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Review Article

A REVIEW ON THERAPEUTIC POTENTIAL OF MEDICINAL PLANTS USED IN TREATMENT OF OCULAR DISEASES

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ABSTRACT

There are many pathological conditions which can affects health of eye due to the pollution, stress, nutritional deficiency and allergic conditions, etc. Glaucoma, uveitis, squint cataract, dry eye and conjunctivitis, etc. are common diseases of eye Due to side effects of allopathic drugs, now a day's huge numbers of herbal drugs are used for treatment of ocular diseases. In recent years, there have been many epidemiological and clinical studies that have demonstrated the beneficial effects of plant-derived compounds. Studies in cell cultures and animal models showed promising results for their uses in eye diseases. While there are many apparent significant correlations, further investigation is needed to uncover the mechanistic pathways of these botanical compounds in order to reach widespread pharmaceutical use and provide non-invasive alternatives for prevention and treatments of the major eye diseases. This review briefly explains the about ocular diseases, phytochemicals & medicinal plants to treat ocular diseases.

Keywords: Eye, Ocular disorders, Medicinal plants, phytochemicals

INTRODUCTION

Vision impairment is a major cause of disability worldwide. In 2015, an estimated 36 million people were blind, 217 million had moderate or severe vision impairment and over a billion people experienced near-vision impairment (presbyopia). Cataract and uncorrected refractive error are correctable conditions which accounted for 78% of global visual impairment that year. Despite reductions in age-specific prevalence, the number of people with vision impairment and blindness is projected to increase due to population growth and ageing. Vision impairment is associated with negative health outcomes, such as having multiple chronic conditions, and increased mortality, and also induces substantial socioeconomic consequences for individuals, and an associated lower quality of life (Bourne *et al*., 2017; Flaxman *et al*., 2017; Garin *et al*., 2014).

The eye is quite possibly the most intricate organs in the human body. There are three layers to the natural eye. The external locale comprises of the cornea and sclera. The cornea likewise sends and communicates light to the focal point and retina and shields the eye from disease and underlying harm in the more profound parts. The sclera frames a layer of connective tissue that shields the eye from inside and outside powers and keeps up with its shape. The cornea and sclera are associated with the limbus.

The noticeable piece of the sclera is covered by a reasonable mucous film, the conjunctiva. The centre layer is comprised of the iris, the ciliary body and the choroid. The iris controls the size of the understudy, so the measure of light arrives at the retina; the ciliary body manages the energy and organization of the focal point and is a wellspring of water creation; and choroid is a layer of conduits that supply oxygen and supplements to the external layers of the retina. The inward layer of the eye is the retina, a perplexing, complex design of tactile nerves that catches and cycles light. The three most clear constructions encompassed by visual layers are called water, glassy and focal point (Muller *et al*., 2003; Rufer *et al*., 2005; Van Buskirk 1989).

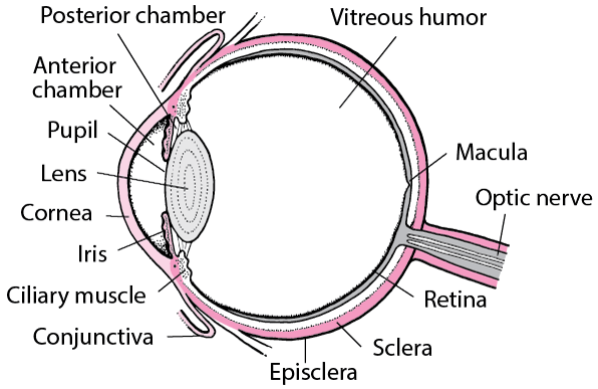

Figure 1: Structure of eye

Some common ocular diseases

Cataracts

Cataract is blurring of the lens of the eye which forestalls clear vision. Albeit most instances of cataract are identified with the maturing cycle, infrequently kids can be brought into the world with the condition, or a waterfall may create after eye wounds, aggravation, and some other eye sicknesses. There are three essential kinds of Cataract re - examined under: Nuclear Sclerotic Cataracts, Cortical Cataracts, Posterior subcapsular cataract (Thompson *et al*., 2015).

Glaucoma

Glaucoma can be a condition that harms your eye's optic nerve. It deteriorates over the long haul. It's regularly connected to a development of weight inside the eye. Glaucoma will in general spat families. You for the most part don't get it until another time throughout daily life. The expanded weight in the eye, called intraocular pressure, can harm the optic nerve, which sends pictures to your mind. On the off chance that the harm intensifies, glaucoma can cause perpetual vision misfortune or even all out visual impairment inside a couple of years. A great many people with glaucoma don't have any early manifestations or torment (Gupta and Chen, 2016).

Corneal Abrasion

It happens quite often when dirt or sand gets trapped in your eye. As you rub your eyes to get rid of it, the dust particle causes a scratch on your eye. This condition is called Corneal Abrasion. You experience pain in your eye and a burning or stinging sensation.

The symptoms are feeling sand or dirt stuck in your eye, Pain in eye, especially when you open or close it, Redness of eyes and teary eyes, Light sensitivity, Blurred vision (Fraser, 2010).

Age-Related Macular Degeneration (AMD)

This is the deterioration of the macula, the central area of the retina that controls visual acuity. Symptoms of Age-related Macular Degeneration include loss of visual acuity, loss of contrast sensitivity, Seeing images distorted in the centre (Bressler *et al*., 1998).

Subconjunctival Haemorrhage

This condition occurs when a tiny blood vessel breaks just below the conjunctiva of your eye. The conjunctiva cannot absorb

blood. This causes the blood to be trapped underneath it. A subconjunctival haemorrhage often occurs without causing any serious harm to your eyes. A strong sneeze or a bout of a cough can even cause haemorrhage of blood vessels in your eyes. The initial symptoms might worry you, but this condition is usually harmless condition and disappears within a week or two (Tarlan and Kiratli, 2013).

Retinal Detachment

This is a serious eye condition. It occurs when your retina located at the back of your eye detaches from the tissue around it. The Retina processes light and a damaged Retina may cause permanent vision loss if it isn't treated right away. You are at risk if you are severely nearsighted or have a family history of retinal detachment (Ghazi and Green, 2002).

Scleritis

This is a painful condition where the white part of the eye (called Sclera) swells. The tissues of the sclera constitute the protective outer layer of your eye. It makes up 83% of your eye's surface. In most of all cases, scleritis is associated with other autoimmune disorder such as rheumatoid arthritis. The two types of scleritis are Anterior and Posterior Scleritis. The symptoms include, severe pain and tenderness in the eye. This pain often extends to other regions of the face such as the jaw, face, or part of head at the affected side, Blurred vision and tearing, extreme sensitivity to light, partial or complete loss of vision (in some cases) (Beardsley *et al*., 2013).

Hyphema

Hyphema is the condition when blood gets accumulated in the front part of your eye. The blood mainly collects between the Cornea and the Iris. This condition occurs when an injury (such as a sharp blow) tears the blood vessels. The less harmful case of the broken blood vessel is called subconjunctival haemorrhage while Hyphema is very painful and can also cause serious vision and eye problems such as Glaucoma or Corneal damage (Bansal *et al*., 2016).

Refractive Errors

Refractive errors, including nearsightedness, farsightedness and astigmatism, are the most common causes of vision loss. Refractive errors occur when light is improperly bent (or "refracted") while passing through the cornea. This produces a flawed image (Schiefer *et al*., 2016).

Dry eyes

Dry Eye is a condition caused by changes in the quantity or quality of your tears. Tears are composed of three main layers that work together to keep your eyes comfortable and protected. If these layers become imbalanced, your tears will evaporate too quickly, causing your eyes to feel dry and irritated (Latkany *et al*., 2008).

Eye allergies

Eye allergies occur when the eyes react to something that irritates them, causing the eyes to produce histamine. Unlike bacterial or viral eye infections, eye allergies can not be spread from person to person. People who suffer from eye allergies usually also have nasal allergies. Eye allergies are usually a temporary condition associated with seasonal allergies. Eye allergies can also develop from exposure to other environmental triggers, such as pet dander, dust, smoke, perfumes, and foods (Bielory *et al*., 2006).

Major Eye Diseases Share Common Mechanistic Pathways

AMD, glaucoma, cataract, and other retinal diseases, including diabetic retinopathy (DR) and retinitis pigmentosa (RP), are the major causes of blindness around the world. An epidemiologic survey conducted by the Eye Diseases Prevalence Research Group indicated that by 2020 an estimated 30.1 million Americans will suffer from cataract. Interestingly, all these diseases are associated with aging, and their etiology or pathophysiologies share some common mechanistic pathways. These pathways include oxidative stress, inflammation, and apoptotic factors, which provide insight for potentially targetable areas. Indeed, in many cases of eye diseases, oxidative stress due to reactive oxygen or nitrogen species and lipid peroxidation lead to ocular cell death. In addition, many pathogenic pathways include inflammatory factors such as the tumor necrosis α (TNF-α) and nuclear factor-kappa B (NF-κB). Interestingly, these pathways often intersect with the mechanism of action of many botanical compounds. Oxidative stress induces the formations of reactive oxygen species, which interact with the mitochondria and activates the JNK pathway leading to apoptosis. Since AMD, DR, RP, and glaucoma all have a significant impact on populations worldwide, this review will focus on these pathologies and the potential benefits of botanical compounds in their prevention and treatment (Gurib-Fakim *et al*., 2006; Klein *et al*., 2004; Congdon *et al*., 2004).

Modern Diagnostic Approach for Eye Diseases:

- Opthalmoscopy is used for the evaluation of problem in posterior segment of eye. Flourescien angiography is used for the diagnosis of retinal lesions.
- Gonioscopy helps in diagnosis of angle of anterior chamber.
- Corneal topography is used for cornea curvature surface mapping, also used to diagnose marginal degeneration and keratoglobus.
- Tonometry is used to analyze intraocular pressure in glaucoma. Perimetry is used for visual field examination in glaucoma.
- Ultrasound biomicroscopy is used to visualize behind the iris.
- Optical coherence tomography is used to assess volume of retina and retinal thickness. Ocular surface staining is applied for the measurement of basal secretion of tears (Gunjal and Gaikwad, 2022).

The treatment of eye disorders with medications that have no side effects remains a problem for the medical system. The medical system continues to struggle with treating eye diseases using chemical treatments that have no adverse effects. Medicinal plants, on the other hand, can overcome these limitations. Herbal medications, on the other hand, have the ability to get over the limitations that come with conventional medications. Due to its efficacy, few side effects, and cost-effectiveness, several attempts have been made to discover new herbal medications from a variety of sources (Salazar-Gómez *et al*., 2023).

Nature has been an unlimited source of biologically-active compounds. Attempts have been made to investigate new

compounds with an aim to provide substantial benefits to eye tissue and vision with less side effects and toxicity. Emerging scientific evidence of antimicrobial, antibacterial, antioxidant, anti-inflammatory, wound-healing, antitumor, and antiangiogenic actions of traditional medicines have encouraged more research investment in this area cent research studies have identified molecular mechanism of action of many of the botanical compounds, which are in use as nutraceuticals or supplements. However, the detail mechanisms of most plant-derived active ingredients are still under investigation, and few research studies have been performed on the efficacy of botanical compounds' effects on human diseases, especially for eye diseases (Memarzadeh *et al*., 2018; Tewari *et al*., 2019).

Phytochemicals used to treat ocular disease

Hesperidin

Hesperetin particularly attractive is their effect on ocular blood flow and vascular permeability. Hesperidin, and especially hesperetin, produces marked increase in ocular blood flow and retinal function recovery following retinal ischemia. Additionally, these compounds have been demonstrated to be effective in the treatment of chronic venous insufficiency. Reports also suggest that hesperidin can prevent microvascular leakage through their capillary wall strengthening action: hesperidin methyl chalcone, given intravenously significantly inhibited the macromolecular permeability-increasing effect of bradykinin, LTB4, and histamine. Furthermore, hesperidin and hesperitin can reduce platelet aggregation, a factor involved in the blockage of retinal blood vessels (Majumdar *et al*., 2009)

Baicalein

Reports also suggest that baicalein is capable of suppressing IL-6 and IL-8 expression in ARPE-19 cell lines and to protect the retinal ganglion cells (RGC) from oxidative stress and ischemia induced cell death. Similar results were observed with ARPE-19 and human RPE cells. Protection of retinal cells against oxidative stress and ischemia/reperfusion (I/R) in vivo were reported for baicalein. The antioxidant activity of baicalein on human retinal pigment epithelium cells, it was found to down regulate the levels of VEGF and MMP-9 (Xiao *et al*., 2014).

Bioflavonoids

Flavonoids have gained prominence in the pharmaceutical arena by virtue of their therapeutically beneficial properties. Bioflavonoids possess antioxidant, anti-angiogenic, and/or anti-inflammatory activities and are also capable of reducing fluid retention and strengthening capillary walls. Interestingly, the etiology of most ocular diseases involve free radical mediated oxidative damage, hypoxia, decreased blood supply to ocular tissues and, in certain conditions, angiogenesis, increased vascular permeability and leakage of vascular contents. Thus, select bioflavonoids may be effective in the prevention or treatment of ocular diseases (e.g., DR and macular degeneration) that lead to vision loss if untreated (Crozier *et al*., 2009; Erickson *et al*., 2007).

Epigallocatechin gallate

Epigallocatechin gallate (EGCG), also known as epigallocatechin 3-gallate, is the ester of epigallocatechin and gallic acid EGCG is also an inhibitor of angiogenesis. EGCG was reported to inhibit angiogenesis by inhibiting

hypoxia-inducible factor-1α protein expression and in turn VEGF expression. The treatment with EGCG (intraperitoneal administration) in nude mice decreased tumor growth, microvessel density and tumor cell proliferation. However, the authors reported that other tea catechins such as (-)-epigallocatechin, (-)-epicatechin gallate, and (-)-epicatechin were ineffective in vitro against Erk1/2 (extracellularly-regulated kinase-1 and -2; important mediators in the up-regulation of VEGF expression) activation, whereas EGCG inhibited Erk1/2 activation in a dose dependent manner (Lee *et al*., 2011; Cavet *et al*., 2011).

Resveratrol

Kubota et al used oral doses of 5, 50, 100, 200 mg/kg of bodyweight in endotoxin induced uveitis (EIU) mice model with RES. They found a significant dose dependent reduction in leukocyte adhesion molecules, ICAM. The levels of ICAM and MCP were also reduced in the retina and RPE-choroid on administration of 50 mg/kg of RES in the EIU mice model. All other inflammatory mediator levels were also diminished. Zhou et al observed increased levels of the glaucoma biomarker, endothelial leukocyte adhesion molecule-1, when acutely treated with H2O2. Chronic treatment resulted in sustained stress response activation. Luna et al observed a significant inhibition of these markers on administration of RES (Kubota et al., 2009).

Curcumin

Curcumin is a natural phenol obtained from Curcuma longa of the Zingiberaceae family. It is the major of the three curcuminoids. Curcumin is used as an anti-inflammatory and anti-oxidant in various pathological conditions. Awasthi et al used an in vitro rat model to establish the activity of curcumin as an antioxidant in treating cataract. When treated with curcumin, 75 mg/kg, there was a significant increase in the glutathione S-transferase isozyme, rGST8-8, which uses 4-hydroxy-2-nonenal/L, a highly electrophilic product of lipid peroxidation, as a substrate and reduces it. It was observed that naphthalene, through an oxidative stress mediated pathway, causes cataract in rat and rabbit models (Awasthi *et al*., 1996).

Although the potential of the phytochemicals as therapeutic agents for oxidative stress associated ocular diseases has been demonstrated, their delivery to the ocular tissues and physiological diffusion barriers encountered has not been investigated. In order to limit/prevent oxidative damage it is imperative that the bioflavonoids reach the deeper ocular tissues such as the neural retina and lens, the sites of free radical induced damage, in effective concentrations.

Commonly used medicinal plants used to treat ocular disease

1. *Emblica officinalies*

Common name: Amlaki, Amla

Chemical constituents: Ellagic acid, gallic acid, phyllantine, chebulic acid, chebulinic acid, tannin, vitamins.

Use: Improve eye sights, Beneficial in the treatment of conjunctivitis and glaucoma and cataract (Suryanarayana *et al.,* 2004).

2. *Terminalia chebula*

Common name: Haritaki

Chemical constituents: Chebulin, ellagic acid, gallic acid, chebulilinic acid, terflavin A-D, tannic acid, ethyl gallate

Use: The prevention of age-related eye disorders like Age-related macular degeneration (ARMD), Senile Cataract,

Open-angle glaucoma and Retinal degeneration (Singh *et al*., 2011).

3. *Terminalia bellerica*

Common name: Vibhitaki

Chemical constituents: Bellericosides, hexahydroxydipjenic acid, methyl ester, beta-sitosterol, gallic acid, ethyl gallate, ellagic acid, chebulagic acid, mannitol, glucose, galloyl glucose

Use: Used in cataract, glaucoma, progressive myopia and conjunctivitis (Ashwini *et al*., 2011).

4. *Nigella sativa*

Common name: Kalonji

Chemical constituents: alanine, arginine, ascorbic-acid, asparagine, campesterol, carvone, cymene, cystine, dehydroascorbic-acid, eicosadienoic-acid, glucose, glutamic acid, glycine, iron, isoleucine, leucine, linolenic-acid, lipase, lysine, methionine, myristic-acid, nigellin, nigellone, oleic-acid, thymoquinone.

Use: Used in Cataract **(**Elkadery *et al*., 2019).

5. *Trigonella foenum*

Common name Graecum, Fenugreek seed

Chemical constituents: Ascorbic acid, carotene, beta-carotene, thiamine, niacin, vitamin C, quercetin, kaempferol.

Use: Used in cataract and as an anti-inflammatory agent (Gupta *et al*., 2010).

6. *Ginkgo biloba*

Chemical constituents: terpene lactones-ginkgolides and diterpenes and ginkgo flavone glycosides-ginkgetin, bilobetin, and sciadopitysin

Use: Used in Glaucoma, dry eyes, improve eye-sights (Fogagnolo *et al*., 2022)

7. *Boerhavia diffusa*

Common name Punarnava

Chemical constituents: Punarnavine, punarvoside, beta-sitosterol, tetracosanoic, hexacosanoic, stearic acid, ursolic acid, oxalic acid, mysristic acid

Use: Prevent night blindness and conjunctivitis (Lakshmi *et al*., 2017).

8. *Ocimum sanctum* linn

Common name Tulasi

Chemical constituents: Carvacrol, camphere, eugenol, ascorbic acid, beta-carotene, apigenin, ascorbic acid, glyocosides, saponin, tannin, sitosterol, palmitic acid and oleic acid.

Use: Help in prevent conjunctivitis and cataract, also used as antiinflammatory and soothing properties that help to protect eyes from environmental damage and free radical (Kumar *et al*., 2011).

9. *Butea monosperma*

Common name: Palash

Chemical constituents: Palasonin, aleuritic acid, butrin, isobutrin, coreospsin, sulphurein, monospermoside, isomonospermoside, tannic acid, gallic acid, bets sitosterol

Use: Used in conjunctivitis and cataract (Malvia *et al*., 2018).

Ayurvedic therapies for eye disorder

Sushruta the father of Indian Ophthalmology mentioned six Kriya Kalpas.- Tarpana, Putapaka, Seka, Aschotana, Anjana, Arka.

Kriya means the therapeutic procedures which cures the disease without causing any adverse effects. Kalpa indicates the specific formulation adapted for the therapeutic procedures.

Therapies for eye disorders:

Fomentation: - Seka

Fomentation with decoction of Kanthakari (Solanum xanthocarpum) root, prepared with milk. Fomentation with concentrated extract of either Nagarmotha (Cyperus scariosus) or

Sendha Namak (Rock Salt) or Mulethi (Glycyrrhiza glabra) or Pippali (Piper longum) prepared with milk

Arka

Steam distillates of plants like Punarnava (Boerhavia diffusa), Palash (Butea monosperma) and Mulethi (Glycyrrhiza glabra), used as eye drop (Verma and Lal, 2014).

Anjan

Paste of Mulethi (Glycyrrhiza glabra), Harida (Curcuma longa) Harad (Terminalia chebula) Devdaru (Cedrus deodara), in equal parts prepared with goat milk or water and concentrated. An Anjan (Collerium) is prepared and applied

Paste

Fine paste of drugs used as ointment

Washing

Washing of eyes with extract of drugs like Triphala comprising of three drugs viz. Amla (Embica officinalis), Harad (Terminalia chebula) and Bahera (Terminalia belerica) (Shastri, 2009; Srikanth, 2011).

CONCLUSION

Ayurveda is one of such inherited tradition of health and longevity. A wide variety of plants have been found to have effective against number of ocular diseases. Botanical compounds have been used throughout history for the prevention and treatment of various diseases. Previously, botanical supplements had not been awarded much scientific consideration; however, in the recent years, researchers and pharmaceutical companies have raised increasing interest for active ingredients from plants and nutraceuticals Collaborative efforts between traditional healers, scientists, and healthcare professionals can bridge the gap between traditional knowledge and modern evidence-based medicine, ultimately benefiting the population's eye health. By combining the wisdom of ancient botanical knowledge with scientific research, we can unlock the full potential of medicinal plants and contribute to the development of more comprehensive and effective eye care treatments in wor

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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