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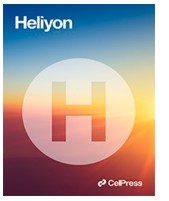

Review article

The powerful antioxidant effects of plant fruits, flowers, and leaves help to improve retinal damage and support the relief of visual fatigue

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ABSTRACT

With the popularization of electronic products, visual fatigue is inevitably frequent. The causes of visual fatigue are varied, but from the perspective of physiological mechanisms, it is mainly closely related to retinal function or structural damage, especially the light source from various mobile devices and office equipments nowadays, which induces oxidative stress damage in the retina and exacerbates the degree of visual fatigue, resulting in the inability to use the eyes for a long period of time, pain in the eyes and periorbital area, blurred vision, dry eyes, tearing, and other discomforts. Food ingredients derived from natural plants have greater application in relieving visual fatigue. Therefore, this paper presents a detailed compilation of six plants that are widely used for their visual fatigue-relieving function, in the hope of providing more raw material choices for the development of products with visual fatigue-relieving functions in the future.

1. Introduction

Eye health has always been neglected, but the eye is an important organ for exploring the external environment and taking in external information, it is almost completely exposed to the external environment and suffers from adverse external influences from time to time, such as light, dust, bacteria, etc [1]. These substances cause damage and functional decline of the ocular surface and even the fundus, thus causing a strong sense of ocular visual fatigue, i.e.: dryness, soreness, blurred vision, and various other ocular discomforts [2]. Blue light produced by electronic products is the main reason for inducing an elevated frequency of visual fatigue [3]. According to statistics, using a computer office for more than 4 h will significantly increase eye discomfort [4]. The prevalence of visual fatigue in the college student population was as high as 67.8 %, with blurred vision being the most frequently reported visual fatigue phenomenon (27.0 %) [5]. The prevalence of visual fatigue in the high school student population between the ages of 12 and 18 years old was 49.4 %, and the most common manifestation of visual fatigue in this group was significant tearing and eye pain accompanying close-up work and during reading [6]. These data suggest that people who work with their eyes for long periods, especially those in the study and work stages, are very vulnerable to visual fatigue. Visual fatigue not only affects the efficiency of study and work but also easily causes mental distress. Therefore, effective strategies to alleviate visual fatigue should be proposed to solve this distress.

Studies have shown that strategies of dietary intervention are effective in ameliorating retinal oxidative stress, inflammatory

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damage and apoptosis, and reducing the frequency of visual fatigue [1,7]. Fig. 1 shows current nutritional intervention strategies to alleviate visual fatigue. The current study found that 4 consecutive weeks of supplementation with omega-3 polyunsaturated fatty acid-rich fish oil, Bilberry (Vaccinium myrtillus L.) extract, and lutein preparations improved subjective symptoms of visual fatigue and mental fatigue in the population [8]. A 3 g taurine supplementation for 12 consecutive days significantly improved visual fatigue caused by visual display terminals (VDT) work [9]. Oral administration of Bilberry extract for 4 weeks (at a dose of 1000 mg/d) was effective in relieving visual fatigue induced by prolonged use of tablet computers [10]. Compound chrysanthemum extract can reduce visual fatigue through multi-component, multi-target and multi-pathway [11]. Besides, food ingredients such as zeaxanthin, polyunsaturated fatty acids, vitamins and minerals have better visual fatigue reduction functions [2]. More studies have been reported on the powerful antioxidant effects exhibited by natural plants and their extracts in ameliorating retinal damage. This suggests that food ingredients of plant origin have greater application value in alleviating visual fatigue function. Therefore, in this paper, the fruits, flowers and leaves of plants with the function of relieving visual fatigue, which are more widely used, were collated in detail, and their mechanisms of action in relieving visual fatigue were summarized, in the hope of providing more choices of raw materials for the development of products with the function of relieving visual fatigue in the future.

2. Oxidative stress and visual fatigue

The eyes are exposed to air for a long time and are easily disturbed by external undesirable factors (e.g., bacteria and bright light). The tear film on the surface of the eye contains a certain amount of lysozyme that can act as the first line of defense of the eye against external bacteria and dust [12], while sufficient nutrients and antioxidants inside the eye provide the necessary support and ocular protection for the visual circulation. The retina in the eye has high energy and oxygen consumption, especially the retinal pigment epithelial (RPE) cells therein, which have the function of supporting and nourishing photoreceptor cells [13] and need to constantly phagocytose and digest the outer ganglionic membrane discs produced by photo-oxidative stimulation of photoreceptor cells to maintain the normal function of photoreceptor cells [13] and to complete visual transduction. However, when people use their eyes for long periods for work, study or recreation, they are prone to produce a large amount of reactive oxygen species (ROS) resulting in a massive depletion of nutrients and antioxidants in the retina, and the intraocular balance is further disrupted with oxidative stress [14], leading to frequent occurrences of visual fatigue [1,7]. This depletion and damage are further enhanced when the eye is subjected to the use of precision instruments (microscopes, etc.).

ROS include hydroxyl radical (·OH), hydrogen peroxide (H_2O_2), superoxide anion ($O_2^{\bullet-}$), peroxyl radical (ROO), and singlet oxygen

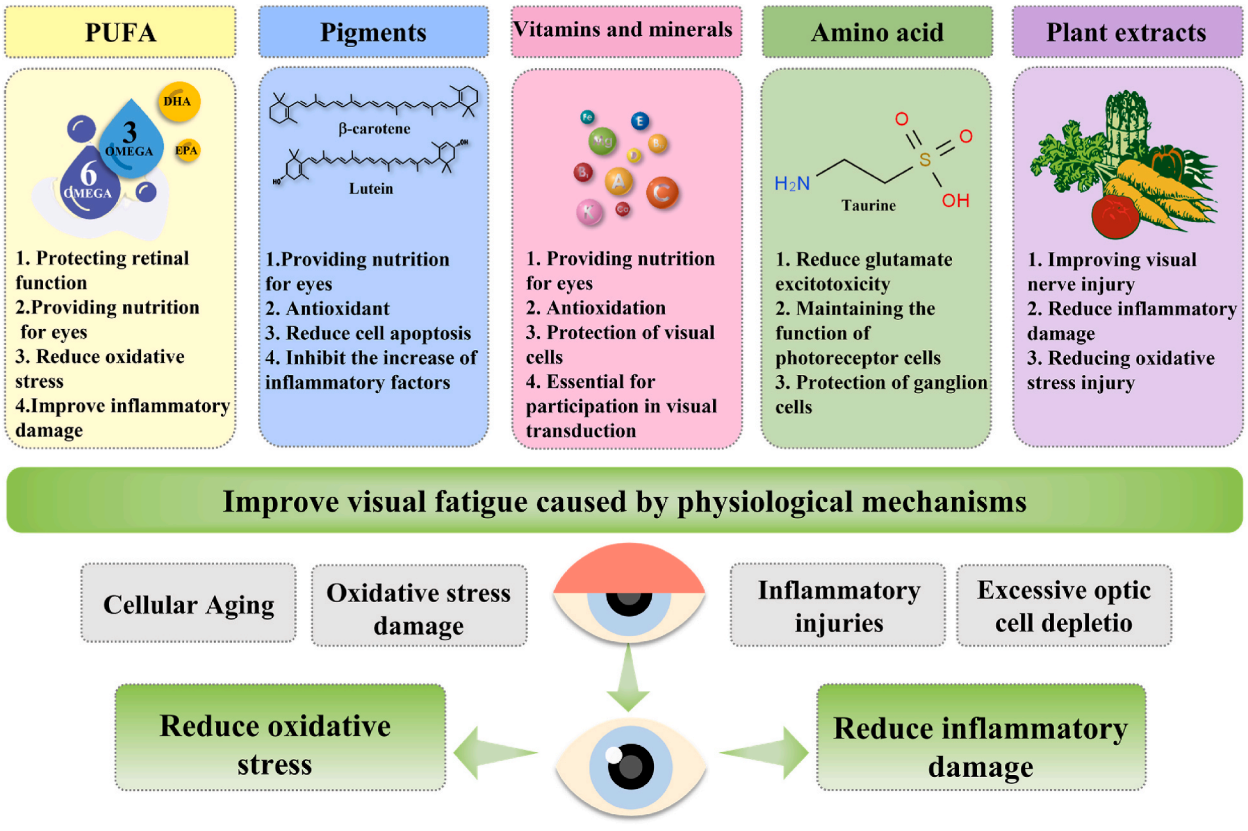

Fig. 1. Nutritional intervention strategies to alleviate visual fatigue.

(O_2) [15]. Of these, O2– is formed by the reduction of oxygen, with the subsequent transformation to H_2O_2 [16], and then the most active ROS (i.e., ·OH) through the Fenton reaction [17], reflecting the fact that cellular damage may be the result of a shift from a redox state to a more oxidative state [15]. The influence of external blue light and UV light, leads to the elevation of ROS in the retina, which causes the death of photoreceptors in the retina [18], resulting in the structural and functional damage of retinal cells [19,20]. Moreover, the RPE ingests large amounts of lipids and proteins in the form of phagocytosed photoreceptor outer segments (OS) [21], and the high concentration of ROS induces an increase in the amount of lipid peroxidation byproducts in the retina, which can bind to each other and proteins and DNA in the cells, exacerbating cellular inflammation and apoptosis [22], and ultimately inducing the onset of visual fatigue [1,7]. In addition, during phagocytosis of the outer segments by RPE cells, N-retinyl-N-retinylidene ethanolamine (A2E) is produced and further aggregated in RPE cells, resulting in an increase in ocular photosensitivity, which leads to a greater tendency to induce ROS production when the eye is subjected to external light, leading to apoptosis of the RPE cells [23], and a decrease in retinal function also declines and ultimately leads to Age-related macular degeneration (AMD) [24]. AMD damages the photoreceptor cell layer, leading to decreased macular function and increasingly frequent visual fatigue. Oxidative stress-induced functional impairment of the eye is shown in Fig. 2.

It can be seen that the development of visual fatigue is closely related to the damage caused by oxidative stress on the retina. Improving the antioxidant defense system and inhibiting the production of ROS is essential for maintaining the structure and function of the retina, especially the RPE, RGC and photoreceptor cells on it, which are key to alleviating visual fatigue.

3. Mechanism of action of plant fruits in alleviating visual fatigue through the antioxidant pathway

Table 1 summaries the mechanisms by which the three plant fruits alleviate visual fatigue.

3.1. Lycium barbarum (wolfberry)

3.1.1. Basic features

Lycium barbarum is the dried mature fruit of the plant wolfberry which is widely distributed in China, Korea, North America, Japan, Europe, and other countries [44]. *Lycium barbarum* is rich in functional components such as polysaccharides, polyphenols, flavonoids, pigments, amino acids, vitamins, trace elements, and so on [45,46], and thus have a wide range of physiological activities, such as vision protection, kidney protection, antioxidant, hepatoprotection, regulation of intestinal flora, enhancement of immunity, and anti-fatigue [47–51]. The polyphenolic components in *Lycium barbarum* are one of the important components of wolfberry to exert antioxidant function [52]. It is generally believed that the phenolic and antioxidant capacity in black wolfberry is much higher than that in red wolfberry, while the carotenoid content in red is much higher than that in black wolfberry [53,54], and both kinds of wolfberries have better antioxidant effects and retinal protection.

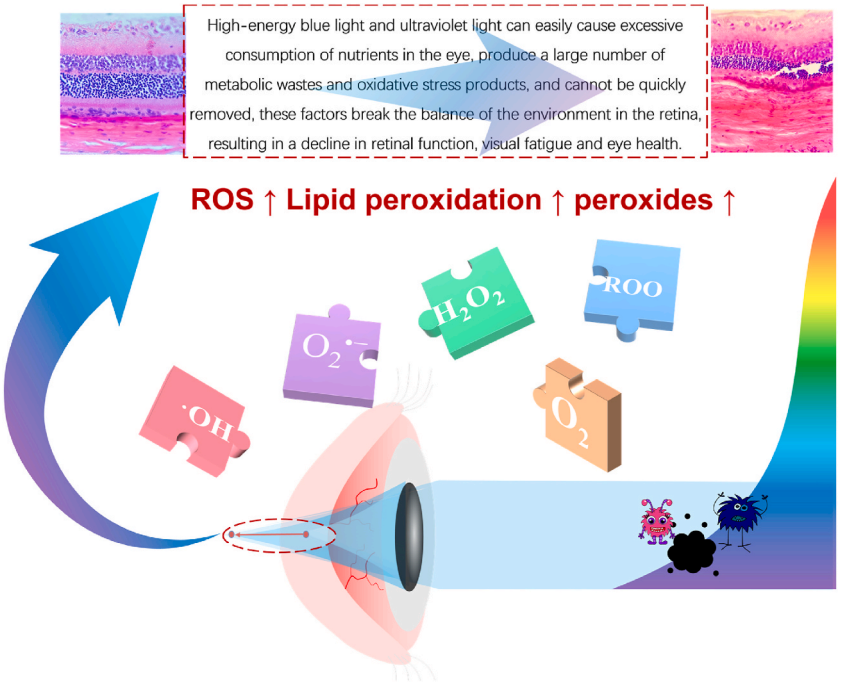

Fig. 2. Oxidative stress-induced functional impairment of the eye.

Table 1
Summarizes the mechanisms by which the three plant fruits alleviate visual fatigue.

vegetative	Materials/ingredients	Subjects/Cells	way	dose	Results or conclusions	Ref.
Lycium barbarum	*Lycium barbarum* aqueous extract	RCS rats	in vivo	1 mg/kg	1、 The aqueous extract of *Lycium barbarum* has a better neuroprotective effect against early retinal injury in RCS rats, possibly by inhibiting the expression of Caspase-2 to protect apoptotic neurons. 2、 Zeaxanthin and lutein in the aqueous extract of *Lycium barbarum* may be important components in the inhibition of apoptosis.	[25]
	Alcoholic extract of *Lycium barbarum*	C57BL/6 mice	in vivo	1.2 g/kg	1、 Ethanolic extract of LBP improves RPE deposition and restores Bruch's membrane organization in AMD mice in vivo.	[26]
	Lutein and zeaxanthin from goji berry sources	ARPE-19	in vitro	200 μmol	1、 Lutein and zeaxanthin from the LBP source restored the viability of ARPE-19 cells under suppressed oxidative stress, regulated the MMP/TIMP system, increased cellular antioxidant activity, and improved the condition of AMD mice.	[26]
	Alcoholic extract of *Lycium barbarum*	ARPE-19	in vitro	50 μg/mL	1、 Both LBP extracts reduced UV-induced RPE cell death and decreased endogenous ROS levels in ARPE-19 cells; 2、 Both LBP	[27]
	Lycium barbarum aqueous extract	ARPE-19	in vitro	50 μg/mL	extracts attenuated UV-induced loss of mitochondrial membrane potential and prevented the loss of mitochondrial membrane potential in UV-irradiated cells; 3、 Both LBP extracts significantly attenuated the activation of γ-h2ax, thereby inhibiting photodamage-induced apoptosis in ARPE-19 cells.	[27]
Vaccinium myrtillus	Bilberry Extract	People with visual fatigue	in vivo	1000 mg/d	A 4-week dose of 1000 mg/d of *Vaccinium myrtillus* extract in people with visual fatigue significantly improved eye pain, inflammation, dryness, fatigue, blurred vision, and visual discomfort, and was effective in relieving symptoms of visual fatigue caused by tablet viewing.	[24]
	Bilberry Extract	ARPE-19	in vitro	100 μg/mL	1、 Both polyphenols and anthocyanins showed dose-dependent protective effects against A2E-aggregated ARPE-19 cells + blue	[28]
	Bilberry polyphenol	ARPE-19	in vitro	50 μg/mL	light-induced apoptosis (polyphenols: 14.7 % at 12.5 μg/mL and 36.35 % at 100 μg/mL; anthocyanins: 17.7 % at 12.5 μg/mL and	[28]
	Bilberry anthocyanin	ARPE-19	in vitro	12.5 μg/mL	34 % at 100 μg/mL). 2、 Treatment of cells with *Vaccinium myrtillus* extract or its fractions before A2E accumulation in ARPE-19 reduced the number of apoptotic cells after blue light damage, suggesting that *Vaccinium myrtillus* extract or its fractions may inhibit the accumulation of A2E in cells. 3、 Blue light reduced cellular A2E levels by 87 %, suggesting an oxidative effect of light irradiation on A2E. In contrast, Bilberry Extract, Bilberry polyphenols, and Bilberry anthocyanins all effectively inhibited the photo-oxidation of A2E in a dose-dependent manner.	[28]
	Bilberry anthocyanin	ARPE-19	in vitro	50 μg/mL	1、 Bilberry anthocyanins significantly increased ARPE19 cell viability. 2、 Bilberry anthocyanins enhanced the resistance of ARPE-19 cells to oxidative damage by inducing HO-1 expression.	[29]
	Bilberry anthocyanin	pigmented rabbits	in vivo	500 mg/d	1、 500 mg/kg Bilberry anthocyanin significantly increased HO-1 expression in the rabbit retina. 2、 Light increased IL-6 protein expression, and 500 mg/kg Bilberry anthocyanin significantly inhibited photo-oxidation-induced elevation of IL-6 protein expression; and inhibited light-induced elevation of NF-κB mRNA levels.	[29]
	Bilberry anthocyanin	pigmented rabbits	in vivo	250 mg/d	1、 The results of electroretinography showed that the reduction of b-wave amplitude was significantly smaller in the animals in the Bilberry anthocyanin intervention group, and the b-wave amplitude increased with the increase of Bilberry anthocyanin concentration, and also effectively suppressed the reduction of the thickness of the ONL of the retina and the length of photoreceptor cells' outer segment of the model rabbits, which indicated that Bilberry anthocyanin could improve the function of the retina. 2、 Light exposure resulted in the up-regulation of the pro-apoptotic protein Bax and the down-regulation of the anti-apoptotic protein Bcl-2, whereas Bilberry anthocyanins not only increased the expression of the anti-apoptotic Bcl-2 but also significantly decreased the expression of Bax, which resulted in the reduction of light-induced apoptosis in the retina of the model rabbit. 3、 It increased the levels of SOD, GSH-Px, CAT, and total antioxidant capacity in the retina, and reduced the level of MDA; it effectively inhibited the light-induced increase in the levels of pro-inflammatory factor IL-1β and angiogenic parameter VEGF, suggesting that Bilberry anthocyanins play a role in protecting the retina by increasing the antioxidant defense mechanism,	[30]

(*continued on next page*)

Table 1 (*continued*)

vegetative	Materials/ingredients	Subjects/Cells	way	dose	Results or conclusions	Ref.
					inhibiting lipid peroxidation and pro-inflammatory factors, and inhibiting retinal cell apoptosis.	
blueberries	blueberry anthocyanin extract (BAE)	ARPE-19	in vitro	5 μg/mL	1、 BAE, Mv, Mv-3-glc, and Mv-3-gal pretreatment increased cell viability and reduced apoptosis to varying degrees, thus	[31]
	Malvidin (Mv)	ARPE-19	in vitro	5 μg/mL	protecting ARPE-19 cells from H_2O_2-induced cytotoxicity, with	[31]
	malvidin-3-glucoside (Mv-3-glc)	ARPE-19	in vitro	5 μg/mL	Mv-3-glc and Mv-3-gal showing more significant protective and anti-apoptotic effects. 2、 BAE, Mv, Mv-3-glc, and Mv-3-gal all reduced ROS production and inhibited MDA production in	[31]
	malvidin-3-galactoside (Mv-3-gla)	ARPE-19	in vitro	5 μg/mL	damaged ARPE-19 cells to different degrees, with Mv-3-gal showing the strongest antioxidant capacity, and Mv-3-glc the strongest inhibitory effect on MDA. 3、 Mv, Mv-3-glc, and Mv-3-gal had better antioxidant and anti-apoptotic effects compared to BAE, and were able to effectively reduce the levels of MAPKs, p38 phosphorylation, Caspase-3, Bax, and VEGF, and differentially increase the Akt/Akt ratio, Bcl-2, SOD, CAT and GSH-Px expression.	[31]
	Blueberry Juice Concentrate (rich in anthocyanins)	BN and albino Wistar rats	in vivo	1 mL	1、 Long-term (7 weeks) and short-term (2 weeks) prophylactic blueberry juice concentrate interventions were protective against light exposure-induced damage to retinal structure and function in Wistar rats. 2、 Different breeds of rats have different susceptibility to light damage, with BN rats being more susceptible to light exposure than albino rats.	[32]
	blueberry anthocyanin	RPE cell	in vitro	0.1 mg/mL	1、 Light-induced RPE cell aging caused a significant increase in intracellular ROS levels, but treatment with blueberry anthocyanins was able to reduce the increase in ROS and improve the antioxidant activity of RPE cells. 2、 Blueberry anthocyanins were able to inhibit the senescence of RPE cells by extending the lifespan of RPE cells, reducing the number of senescent cells after passaging, and inhibiting the increase of intracellular ROS after visible light irradiation. 3、 VEGF overexpression was observed in senescent RPE cells induced by light exposure, and blueberry anthocyanins effectively reduced VEGF expression, demonstrating a protective effect on RPE cells against light-induced injury.	[33]

Note: RCS = Royal College of Surgeon; ARPE-19 = Human adult retinal pigment epithelial cells; AMD = age-related macular degeneration; IL-6 = interleukin-6; HO-1= Heme Oxygenase-1; H_2O_2 = hydrogen peroxide; ONL=Outer nuclear layer; T-SOD = Total superoxide dismutase; SOD= Superoxide Dismutase; GSH-Px = Glutathione peroxidase; CAT= Catalase; MDA = Malonaldehyde; IL-1β = interleukin-1β; VEGF = vascular endothelial growth factor; MAPKs = Mitogen-Activated Protein Kinases; BN = pigmented Brown-Norway.

3.1.2. Relieves the mechanism of visual fatigue

Caspase plays a key role in the initiation and execution of apoptosis [55], and the aqueous extract of *Lycium barbarum* can have a better neuroprotective effect on the early retinal tissues of retinal dystrophy rats by protecting photoreceptors and inhibiting apoptosis of Caspase-2 protein [25]. The ethanol extract of *Lycium barbarum* was able to ameliorate the fundus damage in AMD rats, and the lutein/zeaxanthin derived from *Lycium barbarum* was effective in promoting the proliferation of H2O2-treated ARPE-19 cells, decreasing the expression of MMP-2 and TIMP-1, and decreasing the oxidative stress damage of the retina and protecting the retina [26]. Analysis of comparative experimental studies revealed that both aqueous and alcoholic extracts of *Lycium barbarum* enhanced the antioxidant activity of Human adult RPE cells-19 (ARPE-19) cells and reduced their endogenous ROS levels, reduced light-induced apoptosis, and prevented UV irradiation-induced DNA damage and apoptosis of ARPE cells, but the antioxidant effect of the ethanol extract was significantly stronger than that of the aqueous extract, suggesting that the polyphenol components in the ethanol extract may have enhanced the antioxidant activity of the ethanol extract of *Lycium barbarum* [27]. *Lycium barbarum* polysaccharide (LBP) is one of the main active components in *Lycium barbarum* with good antioxidant effects [56]. It has been reported that LBP can promote M2 polarisation and delay RGC injury by regulating microglia/macrophage activity [57]. And it can have a better protective effect on RPE under oxidative stress by inhibiting miR-181 and affecting the Bcl-2/Beclin1 autophagy signaling pathway [58]. LBP can also eliminate excess oxygen radicals by up-regulating the antioxidant genes nuclear factor erythroid2-related factor 2 (Nrf2) and recombinant thioredoxin reductase 1 (TrxR1), thus reducing the mitochondrial response to oxidative stress, enhancing the antioxidant capacity, and effectively protecting the photoreceptor cells from light-induced retinal damage [59].

The components in wolfberry that can relieve visual fatigue are mainly LBP, carotenoids, *Lycium barbarum* polyphenols, etc. These functional components reduce oxidative stress, and cellular autophagy in the retina and improve the decline in retinal function caused by RPE cell senescence, thus effectively exerting the function of relieving visual fatigue.

Table 2
Summaries the mechanisms by which plant flowers and leaves alleviate visual fatigue.

vegetative	Materials/ingredients	Subjects/Cells	way	dosages	Results or conclusions	Ref
Chrysanthemum	Chrysanthemum Extract	C57BL/6 J mice	in vivo	0.23 g/kg/d	Chrysanthemum extract significantly ameliorated the decrease in cellular activity induced by photodamage and reduced the amount of intracellular ROS.	[34]
		ARPE-19	in vitro	0.2 mg/mL	Intense light caused retinal dysfunction, abnormal retinal structure, and increased apoptosis in RGC and inner and outer nuclear layers. And Chrysanthemum extract can effectively improve the deformation of photoreceptors, ellipsoid zone layer, and myoid zone layer occurred by light damage, improve retinal function, and reduce apoptosis. It produces SOD, CAT, and GSH-Px antioxidant enzymes, improves the antioxidant effect of the retina, and reduces the expression of NF-κb and TNF-α, thus protecting the retina.	[34]
	Combination of chrysanthemum, wolfberry, and blackcurrant extracts and lutein esters	SD rat	in vivo	65.7 mg/kg	1、 The a- and b-waves of ERG in rats were significantly decreased under strong light irradiation for 2 h. The decrease in b-wave at high and low stimulus intensities could be significantly restored after the administration of a plant complex containing various plants such as chrysanthemum. 2、 Intense light exposure resulted in a significant reduction in ONL thickness in rats, which was significantly improved after administration of the complex containing chrysanthemum. 3、 Cellular experiments showed that strong light stimulation led to enhanced phosphorylation of p38 and JNK and reduced HIF expression in ARPE-19 cells, whereas the intervention of chrysanthemum complex significantly reduced the phosphorylation of p38 and JNK and restored HIF expression.	[35]
		ARPE-19	in vitro	100 μg/mL		[35]
	Chrysanthemum Extract	ARPE-19	in vitro	30 μg/mL	1、 Chrysanthemum extract is rich in polyphenols such as phenolic compounds and flavonoids, which showed good antioxidant activity in DPPH, ABTS, and FRAP assays. 2、 Chrysanthemum extract effectively inhibited A2E accumulation and A2E-induced cell death in ARPE19 cells in a dose-dependent manner. 3、 Among the five fractions of chrysanthemum extract, the EtOA fraction had the highest polyphenol content and antioxidant activity, followed by BuOH.n 4、 H_2O fraction had the greatest inhibitory effect on A2E accumulation and A2E-induced apoptosis, followed by BuOH.	[36]
	ethyl acetate fraction (EtOAc)	ARPE-19	in vitro	30 μg/mL		[36]
	butanol fraction (BuOH)	ARPE-19	in vitro	30 μg/mL		[36]
	hexane fraction (Hex)	ARPE-19	in vitro	30 μg/mL		[36]
	Dichloromethane fraction (CH_2Cl_2)	ARPE-19	in vitro	30 μg/mL		[36]
	water fraction (H_2O)	ARPE-19	in vitro	30 μg/mL		[36]
Ginkgo biloba	*Ginkgo biloba* Extract	SD rats	in vivo	100 mg/kg	1、 After 24 h of light exposure, the MDA levels in the model group (M), model + saline group (MN), and model + *Ginkgo biloba* extract group (ME) were significantly higher than those in the normal control group, but the MDA levels in the ME group were significantly lower than those in the M and MN groups.2、 The T-SOD, GSH-Px, and CAT activities of M and MN groups were significantly lower than those of NC and ME groups, indicating that *Ginkgo biloba* extract has some antioxidant activity.3、 After 4 d of exposure, the number of apoptotic photoreceptors in the ONL of the ME group was significantly less than that of the M and MN groups. At 1 and 2 weeks after exposure, the thickness of ONL in the ME group was greater than that in the M and MN groups and less than that in the NC group.	[37]
	Ginkgo biloba Extract	People with vision impairment due to AMD	in vivo	60 mg/d	After the fourth week of administration of *Ginkgo biloba* extract, all the test subjects showed significant improvement in visual acuity, which was even more pronounced after six months.	[38]

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Table 2 (*continued*)

vegetative	Materials/ingredients	Subjects/Cells	way	dosages	Results or conclusions	Ref
	Procyanidin B2	ARPE-19	in vitro	10 μg/mL	1、 Procyanidin B2 and Quercetin-3-*O*-rutinoside were not only well tolerated in ARPE-19 cells but also reduced oxidative damage in RPE cells.2、 Procyanidin B2 and Quercetin-3-*O*-rutinoside were able to promote Nrf2 activation, thereby protecting RPE cells from oxidative stress and apoptosis.3、 Procyanidin B2 and Quercetin-3-*O*-rutinoside inhibit the late pro-apoptotic activation of ERK1/2, a process that may be associated with the upregulation of Nrf2.	[39]
	Quercetin-3-*O*-rutinoside (Rutin)	ARPE-19	in vitro	10 μg/mL		[39]
Teas	Green Tea Extract	healthy population	in vivo	/	1、 Continuous intake of green tea extract significantly improved eye regulation in subjects under 45 years of age and in subjects undergoing daily VDT.2、 VDT subjects who ingested green tea extract significantly improved their visual fatigue after week 4, lower back pain after week 8, and headache at week 12, suggesting that long-term intake of green tea extract can help alleviate visual fatigue.	[40]
	green tea polyphenols	RPE (no. D407)	in vitro	140 mg/L	1、 The viability of RPE cells decreased by 49.2 % under UV irradiation, and the protective effect of green tea extract against UV damage in RPE cells was dependent on the green tea extract concentration and treatment.2、 UV light led to contraction of nucleoli, shedding of outer cell microvilli, deformation of mitochondria, and observation of many vesicular structures in RPE cells. Smaller changes in cell microstructure were observed after both pre-treatment and post-treatment with green tea extract and most mitochondria were able to maintain the original normal cellular morphology, but the improvement effect was more pronounced in the pre-treatment with green tea extract.3、 Dumbbell shapes and long mitochondria were seen in GTP after treatment with both GTP doses, suggesting that GTP attenuates UVB-induced RPE cell damage by both pre-treatment and post-treatment.4、 Green tea extract partially inhibited DNA breakage in both pretreatment and post-treatment groups, but the protective effect of post-treatment on DNA breakage was weaker, especially at 70 mg/L, suggesting that green tea extract inhibited UV-induced DNA breakage and promoted the repair of damaged DNA and that its protective effect was dose-dependent.	[41]
	EGCG	Wistar rat	in vivo	70~80 mg/d	1、 Light exposure significantly reduced retinal and retinal kinase mRNA, and light-induced reductions in retinal mRNA and Ret-P1 protein were significantly ameliorated when EGCG was present in rat drinking water.2、 EGCG was able to partially but significantly attenuate the a- and b-wave amplitudes of ERG in rats with light-induced retinal damage.3、 EGCG significantly reduced the expression of caspase-3 and PARP after 2 days of light exposure, suggesting its neuroprotective role in light-induced apoptosis and cell death early after light exposure.	[42]
	EGCG	Pigmentary retinitis in rats	in vivo	25 mg/kg	1、 EGCG was able to reach the retina and improve visual function in rats.2、 EGCG treatment significantly improved visual and retinal electrical function in rats, with significant increases in contrast sensitivity and b-wave values.3、 EGCG reduces lipid peroxidation, T-AOC, CAT, and SOD activities and improves antioxidant activity	[43]

Note: SD = Sprague Dawley; ERG = electroretinogram; ONL = Outer nuclear layer; T-SOD = Total superoxide dismutase SOD= Superoxide Dismutase; GSH-Px = Glutathione peroxidase; CAT= Catalase; MDA = Malonaldehyde; NF-κb = Nuclear factor-kappa B; TNF-α = tumor necrosis factor;

IL-1β = interleukin-1β; DPPH = 1,1-diphenyl-2-picryl-hydrazyl radical; ABTS = 2, 2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); FRAP = ferric reducing antioxidant power; EGCG = Epigallocatechin gallate; T-AOC = Total antioxidant capacity; VDT = visual display terminals.

3.2. *Vaccinium myrtillus (Bilberry)*

3.2.1. *Basic features*

Bilberry, (Vaccinium myrtillus) is an ancient and economically valuable small berry, a perennial deciduous or evergreen shrubby small-berry fruit tree. The Vaccinium myrtillus is native from eastern Canada to the central and eastern United States and grows mainly in temperate biomes [60], where it is rich in anthocyanins, flavonoids, phenolic acids, proanthocyanidins, and many other active components [61–63]. Bilberry has been reported to contain 15 anthocyanins, which are composed of five anthocyanins, Delphinidin, Cyanidin, Peonidin, Petunidin, Malvidin, and galactose, glucose, and arabinose, which are bound by glycosidic bonds, and they have a powerful antioxidant effect [64]. The ability of anthocyanins to protect RPE and RGC from oxidative stress damage through inhibition of oxidative stress and anti-apoptotic mechanisms has been widely demonstrated [65,66], and anthocyanins have also been shown to promote the regeneration of retinal plasma or to interact directly with retinal plasma molecules [67,68]. Vaccinium myrtillus anthocyanins have also been shown to be a major functional component in protecting the retina from damage, being able to neutralize ROS by providing hydrogen ions, and modulating cell signaling pathways [69]. Clinical studies have shown that a 4-week period of 1000 mg/d of bilberry extract given to people with visual fatigue significantly improved ocular pain, inflammation, dryness, fatigue, blurring of vision, and visual discomfort, and was effective in alleviating symptoms of visual fatigue induced by tablet viewing [24].

3.2.2. *Relieves the mechanism of visual fatigue*

It has been shown that Bcl-2 prevents apoptosis through the antioxidant pathway [70]. Elevated Bax/Bcl-2 ratio is thought to cause apoptosis [71]. Activation of caspase-3 is a death protease that catalyzes the specific cleavage of many key cellular proteins and is often used as an early detector of apoptosis [72]. Exposure of A2E cells to blue light-induced apoptosis in Human adult RPE cells (ARPE-19) by increasing the cleaved form of caspase-3, Bax/Bcl-2, whereas upon administration of bilberry extract this significantly inhibited cell death and the bilberry extract, together with its polyphenol and anthocyanin fractions, not only inhibited the photo-oxidation of A2E via HPLC monitoring also revealed that bilberry extract and its polyphenol and anthocyanin fractions also reduced the intracellular accumulation of A2E, which led to the survival of blue-light-irradiated RPE cells and effective protection of retinal epithelial cells [28]. Heme Oxygenase-1 (HO-1) acts on the degradation of haemoglobin, which results in the production of carbon monoxide, free iron, ferritin, and bilirubin, and it is an important antioxidant enzyme [73]. HO-1 is mediated by the Nrf2 transcription factor in cells and has a key role in the activation of antioxidant response element signaling pathways and antioxidant enzyme activation [74]. Experiments have shown that Vaccinium myrtillus anthocyanins protect ARPE-19 cells from visible light damage, reduce intracellular ROS levels, upregulate HO-1 expression, and significantly inhibit the photo-oxidation-induced increase in the expression of Interleukin-6 (IL-6); and attenuate the expression of the inflammation-related gene nuclear factor κB (NF-κB) [29]. Among them, the transcription factor NF-κB is a key mediator of the inflammatory response, capable of inducing the release of various pro-inflammatory genes and participating in the regulation of inflammation, and dysregulated NF-κB activation promotes a variety of inflammatory responses [75,76]. Therefore, the main mechanism by which Vaccinium myrtillus anthocyanin protects the retina from damage is to attenuate retinal photo-oxidative damage through activation of HO-1 expression and inhibition of NF-κB activation. Outer nuclear layer (ONL) thickness is an indicator for assessing photoreceptor cell survival [77], and light exposure induces apoptosis of photoreceptors, which further leads to a decrease in the amplitude of the b-wave in the electroretinogram (ERG) assay [78]. After the continuous administration of 500 mg/d of Vaccinium myrtillus anthocyanin to light-damaged pigmented rabbits for 7 days, the results of electroretinography (ERG) assay showed that the retinal function was significantly better than that of the control group and effectively suppressed the reduction of the thickness of ONL and the length of photoreceptor outer segment in the model rabbits' retinas; they were able to attenuate the apoptosis induced by light exposure, and increase the superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), catalase (CAT) and total antioxidant capacity in the retina while reducing malondialdehyde (MDA) levels; effectively inhibited light-induced elevation of pro-inflammatory factors IL-1β and vascular endothelial growth factor (VEGF), suggesting that lingonberry anthocyanins increase antioxidant defense mechanisms, inhibit lipid peroxidation and pro-oxidative effects, and reduce the length of the outer segment of light-exposed cells. This suggests that lingonberry anthocyanins play a role in protecting the retina by increasing the antioxidant defense mechanism, inhibiting lipid peroxidation and pro-inflammatory factors, and inhibiting retinal cell apoptosis [30]. In addition, Vaccinium myrtillus has a good protective effect on UV-induced retinal photoreceptor cell damage [79].

In summary, the main components in Vaccinium myrtillus that protect the retina from oxidative stress are polyphenols and anthocyanins, which can improve the retina by inhibiting the accumulation of A2E and photo-oxidation in RPE cells, decreasing the expression of NF-κB, up-regulating the expression of HO-1, SOD, CAT, and GSH-Px, and down-regulating the expression of MDA, caspase-3, Bax/Bcl-2, and inflammatory factors through several pathways, including the inhibition of retinal damage, thereby alleviating visual fatigue.

3.3. *Blueberry*

3.3.1. *Basic features*

Blueberries are one of the commonly used ingredients for the formulation of functional foods to relieve visual fatigue in the market, which are usually used with ingredients such as lutein and zeaxanthin. Currently, blueberries have grown to be one of the largest

consumed berries in the world, with the main origin being the United States [80], and blueberries are also produced in countries such as Canada, China, and Germany. Flavonoids and phenolic compounds are considered the main active components of blueberries, which endow blueberries with powerful antioxidant activity [81,82], and it has been confirmed through in vivo and in vitro studies that blueberries can effectively inhibit ROS production in the organism [83], significantly increase the levels of SOD and CAT in the cells, and inhibit the concentration of MDA [84]. Moreover, the main effect of anthocyanins in rod photoreceptors is on the regeneration of optic violet matter [85], which suggests that anthocyanins are involved in visual transduction and can influence its process.

3.3.2. *Relieves the mechanism of visual fatigue*

Blueberries are rich in phenols, including delphinidin, cyanidin, petunidin, peonidin, malvidin glycosides, malvidin-3-glucoside, malvidin-3-galactoside. Blueberry anthocyanin extract (BAE), malvidin (Mv), malvidin-3-glucoside (Mv-3-glc), and malvidin-3-galactoside (Mv-3-gal) were demonstrated to be effective in reducing ROS and MDA levels by decreasing ROS and MDA levels, as well as increasing the RPE cellular SOD, CAT, and GSH-Px levels, reducing H2O2-induced oxidative stress, apoptosis, where Mv, Mv-3-glc, and Mv-3-gal have stronger antioxidant and anti-apoptotic effects compared to BAE, with protective mechanisms including mitogen-activated protein kinases (MAPKs) including ERK1/2 and p38 pathways, reducing VEGF levels and activating the Akt signaling pathway [31]. This study suggests that the protective effect of phenolic components in blueberries on the retina is achieved through a multi-component, multi-pathway approach. This also suggests that the active ingredients from natural plant sources are endowed with more potent antioxidant and retinal protective effects due to their complex composition. Retinal electrophysiology (ERG) is commonly used to test retinal function based on the bioelectrical potential induced in the retina in response to light stimuli [86]. The administration of high concentrations of blueberry juice concentrate (rich in anthocyanins) to albino and colored rats for either 2 or 7 weeks followed by 2 h of intense light exposure revealed severe retinal damage in the animals in the placebo group, with a significant reduction in the maximum amplitude of the electroretinogram in both species, whereas the maximum amplitude of the

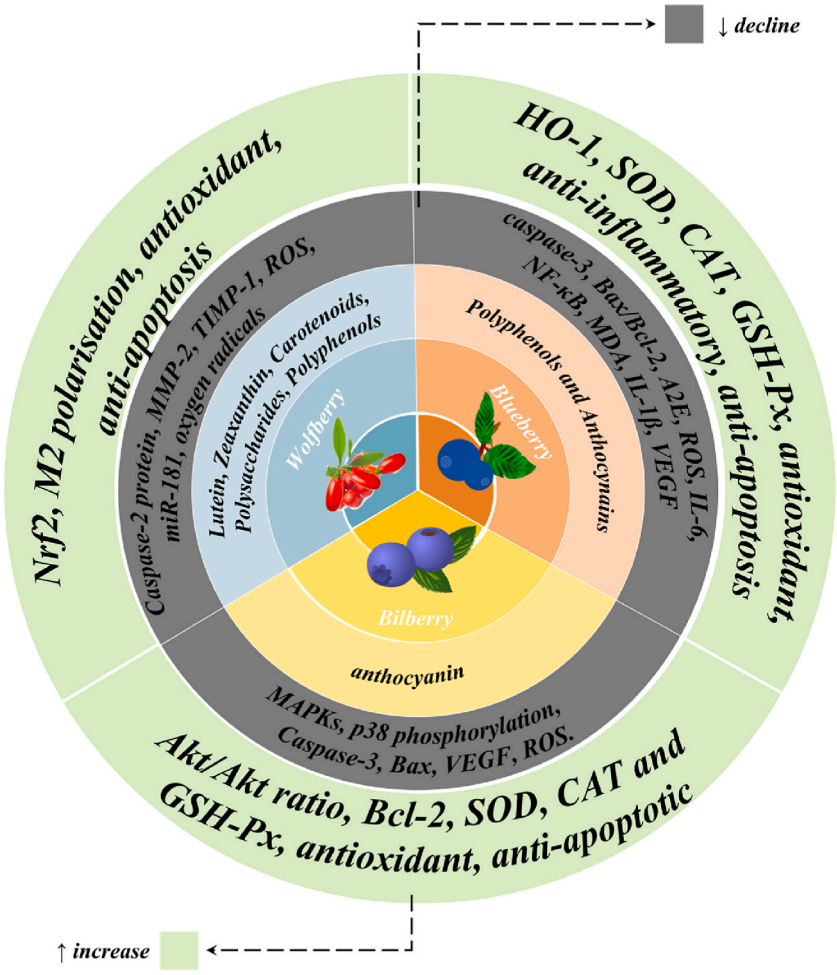

Fig. 3. Main active components and related signaling pathways of three plant fruits to alleviate visual fatigue (IL-6 = interleukin-6; HO-1 = Heme Oxygenase-1; SOD = Superoxide Dismutase; GSH-Px = Glutathione peroxidase; CAT = Catalase; MDA = Malonaldehyde; IL-1β = interleukin-1β; VEGF = vascular endothelial growth factor; MAPKs = Mitogen-Activated Protein Kinases).

electroretinogram of the albino rats in the blueberry juice concentrate intervention group was significantly protected from photodamage, but not observed in the colored rat's Retinal damage was effectively improved; histological observations of retinal sections showed that the outer nuclear layer of the retina was better protected in the albino rats in the blueberry juice concentrate intervention group, whereas severe damage to the upper half of the retina was observed in the placebo group and the colored rats given blueberry juice intervention [32]. This suggests that the sensitivity to light exposure is different in different species of rats. Meanwhile, blueberry anthocyanins have also been reported to protect against aging and light-induced RPE cell damage; light exposure not only leads to senescence of RPE cells but also accelerates cell death and increased VEGF expression, while blueberry anthocyanins effectively protect RPE cells from light-induced damage by inhibiting cell death and mediating VEGF release [33]. In addition, different blueberry polyphenol fractions significantly inhibited lipid peroxidation and cytotoxicity induced by prolonged light exposure in the retina, among which the flavonoid-rich fractions with quercetin as the main component inhibited visible-light-induced lipid peroxidation of DHA significantly better than anthocyanin- and phenolic acid-rich fractions [87].

The above studies have shown that the protective effect of blueberries on the retina mainly comes from the phenolic components, which can improve the antioxidant and anti-apoptotic effects of the retina by reducing the levels of MAPKs, p38 phosphorylation, Caspase-3, Bax, VEGF, and increasing the Akt/Akt ratio, the expression of Bcl-2, SOD, CAT, and GSH-Px, thereby help to alleviate visual fatigue.

Fig. 3 summarizes the main active components and associated signaling pathways of the three plant fruits that alleviate visual fatigue.

4. Mechanisms of action of flowers and leaves of plants in alleviating visual fatigue through antioxidant pathways

Table 2 Summaries the mechanisms by which plant flowers and leaves alleviate visual fatigue.

4.1. Chrysanthemum

4.1.1. Basic features

Chrysanthemum belongs to the ornamental family of plants with active constituents such as flavonoids, terpenoids, and organic acids [88,89]. Many literatures have reported that chrysanthemum has good antioxidant and anti-inflammatory effects, and it can also be used as a natural preservative in food and pharmaceutical preparations [90,91], and it has a positive role in relieving visual fatigue and improving inflammation of the ocular surface [92–94]. Nitric oxide (NO) is involved in the processing and regulation of visual information [95] and plays an important role in relaxing ciliary muscle contraction [96]. In contrast, the local elevation of internal calcium ions ($Ca2+$) leads to ciliary muscle arrest [97], resulting in increased ocular fatigue. Through in vivo and in vitro studies, it was found that eye care products containing chrysanthemum extract can increase the concentration of NO in the eyes, reduce the amount of $Ca2+$, and decrease the mRNA expression of PKA and PKC, which leads to the relaxation of the ciliary muscle and the effective relief of eye fatigue [94].

4.1.2. Relieves the mechanism of visual fatigue

Experiments showed that light damage induced oxidative stress in the retina, leading to a large amount of ROS production in the retina, while chrysanthemum extract could significantly increase the viability of light damage-induced ARPE-19 cells and reduce the intracellular level of ROS; it could be observed that light damage triggered the apoptosis of RGCs and photoreceptor cells and the expression of inflammation-related factors in the nucleus was elevated in the animal experiments, and chrysanthemum extract could protect the retina through the increase of SOD, CAT and GSH-Px activities to reduce ROS production in the retina, effectively reducing oxidative stress and inflammatory damage and protecting the retina [34]. This suggests that chrysanthemum extract, as a natural antioxidant, can provide good protection for the retina. Moreover, by compounding multiple natural antioxidant plants, it can show even more superior antioxidant effects and retinal protection. The function of the retina is usually evaluated using electroretinography (ERG), in which the a-wave reflects the functional integrity of photoreceptors and the b-wave reflects the function of photoreceptors, bipolar cells, and Müller cells [98]. Experiments showed that the a- and b-waves of ERG in rats decreased significantly under strong light irradiation for 2 h, and the decrease in b-wave under high and low stimulus intensities could be significantly restored after administration of complexes containing a variety of plants such as chrysanthemums; strong light irradiation resulted in a significant reduction in the thickness of the ONL in rats, which was significantly improved after administration of the complexes containing chrysanthemums; and cellular experiments showed that strong light stimulation led to the reduction of the thickness of the p38 and JNK in ARPE- 19 cells with enhanced phosphorylation of p38 and JNK and reduced HIF expression, while the intervention of the chrysanthemum complex significantly reduced the phosphorylation of p38 and JNK and restored HIF expression [35]. Among them, JNK and p38 are members of MAPK that play important roles, and excessive phosphorylation of p38 and JNK leads to increased apoptosis [99]. Hypoxia-inducible factor (HIF) has been reported to defend against oxidative stress by directly targeting mitochondria [100], and HIF can regulate the transcription of multiple genes, including VEGF and HO-1 [101,102], thereby reducing retinal oxidative stress. Experiments have confirmed that substances such as phenolic compounds and flavonoids in chrysanthemums confer a better antioxidant and vision-protective effect on chrysanthemums. Using hexane (Hex), dichloromethane ($CH2Cl2$), ethyl acetate (EtOAc), butanol (BuOH), and water ($H2O$) sequentially to extract the chrysanthemum extract, five fractions were obtained, in which the polyphenol content and antioxidant effects were, from largest to smallest, EtOAc > BuO > Hex > $CH2Cl2$ > $H2O$; and the effect of the $H2O$ fraction on the A2E accumulation and A2E-induced cell death was the strongest inhibitory ability, followed by BuOH [36], and since the polyphenol content detected in the water fraction was very trace, it is reasonable to suspect that non-polyphenolic

substances in chrysanthemums may also be involved in the protective effect against A2E. This also suggests that the complexity and diversity of active constituents from natural plant sources provide a variety of possible mechanisms for organismal antioxidation.

In summary, chrysanthemum extract can protect the retina from oxidative stress damage by elevating the expression of SOD, CAT, GSH-Px, and HIF, improving the antioxidant effect of the retina, and reducing the expression of NF-κ b, TNF-α, p38, and the phosphorylation of JNK, and the retina is protected from oxidative stress damage, and its good renoprotective effect may be mainly from the antioxidant effect provided by polyphenol compounds, but we cannot exclude that Its good retinal protective effect may mainly come from the antioxidant effect provided by polyphenolic compounds, but it is not excluded that the non-polyphenolic substances in it exerted retinal protection through other pathways. In conclusion, the antioxidant effect of chrysanthemums provided good retinal protection, thus alleviating the occurrence of visual fatigue.

4.2. Ginkgo biloba

4.2.1. Basic features

Ginkgo biloba is the dried leaves of ginkgo obtained by harvesting and drying the leaves in autumn when they are just turning green. Ginkgo is the world's oldest surviving tree species and the only surviving member of the ginkgo family [103], whose main origin is in China. The main active components in Ginkgo biloba are flavonoids, lactone compounds, and phenolic acids [104–106]. Ginkgo biloba extract has a positive effect on blood circulation; thus, it has been widely used in the treatment of peripheral circulation, cerebral blood supply insufficiency, and other diseases [107], and the corresponding clinical drugs have been formed. And it also has good applications in improving antioxidants, Alzheimer's disease, mild to moderate dementia, neuroprotection, and anti-inflammation [108–110]. In ophthalmological applications, it has a better neuroprotective effect on RGC cell hypoxia-induced damage [111]. It can significantly reduce inflammatory cell infiltration in the retina and damage to the outer retinal layer [112].

4.2.2. Relieves the mechanism of visual fatigue

Ginkgo biloba extract is considered to have strong antioxidant and neurotoxicity-reducing effects and can reduce RGC neurotoxicity induced by retinal injury, which has a good application value in improving retinal injury [113,114]. Moreover, the administration of 100 mg/kg of Ginkgo biloba extract to rats with retinal injury induced by photodamage was able to effectively reduce the apoptosis of retinal photoreceptor cells, increase the activity of antioxidant enzymes, and decrease the amount of oxidative stress-related factors produced [37]. The occurrence of AMD is believed to be closely associated with vascular factors and oxidative stress. Previous studies have shown that Ginkgo biloba extract has a promising application in AMD [115]. In a clinical study, 99 patients with visual impairment due to AMD were given Ginkgo biloba extract for a period of six months (50 patients in group I given 240 mg/d and 49 patients in group II given 60 mg/d), and it was found that after the fourth week of Ginkgo biloba administration, visual acuity in both groups improved significantly, and the improvement was more pronounced in group I and the improvement of visual acuity was even more significant in both groups after six months. The improvement in visual acuity was even more significant in group I, and after six months in both groups [38], this result proved that Ginkgo biloba extract has a significant ameliorative effect on AMD and a better promotional effect on vision. Studies have reported that different subfamilies of MAPK include Erk1/2 and JNK, which are activated by oxidative stimuli and induced cellular oxidative stress damage [116,117]. Procyanidin B2 and rutin extracted from Ginkgo biloba were shown to protect RPE from oxidative stress injury by modulating Nrf2 and Erk1/2 signaling pathways [39].

In summary, Ginkgo biloba extract exerts its role in alleviating retinal damage mainly through neuroprotection and regulation of various signaling molecules in the antioxidant pathway, thus effectively alleviating the occurrence of visual fatigue.

4.3. Tea

4.3.1. Basic features

Tea is one of the most widely used beverages in the world, which can be made into special flavored beverages through further processing, and is generally classified into three types according to the production process, namely green tea (unfermented), oolong tea (semi-fermented), and black tea (fermented) [118], whose main active components are polyphenols, polysaccharides, theanine, and caffeine, etc. [119], and thus possesses a wide range of physiological activities such as anti-oxidation, anti-tumor, and anti-inflammatory activities [120–122]. Currently, the main countries producing tea are China, India, Japan, Sri Lanka, Indonesia, and Central African countries [118]. Studies have shown that long-term intake of green tea can help reduce visual fatigue and improve visual function [40]. A questionnaire study with 35,557 participants reported a positive correlation between tea intake and macular retinal nerve fiber layer (mRNFL) thickness, which was found to be significantly higher in tea-drinking populations than in non-tea-drinking populations, especially those who drank more than four cups of tea per day [123], suggesting that tea intake may have some neuroprotective effects on the retina.

4.3.2. Relieves the mechanism of visual fatigue

Catechins are the most abundant polyphenols in green tea and confer a powerful antioxidant effect [124]. The highest concentration of catechins was found in the rat retina after feeding Sprague Dawley (SD) rats with catechin-rich green tea extracts, suggesting that catechins have a better antioxidant protective effect on the retina [125]. Indeed, it has been confirmed in several research reports that green tea catechin-like constituents help to ameliorate oxidative stress, and inflammation-induced retinal damage [126,127]. Polyphenolic constituents in green tea also protect RPE cells from UV damage by increasing survivin gene expression, inhibiting mitochondrial dysfunction, and DNA breaks [41]. Epigallocatechin gallate (EGCG), one of the representative components of strong

antioxidants in green tea, was shown to be able to reach the retina by oral administration and effectively attenuate light-induced oxidative stress in the retina and ameliorate the degree of light-induced photoreceptor damage [42]. Moreover, EGCG treatment given once a week for 100–160 days after birth to rats with retinitis pigmentosa significantly improved visual function and retinal function, effectively increased the b-wave value in the ERG assay, reduced lipid peroxidation in the retina, and increased the total antioxidant capacity and the activities of CAT and SOD, suggesting that EGCG not only attenuates the visual function loss but also attenuates oxidative damage and reverses the retinal damage condition in rats by acting on different antioxidant enzymes [43].

The abundant antioxidant active ingredients in tea, especially polyphenols, can protect RPE cells from oxidative damage by activating anti-apoptotic and endogenous antioxidant enzyme signaling pathways, thus improving visual fatigue.

Fig. 4 summarizes the main active components and associated signaling pathways of plant flowers and leaves for relieving visual fatigue.

5. Conclusions

The fruits, flowers, and leaves of natural plants are rich in strong antioxidants such as polyphenols, polysaccharides, and flavonoids, thus endowing natural plants with powerful antioxidant effects, and more and more research reports have further revealed their antioxidant, anti-inflammatory, anti-apoptotic, and neuroprotective mechanism, and potential application value. Moreover, natural plants are rich in active ingredients, and some trace elements may also promote the efficacy of antioxidants in plants. This article reviews the application potential of several plant fruits, flowers, and leaves that are widely used in the market in alleviating visual fatigue. In addition to the fruits, flowers, and leaves of several natural plants reviewed in this paper, some studies have reported that cranberry, ginseng berry extract, and Aronia melanocarpa fruit extract have good applications in improving retinal damage, but the research content is small and the mechanism of action is not clear enough, so it is not reviewed here. This also suggests that in future research, the raw material mining and raw material mechanism of natural plant fruits, flowers, and leaves are worth further exploration. The occurrence of visual fatigue is mainly closely related to retinal damage, and plant fruits, flowers, and leaves can promote antioxidant enzyme activity, inhibit peroxidation, and inflammatory reactions, reduce retinal damage, and reverse retinal damage or death by regulating antioxidant and anti-apoptotic signaling pathways, thereby repairing damaged retinas, and alleviating or reducing visual fatigue.

The blood-retinal barrier (BRB) consists of tightly packed capillary endothelial cells. Because of the presence of the BRB, this results in a strong selectivity of active ingredients that can reach the retina. The fruits, flowers, and leaves of several natural plants reviewed in this paper were able to reach the retina by oral administration and exerted strong antioxidant protection. This once again confirms the potential value and possibility of the application of fruits, flowers, and leaves of natural plants for the relief of visual fatigue. Of course, the rich active ingredients of natural plants give them powerful antioxidant activities and better physiological functions on the one hand, but on the other hand, they also reflect the complexity of natural plant compositions. Therefore, the safe range of doses and the optimal starting dose for their relief of visual fatigue should be determined in specific applications. Secondly, the extraction method of natural plants also affects their efficacy in relieving visual fatigue, and it is worthwhile to further study in future research to determine the differences of different extraction components of natural plants in relieving visual fatigue, and further discuss the differences of the main components of different components, to analyses and excavate the natural components that play a role in relieving visual fatigue, and to give more help to the application of natural plants in relieving visual fatigue. The results of this study will be used to analyze and explore the natural components in plants that play a role in relieving visual fatigue and to provide more help for the application of natural plants in relieving visual fatigue.

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Hao Duan: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Diandian Wang:** Data curation. **Yue Zheng:** Data curation. **Yaxi Zhou:** Data curation. **Wenjie Yan:** Supervision, Resources, Investigation, Funding acquisition.

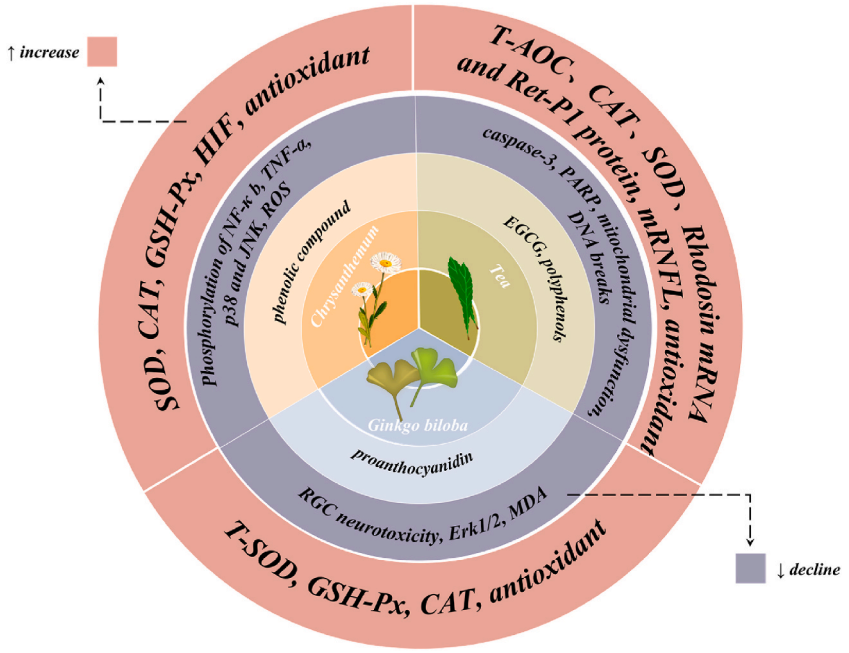

Fig. 4. Main active components and related signaling pathways in plant flowers and leaves to alleviate visual fatigue (T-SOD = Total superoxide dismutase; SOD= Superoxide Dismutase; GSH-Px = Glutathione peroxidase; CAT= Catalase; MDA = Malonaldehyde; NF-κb = Nuclear factor-kappa B; TNF-α = tumor necrosis factor; EGCG = Epigallocatechin gallate; T-AOC = Total antioxidant capacity).

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Wenjie Yan reports financial support and article publishing charges were provided by the National Key Research and Development Program of China. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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