. Zhao PY, Rahmathullah R, Stagg BC, Almobarak F, Edward DP, et al. (2018) A Worldwide Price Comparison of Glaucoma Medications, Laser Trabeculoplasty, and Trabeculectomy Surgery. JAMA Ophthalmol 136(11): 1271-1279.
5. Kang JM, Tanna AP (2021) Glaucoma. Med Clin North Am 105(3): 493-510.
6. Quigley HA (2011) Glaucoma. Lancet 377(9774): 1367-1377.
7. Ramdas WD (2018) The relation between dietary intake and glaucoma: a systematic review. Acta Ophthalmol 96(6): 550-556.
8. Zarnowski T, Tulidowicz-Bielak M, Kosior-Jarecka E, Zarnowska I, Turski WA, et al. (2012) A ketogenic diet may offer neuroprotection in glaucoma and mitochondrial diseases of the optic nerve. Med hypothesis Discov Innov Ophthalmol J 1(3): 45-49.
9. Hanyuda A, Rosner BA, Wiggs JL, Walter CW, Kazuo T, et al. (2020) Low-carbohydrate-diet scores and the risk of primary open-angle glaucoma: data from three US cohorts. Eye 34(8): 1465-1475.
10. Moreno-Montanes J, Gandara E, Moreno-Galarraga L, Hershey MS, López-Gil JF, et al. (2022) ACE-Vitamin Index and Risk of Glaucoma: The SUN Project. Nutrients 14(23): 5129.
11. Knecht KT, Chiriac G, Guan HD (2024) The potential impact of a vegetarian diet on glaucoma. Surv Ophthalmol 69(5): 833-841.
12. Kinouchi R, Ishiko S, Hanada K, Hayashi H, Mikami D, et al. (2018) A low meat diet increases the risk of open-angle glaucoma in women-The results of population-based, cross-sectional study in Japan. PLoS One 13(10): e0204955.
13. Lee JY, Kim JM, Lee KY, Kim B, Lee MY, et al. (2020) Relationships between Obesity, Nutrient Supply and Primary Open Angle Glaucoma in Koreans. Nutrients 12(3): 878.
14. Mylona I, Chourdakis M, Makedou K, Tsinopoulos I (2020) Dietary habits are useful as risk factors for primary open-angle glaucoma while controlling for heredity and metabolic disease. Nutr Health 26(3): 163-166.
15. Braakhuis A, Raman R, Vaghefi E (2017) The Association between Dietary Intake of Antioxidants and Ocular Disease. Diseases 5(1): 3.
16. Downie LE, Vingrys AJ (2018) Oral Omega-3 Supplementation Lowers Intraocular Pressure in Normotensive Adults. Transl Vis Sci Technol 7(3): 1.
17. Romeo VS, Rodriguez GE, Sagastagoia EO, Alvarez DMD, Domingo PJC (2018) Effects of Oral Supplementation with Docosahexaenoic Acid (DHA) plus Antioxidants in Pseudoexfoliative Glaucoma: A 6-Month Open-Label Randomized Trial. J Ophthalmol 2018: 8259371.
18. Kang JH, Pasquale LR, Willett WC, Bernard AR, Kathleen ME, et al. (2004) Dietary fat consumption and primary open-angle glaucoma. Am J Clin Nutr 79(5): 755-764.
19. Wang YE, Tseng VL, Yu F, Caprioli J, Coleman AL (2018) Association of Dietary Fatty Acid Intake With Glaucoma in the United States. JAMA Ophthalmol 136(2): 141-147.
20. Ramdas WD, Wolfs RCW, Kiefte-de JJC, Hofman A, de Jong PT, et al. (2012) Nutrient intake and risk of open-angle glaucoma: the Rotterdam Study. Eur J Epidemiol 27(5): 385-393.
21. Garcia-Medina JJ, Garcia-Medina M, Garrido-Fernandez P, Galvan-Espinosa J, Garcia-Maturana C, et al. (2015) A two-year follow-up of oral antioxidant supplementation in primary open-angle glaucoma: an open-label,

randomized, controlled trial. Acta Ophthalmol 93(6): 546-554.

22. Lee JY, Kim JM, Lee KY, Kim B, Lee MY, et al. (2020) Relationships between obesity, nutrient supply and primary open angle glaucoma in Koreans. Nutrients 12(3): 1-13.

23. Lee SY, Tseng VL, Kitayama K, Thomas JA, Fei Y, et al. (2023) Associations Between Niacin Intake and Glaucoma in the National Health and Nutrition Examination Survey. J Glaucoma 32(6): 443-450.

24. Taechameekietichai T, Chansangpetch S, Peerawaranun P, Lin SC (2021) Association between Daily Niacin Intake and Glaucoma: National Health and Nutrition Examination Survey. Nutrients 13(12): 4263.

25. Tittler EH, de Barros DSM, Navarro JBVK, Freitas DG, Gheith ME, et al. (2008) Oral niacin can increase intraocular pressure. Ophthalmic surgery, lasers imaging 39(4): 341-342.

26. Turgut B, Kaya M, Arslan S, Demir T, Guler M, et al. (2010) Levels of circulating homocysteine, vitamin B6, vitamin B12, and folate in different types of open-angle glaucoma. Clin Interv Aging 5: 133-139.

27. Kang JH, Loomis SJ, Wiggs JL, Willett WC, Pasquale LR (2014) A Prospective Study of Folate, Vitamin B6, and Vitamin B12 Intake in Relation to Exfoliation Glaucoma or Suspected Exfoliation Glaucoma. JAMA Ophthalmol 132(5): 549-559.

28. Atalay K, Savur FG, Kirgiz A, Kaldırım HE, Zengi O (2019) Serum levels of thyroid hormone, vitamin D, vitamin B12, folic acid, C-reactive protein, and hemoglobin in Pseudoexfoliation and primary open angle Glaucoma. J Fr Ophtalmol 42(7): 730-738.

29. Turkcu FM, Koz OG, Yarangumeli A, Oner V, Kural G (2013) Plasma homocysteine, folic acid, and vitamin B_{12} levels in patients with pseudoexfoliation syndrome, pseudoexfoliation glaucoma, and normotensive glaucoma. Medicina (Kaunas) 49(5): 214-218.

30. Wang SY, Singh K, Lin SC (2013) Glaucoma and vitamins A, C, and E supplement intake and serum levels in a population-based sample of the United States. Eye 27(4): 487-494.

31. Yuki K, Murat D, Kimura I, Ohtake Y, Tsubota K (2010) Reduced-serum vitamin C and increased uric acid levels in normal-tension glaucoma. Graefe's Arch Clin Exp Ophthalmol 248(2): 243-248.

32. Krefting EA, Jorde R, Christoffersen T, Grimnes G (2014) Vitamin D and intraocular pressure - results from a case -control and an intervention study. Acta Ophthalmol 92(4): 345-349.

33. Vukovic AZ, Knezevic PM, Miskic B, Vatavuk Z, Vukovic RJ, et al. (2016) Association Between Serum Vitamin D Level and Glaucoma in Women. Acta Clin Croat 55(2): 203-208.

34. Kim HT, Kim JM, Kim JH, Lee MY, Won YS, et al. (2016) The Relationship between Vitamin D and Glaucoma: A Kangbuk Samsung Health Study. Korean J Ophthalmol 30(6): 426-433.

35. Yoo TK, Oh E, Hong S (2014) Is vitamin D status associated with open-angle glaucoma? A cross-sectional study from South Korea. Public Health Nutr 17(4): 833-843.

36. Li S, Li D, Shao M, Cao W, Sun X (2017) Lack of Association between Serum Vitamin B_6, Vitamin B_{12}, and Vitamin D Levels with Different Types of Glaucoma: A Systematic Review and Meta-Analysis. Nutrients 9(6): 636.

37. Lee T, Jammal AA, Medeiros FA (2022) Association Between Serum Vitamin D Level and Rates of Structural and Functional Glaucomatous Progression. J Glaucoma 31(7): 614-621.

38. Dikci S, Ozturk E, Fırat PG, Yılmaz T, Taskapan MC, et al. (2019) The Association of Serum Vitamin D Levels with Pseudoexfoliation Glaucoma/Syndrome. Endocr Metab Immune Disord Drug Targets 19(2): 166-170.

39. Yu AL, Moriniere J, Welge-Lussen U (2013) Vitamin E reduces TGF-beta2-induced changes in human trabecular meshwork cells. Curr Eye Res 38(9): 952-958.

40. Szeto SKH, Chan TCY, Wong RLM, Ng ALK, Li EYM, et al. (2017) Prevalence of Ocular Manifestations and Visual Outcomes in Patients With Herpes Zoster Ophthalmicus. Cornea 36(3): 338-342.

41. Marino PF, Rossi GCM, Campagna G, Capobianco D, Costagliola C, et al. (2020) Effects of Citicoline, Homotaurine, and Vitamin E on Contrast Sensitivity and Visual-Related Quality of Life in Patients with Primary Open-Angle Glaucoma: A Preliminary Study. Molecules 25(23): 5614.

42. Parisi V, Centofanti M, Gandolfi S, Marangoni D, Rossetti L, et al. (2014) Effects of coenzyme Q10 in conjunction with vitamin E on retinal-evoked and cortical-evoked responses in patients with open-angle glaucoma. J Glaucoma 23(6): 391-404.

43. Xiong K, Zhang Q, Mao H, Congdon N, Liang Y (2024) Assessment of Causality Between Diet-Derived

Antioxidants and Primary Open-Angle Glaucoma: A Mendelian Randomization Study. Translational Vision Science & Technology 13(2): 20.

44. Goldblum D, Meyenberg A, Mojon D, Tappeiner C, Frueh BE (2009) Dietary tocopherol supplementation after trabeculectomy and phacotrabeculectomy: double-blind randomized placebo-controlled trial. Ophthalmologica 223(4): 228-232.

45. Engin KN, Engin G, Kucuksahin H, Oncu M, Engin G, et al. (2007) Clinical evaluation of the neuroprotective effect of alpha-tocopherol against glaucomatous damage. Eur J Ophthalmol 17(4): 528-533.

46. Zhang Y, Zhao Z, Ma Q, Li K, Zhao X, et al. (2023) Association between dietary calcium, potassium, and magnesium consumption and glaucoma. PLoS One 18(10): e0292883.

47. Wang SY, Singh K, Lin SC (2012) The Association between Glaucoma Prevalence and Supplementation with the Oxidants Calcium and Iron. Invest Ophthalmol Vis Sci 53(2): 725-731.

48. Kang JH, Ivey KL, Boumenna T, Rosner B, Wiggs JL, et al. (2018) Prospective study of flavonoid intake and risk of primary open-angle glaucoma. Acta Ophthalmol 96(6): e692-e700.

49. Keech AC, Mitchell P, Summanen PA, O'Day J, Davis TM, et al. (2007) Effect of fenofibrate on the need for laser treatment for diabetic retinopathy (FIELD study): a randomised controlled trial. Lancet 370(9600): 1687-1697.

50. Giaconi JA, Yu F, Stone KL, Pedula KL, Ensrud KE, et al. (2012) The association of consumption of fruits/ vegetables with decreased risk of glaucoma among older African-American women in the study of osteoporotic fractures. Am J Ophthalmol 154(4): 635-644.

51. Park JW, Kwon HJ, Chung WS, Kim CY, Seong GJ (2011) Short-term effects of Ginkgo biloba extract on peripapillary retinal blood flow in normal tension glaucoma. Korean J Ophthalmol 25(5): 323-328.

52. Quaranta L, Bettelli S, Uva MG, Semeraro F, Turano R, et al. (2003) Effect of Ginkgo biloba extract on preexisting visual field damage in normal tension glaucoma. Ophthalmology 110(2): 354-359.

53. Guo X, Kong X, Huang R, Jin L, Ding X, et al. (2014) Effect of Ginkgo biloba on visual field and contrast sensitivity in Chinese patients with normal tension glaucoma: a randomized, crossover clinical trial. Invest Ophthalmol Vis Sci 55(1): 110-116.

54. Shim SH, Kim JM, Choi CY, Kim CY, Park KH (2012) Ginkgo biloba extract and bilberry anthocyanins improve visual function in patients with normal tension glaucoma. J Med Food 15(9): 818-823.

55. Ohguro H, Ohguro I, Katai M, Tanaka S (2012) Two-year randomized, placebo-controlled study of black currant anthocyanins on visual field in glaucoma. Ophthalmologica 228(1): 26-35.

56. Ohguro H, Ohguro I, Yagi S (2013) Effects of black currant anthocyanins on intraocular pressure in healthy volunteers and patients with glaucoma. Journal of Ocular Pharmacology and Therapeutics 29(1): 61-67.

57. Terai N, Gedenk A, Spoerl E, Pillunat LE, Stodtmeister R (2014) The short-term effect of flavonoid-rich dark chocolate on retinal vessel diameter in glaucoma patients and age-matched controls. Acta Ophthalmol 92(5): e341-5.

58. Wu CM, Wu AM, Tseng VL, Yu F, Coleman AL (2018) Frequency of a diagnosis of glaucoma in individuals who consume coffee, tea and/or soft drinks. Br J Ophthalmol 102(8): 1127-1133.

59. Bae JH, Kim JM, Lee JM, Song JE, Lee MY, et al. (2020) Effects of consumption of coffee, tea, or soft drinks on open-angle glaucoma: Korea National Health and Nutrition Examination Survey 2010 to 2011. PLoS One 15(7): e0236152.

60. Chandrasekaran S, Rochtchina E, Mitchell P (2005) Effects of caffeine on intraocular pressure: the Blue Mountains Eye Study. J Glaucoma 14(6): 504-507.

61. Kang JH, Willett WC, Rosner BA, Hankinson SE, Pasquale LR (2008) Caffeine consumption and the risk of primary open-angle glaucoma: a prospective cohort study. Invest Ophthalmol Vis Sci 49(5): 1924-1931.

62. Jiwani AZ, Rhee DJ, Brauner SC, Gardiner MF, Chen TC, et al. (2012) Effects of caffeinated coffee consumption on intraocular pressure, ocular perfusion pressure, and ocular pulse amplitude: a randomized controlled trial. Eye (Lond) 26(8): 1122-1130.

63. Pasquale LR, Wiggs JL, Willett WC, Kang JH (2012) The Relationship between caffeine and coffee consumption and exfoliation glaucoma or glaucoma suspect: a prospective study in two cohorts. Invest Ophthalmol Vis Sci 53(10): 6427-6433.

64. Kang JH, Pasquale LR, Willett W, Rosner B, Egan KM, et al. (2003) Antioxidant intake and primary open-angle

glaucoma: a prospective study. Am J Epidemiol 158(4): 337-346.

65. Aydin B, Onol M, Hondur A, Kaya MG, Ozdemir H, et al. (2010) The effect of oral magnesium therapy on visual field and ocular blood flow in normotensive glaucoma. Eur J Ophthalmo 20(1): 131-135.
66. Akyol N, Değer O, Keha EE, Kiliç S (1990) Aqueous humour and serum zinc and copper concentrations of patients with glaucoma and cataract. Br J Ophthalmol 74(11): 661-662.
67. Hohberger B, Chaudhri MA, Michalke B, Lucio M, Nowomiejska K, et al. (2018) Levels of aqueous humor trace elements in patients with open-angle glaucoma. J Trace Elem Med Biol 45: 150-155.
68. Bruhn RL, Stamer WD, Herrygers LA, Levine JM, Noecker RJ (2009) Relationship between glaucoma and selenium levels in plasma and aqueous humour. Br J Ophthalmol 93(9): 1155-1158.
69. Zhao R, Liu T, Zhao B (2024) Association of daily selenium intake and glaucoma: A cross-sectional study. Medicine 103(36): e39573.
70. Zawadzka I, Młynarczyk M, Falkowska M, Socha K KJ (2024) Dietary patterns; serum concentrations of selenium, copper, and zinc; copper/zinc ratio; and total antioxidant status in patients with glaucoma. PLoS One 19(4): e0301511.
71. Choi JS, Lee MS, Jeong JW (2010) Ethyl pyruvate has a neuroprotective effect through activation of extracellular signal-regulated kinase in Parkinson's disease model. Biochem Biophys Res Commun 394(3): 854-858.
72. Williams PA, Casson RJ (2024) Glycolysis and glucose metabolism as a target for bioenergetic and neuronal protection in glaucoma. Neural Regen Res 19(8): 1637-1638.
73. Buckingham T, Young R (1986) The rise and fall of intra-ocular pressure: the influence of physiological factors. Ophthalmic Physiol Opt 6(1): 95-99.
74. Kahn HA, Milton RC (1980) Alternative definitions of open-angle glaucoma. Effect on prevalence and associations in the Framingham eye study. Arch Ophthalmol 98(12): 2172-2177.
75. Xu L, You QS, Jonas JB (2009) Prevalence of alcohol consumption and risk of ocular diseases in a general population: the Beijing Eye Study. Ophthalmology 116(10): 1872-1879.
76. Kang JH, Willett WC, Rosner BA, Hankinson SE, Pasquale LR (2007) Prospective study of alcohol consumption and the risk of primary open-angle glaucoma. Ophthalmic Epidemiol 14(3): 141-147.
77. Bonyadi MHJ, Yazdani S, Saadat S (2014) The ocular hypotensive effect of saffron extract in primary open angle glaucoma: a pilot study. BMC Complement Altern Med 14: 399.