

# Gut microbiome and dry eye: exploring the link and therapeutic potential



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## Abstract

The gut microbiome plays a crucial role in ocular surface health and inflammation. This involvement is referred to as the gut-eye axis. The imbalance ratio of gut microbiomes affects the immune response, metabolism, and production of metabolites, and stimulates systemic inflammation that potentially disrupts the tear film and ocular homeostasis. Studies indicate that the gut microbiome influenced the severity of dry eye disease (DED) through metabolic, immunological and neuroendocrine pathways. This concept of the eye-axis approach to personalised microbiome-based therapy aims to retain and repair ocular health.

**Keywords:** dry eye disease, gut-ocular microbiome axis, ocular dysbiosis

## 1. Introduction

The human microbiome, including bacteria, fungi, viruses, and archaea, is found on the skin, nasal mucosa, gut, oral cavity, and ocular surface (1). This microbiome maintains physiological conditions and homeostasis (2). Additionally, gut microbiomes and ocular microbiomes contribute to ocular surface health. Some clinical evidence supports the connection between the gut microbiome and ocular health (3). An imbalance in this microbiome can negatively impact ocular surface health and lead to dry eye disease (4). This article reviews the immunological and metabolic functions of the gut-eye axis, as well as treatments like probiotics and synbiotics that influence the microbiome and help maintain the stability of the eye surface (5).

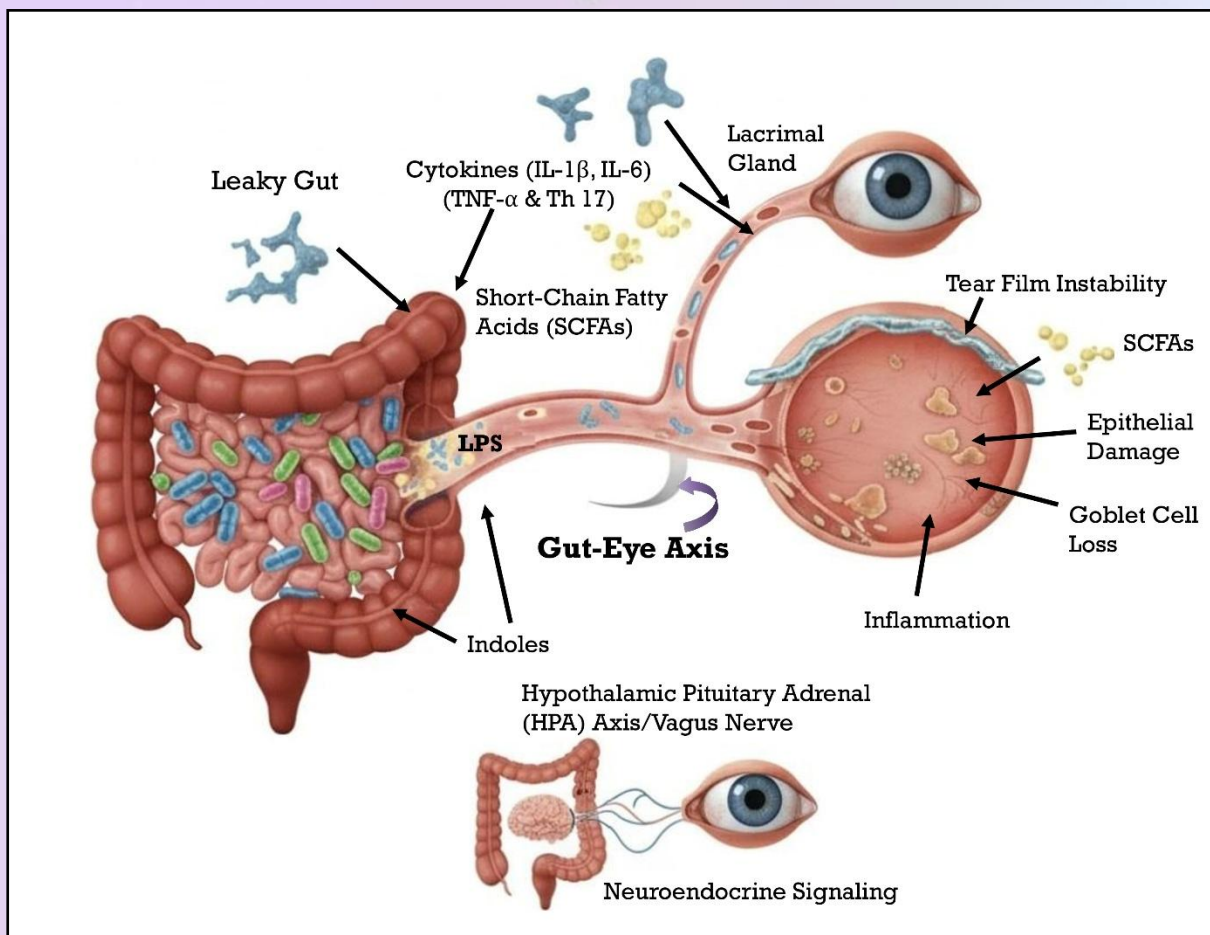
## 2. Pathophysiology of gut-eye axis in DED

One of the novel concepts giving a mechanistic explanation for the role of gut microbiota in the pathogenesis of DED is the gut-eye axis (6). Dysbiosis of the gut disrupts the gut barrier of the intestinal epithelium, increasing permeability and permitting the movement of microbial components like lipopolysaccharide (LPS) into the circulation (7). The activation of macrophages and dendritic cells by these microbial products results in systemic release of pro-inflammatory cytokines like IL-1 $\beta$ , IL-6 and TNF- $\alpha$  that become available on the ocular surface and lacrimal glands, resulting in local inflammation, goblet cell destruction and instability of the tear film (8). Short-chain fatty acids (SCFAs). These SCFAs usually improve immune homeostasis and control T-cell function (9). Dysbiosis reduces SCFA concentrations that tip the balance of the immune response towards pro-inflammatory Th17 responses that exacerbate

ocular surface damage (10). Molecular mimicry may cause autoreactive T-cells to be activated by microbial antigens that resemble ocular surface proteins, leading to a chronic inflammation of the eye's surface (11). Furthermore, microorganisms in the gut also influence neuroendocrine signaling directly through the GBA and therefore affect the hypothalamic pituitary adrenal (HPA) axis and autonomic nervous system, which can reduce the production of tears by lacrimal glands (12). It has been reported that changes in microbial metabolism that result from altered production of vitamins and vital molecules might have an impact on mucin stability (13). Figure 1 shows the role of the gut-eye axis in the development of DED.

### 3. The gut microbiota's function in DED

The function of gut microbiota in DED has been studied. It has been reported that, as compared to normal individuals, the DED patients have clear differences, such as less microbial variety, more proinflammatory bacteria and fewer genera that create short-chain fatty acids (14). These variations may contribute to inflammation in the eye. Treatments, like probiotics or fecal microbiota transplant, have been studied (15). Animal studies also suggest that gut dysbiosis can change immune modulation, T-cell responses, the production of beneficial metabolites and the blood retinal barrier (16). This alteration elevated eye inflammation and disease progression in a mouse model of experimental Graves orbitopathy. These results indicate that the gut-eye axis may be targeted for treatment of DED (17), and Table 1 highlights the studies conducted.



**Figure 1.** Gut-Eye Axis Mechanisms in DED Development

**Table 1.** Preclinical and Clinical Evidence Linking Gut Microbiota to DED

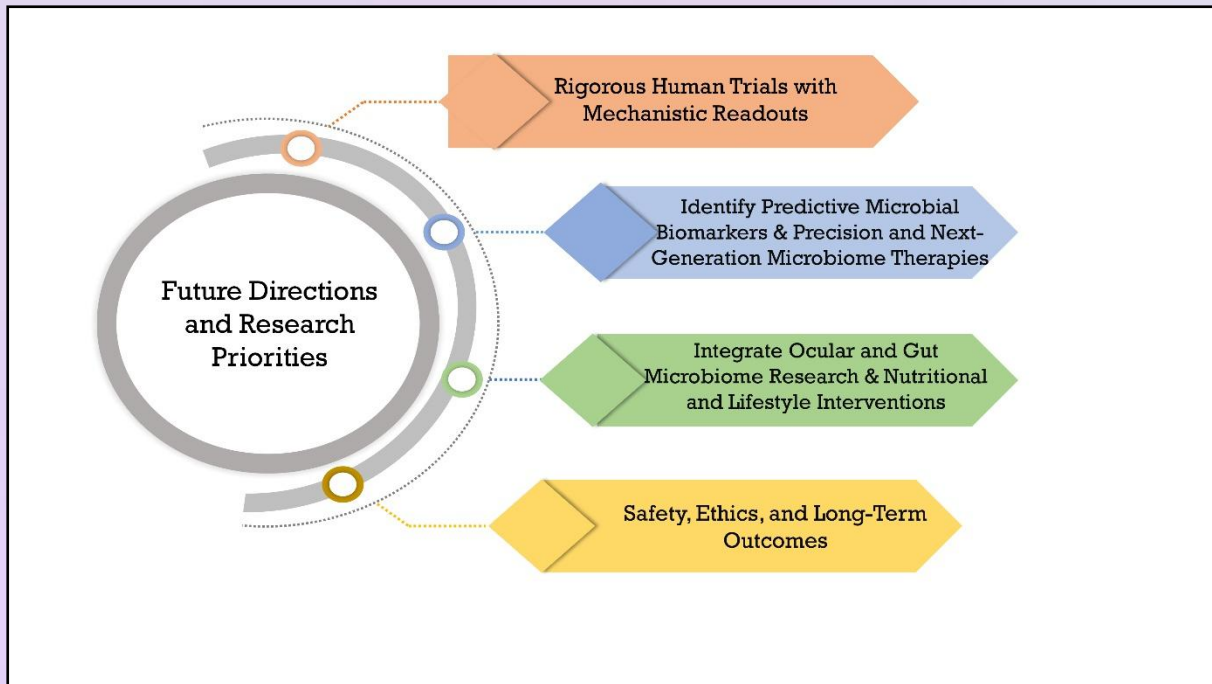
Sr. No.	Study	Outcome	References
1.	Preclinical	Mouse model gut dysbiosis worsens ocular surface inflammation. Prebiotics restore tear production and reduce inflammatory cytokines	(18)
2.	Clinical	DED patients show gut dysbiosis, reduced beneficial bacteria, and increased inflammation markers, and microbiota linked to tear stability and ocular surface health	(19)

#### 4. Therapeutic strategies to attain a healthy gut balance and potential DED effects

Restoring gut microbial balance is recognized as a treatment option that may help treat DED by reducing inflammation and enhancing the ocular surface health (20). Therapeutic options such as dietary supplements, probiotics, prebiotics and microbial metabolites reduce ocular inflammation and promote ocular health (21). Table 2 highlights the gut-targeted therapeutic approaches for dry eye diseases. Figure 2 shows future directions and research priorities of dry eye disease.

**Table 2.** Gut-Targeted Therapeutic Approaches for Dry Eye Diseases

Sr. No.	Treatment (Model)	Gut Mechanism	Ocular Effect	References
1.	Probiotic + Prebiotic (Human RCT Model)	Modulate gut flora & ↓ inflammation	↓Ocular Surface Disease Index & ↑TBUT	(22)
2.	<i>S. Thermophilus</i> iHA318 (Human)	Alter microbiota, ↓ inflammation	↑Tear volume, ↑TBUT	(23)
3.	IRT5 Probiotic (Mouse)	Modulates Gut immunity	↑ Tear secretion	(24)
4.	<i>L. Reuteri</i> DMS17938(Mouse)	Modulates Gut immunity	↑ Tear secretion	(25)
5.	Diet/Microbiota (Human)	Gut Dysbiosis	Correlation with DED severity	(26)
6.	Gut Eye Axis	Modulates systemic immunity	Proposed Ocular Benefit	(27)
7.	Gut Microbiota	Dysbiosis in eye disease	DED, Uveitis	(28)
8.	Autoimmune Dry Eye (Human)	Dysbiosis in Sjögren's	Correlated with severity	(29)
9.	Ocular Surface Microbiome	Altered Flora	DED vs Control	(30)
10.	Conjunctival Diversity	Microbiota Diversity	DED Patient	(31)



**Figure 2.** Future directions and research priorities of dry eye disease

## 5. Conclusion

In conclusion, the gut microbiome maintained ocular health by modulating immune system balance. Gut eye dysbiosis can cause inflammation. Gut eye dysbiosis is mainly caused by pharmacological factors like inflammation and immune imbalance. The ocular diseases are linked to inflammatory factors that involve microbial translocation, cytokine signalling and SCFAs that recognized as the gut-ocular axis. The treatment of ocular disease by regulating gut microbiome may be done by microbiome-based therapy, dietary modulation and use of probiotics and prebiotics. This therapy recovers microbiome balance and maintains the gut-ocular axis. Combining this advancement with personalized medicine, multi-disciplinary and integrative omics therapies will signify a transformative and scientifically critical path for future clinical pharmacy and ocular healthcare.

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