Review Article

A Comprehensive Review on Ocular Vision Enhancement and Reduction of Inflammation of Eyes by *Foeniculum vulgare* Seeds Extract.

Wankhede Siddhi[1*], Lanjewar Kalyani[2], Agala Dr. V.S. Babu [3]

1. Student, G H Raisoni Institute of Life Sciences, Hingna, Nagpur, Maharashtra, India.
2. Assistant Professor, G H Raisoni Skill Tech University, Hingna, Nagpur, Maharashtra, India.
3. Dean, G.H. Raisoni Skill tech University, Nagpur, Maharashtra, India.

***Corresponding author's E-mail:** siddhiwankhede08@gmail.com

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ABSTRACT

Ocular health is vital for clear vision. However, people still face issues like dryness, irritation, inflammation, and progressive vision loss. Recent interest in herbal treatments has brought fennel (Foeniculum vulgare) seed extracted into the spotlight as a promising natural aid for eye health. This review explores the potential of fennel seed extract to improve vision and reduce inflammation-related eye disorders. Fennel seeds contain bioactive compounds, including flavonoids, volatile oils, and phenolic antioxidants. These compounds have anti-inflammatory, antimicrobial, and soothing effects. Fennel seed extracts may help relieve eye irritation, reduce inflammation in the conjunctiva and cornea, increase tear production, and protect eye tissues from oxidative damage. Together, these benefits can lead to better visual comfort and possibly improved visual performance. This review aims to clarify how fennel seed extract can be a helpful approach for addressing eye issues and promoting healthier vision. It also points out areas where more research is needed.

Keywords: Anti-inflammatory effect, Bioactive compounds, Dryness, Eye irritation, Foeniculum Vulgare, Fennel Seed extract, Oxidative damage protection, Ocular Inflammation.

INTRODUCTION

Ocular vision refers to the function of the eye in terms of the formation of an image upon the retina and, further, sending that information to the brain. During normal vision, the ocular motor system works to fixate, track, and hold images steadily on the retina, which ensures good visual acuity[1]. Ocular inflammation denotes an immune response within one or more segments of the eye, including the surface of the eye (conjunctiva, cornea), the uvea (iris, ciliary body, choroid), the retina, the optic nerve, or other structures. It consists of the influx of immune cells, liberation of inflammatory mediators, such as cytokines, and ranges from mild, self-limited conditions up to severe, vision-threatening disorders[2]. Causes of ocular inflammation include infection by bacteria, viruses, and fungi; trauma; chemical irritants; and systemic inflammatory diseases, especially autoimmune disorders[3]. At the very centre of dry eye disease is inflammation. Poor quality or quantity of tears results in chronic damage and inflammation of the ocular surface, that is, the cornea, conjunctiva, and eyelids[4].

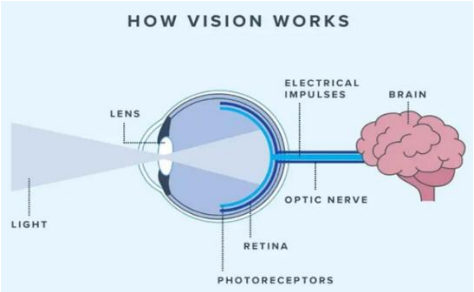

Figure 1: Mechanism of vision[7]

An aqueous extract of Foeniculum vulgare seeds was reported to reduce IOP significantly in rabbit models. Single-drop application at concentrations of 0.3%, 0.6%, and 1.2% w/v resulted in ~17.5, ~21.2, and ~22.0% reductions in normal normotensive eyes.[5] In a study on selenite-induced cataract in rabbits, 0.5% eye-drops prepared from aqueous fennel seed extract considerably decreased the lens opacity as compared to the untreated cataract eyes. The same study showed that the lenses treated with fennel extract had reduced MDA levels, a marker of oxidative stress, indicating that fennel extract protects the lens against oxidative damage[6]. The methanolic extract of F. vulgare fruit (seeds) has been reported in rodents to significantly reduce inflammation, increase antioxidant enzyme activities (SOD, catalase), and lower lipid peroxidation (MDA)[7].

Inflammation is an 'organized response of the body to injury or infection.' That is, it is the body's response to injurious stimuli such as infection and injury. Inflammation entails the cells and mediators that are responsible for vascular changes, increased cell migration, and tissue response. In vision, there are different forms of inflammation that can occur in different parts of the vision system, such as the cornea, uvea, or retina. These can manifest in the form of pain or redness[8].

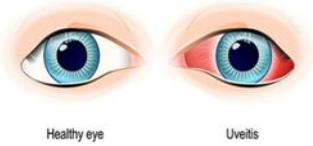

Figure 2: Healthy eye Vs Eye with Uveitis[23]

Mechanisms of Ocular Inflammation:

1. Immune Activation:

Injury or infection, or autoimmune stimuli, trigger innate immune cells (macrophages, dendritic cells, microglial cells). These cells secrete pro-inflammatory cytokines (such as TNF-alpha, IL-1 beta, IL-6) as well as reactive oxygen species (ROS).[9]

2. NF-κB Pathway:

NF-κB (nuclear factor kappa B) is a major transcription factor that Upon activation, NF-κB travels to the nucleus and upregulates pro-inflammatory genes such as COX-2 and iNOS (inducible nitric oxide synthase).[10]

3. MAPK and STAT Pathways:

MAPK pathways (ERK, JNK, p38) mediate inflammation and cytokine release in ocular cells.

The STAT pathway is also involved in inflammation gene expression in epithelial and immune cells.[9]

4. Breakdown of blood-ocular Barriers:

Breakdown of Blood-Ocular Barriers Inflammation compromises the blood-aqueous and blood-retinal barrier tight junctions, leading to increased permeability and immune cells infiltration.

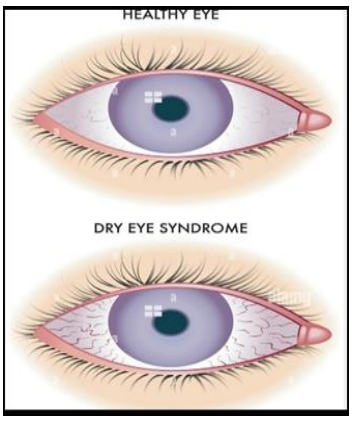

Figure 3: Healthy Eye with an eye affected by Dry Eye[20,24]

Treatment:

- **Treatments for Vision Enhancement:-**

  Non-Surgical treatment: corrective glasses & contact lenses Low-vision aids (magnifiers, special lenses).

  Surgical treatment: LASIK, PRK (laser vision correction) Cataract surgery (lens replacement), Intraocular lens implants.

- **Treatments for Inflammation:**

  Pharmacological treatment:

  Corticosteroids: Prednisolone, dexamethasone

  NSAIDs: Ketorolac, diclofenac

  Antibiotics/ Antivirals: For infectious causes

  Antihistamines: For allergic conjunctivitis

  Immunosuppressants: For chronic or autoimmune uveitis

Is herbal preparation better than marketed preparation?

Multi-Targeted and synergistic:

Herbal medicines act on more than one mechanism, while a large number of conventional medicines act on just one mechanism. Plants have compounds like phytochemicals, which collectively act on anti-inflammatory, antioxidant, immunomodulatory, and vasculoprotective mechanisms, which are useful in managing complex multifactorial conditions such as eye inflammation and vision anomalies. Herbal medicines contain more than one active agent, which acts simultaneously. Conventional medicines typically interact with just one mechanism of action, such as the mechanism of action of NSAIDs, where it acts as an inhibitor of COX enzymes, but herbs act as inhibitors of cytokines, ROS, immune activation, and more.

Generally Fewer and Milder Side Effects:

Herbal medicines are also felt to be safe compared to conventional medicines when taken alone.

• Even prospective clinical studies involving humans revealed patients who took only herbal medications had a low occurrence of systemic-related adverse reactions (such as no liver involvement in one in-hospital clinical research), but patients who combined the herbal and conventional medications had a higher possibility of aforementioned reactions.

• Pharmaceutical anti-inflammatory drugs available in the market, like corticosteroids and NSAIDs, can lead to serious ocular and systemic adverse effects, such as increased IOP, cataracts, renal complications, or gastrointestinal mucosal damage, when taken on a long-term basis.

Improved Patient Acceptance and Compliance:

Herbal medicines could be more acceptable to the patient. This could be the case when the HER2-positive cancers would have to be treated with supporting care over a long span of time.

In addition, natural medicine is thought to be less harsh on the body than conventional medicine, and usability is a factor which could help improve patient compliance regarding therapy, especially where chronic conditions like inflammation or age-related vision problems are being treated.

Herbal medicines can also be used for preparing herbal drugs, and their use can result in increased satisfaction on the part of the patient's compared to conventional medicines.

Plant profile:

- Biological source: Fennel is a medicinal plant belonging to the Umbelliferae (Apiaceae) family.
- Chemical constituents: It consist of 3 to 7% of volatile oil, about 20%each of fixed oil. The chief active

constituent of volatile oil is ketone, fenchone and a phenolic ether anethole.

The chief active constituent of volatile oil is ketone, fenchone and a phenolic ether anethole. Uses: The fruit and root infusions are used as relaxant, estrogenic, analgesic and anti-inflammatory medicines in traditional medicine. Fennel seeds have exhibited estrogenic, antioxidant, and antihirsutism activities; it increases milk secretion, promotes menstruation, facilitates birth and alleviates the symptoms of dysmenorrhea.[11,17]

Figure 4: *Foeniculum vulgare* miller[12]

Table 1: Organoleptic properties of Fennel[12]

Colour	**Green to yellowish brown**
Odour	Sweet aromatic
Taste	Strongly aromatic
Size	5-10 x 2-4mm
Shape	Straight or slightly curved
Condition	straight or slightly curved Cremo carp that has been dried
Surface	Glabrous

Table 2: Microscopic properties of Fennel:[12]

Pericarp: [a] Epicarp	A layer of quadrangular to polygonal cells, with smooth cuticle
[b]Mesocarp	Reticular, lignified parenchyma surrounding the vascular bundles
[c]Vascular bundles	Five in number, bicollateral present below ridge (primary ridge)
[d]Vittae	Schizogenous oil cells, 4 on dorsal side, 2on commissural surface/ventral surface. About 250 micron in maximum width, the walls are brown.
[e]Endocarp	Consist of narrow elongated cells having a parquetry arrangement
Seed: [a]Testa	Single layered yellowish brown in colour
[b]Endosperm	Thick walled, polygonal, cellulosic parenchyma containing oil globules, aleurone, grains and rosette crystal of calcium oxalate
[c]Raphe	A single ridge of vascular strands appears in the middle of commissural surface
[d]Carpophore	With very thick walled sclerenchyma in 2 strands

MATERIALS AND METHODS

Material used: fennel seed, powdered seeds, n-hexane, methanol

Extraction Method:

1. Maceration process

This processing will prevent loss of the chemical components and keep the samples were housed in a secure environment to safeguard the quality of the samples. In this study, n-hexane, methanol, and other chemicals and reagents were used. Each one of the compounds and agents was either laboratory or analytical grade. The volatile compounds from the seeds of F. vulgare were extracted using the technique of maceration. Using, the weight-to-solvent ratio is 7:3, that is, water to methanol; weight of sample added is 25g in a total volume of 100ml. The duration spent in the maceration process is approximately 7 days. Extraction of Bioactive Compounds: The bioactive compounds were extracted by Using Maceration process. A weight amount of sample is placed (25g) in a solvent of total100ml using a ratio of 7:3 i.e. Water (70%) Methanol (30%). The maceration process is done for 7days.[12]

Procedure:

plant material, crushed or small to moderately coarse powder

Fennel seeds

↓

Placed in closed vessel

↓

Whole of the selected solvent added

↓

Allowed to stand for 7 days, shaking occasionally

↓

Liquid strained off Solid residue (marc) pressed to recover as much occluded solution

↓

Strained and expressed liquid combined

↓

Caused by subsidence or filtration

↓

Evaporation and concentration

Pharmacological properties of Fennel[19]:

Antioxidant activity:

Fennel extracts have antioxidant potential: the aqueous, hydroethanolic, decoction, and essential oil extracts of F. vulgare demonstrated their potency in DPPH, FRAP, and Total Antioxidant Capacity (TAC) assays in an in vitro study. The essential oil had the highest antioxidant effect, with an IC_{50} value of 51.45 µg/mL.[15]

The same study (Unveiling the Chemical Composition…) correlated the antioxidant capacity with the phenolic compounds: e.g., butyl ferulate, chlorogenic acid, and dihydrocaffeic acid were abundant and likely contributed significantly.[13,22]

Antimicrobial / Antifungal Activity:

The antimicrobial activity of F. vulgare extracts and essential oils has been reported; they noticed inhibition of

microorganisms by an essential oil rich in fenchone and trans-anethole, as well as by phenolic extracts in the presented in vitro + in silico study. For instance, Candida albicans was inhibited with MIC = 3.13 mg/mL, while Aspergillus niger was inhibited with MIC = 6.25 mg/mL. The same study performed in silico molecular docking to illustrate that the phenolic compounds, chlorogenic acid and quercetin-3-glucuronide, interact strongly with microbial target proteins, thereby providing a mechanistic basis for the antimicrobial effect. Another study conducted with seeds showed a weak antimicrobial activity for some bacterial strains, such as *P. fragi, S. putrefaciens*, and *C. jejuni*, using conventional extraction; the MIC was 2-4 mg/mL, which is generally relatively weak compared to potent antimicrobials.[2,16]

Anti-inflammatory activity:

Anti-inflammatory activity stands out among the pharmacological effects of the fennel plant. Studies point to its strong potential in this area. Researchers have found that the methanol extract from fennel carries clear anti-inflammatory effects. When given orally at 200 mg per kg body weight, the methanol extract of fennel fruit helps inhibit both acute and subacute inflammatory conditions. It also curbs type 4 allergic reactions pretty effectively. On top of that, this extract lowers the activities of superoxide dismutase, known as SOD, and catalase, or CAT. Meanwhile, it boosts plasma levels of HDL cholesterol in a significant way. At the same time, the extract cuts down the level of malondialdehyde, which measures lipid peroxidation. All these findings suggest the methanol extract of fennel fruit works well to reduce inflammation overall. Kataoka and colleagues looked into the anti-inflammatory effects of fennel too. Their results indicated that the methanol extract from fennel seeds blocks inflammation by acting on cyclooxygenase pathways. It does the same through lipoxygenase pathways as well. Choi and team also checked out the anti-inflammatory effects of fennel methanol extract. They saw that it shows activity tied to both central and peripheral mechanisms.[18]

Anti-anxiety activity:

Researchers have reported the anxiolytic activity of the crude extract from fennel. This plant contains phytoestrogens, which give it extensive therapeutic uses in treating estrogen deficiency abnormalities. Estrogens function as hormones that play a role in anxiety phenomena, and they seem to work through GABA A receptors. One study found that the plant led to a significant increase in time spent in the open arm, showing a clear anxiolytic effect. Picrotoxin, which acts as a GABA receptor antagonist, along with Tamoxifen, blocked this anxiolytic effect. So, fennel likely serves as an herbal remedy with anxiolytic effects that involve the GABA-ergic system and estrogen receptors, according to Kooti W and colleagues. Mesfin and others examined the anxiolytic activity of fennel in adult mice. They showed that stress levels dropped significantly in the group treated with fennel essence when compared to the control group. From this, it seems reasonable to conclude that the plant offers promising effects for treating anxiety and stress. Koppula and team looked into the properties of fennel extract for reducing stress and enhancing memory in rats. Their study indicated that this herb, with its various functions like anti-stress actions, memory improvement, and antioxidant effects, could help lower stress and related disorders.[14]

Hepatoprotective activity:

Fennel essential oil shows hepatoprotective properties in research. Studies indicate that it helps protect the liver from damage. In one particular study, researchers examined the effects of this oil on liver toxicity caused by an acute injection of CCl4. They noticed a clear decrease in levels of key blood enzymes. This included aspartate Alkaline aminotransferase, known as AST. There was also alanine aminotransferase, or ALT. phosphatase, called ALP, dropped too. Even bilirubin levels went down. All this points to the oil's protective role against such toxicity.

Oestrogenic activity:

F. vulgare has traditionally been used for many years as an oestrogenic agent. It is reported to enhance libido, stimulate menstruation, make labour and delivery easier, increase milk production, and minimize symptoms of male climacteric. It is thought that anethole, making up the bulk of the oil, is the active oestrogenic Component in Fennel essential oil. According to several other studies, the actual pharmacologically active

Some compounds are polymers of anethole such as dianethole an photoanethole.[12]

CONCLUSION

Foeniculum vulgare Miller (fennel) (Active Constituents are Fenchone, Anethole) seed extract indicates promising potential by several mechanisms in maintaining ocular health. It contains a high number of flavonoids, phenolic substances, and essential oils, which contribute to its remarkable antioxidant and anti-inflammatory effects, potentially capable of reducing oxidative stress and inflammation within ocular tissues. Several preclinical studies have indicated that the extract may improve visual function, protect retinal and corneal cells, and reduce irritations, dryness, or other types of inflammatory insult to the ocular surface. Moreover, neuroprotective and cytoprotective properties also imply possible uses in preserving optic nerve and retinal integrity.

Future Scope:

Future studies will be done in terms of controlled clinical trials, ocular-specific mechanistic studies, and a standardized extraction method to confirm its efficacy, safety, and therapeutic dosage in visual enhancement and eye anti-inflammation. Overall, fennel seed extract holds promise as a natural adjunct for promoting ocular health and preventing vision-related disorders.

Preclinical ocular-specific studies to investigate mechanisms within tissues of the retina, cornea, and optic

nerve. Standardization of extracts to ensure uniformity of active compounds and quality control.

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