

# **Anti-Inflammatory Mechanisms of Homoeopathic Eye Drops in Ocular Surface Disorder: A Literature Review**

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## **Abstract**

### **Background and Objective**

Ocular Surface disorder comprises group of Various ocular surface related conditions including Blepharitis, Conjunctivitis, Dry Eye Disease, Meibomian gland dysfunction, etc. are considered as low-grade inflammations of ocular surface epithelium. OSD have a substantial impact on quality of life and visual comfort. Ocular Surface Inflammation and immunological dysregulation are the shared pathological underpinning of these illnesses, despite their diverse etiologies. Homoeopathic eye drop attracted clinical and research interest as potential anti-inflammatory alternatives in this context.

### **Methods**

A thorough review of literature was carried out using online databases like Scopus, PubMed, research gate, web of science, google scholar, Science Direct and various Homoeopathic journals. This article reviews the research and clinical trials in homoeopathic ophthalmic preparations for the treatment of Ocular Surface Disorders

### **Interpretation and Conclusion**

This article combines various in vitro, experimental and clinical trials of homoeopathic ophthalmic preparations for anti-inflammatory action against Ocular surface disorder. In vitro studies demonstrates that the homoeopathic ophthalmic preparations containing phytochemically active concentrations of Euphrasia, calendula, cineraria can reduce pro inflammatory cytokines Interleukins (IL-1 $\beta$ , IL-6, TNF- $\alpha$ ) and inhibit Cyclooxygenase (COX-2) expression in Corneal cell modules demonstrating their potential anti-inflammatory, antioxidant and cytoprotective activity. Clinical studies showed overall improvement in the presenting symptoms of the various Ocular surface disorders.

### **Keywords**

Ocular surface disorder, cytokines, dry eye disease, Homoeopathy, Euphrasia officinalis, Calendula officinalis.

## 1. Introduction

The Inflammatory basis of Ocular Surface Disorder (OSD) –

Ocular surface disorder is a term used to describe various spectrum of condition like Allergic conjunctivitis, dry eye disease (DED), blepharitis, vernal keratoconjunctivitis, meibomian gland dysfunction. The structures of the eye and adnexa such as cornea, conjunctiva, eyelids, lashes, tear film, lacrimal glands and meibomian glands are collectively referred to as ocular surface. Dysregulated inflammation at the ocular surface epithelium, conjunctival stroma and accessory lacrimal apparatus is a crucial mechanistic thread that unites these disorders despite their varied etiologies. Tear film instability, hyperosmolarity and mechanical stress trigger the inflammatory cascade in dry eye disorder, a multifactorial disease. This triggers the nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B) signaling pathway in corneal and conjunctival epithelial cells(1). Goblet cell apoptosis, corneal nerve damage, and the continuation of the inflammatory cycle are all caused by the production of interleukins (IL-1 $\beta$ , IL-6, IL-8, and IL-17), tumor necrosis factor-alpha (TNF- $\alpha$ ), matrix metalloproteinases (MMP-9), and intercellular adhesion molecule-1(ICAM-1)

The surface of eye is a highly exposed mucosa. It is protected by specialized stratified epithelium. It contains a range of resident immune cells, including natural killer cells, dendritic cells, macrophages, CD4 and CD8<sup>2</sup>T cells mostly involved in antimicrobial activity but may contribute to pathogenesis of dry eye. Multiple risk factors and dysfunction of tear producing glands that cause an unstable tear film which is accompanied by elevated tear osmolarity, triggers the production of innate inflammatory molecules and activates stress signaling pathways(2). Together with the tear film, the corneal epithelium acts as a barrier to external environment and is crucial to the eye's refractive power(3). Although tear fluid (TF) is not commonly used it is an excellent source for non-invasive research. Consequently, various ocular conditions like glaucoma, DED, etc. have been diagnosed using TF(4).

Innate and adaptive immune cells, together with non-immune cells, produce inflammatory mediators (cytokines, chemokines and others) to act on various target tissues in inflammation. These mechanisms involves prostaglandin E2 (PGE2) and Cyclooxygenase (COX-1 and 2).IL-8 is a marker for a number of inflammatory diseases including ocular inflammations where elevated levels contribute to angiogenesis resulting in Inflammation(5)

Therapeutic Landscape and the case alternative anti-inflammatory strategies –

Commercially available and Widely used Homoeopathic preparations claims to have Anti-inflammatory, anti-allergic and lubricant properties. Homoeopathic Ophthalmic preparations including Euphrasia officinalis, Calendula officinalis and Cineraria Maritima have documented anti-inflammatory pharmacological or phytochemical properties at low potencies. Existing evaluations have not thoroughly examined whether these qualities are maintained, improved or eliminated by the severe dilutions used in homoeopathic potentization.

## 2. Methodology

A systematic computerized search was done through online literature available in Scopus, PubMed, research gate, web of science, google scholar, Medline, Science Direct and various Homoeopathic journals. This article reviews the research and clinical trials on the treatment of Ocular Surface Disorders

Articles from the year 2014 to year 2025 were included for the review. In vitro studies, clinical trials, observational studies and review articles are included. Articles without clear conclusion were eliminated.

### 3. Discussion

Table 1. In vitro and experimental studies for anti-inflammatory activities

Author and year	Preparation	Type of study	Inflammatory targets	Key outcome
Bigagli E, Cinci L (2017)	Euphrasia officinalis and Matricaria chamomilla eye drop	In vitro study on Human corneal cell	COX-2,IL-1 $\beta$ and iNOS	COX-2,IL-1 $\beta$ and iNOS reduced
Paduch R, Wozniak A (2014)	Euphrasia Officinalis extract	In vitro study on Human corneal cell	<i>IL-1<math>\beta</math>, IL-6 and TNF-<math>\alpha</math></i>	<i>IL-1<math>\beta</math>, IL-6 and TNF-<math>\alpha</math> reduced IL-10 raised</i>
Ying L, Senghyun kim (2019)	Euphrasia Officinalis extract	In vitro study on RAW264.7 macrophages	<i>NF-<math>\kappa</math>B and JAK/STAT pathway in LPS stimulation</i>	<i>Suppressed NF-<math>\kappa</math>B and JAK/STAT pathways</i>
Silva D, Salvador M (2021)	Calendulla officinalis	In vitro study on RAW264.7 macrophages		50% NO inhabitation
Catarina A, Cunha A, Hilana B (2025)	Viscum Album Eye drop	Human Keratinocytes	IL-8 and IL-10	Marked reduction in IL-8 and IL-10
Valle V, Cunha A (2024)	Cineraria maritima eye drop	Human Keratinocytes	IL-8	Reduction in release of IL-8

#### Euphrasia officinalis – Mechanistic evidence

The well characterized phytochemical repertoire of Euphrasia officinalis includes the flavonoids luteolin and quercetin, phenylpropanoids, tannins and iridoid glycoside aucubin. In human corneal epithelial cells exposed to UVB radiation, the herbal eye drop formulation including Matricaria Chamomilla and Euphrasia Officinalis showed notable anti-inflammatory, antioxidant, cytoprotective and wound healing properties. Inflammatory markers like IL-1 $\beta$  and inducible Nitric Oxide synthase (iNOS) were raised due to UVB radiation. By normalizing the expression of HO-1, SOD-2 and GSS, treatment with homeopathic eye drop restored antioxidant defense pathway and drastically decreased the expression of inflammatory genes (COX-2, IL-1  $\beta$  and iNOS) (6).

Normal human corneal epithelial cells were exposed to Euphrasia officinalis extract, revealing significant findings through various assays. The heptane extract reduced mitochondrial metabolism and cell viability at concentrations above 25  $\mu$ g/mL with an IC<sub>50</sub> value of 72.77  $\mu$ g/mL. Higher concentration of ethyl acetate and heptane extracts were associated with increased nitric oxide reducing activity. Treatment with Euphrasia resulted in decreased pro inflammatory cytokines (IL-1 $\beta$ , IL-6 and TNF- $\alpha$ ) and an increase in anti-inflammatory cytokine (IL-10) levels. Concluded that Ethanol and ethyl acetate extracts were non toxic even at 125  $\mu$ g/mL, but heptane extracts became toxic above 75  $\mu$ g/mL, highlighting the importance of extraction solvents. (7)

Another study analyses the cytotoxicity of ethanol extract of *Euphrasia Officinalis* - silver nanoparticles (AuNPs) on RAW264.7 macrophage using the MTT assay. The extract reduced  $\text{H}_2\text{O}_2$  to synthesize AuNPs, which significantly blocked LPS- induced releases of TNF- $\alpha$ , IL-1 $\beta$  and IL-6 in a dose dependent manner. EO-AuNPs inhibited the translocation of the transcription factor NF- $\kappa$ B from cytoplasm to the nucleus, indicating their anti-inflammatory effects. The findings suggested that EO-AuNPs decrease inflammatory mediators by suppressing NF- $\kappa$ B and JAK/STAT pathways in LPS-stimulated RAW264.7 cells(8).

#### *Calendula officinalis* – Evidence and interpretive challenges

*Calendula officinalis* contains oleanolic acid, betulinic acid, and the flavonoid isorhamnetin, which inhibit pro inflammatory cytokines and COX-2. A mouse macrophage cell line (RAW264.7) was studied, stimulated with LPS. 50% NO inhibition was the outcome of the study, presenting a safety profile and an anti-inflammatory property of the *calendula officinalis*(5)

*Viscum Album* contains Flavonoids, Viscotoxins and possess anti-inflammatory activity. To evaluate cell migration and viability of the cell, a study assessing on MTT and Scratch assay, was done comparing treatment and control group. 102% cell viability was exhibited by the treatment group showing that the eye drop was non cytotoxic. A marked reduction in the levels of IL-8 and IL-10 was observed after administration of *Viscum 6DH* homoeopathic eye drop(9)

*Cineraria Maritima* – potential of a homoeopathic eye drop – study revealed reduction in the release of IL-8 ( $p < 0.0001$ ) in the treatment group with *Cineraria 4CH* eye drop. Cytotoxicity towards the cell line was not shown also it promoted scratch closure as compared to the control group ( $p = 0.0201$ )(10).

Various reviewers stated that ocular problems are often misdiagnosed or undertreated and it should be regarded as a separate clinical illness since it severely impairs patient quality of life, especially for those with chronic moderate to severe ocular symptoms(11). Numerous ailments including inflammation, ulcers, skin illnesses, etc. have historically treated by *Calendula*. Various pharmacological activities including anti-inflammatory, antioxidant, antimicrobial, etc. have been shown by scientific research on *calendula officinalis*(12).

A broad range of conditions affecting the eyes in children, such as refractive errors, conjunctival disease, lachrymal duct obstruction and congenital abnormalities If not identified and treated they may result in vision impairments. To lessen it preventive strategies like limiting screen time, appropriate lighting and 20-20-20 rule are advices. The review investigates the possible relevance of homoeopathy in pediatric eye complains(13). Most commonly and widely used homoeopathic remedies include *Euphrasia officinalis*, *Allium cepa*, *Aconitum napellus*, *Pulsatilla nigricans*, *Apis mel*, *Mercuris Solubilis*, *Arsenicum album*, *Ruta Graveolans*, *Argentum Nitricum* are believed to reduce ocular inflammation and supports healing response of the body(14). Homoeopathic medicines such as *Conium mac*, *Silicea*, *Thuja*, *Apis mel*, *Pulsatilla*, *Hepar Sulph*, *Staphysagria*, *Calc flour*, *Calc carb*, *Sulphur*, etc. are effective reducing symptoms of Chalazion like pain, redness, swelling and discomfort there by reducing the sensitivity towards chalazion and also stopping the recurrence(15).

Table 2 - Clinical and experimental studies for anti-inflammatory activities

Author and Year	Study Design	Intervention	Comparator	outcome
B. Mortemousque, P.J. Pisella	Randomised comparative study	Homeoptic eye drop	Larmabak (lubricant)	Intervention more effective than comparator
Meier-Girard D, Gerstenberg G	RCT	Euphrasia eye drop	Placebo	Invervention reduced ocular discharge
Huff ML, Fikse D, Surmaitis RM	Case report	Similasan pink eye relief eye drop	-	Reported adverse effect
Dokania S, Aphale P, Mishra N	Clinical Trial	Euphrasia Eye Drop	-	Significant improvement in TBUT
Jung GT, Kim M, Song JS, Kim TI	Prospective Double Blind Study	Tear Proteomic Analysis 0.1% cyclosporine, 0.05% cyclosporine, or 3% diquafosol eye drops.	-	Indicating their potential role as biomarkers

#### Anti-Inflammatory outcomes across Ocular Surface Disorders Subtypes-

Comparative study between Homeoptic eye drop and Larmabak lubricant for (n=93) revealed that the mean Visual Analogue Scale (VAS) score for Homeoptic group was  $26 \pm 18.8$  and that for Larmabak group was  $32.8 \pm 21.2$ . VAS for Homeoptic also detected dry eye sensation ( $p=0.009$ ) and burning ( $p=0.004$ ) and this was in favor of Homeoptic(16). A double blind RCT comparative study between Euphrasia eye drop and placebo in pediatric age group revealed the Euphrasia eye drop group responded well to the study. Signs of redness during 96 hour intervention tended to be lowered in Euphrasia group more than the placebo group(17).

Similasan eye drop – pink eye relief case report states that a 55year female presented with 5 days history of left eye redness, swelling, tearing and foreign body sensation with hazy appearance of left cornea. Examination revealed increased intra ocular pressure, suggestive of Acute Angle Closure Glaucoma. History of Application of eye drop reveal its contents to be Atropa Belladonna resulting in the adverse effect of Belladonna containing eye drop(18). Homoeopathy has been investigated as a possible supplementary strategy for the treatment of myopia. Ruta Graveolens and Physostigma Venenosum are studied to have potential to delay growth of myopia. Besides, Individual Homoeopathic medicines may be helpful in preventing future advancements and lowering refractive error(19).

In a Clinical trial Homoeopathic case report assessment scale was used and participants were advised to administer one drop of Euphrasia eye drop in both eyes and the results were compared on 15<sup>th</sup> and 30<sup>th</sup> day with the baseline and a significant improvement in Tear break up test (TBUT) was observed and an overall improvement in symptoms of patient was recorded with conclusive findings from HCRAS value(20). A prospective double blind, multicentric investigation was conducted to use proteome analysis to find possible tear protein biomarkers in Dry eye disease (n=80) were treated with either 3%

diquafosol eye drop, 0.05% cyclosporine or 0.1% cyclosporine. Assessed tear sample both before and after treatment, the finding showed that a number of tear proteins were significantly altered in individual with dry eye. Tear proteomics can offer important insights to the pathophysiology of DED and therapy response(21).

#### 4. Conclusion

Tear film instability, oxidative stress and the activation of inflammatory signaling pathways are the main cause of chronic inflammation in a group of multifactorial condition Ocular surface disorder. On the surface of the eye these mediators support a self-sustaining inflammatory cycle and cause epithelial damage.

Several homoeopathic ophthalmic preparations appears to have anti-inflammatory, antioxidant and cytoprotective effects in experimental and clinical studies. According to the evidence reviewed in this article, these preparations seem to promote ocular surface repair, lower cytokine expression and regulate inflammatory mediators.

The majority of the research is restricted to the in vitro tests, short clinical trials or observational data, the current finding suggests that homoeopathic eye drops may have therapeutic advantages in treating ocular surface disorders but further RCTs, mechanistic research, more thorough clinical trials are needed to determine the clinical relevance

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