# Chapter 7

# MEDICINAL PLANTS AND SECONDARY METABOLITES FOR OCULAR DISEASES

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## INTRODUCTION

Ancient civilisations have traditionally used medicinal herbs for their therapeutic benefits (1). The usage of medical plants is still common in the rural regions of developing nations today, while the demand for herbal medicinal products in developed nations is rising steadily (2).

The eye is one of the most sensitive organs in the human body, because it is in contact with the external world, and ocular disorders caused by infection, allergies, or trauma can develop rapidly. Due to their secondary metabolites, several plant parts from various families, including those from the Lamiaceae, Malvaceae, Rosaceae, and Asteraceae, have a variety of therapeutic effects on eye diseases (3). It has been stated by different researchers that the use of plants in eye diseases is included in traditional Cameroon, Chinese, Indian and Tanzanian medicine (4-7). Despite advanced technologies that allow the development of novel molecules, extensive research into secondary metabolites isolated from plants continues. Many of these naturally occurring compounds, however, have yet to be adequately investigated for effect in ocular tissues. As a reason, in the present review, we have chosen herbal extracts and natural compounds that have a considerable body of evidence from controlled research in the current scientific literature supporting their use in ocular diseases.

### Anatomy and Physiology of Eye

The orbital bones protect the eyeball (Bulbus oculi), which is located in the orbita. The lens separates the eye into two sections, anterior and posterior (8). The cornea, pupil, aqueous humor, and iris-ciliary body comprise the anterior

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segment, whereas the sclera, choroid, retinal pigment epithelium, retina, and vitreous humor comprise the posterior segment. Because the eye is an organ that is in contact with the outside world, it has biological barriers to protect its integrity. Ocular barriers are the tear film, cornea, conjunctiva, sclera, blood-aqueous humor or iris-ciliary body, lens, and blood/retina barriers in anatomical order (9).

## MEDICINAL PLANTS AND THEIR SECONDARY METABOLITES FOR OCULAR DISEASES

Herbal remedies, which are useful for treating numerous disorders such as glaucoma, cataracts, bacterial eye infections, fungal eye infections, viral eye infections, and ocular traumas, have also been pioneers in the development of novel molecules.

The pharmacological activities of *Aloe barbadensis* (Liliaceae) include antibacterial, immunomodulatory, wound-healing antiviral, anti-inflammatory, antioxidant, and antifungal activities (10). It has been determined that *A. barbadensis* leaf juice contains many compounds including flavonoids, anthraquinones, mucilage, and phenolic acids (11). In the study of Wozniak et al., it was determined that the *A. barbadensis* has anti-inflammatory activity on the cornea, and it has also been revealed that it has low toxicity and immunomodulatory effect (12). In another study, Curto et al. found that barbadensis accelerated re-epitilization and reduced fibrosis on corneal lesions (Table 1) (10).

*Ginkgo biloba* (Ginkgoaceae) leaf extract; It is known that it has been used by Japanese, Chinese, and Korean cultures for centuries in various ailments. Ginkgo biloba leaves contain flavone glycosides, phenolic acids, and terpene lactones (13). *G. biloba* has been demonstrated to increase the rate of ocular blood flow in healthy adult volunteers, indicating that it may enhance circulation to the optic nerve head and protect retinal ganglion cells in glaucoma patients (Table 1) (13).

*Euterpe oleracea* (Arecaceae) is a palm tree that grows in the South American regions and has a purple round fruit that is widely used in the Brazilian diet and cuisine (14). The fruit contains anthocyanin, tannin, and flavonoid (14-16). Bersanetti et al. provided evidence that *E. oleracea* extract was successful in corneal cross-linking in rabbit corneas, addressing potential applications in corneal illness (Table 1) (17).

*Linum usitatissimum*, known in Turkey as keten, is a small plant belonging to the Linaceae family. Essential fatty acids like omega 6 (linoleic acid) and omega 3 (linoleic acid) are plentiful in their oilseeds. Pinheiro and colleagues A controlled trial in patients with Sjögren's syndrome treated with 1 g or 2 g oil of *L. usitatissimum* daily discovered that L. usitatissimum decreased ocular inflammation when compared to a placebo (Table 1) (18).

*Heliotropium indicum* (Boraginaceae) can be grown in both tropical and non-tropical regions. It is commonly found in moist rich soils in the lowland tropics along rivers and lakes, on roadsides, and in waste areas. Extracts obtained from the aerial parts of *H. indicum* are used as medicine in the treatment of fever, urticaria, ulcer, wound, local inflammation, gonorrhea, ringworm, and rheumatism (19). It is emphasized that the use of *H. indicum* in many diseases among people is due to the presence of alkaloids such as indisine, acetyl-indisine, and indisine-N-oxide (20). Kyei et al. (2015) evaluated the activity of an aqueous extract of *H. indicum* in rabbit eyes and discovered a significant hypotensive activity as well as anti-oxidant and neuroprotective activities (20). In addition, in 2 different studies conducted by the same authors in 2016, it was determined that the plant has both anti-inflammatory effects and effective against cataracts (Table 1) (21, 22).

*Scutellaria baicalensis* (Lamiaceae) is a flavonoid-rich plant that has long been utilized as a medicinal herb in Asian nations such as China. Hurst and Bazan found that the plant provided corneal healing (23), while Li et al. found that it was effective in cataracts because it inhibited aldose reductase (24). In addition to these findings, Nagaki et al discovered that the plant extract had high anti-inflammatory activity in a rabbit uveitis model (Table 1) (25).

*Lycium barbarum* (Solanaceae) known as the goji berry or wolfberry has been used for centuries in traditional Chinese medicine to treat hepatic and ocular diseases. It has immunomodulatory, neuroprotective, anti-inflammatory, and antioxidant effects. These have been associated with the presence of polysaccharides, which account for around 40% of *L. barbarum* composition (26). Studies on rats have shown that ingesting *L. barbarum* extract has a neuroprotective effect in experimental models of retinal ischemia and optic nerve damage (26). In cultures of human lens epithelial cells, Qi et al. reported that the plant's secondary metabolites also showed protection against oxidative and apoptotic effects (Table 1) (27).

**Table 1. List of medicinal plants used in various types of ocular diseases**

| Natural source | Part used | Action location | Activity | References |
|---|---|---|---|---|
| *Aloe barbadensis* | Leaf juice | Cornea<br>Cornea | Anti-inflammatory<br>Wound-healing | Wozniak et al.(12)<br>Curto et al.(10) |
| *Ginkgo biloba* | Leaf | Optic nerve | Neuroprotection | Cybulska-Heinrich et al.(13) |
| *Euterpe oleracea* | Fruit | Cornea | Cross-linking | Bersanetti et al.(17) |
| *Linum usitatissimum* | Seed | Cornea | Anti-inflammatory | Pinheiro et al.(18) |
| *Heliotropium indicum* | Aerial parts<br>Aerial parts<br>Aerial parts | Ciliary muscle<br>Anterior chamber<br>Lens | Ocular hypotensive effect<br>Anti-inflammatory<br>Anticataract | Kyei et al.(20)<br>Kyei et al.(21)<br>Kyei et al.(22) |
| *Scutellaria baicalensis* | Root<br>Root<br>Root | Lens<br>Anterior chamber<br>Cornea | Anticataract<br>Anti-inflammatory<br>Wound healing | Li et al.(24)<br>Nagaki et al.(25)<br>Hurst and Bazan.(23) |
| *Lycium barbarum* | Fruit<br>Fruit | Retina<br>Lens | Neuroprotection<br>Antioxidant | Wang H et al.(26)<br>Qi et al.(27) |
| *Vaccinium myrtillus* | Fruit<br>Fruit<br>Fruit<br>Fruit | Lens<br>Cornea<br>Anterior chamber<br>Retina | Anticataract<br>Antioxidant<br>Anti-inflammatory<br>Neuroprotection | Bravetti et al.(27)<br>Riva et al.(30)<br>Yao et al.(29)<br>Matsunaga et al.(31) |
| *Camellia sinensis* | Leaf | Lens | Anticataract | Gupta et al.(33) |
| *Hydrastis canadensis* | Root | Cornea | Conjunctivitis | Babbar and Ray(35) |
| *Panax ginseng* | Root | Anterior chamber | Anti-inflammatory | Kim et al. (37) |

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|---|---|---|---|---|
| *Salvia miltiorrhiza* | Aerial parts<br>Aerial parts | Anterior chamber<br>Retina | Anti-inflammatory<br>Neuroprotection | Zhang et al.(38)<br>Zhu et al.(39) |
| *Buddleja officinalis* | Flower bud | Cornea | Increased tear volume | Peng et al.(40) |
| *Prunus armeniaca* | Fruit | Cornea | Increased tear volume | Kim et al.(41) |
| *Aristotelia chilensis* | Fruit | Cornea | Increased tear volume | Hitoe et al.(42) |
| *Hippophae rhamnoides* | Fruit | Cornea | Increased tear volume | Nakamura et al.(44) |
| *Rhynchosia volubilis* | Seed | Cornea | Antioxidant | Kang et al.(45) |
| *Matricaria chamomilla* | Aerial parts | Cornea | Antioxidant | Bigagli et al.(46) |
| *Euphrasia officinalis* | Aerial parts | Cornea | Antioxidant | Bigagli et al.(46) |
| *Allium sativum* | Bulbus | Lens | Antioxidant | Raju et al.(49) |
| *Capsicum annuum* | Fruit<br>Fruit | Cornea<br>Cornea | Increased tear volume<br>Antioxidant | Shanmugham and Subban(48)<br>Shanmugham and Subban(48) |
| *Moringa oleifera* | Leaf | Cornea<br>Lens | Antibacterial<br>Anticataract | Hossain et al.(51)<br>Hossain et al.(51) |

*Vaccinium myrtillus* (Ericaceae) known as the bilberry found in the mountainous regions of Europe and the northern United States (28). Currently, bilberry is utilized in a wide range of pharmaceutical and food products that are advised for the treatment of vascular and visual diseases (28). Studies have shown that Bilberry is anticataract on the lens (27), anti-inflammatory (29), and antioxidant (30) on the cornea, and neuroprotective on the retina (Table 1) (31).

*Camellia sinensis* (Theaceae) is generally known as green tea. *C. sinensis* is mostly grown in India and China. It has immunomodulatory, hepatoprotective, antimicrobial, neuroprotective, anti-inflammatory, antidiabetic, and antioxidant effects (32). In the study in which an *in vivo* cataract model was created, green tea extract was administered intraperitoneally. Improvements in biochemical parameters were observed in rats given green tea extract compared to positive control (Table 1) (33).

The perennial herb *Hydrastis Canadensis* (Ranunculaceae), also known as Goldenseal, is native to southeastern Canada and the eastern United States. Goldenseal is used to treat gastroenteritis, diarrhea, and hemorrhoids, as well as upper respiratory tract infections, clogged noses, peptic ulcers and colitis, wound healing, stomach, intestinal disorders, and allergic rhinitis. Goldenseal includes alkaloids such berberine, hydrastine, palmatine, canadine, 6-desmethyl-sideroxylene, as well as flavonoids like sideroxylin, 8-desmethyl-sideroxylene (34). Studies have shown that goldenseal root and its major alkaloid berberin can be used as eyewash in the treatment of stage-1 of trachoma (Table 1) (35).

Ginseng is the root of *Panax ginseng* and has long been utilized in Chinese medicine. Ginseng's major active constituents are ginsenosides, which are a kind of steroidal saponin that may target various tissues and cause a wide range of pharmacological effects (36). Ginseng oral treatment significantly increased retinal blood flow in the temporal peripapillary areas in clinical studies on glaucoma patients (Table 1) (37).

*Salvia miltiorrhiza* (Lamiaceae) is perennial herb. It possesses antiarrhythmic, anti-artherosclerosis, enhancing microcirculation, protecting the myocardium, antioxidant, hepatoprotective, suppressing and releasing platelet aggregation, improving coronary, and anti-inflammatory properties (38). Zhang et al. showed that *S. miltiorrhiza* has a protective effect by suppressing inflammatory agents in rats with a diabetic retinopathy model formed through the blood-ocular barrier (38). Also, Zhu et al. showed that *S. miltiorrhiza* extracts decreased cell

loss as glaucoma progressed but were unable to stop the increase in intraocular pressure (IOP) in the laser-induced glaucoma model (Table 1) (39).

*Buddleja officinalis* (Buddlejaceae) has long been utilized in Chinese medicine. Flower of *B. Officinalis* includes flavonoids phenolic acid, and phenylethanoid. It possesses antioxidant and antimicrobial activities (40). Peng et al. found that The aqueous extract of *B. officinalis* has been found to increase tear volume on the cornea (Table 1) (40). Likewise, it has been determined that the plants of *Prunus armeniaca* (Rosaceae) (41) and *Aristotelia chilensis* (Elaeocarpaceae) (42) increased the tear volume on the cornea. *Hippophae rhamnoides* (synonym: *Elaeagnus rhamnoides*) (Elaeagnaceae) is an important plant with biological activities that includes anticancer, antioxidant, antibacterial, hepatoprotective, and atopic dermatitis (43). Nakamura et al. also, showed that *H. rhamnoides* fruit increased the tear volume on the cornea (Table 1) (44).

In another study, *Rhynchosia volubilis* (Fabaceae) ethanol extract was tested in an *in vivo* dry eye model. Compared to the control group, it was stated that ethanol extract prepared from *R. volubilis* strongly suppressed inflammation agents and could be used in dry eye syndrome (Table 1) (45).

*Matricaria chamomilla* (Asteraceae) and *Euphrasia officinalis* (Orobanchaceae) extracts were tested on human corneal epithelial cells against oxidative stress and inflammation caused by UVB radiation. Bigagli et al. determined that both plant extracts prevented oxidative damage to the cornea (Table 1) (46). *Capsicum annuum* (Solanaceae) has long been used as a spice in various parts of the world due to its distinct flavor, color, and aroma (47). It includes favonoids (quercetin, kaempferol, catechin, epicatechin, rutin, luteolin), capsaicinoids (capsaicin, dihydrocapsaicin), carotenoids (lutein, zeaxanthin, capsorubin, $\beta$-carotene), and steroid saponins (capsicidine, capsicoside E, F, G) (46). According to Shanmugham and Subban's study, it was determined that *Capsicum annuum* fruit extract both reduced intraocular pressure (IOP) and reduced inflammation on the corneal surface (Table 1) (48).

*Allium sativum* (Liliaceae) is an important plant with biological activities that include antimicrobial, antioxidant, anticancer, antidiabetic, hepatoprotective, antihypertensive, and antiobesity. *A. sativum* contains secondary metabolites of alliin, allicin, ajoene, S-allyl-cysteine, S-trityl-L-cysteine, diallyl sulfide, and S-allylmercaptocysteine (49). Raju et al. found that Garlic extract was reported to reduce rat lens opacity in an *in vitro* diabetic cataract model study(Table 1) (49).

One of the most delicious foods in the world, *Moringa oleifera* (moringa), is also consumed by humans and used in medicine for its antioxidant, antibacterial, antidiabetic, hepatoprotective, cardioprotective, immunomodulatory, radioprotective, analgesic, antiulcer, and antihypertensive activities. The observed effects are thought to be caused by a wide range of polyphenols and phenolic acids, as well as flavonoids, glucosinolates, and alkaloids (50). In an isolated goat lens model, *M. oleifera* showed significant *in vitro* action against glucose cataracts, and it was also effective in treating conjunctivitis (Table 1) (51).

Atropine is an alkaloid isolated from *Hyoscyamus niger, Atropa belladonna*. It has been commercialized in sulfate form as eye drops at 0.5% and 1% doses to induce mydriasis and cycloplegia.(52) The secondary metabolites competing with acetylcholine as an antagonist at the muscarinic receptors found in the ciliary muscle and iris sphincter (52, 53). Atropine in the treatment of myopia, a clinical experiment conducted in 2006, found that atropine eye drops reduced the progression of myopia in Asian children (54). Also, Chia et al. showed in 2016 that a reduced daily dose of 0.01% atropine eye drops prevented the progression of myopia and causing less rebound and side effects than regularly used higher doses (Table 2) (55).

Pilocarpine is an alkaloid isolated from *Pilocarpus microphyllus. P. microphyllust is* indigenous to South America and was used to treat glaucoma. Pilocarpine enhances aqueous humour drainage via the trabecular meshwork at the iridocorneal angle and stimulates ciliary muscle contraction (56). The use of pilocarpine for glaucoma therapy has decreased as a result of modern anti-glaucoma medicines with reduced risk profiles, although it is still marketed (Table 2) (56).

Caffeine is an alkaloid isolated from *Coffea arabica* and *Coffea canephora*. Eye drops containing caffeine are highly stable and resistant to photodynamic degradation. It has been evaluated for cataract prevention by providing ultraviolet (UV) protection. Kronschläger et al. reported that applying caffeine eye drops containing 0.9% hydroxypropylmethyl cellulose protected rats against cataracts caused by UV-B-type radiation exposure (57). Zhang et al. discovered that caffeine protects against oxygen-induced retinopathy in rats, which is a different effect (Table 2) (58).

Berberine is an isoquinoline alkaloid isolated from *Hydrastis canadensis*, *Berberis aristata*, *Coptis chinensis*, *Coptis rhizome*, *Coptis japonica*, *Phellodendron*

*amurense*, and *Phellodendron chinense* (59). It has antimicrobial, antifungal, anticancer, and antidiabetic activities (60). In a study on berberine Babbar and Roy found that berberine can be used as eyewash in the treatment of stage-1 of trachoma (Table 2) (35).

Homoharringtonine is an alkaloid isolated from *Cephalotaxus fortunei*. It has been approved by the US FDA for the treatment of chronic myeloid leukemia in Chinese medicine. In the study, it has been determined that the use of homoharringtonine in high doses contributes to the formation of corneal neovascularization (Table 2) (61).

Δ9-Tetrahydrocannabinol is a cannabinoid isolated from *Cannabis sativa*, *C. ruderalis*, and *C. indica.* The interest in cannabinoids in ocular diseases began in the 1970s when Hepler et al. demonstrated a reduction in intraocular pressure (IOP) in patients who smoked marijuana (62). Smoking marijuana or administering cannabinoids orally or intravenously causes a 25% drop in IOP that lasts 3 to 4 hours (63). Kokana et al. Also showed that Δ9-Tetrahydrocannabinol suppressed inflammation on the retina (Table 2) (64).

Curcumin was called after Vogel and Pelletier, who were the first to isolate a "yellow coloring material" from *Curcuma longa* rhizomes (turmeric) in 1815 (65). Curcumin has antibacterial (66), antiviral (67), antioxidant (68), antifungal (69), anti-arthritic (70), hepatoprotective (71), antithrombotic (72), cardioprotective (73), antidiabetic (74), anti-allergic (75), wound-healing (76), anti-inflammatory (77), and anticancer (78). Chung et al. demonstrated that Curcumin showed to decrease the expression of ovalbumin-induced proinflammatory cytokines like IL-4 and IL-5 in rat conjunctiva (79). In addition, another in *vitro* study discovered that curcumin protected hyperosmoticity-induced IL-1$\beta$ upregulation in the corneal epithelial cell via p38 mitogen activated protein kinase pathways (Table 2) (80).

Lutein and zeaxanthin are carotenoids from the xanthophyll family, which are secondary metabolites produced by some plants. Kale, savoy cabbage, spinach, broccoli, peas, parsley, maize, and egg yolks are rich sources of these carotenoids. The daily recommended lutein consumption is about 10.0 mg, while the daily recommended zeaxanthin intake is 2 mg (81). It has been demonstrated that supportive treatment with lutein and zeaxanthin can help to slow the development of age-related macular degeneration (AMD) (Table 2) (81).

Saffron isolated from the flower of *Crocus sativus*, is used in food as a flavor and coloring ingredient (82). Several studies have demonstrated that saffron provides several biological effects, including anti-inflammatory (83), free radical scavenging (84), anti-aging (84), anti-depressant (85), anti-bacterial (86), antiangiogenesis (87), antidiabetic (88), neuroprotective (89), and cardioprotective (90) activities. Saffron treatment, according to Manesh et al., has a beneficial effect on LGE (Lacrimal gland excision)-induced dry eye syndrome in rats due to its anti-inflammatory activities (Table 2) (91).

Kaempferol is a flavonol, which is a flavonoid found in plants including beans, strawberries, broccoli, apples, lemon, pineapple, peach, apricot, pear, grape, and spinach (92). Kaempferol has antibacterial (93), antioxidant (93), antidiabetic (94), anti-inflammatory (95), and anticancer (96) activities. Kaempferol-loaded gelatin nanoparticles have been reported *in vitro* to inhibit human umbilical vein endothelial cells and promote corneal neovascularization (Table 2) (97).

Quercetin is a flavonol that is rich in a wide range of fruits and vegetables. Many investigations on quercetin and its glycosides have been conducted. Quercetin has been shown to have anticancer, anti-inflammatory, anti-fibrosis, immunomodulatory, vascular protection, neuroprotection, antibacterial, antiviral, antidiabetic, and antihyperlipidemic properties (98). In a study on quercetin, it was determined that it has anti-inflammatory activity in the cornea (99). In another study on quercetin, it was revealed that it increases retinal optic nerve blood circulation and has an effect on glaucoma (Table 2) (100).

Myricetin is a flavonol with several pharmacological effects, including anti-inflammatory, antioxidant, anticancer, and antibacterial properties (101). The effect of myricetin on dry eye disease by reducing oxidative stress has been determined in the study (Table 2) (102).

Rutin is a flavonol glycoside with several pharmacological effects, including anti-inflammatory, antioxidant, anticancer, and antibacterial properties (103). The effect of rutin on diabetic retinopathy by reducing oxidative stress has been determined in the study (Table 2) (104).

Naringenin is a flavanone that is rich in a wide range of fruits and vegetables. Naringenin has been shown antioxidant, anticancer, antiviral, antibacterial, anti-inflammatory, antiadipogenic, and cardioprotective activities (105). According to Li et al., an *in vivo* study found that naringenin increased tear volume on the cornea. (Table 2) (106).

Cyanidin-3-glycoside is a potent antioxidant and anti-inflammatory found in fruits and vegetables (107). Morimitsu et al. Found that doses greater than 10 mM were reported to reduce rat lens opacity in an *in vitro* diabetic cataract model study. (Table 2) (108).

Silymarin is isolated from *Silybum marianum* (Asteraceae). Silymarin is a polyphenolic compound with seven secondary metabolites: taxifolin, silychristin, silydianin, silybin A, silybin B, isosilybin A, and isosilybin B. It has hepatoprotective, antioxidant, anticancer, and antiviral (109). In an *in vivo* study on silymarin, it was determined that the oxidative stress on the corneal surface was eliminated (Table 2) (110).

Genistein, an isoflavonoid, is abundant in soybeans. Along with its tyrosine kinase inhibitory properties, genistein has biological activities including antioxidant and aldose reductase inhibitory, anti-inflammatory, anticancer, and antioxidant activities (111). Genistein-amphiphilic polymer micelle have been reported *in vitro* to inhibit human umbilical vein endothelial cells and promote corneal neovascularization (Table 2) (112).

Puerarin an isoflavonoid, is isolated from *Puerariae lobatae*. It is commonly used as an adjuvant therapy for neurodegenerative disorders, diabetes and its complications, cardiovascular and cerebrovascular diseases, and cancer (113). Fathalipour et al. found that Puerarin attenuates retinal neovascularization (Table 2) (114).

Resveratrol (stilbene structure) is a polyphenol isolated from blueberries, bilberries, grapes, peanuts, cocoa, and cranberries. Resveratrol is well-known for its antiaging, anticancer, antidiabetic, neuroprotective, and cardioprotective effects (115). In a study on resveratrol, its ocular hypotensive effect was determined (Table 2) (116).

Glycyrrhizin is a saponosides isolated from the root of the Liquorice and ıt has an anti-inflammatory, antihypertensive, and immunosuppressive drug widely used in clinics (117). According to Li et al., glycyrrhizin has been used to inhibit eye surface inflammation and improve tear film quality in eye drops (Table 2) (106).

Meliacine is a triterpenoid isolated from *Melia azedarach*. It has antiviral, antihelmintic, emmenagogue, and anticancer activities (118). Alche et al. found that Meliacin exerted a potent antiviral effect on HSV-1-induced ocular disease in mice without evidence of toxic effects (Table 2) (119).

Forskolin is a diterpene isolated from *Coleeus forskohlii.* Forskolin has antiobesity, antidiabetic, antithrombotic, antioxidant, anti-inflammatory activity, antiasthma, antihypertension, and anticancer activities (120). According to Caprioli and Sears, Topical ocular administration of forskolin, which raises intracellular cyclic adenosine monophosphate by directly activating adenylate cyclase without cell surface mediation, reduced intraocular pressure (IOP) in healthy rabbits, monkeys, and volunteers (Table 2) (121).

Ferulic acid is a phenolic acid derrivates from fruits and vegetable includes such as *Angelica sinensis*, *Cimicifuga heracleifolia,* and *Lignsticum chuangxiong*. Ferulic acid has antioxidant, antimicrobial, anti-inflammatory, antithrombosis, and anticancer activities. It also helps prevent coronary artery disease, reduces cholesterol, and enhances sperm viability (122). In an *in vivo* study, it was emphasized that ferulic acid suppresses high levels of inflammation agents compared to the control group, therefore it can be used in dry eye syndrome (Table 2) (123).

Chlorogenic acid is a phenolic acid found in coffee, beans, potatoes, and apples that is synthesized via the esterification of caffeic and quinic acids. Many research have shown that chlorogenic acid has antibacterial (124), anti-inflammatory (125), antioxidant (124), antidiabetic (126), and anticancer (127) properties. According to Shin et al. found that chlorogenic acid suppresses high levels of inflammation agents compared to the control group therefore it can be used for diabetic retinopathy (Table 2) (128).

## CONCLUSIONS

Ocular diseases can be effectively treated with a wide range of plants and their secondary metabolites and their uses are documented in this book chapter. This review benefits researchers in finding better therapeutics for ocular disorders; these developments will ultimately benefit society as a whole.

| Table 2. List of secondary metabolites used in various types of ocular diseases | | | |
|---|---|---|---|
| **Secondary Metabolites** | **Action location** | **Activity** | **References** |
| Atropine | Ciliary body | Decreased myopia | Chia et al.(55) |
| Pilocarpine | Ciliary body and Cornea | Ocular hypotensive effect | Bachu et al. (56) |
| Caffeine | Lens<br>Retina | UV protection<br>Antiangiogenic | Kronschläger et al.(57)<br>Zhang et al.(58) |
| Homoharringtonine | Cornea | Neovascularization | Xu et al.(61) |
| Δ9-tetrahydrocannabinol | Ciliary body<br>Retina | Ocular hypotensive effect<br>Anti-inflammatory | Hepler et al. (62)<br>Kokona et al. (64) |
| Curcumin | Cornea<br>Anterior chamber | Anti-inflammatory<br>Anti-inflammatory | Chung et al.(79)<br>Chen et al.(80) |
| Lutein and Zeaxanthin | Retina | Anti- AMD | Mrowicka et al.(81) |
| Saffron | Anterior chamber | Anti-inflammatory | Manesh et al.(91) |
| Kaempferol | Cornea | Neovascularization | Chuang et al.(97) |
| Resveratrol | Ciliary body and Cornea | Ocular hypotensive effect | Liu et al.(116) |
| Quercetin | Cornea<br>Retina | Anti-inflammatory<br>Neuroprotection | Ding et al.(99)<br>He et al.(100) |
| Myricetin | Cornea | Anti-inflammatory | Yin et al.(102) |
| Rutin | Retina | Antioxidant | Ola et al.(104) |
| Naringenin | Cornea | Increased tear volume | Li et al.(106) |
| Cyanidin-3-glycoside | Lens | Anti-inflammatory | Morimitsu et al.(108) |
| Silymarin | Cornea | Antioxidant | Fallah Huseini et al.(110) |
| Genistein | Retina | Neovascularization | Cong et al.(112) |
| Puerarin | Retina | Neovascularization | Fathalipour et al.(114) |
| Berberine | Cornea | Conjunctivitis | Babbar and Ray(35) |
| Glycyrrhizin | Cornea | Anti-inflammatory | Li et al.(106) |
| Meliacine | Cornea | Antiviral | Alche ' et al.(119) |
| Forskolin | Ciliary body and Cornea | Ocular hypotensive effect | Caprioli and Sears(121) |
| Ferulic acid | Cornea | Anti-inflammatory | Chen et al.(123) |
| Chlorogenic acid | Cornea | Anti-inflammatory | Shin et al.(128) |

AMD: age-related macular degeneration

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