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Unique Australian Native Botanical - Lemon Myrtle as a Natural Source of Ocular Health Super-Nutrient

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Abstract

A uniquely Australian botanical called lemon myrtle or Backhousia citriodora has been used for thousands of years by Indigenous Australians for food and health purposes.

Some of the key nutrients of lemon myrtle are lutein, other antioxidants like vitamin E and polyphenols, magnesium, and calcium. Lutein is a naturally occurring carotenoid antioxidant which can reduce the risk of ocular diseases like cataracts and Age-Related Macular Degeneration (AMD). Additionally, vitamin E present in the lemon myrtle may neutralise the effect of solar radiations and Reactive Oxygen Species (ROS) and in turn reduce the risk of developing AMD. Additionally, vitamin E along with lutein and zeaxanthin has been found to decrease the risk of cataracts. Magnesium in lemon myrtle can maintain normal metabolism and ionic balances in ocular tissues and reduce ocular diseases such as glaucoma, cataracts, and diabetic retinopathy.

As such, dietary requirements for lutein have not been established so far. A recommended daily allowance (RDA) or a recommended daily intake (RDI) of 10 mg/day of lutein is suggested by the American Optometric Association. Lemon myrtle, which is mostly used as a flavor and fragrance food ingredient, can help to achieve a substantial part of RDA or RDI through foods or nutraceutical supplements.

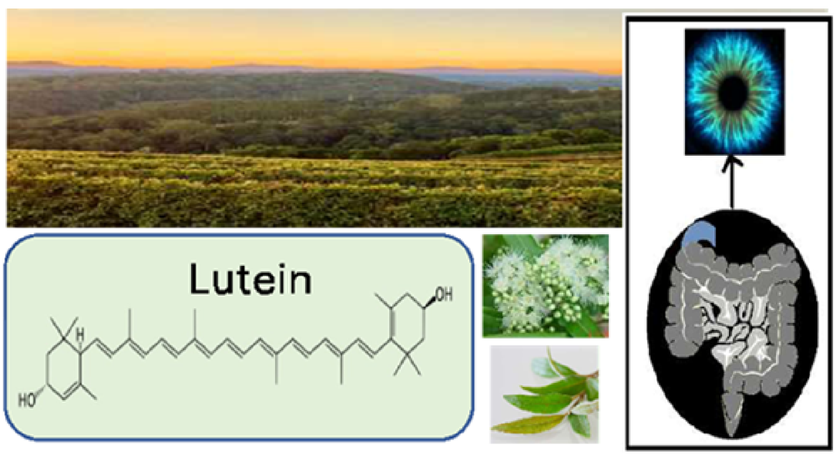
Combining Lutein with other antioxidants (vitamin E and polyphenols), calcium, magnesium, phenolics, flavonoids, and folate make lemon myrtle a super-nutrient for ocular health nutritional products.

Graphical Abstract

A uniquely Australian native botanical - lemon myrtle (Backhousia Citriodora) exhibits a potent combination of antioxidants (lutein, vitamin E and polyphenols), magnesium and calcium that can be used to explore the gut - retina axis and develop ocular (beauty and wellness) products (Graphical Abstract Figure).

Article Highlights

- This may be the first article to highlight the potential use of the unique Australian



Abstract Figure: Unique Australian Native Botanical -Backhousia Citriodora As A Natural Source of Ocular Health Nutrient

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botanical, lemon myrtle, for ocular health.

- Lemon myrtle is a natural phytoalexin and a plant-based source of lutein and other micronutrients that can be used for the gut-retina axis research and ocular health benefits
- Not many plant-based sources of lutein are currently available, therefore lemon myrtle provides opportunities to develop lutein-based eye wellness products
- Considered to be the queen of lemon flavour and fragrance, lemon myrtle can be used to develop uniquely lemon flavoured ocular health nutraceutical products

Keywords

Lemon Myrtle; Lutein; Magnesium; Vitamin E; Calcium; Australian Native Botanicals; AMD; Cataracts; Glaucoma; Nutrition; Ocular Health

Abbreviations

Alpha-TC: Alpha-Tocopherol; ATP: Adenosinetriphosphate; AMD: Age-Related Macular Degeneration; ARC: Age-Related Cataract; AREDS: Age-Related Eye Disease Study; AREDS2 Age-Related Eye Disease Study 2 ARM: Age-Related Maculopathy; HLE: Human Lens Epithelial; IL: interleukin; IU: International Units; JNK: c-JUN NH2-Terminal Kinase; ORAC: Oxygen Radical Absorbance Capacity; OSL: Observed Safe Level; RDA: Recommended Daily Allowance; RDI: Recommended Daily Intake; ROS: Reactive Oxygen Species; RIRDC: Rural Industries Research & Development Centre; UVB: Ultraviolet B

Introduction

Background of Lemon Myrtle

Lemon myrtle, a unique Australian botanical, is endemic to subtropical rainforests of the central and south-eastern Queensland region of Australia [1]. It is one of the Australian native botanicals which exhibits both unique beauty, and wellness properties. Lemon myrtle has been used by Indigenous Australians for food and healthcare purposes for thousands of years [2,3]. Its botanical name is "Backhousia citriodora" and the most common chemotype is "Backhouse citriodora F. Muell" [4].

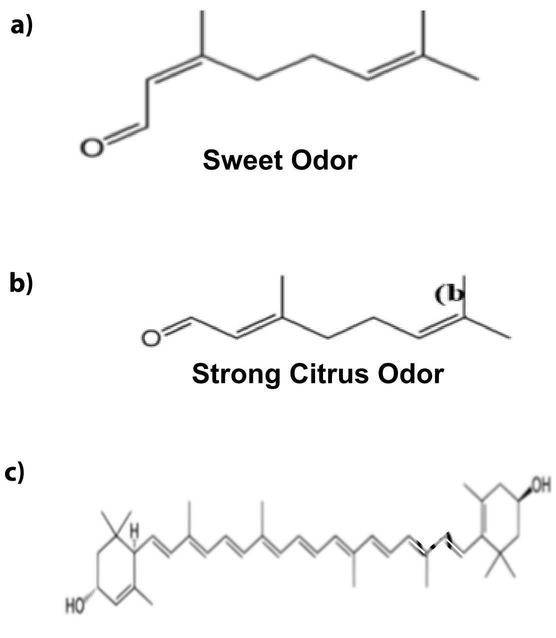

Figure 1: a: Chemical structure of Neral (Citral α)
b) Chemical structure of Geranial (Citral β)
C) Chemical structure of Lutein

Lemon myrtle was named as Backhousia citriodora after James Backhouse in 1853 [2]. Schimmel and Co of Dresden Pharmaceutical Company isolated and identified the high citral content (>90%) in leaf oil in 1888 [4]. During World War II, lemon myrtle leaf oil was used (due to a shortage of lemons) in soft drinks by Tarax Pty Ltd and exported to the Australian troops in the Pacific. From the early 1900s, the foliage was harvested from lemon myrtle trees in Queensland, with the distilled lemon myrtle oil then exported to Europe and the United States.

The flavour lexicon is refreshingly intense with citrus notes that originate from the presence of neral (Citral α) (Figure 1a) which imparts a lemon note and geranial (Citral β) (Figure 1b) which imparts a sweet note [5]. Due to its unique fragrance, lemon myrtle is considered to be the queen of lemon fragrance.

Lemon myrtle is an unique botanical as it has the highest natural source of citral (90-96%) in the world when compared to litsea citrata (90%), litsea cubeba (70-85%), lemongrass (65-85%), lemon tea-tree (70-80%), ocimum gratissimum (66.5%), lindera citriodora (about 65%), calypranthes parriculata (about 62%), petitgrain (36%), lemon verbena (30-35%), lemon ironbark (26%), lemon balm (11%), lime (6-9%), lemon (2-5%), and orange (2-5%) [6].

In addition to citral, lemon myrtle also contains key micronutrients such as magnesium, calcium, antioxidants such as lutein (Figure 1c), vitamin E and phenolics (ellagic acid, cinnamic acid and flavonoids), and folate (Table 1) [5,7]. Table 1 summarises lemon myrtle's key micronutrients and their functions in comparison to other plant-based ingredients. Lemon myrtle exhibits better antioxidant properties than green tea, pomegranate, goji berry, blueberry, etc., and better antimicrobial properties than tea tree oil [8,9,10,11].

Lemon myrtle is recognized as a food ingredient under the European novel food category, European Herbal Infusions Association, Food Standards Australia New Zealand, and the CODEX Alimentarius. These regulations allow it to be used in food as well as in nutraceutical foods. The tolerable upper intake level of lutein is not set by the U.S. Food and Drug Administration or the European Food Safety Authority so far as it is not considered an essential nutrient. OSL of lutein for humans is 20 mg/day based on a non-government organization evaluation [12]. Shao and Hathcock [12] have found no adverse effects for high levels of lutein, but more work is needed to establish its long-term safety.

Ocular Diseases

Cataracts, glaucoma, and AMD are some of the common causes of blindness. Glaucoma is a leading cause of irreversible vision loss globally [13,14]. AMD is a complex multifactorial disease which can cause legal and irreversible blindness among individuals aged ≥65 years in developed countries. It affects 30-50 million people globally and is projected to increase by around 200 million by 2020 (at a cost of $300 billion) [15, 16] and 300 million by 2040 [17]. Early detection biomarkers developed for AMD are not yet developed [16]. A loss of vision is commonly associated with the elderly population with ARC and ARM being two major causes of blindness globally [18].

A low density of macular pigments can lead to greater blue light damage, leading to one of the key risk factors for AMD [19].

The dietary impact on the gut - retina axis (Figure 2) has been recently explored by Rowan et al. [16]. Low-grade inflammation sustained by dysbiosis and a leaky gut can cause AMD [16]. Micronutrients can alter gut microbiota and reduce leaky gut or other gut associated diseases, which can be associated with ocular issues such as AMD [17]. Other lifestyle factors such as obesity, smoking, and inadequate intake of antioxidants can affect ocular health [20]. Excessive exposure to solar radiation, stress, alcohol, etc. can produce the oxidative stress and inflammation which is responsible for the age-related ocular issues such as glaucoma, cataracts, diabetic

Micronutrient	Benefit	Lemon Myrtle (100g)	Compare	Score (/100g)
Ca	Build and maintain strong bones. Help heart, muscles and nerves to function properly	1583 mg	Spinach Other plants (Refer Table 5)	305mg
Mg	Bone Health. Assimilation of calcium into bone and activate vitamin D in kidneys Calming	188 mg	Spinach Other plants (Refer Table 4)	270mg
ORAC-T value (µ mol TE)	Oxygen Radical Absorbance Capacity (ORAC) assay measures the ability of a food extract to reduce free radicals in vitro. Higher ORAC-T score, better is antioxidant capacity	3360	Blueberry Green Tea Pomegranate Goji Berry Oranges	440 1,253 2860 3290 2103
Phenolics-ellagic acid, cinnamic acid and flavonoids (Antioxidants)	Improve antioxidant efficiency	175 mg	Boysenberry	150mg
Vitamin E (lipophilic vitamin & antioxidant)	May protect cells from damage caused by free radicals	21.2 mg	Almonds Other plants (Refer Table 3)	26.2mg
Lutein (Antioxidant)	Good for eye health. May help to improve visual function and symptoms of atrophic age-related macular degeneration	6.6 mg	Avocado Other plants (Refer Table 2)	0.6-1.1mg
Folate	May help repair & synthesis of DNA	71 g	Blueberry	39 g

Table 1: Micronutrients of lemon myrtle and their functions

retinopathy, macular degeneration, and the progressive loss of vision and blindness [21]. Oxidative stress in particular has been associated with compromised lens and retina [18]. Additionally, Chiu and Taylor [18] have showed that glycation and glycoxidation are major molecular insults resulting in oxidative stress, which can damage the vision.

Role of Plants - Based Nutrients

Phytochemicals such as antioxidants and anti-inflammatory agents may prevent or delay the progression of ocular diseases [20]. The research on nutrition-based preventions can be cost-effective in terms of considerable financial savings and improvements in the quality of health [18]. Nutrition, particularly antioxidants, may help to reduce the risk of ARC and ARM [18]. Nutrition therapy can be helpful for the ocular health of the growing elderly population globally as surgical resources are insufficient in providing economical and safe treatments for cataracts or cure ARM.

Researchers have identified some of vegetables or plant-based ingredients that can help to protect or improve ocular health [21] and have demonstrated that plant-based antioxidants can help reduce the effect of solar or air pollution and subsequently reduce the free radicals such as ROS. Rhone et al. [20] have suggested that phytochemicals such as green tea catechins, anthocyanins, resveratrol, and ginkgo biloba can ameliorate ocular ocular oxidative stress [22]. Additionally antioxidants and antioxidant cofactors such as vitamins A, C, zinc, anti-free-radicals such as beta-carotene, carotenoids (lutein and zeaxanthin), micronutrients can protect from blue light [20]. Moreover, the components of the membranes of the photoreceptors of docosahexaenoic acid that are involved in the pathogenesis of AMD can help to protect ocular systems against environmental risks factors such as smoking and chronic blue light exposure [20]. Initial studies have demonstrated positive effects of above-mentioned nutrients at stages 3 and 4 of AMD. Hogg and Charkavarthy [23] have demonstrated that antioxidant supplements can help to prevent progression of ARM to AMD (which is the late-stage manifestations of ARM). Plant-based antioxidants such as resveratrol have been studied to protect or improve ocular health. Resveratrol, a natural phytophenol obtained from grapes, exhibits pleiotropic properties [24]. It has been widely studied to minimise numerous pathways including oxidative stress, inflammation, mitochondrial dysfunction, apoptosis, pro-survival, or angiogenesis that are implicated in the pathogenesis of age-related ocular disorders [21]. In addition to polyphenols, flavonoids such as curcumin can help minimise retinal diseases [25,26]. Moreover, higher dietary nitrate and leafy green vegetable intake can help to reduce the primary open-angle glaucoma risk [27].

The present article focuses on some on the micronutrients present in lemon myrtle and their potential use for ocular health.

Micronutrients of Lemon Myrtle and their Potential Use in Ocular Healthcare

As seen in from table 1, lemon myrtle contains antioxidants such as lutein, vitamin E and polyphenols, and magnesium, and calcium.

Role of Lutein for Ocular Health

Lutein is related to beta-carotene and vitamin A, and is synthesized mostly by plants. Some of the current well-known sources of lutein are leafy green vegetables, broccoli, corn, kiwi fruit, grapes, orange, zucchini, and squash. Lutein is lipophilic in nature and is absorbed easily in tissues from a high-fat diet. Lutein is found in the lens, retina, and macula of the eyes and acts as a light filter to protect the ocular tissues from harmful high-energy light waves like ultraviolet rays in sunlight [28]. The presence of high levels of both lutein and zeaxanthin in ocular tissues like the lens, retina, and macula is linked with better vision, especially in dim light or where glare is a problem [28]. Extensive research has been conducted on

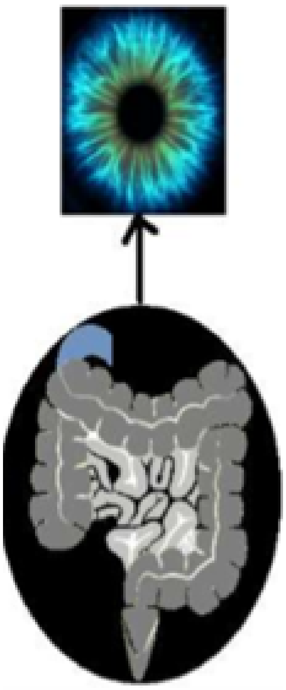

Figure 2: Schematic of Gut-retina axis

lutein and its benefits for ocular health. Some of the literature is discussed as follows.

Dietary xanthophylls lutein, zeaxanthin, and another xanthophyll, meso-zeaxanthin, impart a yellow colour to the macular region of the primate retina [29]. These pigments can absorb blue-light and protect the underlying photoreceptor cell layer from light damage, possibly initiated by the formation of ROS during a photosensitized reaction. There is ample epidemiological evidence available to demonstrate that the concentration of macular pigments is inversely associated with the incidence of ADM. The high concentrations of lutein and zeaxanthin in the retina and lens have found potential applications in the prevention and treatment of age-related diseases such as macular degeneration, cataracts, and retinitis pigmentosa, and blue-light filtering activities [30]. Recently, Bungau et al. [31] have also demonstrated that phytochemicals like carotenoids (e.g. lutein, zeaxanthin, and mezoxanthin) and polyphenols (e.g. anthocyanins, ginkgo biloba, quercetin, and resveratrol) with their antioxidant and anti-inflammatory activities can help to reduce age-related ocular abnormalities such as cataracts, glaucoma, diabetic retinopathy, and macular degeneration. These antioxidants can mitigate the production of ROS, inhibit the tumour necrosis factor-α and vascular endothelial growth factor pathways, suppress p53-dependent apoptosis, and suppress the production of inflammatory markers such as IL-8, IL-6, IL-1a and endothelial leucocyte adhesion molecule-1. These mechanisms of carotenoids and polyphenols and their combinations can help prevent and/or treat age-related eye diseases that are induced or augmented by oxidative stress and inflammation.

Stahl [33] has reported that lutein and zeaxanthin can quench the excited triplet state molecules or singlet molecular oxygen and scavenge further ROS like lipid peroxides or the superoxide radical anion and protect ocular tissues from photooxidative Damage. Trevithick-Sutton et al. [32] have studied the scavenging of superoxide and hydroxyl radicals by mixtures of carotenoids (Lycopene, beta-carotene, zeaxanthin and lutein) using the Electron Spin Resonance (ESR) and luminescent assay, and found that these carotenoids can scavenge the hydroxyl radicals more effectively than superoxide radicals, and that lycopene and beta-carotene are better than zeaxanthin and lutein in scavenging hydroxyl radicals. However, Siems et al. [34] have suggested that major carotenoids of human plasma and tissues are susceptible to radical-initiated autoxidation conditions. Authors (Siems et al.) [34] have compared the stability of lutein and zeaxanthin with lycopene and beta-carotene. Lycopene and beta-carotene are the most effective quenchers of singlet oxygen in plasma. Authors (Siems et al. 1999) [34] have found that lycopene and beta-carotene degrade faster than that of lutein and zeaxanthin under all conditions of free radical-initiated autoxidation of carotenoids.

When exposed to UV light in the presence of Rose Bengal, beta-carotene exhibits a higher breakdown rate than lycopene. Bleaching of carotenoid mixtures using NaOCl, in addition with azo-bis-isobutyronitril, and the photoirradiation of carotenoid mixtures by natural sunlight lead, to the following sequence of breakdown rates: lycopene > beta-carotene > zeaxanthin > lutein. The slow degradation of the xanthophylls zeaxanthin and lutein can be attributed to the fact that these two xanthophylls reside in the human retina and are protected against solar degradation. Beta-carotene and lycopene are not present in the human retina, which may explain their rapid degradation when exposed to natural sunlight and UV light. However, more research needs to be done to confirm these findings.

Bone et al. [35] have showed that lutein exceeds zeaxanthin in plasma but that the combined zeaxanthin stereoisomers exceed lutein in the retina. Lutein, zeaxanthin, and meso-zeaxanthin are three predominant macular pigments [36] which exhibit dual functions as filters and antioxidants, and protect the macula, particularly in ADM. Thus, high levels of these macular pigments can be correlated with a decreased risk of ADM [36]. Indeed, oral supplements of lutein and zeaxanthin have been found to increase the levels of macular pigments in the retina and plasma and reduce ADM [36,20]. Rhone et al [20]. have demonstrated that women in the highest quintiles of lutein/zeaxanthin intake (6.7 mg/day) exhibited a significantly lower risk of developing cataracts compared to women in the lowest dose (1.2 mg/day). Additionally, in the 6–12-month 'Lutein Xanthophyll Eye Accumulation' study involving 101 healthy Caucasian males receiving daily supplementation of either lutein (11 mg), zeaxanthin (13 mg), or a combination (10 mg lutein with 12 mg zeaxanthin), has demonstrated a significant improvement in macular pigment optical density responses compared to placebo. Furthermore, clinical trials have showed that lutein and zeaxanthin are safe at higher doses and can improve the macular pigment optical density, visual acuity, and glare sensitivity [37,38]. Based on these findings, Rhone et al. [20] have suggested incorporating 2-3 daily servings of green leafy vegetables that contained lutein and zeaxanthin in addition to green tea, grapes, and berries in the diet, practicing weight management and avoiding certain unhealthy lifestyle factors to preserve the ocular health. Moreover, from AREDS, Desmettre et al. [22] have developed a cocktail of micronutrients containing lutein and zeaxanthin, and found that these micronutrients are better than beta-carotenes to prevent complications of AMD (as a secondary prevention). Recently, [39] have showed that lower levels of lutein and zeaxanthin have a significant relationship with adverse quantitative measures of retinal vasculature in elderly Singaporean Chinese healthy subjects.

Landrum and Bone [40] have demonstrated that increased macular carotenoid pigments (lutein, zeaxanthin, and meso-zeaxanthin) through dietary supplements can protect against light-induced retinal damage and AMD. Additionally, Bone et al. [41] confirmed that low levels of lutein and zeaxanthin in the diet, serum or retina, and the excessive exposure to blue light can lead to photoreceptor death within the macula and AMD. Light-screening capacity and antioxidant activity of these two macular pigments may reduce photooxidation in the central retina.

Moeller et al. [42] have studied a relationship between macular pigment optical density, the concentration of a marker of lutein and zeaxanthin in the macula, lens optical density, and an antecedent of cataractous changes. Authors Moeller et al. [42] have found that the xanthophylls may act to protect the eye from ultraviolet phototoxicity via quenching ROS and/or other mechanisms. Moreover, Moeller et al. [42] have found that generous intakes of lutein and zeaxanthin, particularly from certain xanthophyll-rich foods like spinach, broccoli and eggs, are associated with up to 20% reduction in the risk for cataracts and up to 40% reduction for ADM. Even though the pathophysiology of cataracts and ADM is complex due to environmental and genetic factors, dietary supplements including antioxidant vitamins and xanthophylls may contribute to a reduction in the risk of these degenerative eye diseases.

Landrum et al. [19] have studied the effects of a lutein supplement for 140 days on two subjects and measured the optical density of macular pigment using the heterochromatic flicker photometry method and analysing blood samples by the high-performance liquid chromatography method. They found that a lutein supplement helps to reduce blue light penetration by 30-40% the vulnerable tissues affected by AMD such as the photoreceptors, Bruch's membrane, and the retinal pigment epithelium. Additionally, Authors [19] have found that people who ate green vegetables rich in zeaxanthin like spinach, kale, and broccoli may be half as likely to get cataracts. Therefore, the supplements containing lutein and zeaxanthin can slow down the macular degeneration process and in turn can help to reduce damage to the middle of retina and central vision.

Chitchumroonchokchai et al. [43] have studied the effects of lutein, zeaxanthin, astaxanthin, and alpha-TC on the lipid peroxidation and the mitogen-activated stress signalling pathways in HLE cells following the Ultraviolet B (UVB) light irradiation. When a combination of lutein, zeaxanthin, astaxanthin, and methyl-beta-cyclodextrin complexes of alpha-TC were applied to HLE cells, the HLE cells were found to accumulate the lipophiles in a concentration-dependent and time-dependent manner with an uptake of lutein exceeding that of zeaxanthin and astaxanthin. Chitchumroonchokchai et al. [43] have found that the pre-treatment of cultures with either 2 micromol/L xanthophyll or 10 micromol/L alpha-TC for 4 hours before the exposure to 300 J/m^2 UVB radiation had decreased the lipid peroxidation by 47-57% in comparison to UVB-treated control HLE cells. The pre-treatment of HLE cells with the xanthophylls and alpha-TC also inhibited the UVB-induced activation of JNK and p38 by 50-60% and 25-32%, respectively.

Additionally, a substantial inhibition of UVB-induced JNK and p38 activation is released for the cells containing <0.20 nmol xanthophylls/mg and approximately 0.30 nmol xanthophylls/mg respectively, whereas >2.3 nmol alpha-TC/mg protein required to significantly decrease UVB-induced stress signalling. Based on this data, authors [42] have suggested that xanthophylls are more potent than alpha-TC for protecting human lens epithelial cells against UVB insult.

Plant-based sources of lutein-zeaxanthin [44] are provided in Table 2. Lemon myrtle contains a substantial amount of lutein compared to other plant based ingredients and can be used for ocular health.

Source	Lutein/Zeaxanthin (mg)
Kale (Cooked)	19.7
Spinach (Cooked)	11.31
Collards (Cooked)	10.9
Turnip Greens (Cooked)	8.44
Garden Cress (Cooked)	8.4
Lemon Myrtle (Raw)	6.6
Mustard Green (Cooked)	5.96
Arugula (Raw)	3.55
Dandelion Green (Cooked)	3.4
Sweet Potato leaves (Cooked)	2.63
Green Peas (Cooked)	2.59
Beet Greens (Cooked)	1.82
Broccoli Rabe (Cooked)	1.68
Brussels Sprouts (Cooked)	1.29
Yellow Sweet Corn	1.05
Pumpkin (Cooked)	1.29
Carrots (Raw)	0.36

Table 2: Plant based sources of lutein/zeaxanthin [44].

Role of Vitamin E and Polyphenols (Antioxidants) for Ocular Health

Chiu and Taylor [18] have reviewed epidemiological literature about ARC and ARM with emphasis on functions of vitamins C and E and carotenoids and suggested that AMD and cataracts, which are due to the cumulative effects of oxidative stress, can be cured or prevented using antioxidant nutrients such as vitamin E. Prospective cohort studies completed by Chong et al. [45] and Evans [65] have found that people with relatively high dietary intakes of vitamin E (30 IU/day) have an approximately 20% lower risk of developing AMD than people with low intakes (<15 IU/day). Moreover, the AREDS's clinical trial (AREDS, 2001) [46] has demonstrated that people with high risk of developing the advanced AMD (either with intermediate AMD or with advanced AMD in one eye) have reduced the risk of developing advanced AMD by 25% by consuming a daily supplement containing 400 IU dl-alpha-tocopherol acetate along with 15mg beta-carotene, 500mg vitamin C, 80mg zinc, and 2mg copper compared to participants taking a placebo over 5 years. Also, Leske et al. [47] have showed that the dietary composition containing vitamin E (as an antioxidant) can protect against cortical, nuclear, and mixed cataracts.

Additionally, Leske et al. [48] have demonstrated that the lens clarity is superior with participants who took vitamin E supplements or with higher blood levels of vitamin E. Also, a long-term use of vitamin E supplements has been associated with slower progression of age-related lens opacification [49]. However, the AREDS trial [50] has demonstrated that the use of a vitamin E-containing formulation do not have any effect on the development or progression of cataracts over an average of 6.3 years. The AREDS2 study [51] also confirmed that the formulations containing 400 IU vitamin E do not affect the progression of age-related lens opacification. The overall results are inconsistent with vitamin E supplements either taken alone or in combination with other antioxidants that reduce the risk of developing AMD or cataracts. At the same time, the formulations containing vitamin E with other antioxidants, zinc, and copper used in AREDS showed some promise for slowing the progression of AMD in people at high risk of developing advanced AMD.

Plant based sources of vitamin E are provided in table 3 and shows that lemon myrtle has asubstantial amount of vitamin E when compared to other plant-based sources and can be used for ocular health.

Role of Magnesium for Ocular Health

Magnesium helps to maintain the structural and functional integrity of several vital ocular tissues such as cornea, lens, and retina. The magnesium content of lens, particularly in its peripheral part, is higher than that in aqueous and vitreous humor.

Recently, Agarwal et al. [52,53,54,55] have studied the effect of magnesium on ocular health which is discussed as follows. Membrane associated ATPase functions that are crucial in regulating the intracellular ionic environment are dependent on magnesium. Additionally, the enzymes involved in the ATP production and hydrolysis need magnesium. A magnesium deficiency can interfere with ATPase functions, calcium and sodium levels, decrease the intracellular potassium concentration and create the ionic imbalances which can alter the other cellular enzymatic reactions and lead magnesium deficient ocular diseases such as cataracts. In addition to cataracts, the magnesium deficiency can cause an imbalance between mediators of vasoconstriction and vasorelaxation resulting in vasospasm, which is one of the pathogenic factors in primary open angle glaucoma. Furthermore, magnesium deficiency can contribute to increased oxidative stress and inducible NOS stimulation that can further contribute in the initiation and progression of ocular pathologies such as cataracts, glaucoma, and diabetic retinopathy.

The association of hypomagnesemia and supplementation of magnesium in the management of eye diseases was recently studied by Ajith [56]. Glaucoma, senile cataracts, and diabetic retinopathy are attributed with a low level of extracellular magnesium [56]. The neurovascular protective effects of magnesium are generally mediated through the activation of endothelial nitric oxide synthase and the inhibition of endothelin-1, which result in vasodilatation of the retinal vessels. It can maintain the lens sodium pump activity, antioxidant status, block the calcium ion channels, and release glutamate in nerve endings. Additionally, magnesium can prevent the apoptosis of retinal ganglion cells. Therefore, magnesium can be considered as a pharmacological agent to manage glaucoma, cataracts, and diabetic retinopathy. However, more clinical trials are required confirm the findings and establish more links between magnesium and ocular health.

Table 4 shows that lemon myrtle has a substantial amount of magnesium when compared to many plant-based sources and can be used for ocular health.

Role of Calcium for Ocular Health

Krizaj and Copenhagen [57] has studied the intricate mechanisms through which calcium ion contributes to detection, transduction, and synaptic transfer of light stimuli in rod and cone photoreceptors. These authors (Krizaj and Copenhagen, 2002) [57] have found that the function of calcium is highly compartmentalized with the outer segment where calcium controls the photoreceptor light adaptation by independently adjusting the gain of phototransduction at several stages in the transduction chain, whereas in the inner segment and synaptic terminal, it regulates cells metabolism, glutamate release, cytoskeletal dynamics, gene expression, and cell death. Calcium acts as an integrator of intracellular signalling pathways and a second messenger in neuromodulation of photoreceptor signalling by extracellular ligands such as dopamine, adenosine, and somatostatin. The dysfunction in photoreceptor calcium homeostasis and pathologies leads to retinal dysfunction and blindness.

Cataractous lenses have a distribution of the intracellular ionic environment with relatively decreasing concentrations of potassium and magnesium and relatively increasing concentrations of sodium and calcium,compared to the concentration of cytosol of most of the cells [58]. The above-mentioned changes in the ionic environment arises from changes to lens membrane characteristics due to normal aging of the human, lens which results in an increase in lens membrane permeability. In the normal human lens calcium is 0.15-0.5 micromol/g of fresh lens weight whereas in senile cataracts calcium can increase to up to 9.31 micromol/g. The normal levels of sodium, magnesium, and potassium are 20 micromol/g, 5.5 micromol/g and 60 micromol/g respectively, whereas in cataractous senile human lenses sodium, magnesium and potassium are found to be 136.10 micromol/g, 3.60 micromol/g and 9.33 micromol/g which can be attributed cataractogenesis.

Miller et al. [59] have showed that rod and cone photoreceptors respond to light with distinct sensitivity and kinetics. Light or voltage stimulation generates changes in the cytoplasmic concentration of calcium in the outer segments that are far larger and faster in cones than in rods. This distinction reflects rod-cone differences in each of the elements that control calcium homeostasis (such as cell volume, the rate of calcium ion clearance) from the outer segment, the cytoplasmic calcium ion buffering, and the calcium ion influx through cGMP-gated ion channels. This shows that calcium is an important micronutrient to control the functions of rods and cones of the eyes. Lemon myrtle contains a substantial (Table 5) amount of calcium in comparison to other plant-based ingredients and can be used for ocular health.

Potential of Lemon Myrtle for Ocular Health

A uniquely Australian botanical called lemon myrtle (Backhousia Citriodora) has been used for thousands of years for health purposes by Indigenous Australians. Lemon myrtle flowers and leaves are depicted in (Figure 3).

As discussed in the present article, lutein is a naturally occurring carotenoid which can reduce the risk of cataracts and AMD. Additionally, vitamin E can be used to neutralise the effect of solar radiations, subsequent formation of ROS, and in turn may help to reduce the risk of developing advanced AMD. Vitamin E, along with lutein and zeaxanthin, may decrease the risk of cataracts. Magnesium may help to maintain normal metabolism and ionic balances in ocular tissues and reduce ocular diseases such as glaucoma, cataracts, and diabetic retinopathy. Calcium is important for the functions of cones and rods.

Lemon myrtle contains a substantial amount of lutein (Table 2), antioxidants such as vitamin E (Table 3), polyphenols, magnesium, (Table 4) and calcium (Table 5) that can help ocular health.

Lemon myrtle (100g) contains 6.6mg of lutein, which is higher than lutein and zeaxanthin found in other plants (Table 2), and is useful for a broad range of ocular health related functions. The dietary requirements for lutein have not been established so far. RDA or RDI of 10mg/day of lutein is suggested by the American optometric association. Lemon myrtle can provide substantial part of RDI or RDA of lutein.

Figure 3: Leaves and flowers of lemon myrtle

Source	Vitamin E (mg)
Sunflower Seeds	26.1
Almonds	25.6
Lemon Myrtle	21.2
Olive Oil	14.4
Avocados	2.1
Spinach	2.1
Kiwifruit	1.5
Broccoli	1.5
Butternut Squash	1.3

Table 3: Plant based sources of vitamin E [62].

Source	Magnesium (mg)
Cacao	272
Hemp Seeds	256
Lemon Myrtle	188
Pumpkin Seeds	184
Chia Seeds	130
Sesame Seeds	126
Sunflower Seeds	113
Cashews	110
Almonds	100
Spinach	79
Swiss Chard	81
Beet Greens	70
Black Beans	70
Quinoa	64
Buckwheat	51
Pinto Beans	50
Green Peas	33
Turnip Greens	31
Avocado	29
Beets	23

Table 4: Some plant-based sources of magnesium [64].

Vitamin E (21.2mg/100g) present in the lemon myrtle, can be used to neutralise the effect of solar radiations and subsequent ROS and in turn may help to reduce the risk of developing advanced AMD. Additionally, vitamin E along with lutein and zeaxanthin may decrease the risk of cataracts.

The ORAC value of lemon myrtle is higher than well-known nutrients or superfoods such as blueberry, green tea, pomegranate, goji berry, and oranges (Table 1). Additionally, amounts of phenolics such as ellagic acid, cinnamic acid, and flavonoids present in lemon myrtle are higher than that of boysenberry (Table 1). Therefore, lemon myrtle can help protect eyes from solar and ROS pollutions.

Magnesium (188mg/100g) present in lemon myrtle may help to maintain normal metabolism and ionic balances in ocular tissues and reduce ocular diseases such as glaucoma, cataracts, and diabetic retinopathy.

Calcium (1583mg/100g) present in lemon myrtle can be used for the health of cones and rods.

Other plant-based ingredients [60] such as resveratrol, curcumin, and leafy green vegetables that contained either vitamins, antioxidants, or micronutrients may not contain most of these micronutrients and provide pleasant sensorial effects (aroma or flavour) to consumers.

Lutein, with other antioxidants (vitamin E and polyphenols), calcium, magnesium, phenolics, flavonoids, and folate make lemon myrtle a super-nutrient for use in ocular health nutritional products.

The key ocular nutrients of lemon myrtle, along with its antimicrobial properties, can be explored to understand gut-retina axis and find new mechanisms for ocular health. In addition to important ocular nutrients, lemon myrtle also exhibits a unique flavour and fragrance due to presence of neral and geranial and is referred as the queen of lemon flavour or fragrance.

All of these properties hold lemon myrtle as a potential super-nutrient that can be used to develop a broad range of novel foods or

Source	Calcium (mg)
Basil (Dried)	2240
Sage (Ground)	1652
Lemon Myrtle	1538
Rosemary (Dried)	1280
Cinnamon	1002
Sesame Seeds(Unhulled)	975
Chives	813
Maca Powder	740
Cloves	632
Chia Seeds	631
Spirulina	460
Black Pepper	443
Thyme	405
Carob Powder	348
Almond Butter	347
Soybeans	277
Almonds (Natural)	269
Flaxseed	255
Collard Greens	232
Goji Berry	190
Kelp	168

Table 5: Some plant-based sources of calcium [60]

nutraceutical-based products in the ocular health segment.

Conclusions

Lutein is a naturally occurring carotenoid which can reduce the risk of cataracts and AMD.

Lemon myrtle (100g) contains 6.6mg of lutein, which is higher than lutein and zeaxanthin found in other plants (Table 2) and is useful for a broad range of ocular functions. Additionally, vitamin E (21.2mg/100g), present in lemon myrtle, can be used to neutralise the effect of solar radiations and subsequent ROS and in turn may help to reduce the risk of developing advanced AMD. Vitamin E, along with lutein and zeaxanthin, may decrease the risk of cataracts. Magnesium (188mg/100g) in lemon myrtle may help to maintain normal metabolism and ionic balances in ocular tissues and reduce ocular diseases such as glaucoma, cataracts, and diabetic retinopathy. Calcium (1583mg/100g) present in lemon myrtle can be used for the health of cones and rods.

Additionally, folate present in lemon myrtle may help with exfoliation glaucoma or exfoliation glaucoma suspect [61], but more research is needed.

As such dietary requirements for lutein has not been established so far. RDA or RDI of 10 mg/day of lutein is suggested by the American Optometric Association. Lemon myrtle, which is mostly used as a flavour and fragrance food ingredient [62], can help to achieve RDA or RDI of lutein using lemon myrtle containing foods or nutraceutical supplements.

Lutein with antioxidants (vitamin E and polyphenols),magnesium, calcium, and folate make lemon myrtle a super-nutrient for ocular health.

Conflict of Interest Statement

Author works for Australian Native Products. The article is based

on the literature review which is not sponsored by the company.

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