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ANTIOXIDANT PROPERTIES OF MATCHA IN DRY EYE DISEASE PREVENTION: CAN MATCHA POLYPHENOLS IMPROVE OCULAR HYDRATION?

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# ANTIOXIDANT PROPERTIES OF MATCHA IN DRY EYE DISEASE PREVENTION: CAN MATCHA POLYPHENOLS IMPROVE OCULAR HYDRATION?

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## ABSTRACT

Dry eye disease (DED), characterized by unstable tear film and damage to the eye's surface, is becoming more common because of environmental and lifestyle factors. Conventional treatments often don't fix the problems of oxidative stress and inflammation that cause it. This has led to interest in natural antioxidants like matcha, a type of green tea powder grown in the shade. Unlike conventional green tea, matcha contains higher concentrations of polyphenols, particularly epigallocatechin gallate (EGCG). These polyphenols have strong antioxidant and anti-inflammatory effects. This review explores matcha's potential in preventing DED by analyzing its mechanisms of action, such as by removing reactive oxygen species (ROS) and increasing endogenous antioxidants (e.g., superoxide dismutase). It also looks at how matcha reduces pro-inflammatory cytokines (e.g., TNF- $\alpha$ , IL-6) through the NF- $\kappa$ B and MAPK pathways. The discussion also covers matcha's effects on tear film stability through enhanced mucin secretion and meibomian gland function.

Studies show that green tea polyphenols can improve tear production and reduce corneal staining, though matcha-specific studies remain limited. New research shows that it has systemic benefits, including modulation of gut microbiota, which may indirectly support ocular health.

Challenges include optimizing dosage and delivery methods, but matcha's bioavailability and ability to act on many targets make it a potentially helpful additional treatment. More clinical trials are needed to prove its efficacy. However, current information suggests it could help with the many factors that cause DED by balancing redox and reducing inflammation.

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## KEYWORDS

Matcha, Dry Eye Disease, Catechins, Polyphenols, Oxidative Stress

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## Introduction.

Dry eye disease (DED) is a multifactorial condition characterized by a loss of homeostasis of the tear film. This leads to ocular symptoms such as discomfort, blurry vision, and tear film instability, which can potentially damage the ocular surface (1). DED is becoming more common because of factors such as prolonged screen time, environmental pollution, and aging populations. It affects 5% to 50% of people worldwide and can significantly impact quality of life (2). Current treatments, like artificial tears and anti-inflammatory medicines, often only relieve the symptoms. This shows that we need new treatments that target the oxidative stress and inflammation that cause the problem (1). There is increasing interest in natural antioxidants as extra treatments. One of these is matcha, a powdered green tea (*Camellia sinensis*) that is rich in polyphenols. It has become a potential candidate due to its strong antioxidant and anti-inflammatory properties (3, 4). Matcha, a powdered form of green tea (*Camellia sinensis*), is unique among green teas because it is grown in the shade. This makes it have more chlorophyll and amino acids. It also increases the amount of active compounds like polyphenols, especially catechins like epigallocatechin gallate (EGCG). These have strong antioxidant, anti-inflammatory, and anti-apoptotic effects (4, 5). New evidence suggests that these active compounds may help keep the eye's surface balanced. It is done by getting rid of reactive oxygen species (ROS), reducing pro-inflammatory cytokines (like TNF- $\alpha$  and IL-6), and keeping the tear film stable (3, 4). For example, green tea polyphenols have been shown to improve the function of the meibomian glands and reduce corneal staining in patients with DED (3). Also, taking oral formulations combining polyphenols and omega-3 fatty acids can improve tear film quality (6). Unlike conventional green tea, where leaves are steeped and discarded, matcha is consumed in its entirety, providing a more concentrated dose of antioxidants. However, the specific role of matcha a concentrated source of catechins with higher bioavailability than traditional green tea in preventing DED is not well understood. This review summarizes current knowledge on how polyphenols from matcha may alleviate dry eye symptoms. It highlights their role in reducing oxidative stress by neutralizing reactive oxygen species (ROS) and increasing natural antioxidant defenses such as superoxide dismutase (SOD) and glutathione (5, 7). It also analyzes the reduction of inflammation by suppressing NF- $\kappa$ B and MAPK signaling pathways (4, 5), as well as their potential to improve tear quality by stabilizing mucin and reinforcing the lipid layer (6).

## The Pathophysiology and Role of Oxidative Stress in Dry Eye Disease

Dry eye disease arises from an imbalance between tear production and evaporation, primarily driven by meibomian gland dysfunction (MGD) and ocular surface inflammation. Evaporative dry eye, which is the most common type, happens when the meibomian glands fail to secrete sufficient lipids, causing excessive tear evaporation (8). Chronic inflammation in DED causes the release of pro-inflammatory cytokines, like interleukin-1 $\beta$  (IL-1 $\beta$ ), IL-6, IL-8 and tumor necrosis factor-alpha (TNF- $\alpha$ ). These cytokines disrupt the tear film and damage corneal epithelial cells. Meta-analyses show that DED patients have higher levels of these cytokines in their tears compared to healthy people (9, 10).

Oxidative stress is very important in the development of DED. The cornea and conjunctiva are easily damaged by oxidation because they are always exposed to things in the environment like UV radiation, air pollution, and digital screens (11). Reactive oxygen species (ROS) overwhelm the ocular surface's antioxidant defenses (e.g., glutathione peroxidase, superoxide dismutase). This leads to lipid peroxidation, DNA damage, and cellular apoptosis (12, 13). In DED, excessive ROS production leads to problems with the lacrimal gland, loss of goblet cells, and damage to the corneal epithelium, making the tear film even less stable (14, 15). Antioxidant mechanisms are compromised in DED. Normally, tear film components like lactoferrin, ascorbate, and uric acid neutralize ROS (12). But in DED, the ability to fight oxidation is reduced, leading to a cycle of inflammation and oxidative damage (13). Exogenous antioxidants, like polyphenols such as EGCG in matcha from food may help restore balance by neutralizing free radicals and changing inflammatory pathways (3). Environmental factors like low humidity, air conditioning, prolonged screen, and pollution increase tear evaporation, reduce blinking, and directly cause oxidative stress and inflammation on the ocular surface, making symptoms worse (11, 16).

## Matcha as a superior source of antioxidants

Matcha is distinguished among teas by its exceptionally high antioxidant capacity, attributed to its unique cultivation and processing. Shade-growing tea for 20–30 days before harvest makes it have more chlorophyll and L-theanine levels. It also makes it less bitter by reducing catechin oxidation (17, 18). The first picking (ichibancha) yields the highest quality matcha. It has a brighter green color and more nutrients than

matcha from later pickings (19, 20). The main antioxidants in matcha are catechins (especially EGCG). EGCG can be up to 60% of all the catechins in matcha (18, 21). Research shows that matcha has much more EGCG than regular green tea, but this depends on how it is prepared (18, 22).

Other bioactive compounds in matcha include phenolic acids (gallic acid, chlorogenic acid), flavonoids (quercetin, rutin), and vitamins (vitamin C, E), all contributing to its free radical-scavenging capacity (21, 23).

### **Matcha polyphenols and their mechanism of action**

Matcha has a much higher amount of bioactive compounds than regular green tea because of its unique cultivation process. Growing matcha in the shade helps it make more chlorophyll and increases the amount of polyphenols, especially epigallocatechin gallate (EGCG), which is the most plentiful and active catechin.

EGCG is known for its strong antioxidant and anti-inflammatory effects, as well as other catechins (5). This growing method makes matcha's antioxidant capacity by up to 137 times stronger than regular green tea, based on ORAC (Oxygen Radical Absorbance Capacity) measurements (22).

The main polyphenols in matcha, especially EGCG, are very highly effective at getting rid of reactive oxygen species (ROS), as shown in lab and animal studies of eye surface diseases (4, 15). ROS contribute to dry eye disease (DED) pathogenesis by causing lipid peroxidation in meibomian gland secretions, harming corneal epithelial cells, and making the tear film unstable (7, 15).

Matcha polyphenols counteract oxidative stress by both directly neutralizing free radicals and by boosting the production of antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) through the activation of the Nrf2/ARE pathway (15, 24). This two-way action helps keep the ocular surface from oxidative damage and keeps tear film homeostasis. Inflammation is a major cause of DED progression. High levels of inflammatory cytokines like TNF- $\alpha$ , IL-6, and IL-1 $\beta$  make symptoms worse and cause ongoing damage to the ocular surface (1, 25). Matcha polyphenols are strong anti-inflammatories. They change important signaling pathways like NF- $\kappa$ B and MAPK, which control cytokine production (3, 4). In vitro studies show that EGCG suppresses NF- $\kappa$ B nuclear translocation and prevents I $\kappa$ B $\alpha$  from being phosphorylated, this lowers the production of inflammatory substances (3, 26). Clinical studies also support these findings. Green tea extract supplements are linked to lower levels of TNF- $\alpha$  and IL-6 in the tears of DED patients (3, 5). Matcha's anti-inflammatory benefits also extend to the meibomian glands. It lessens gland problems that cause evaporative dry eye by reducing inflammation around the glands and improving the quality of lipid secretion (3, 14).

Besides their antioxidant and anti-inflammatory effects, matcha polyphenols improve tear film quality in several ways. They stabilize mucin secretion, which helps the tear film adherence to the eye's surface. They also strengthen the lipid layer, which prevents excessive evaporation (6).

Research shows that polyphenols increase the production of membrane-associated mucins (MUC1, MUC4, and MUC16) by activating the EGFR/MAPK signaling pathway, thereby improving corneal wettability (6, 27). Also, matcha's active compounds help meibum secretion by making the lipid composition of meibomian gland secretions normal, which is often changed in DED (14, 28). A recent study also showed that EGCG boosts the activity of lipogenic enzymes in meibocytes, leading to better meibum fluidity and tear film stability (29). These multifaceted actions make matcha polyphenols as a promising treatment for both aqueous-deficient and evaporative dry eye types. Unlike regular green tea, where active compounds are taken out through infusion, matcha consumption involves ingesting the whole leaf. This makes sure higher bioavailability of these compounds (7). Research shows that when matcha polyphenols are orally consumed, they are absorbed into the bloodstream and may reach ocular tissues this could affect tear secretion and cornea health (24).

### **Clinical evidence supporting matcha in dry eye disease management**

Clinical evidence shows that green tea polyphenols, especially epigallocatechin gallate (EGCG), can help manage dry eye disease (DED). A study where people were randomly assigned to different groups showed that a single dose of green tea extract greatly improved tear production (Schirmer's test) and tear film stability (tear breakup time, TBUT) in healthy people. This suggests that it can quickly help the ocular surface stay balanced (14). Another study supported this by giving DED patients oral green tea extract supplements. The study found that this not only reduced corneal staining (a sign of damage to the eye's surface) but also improved the function of the meibomian glands, which are important for the lipid layer of tears (14).

Although there aren't many direct studies on matcha, its strong antioxidant and anti-inflammatory properties suggest it could have even more therapeutic potential (5). For example, a study on mice with dry

eye showed that green tea catechins significantly lowered oxidative stress and improved the condition of the eye's surface (30). When these results were applied to humans, a study where people were randomly assigned to different groups found that a combination of oral green tea polyphenols and omega-3 fatty acids together improved TBUT and how patients felt (e.g., on the OSDI questionnaire) in DED patients (31). Additionally, another study found that EGCG lowered key inflammatory markers (e.g., IL-6, TNF- $\alpha$ ) in eye surface diseases, further showing how it helps reduce DED (32).

New research also highlights the overall health benefits of matcha's active ingredients. Studies showed that polyphenols change how oxidative stress pathways work in the lacrimal glands. Also, an analysis of genes and metabolites showed that green tea can restore lipid metabolism in the meibomian glands, which helps with evaporative dry eye (33, 34). Although more studies specifically on matcha are needed, the current data suggest it could be a helpful additional treatment for DED (5).

Also, animal studies suggest that green tea catechins help the lacrimal gland work better by increasing aquaporin-5, a protein that is important for tear fluid production (35). If matcha has similar effects, it could improve tear production in people with DED. However, more human studies are needed to confirm how well matcha works, optimal dose, and its long-term safety. Current evidence suggests that drinking 1–2 cups of matcha daily (providing ~200–300 mg EGCG) may be helpful without going over safe caffeine limits (36, 37).

### **Protection of the Corneal Epithelium**

The corneal epithelium is highly susceptible to oxidative damage. EGCG helps the cornea heal by helping cells move and reducing cell death (27). Green tea extracts applied to the surface of the eye have shown good results in preclinical models. This suggests that products made from matcha could be tested to see if they can hydrate the surface of the eye (28).

### **Beyond Antioxidants: Matcha's EGCG Targets VEGF Signaling and Corneal Nerve Protection in Dry Eye Pathophysiology**

Vascular endothelial growth factor (VEGF) has anti-angiogenic and neuroprotective effects and is a key factor in eye surface inflammation and DED. VEGF helps create new blood vessels and makes blood vessels more permeable, which can exacerbate corneal inflammation and the growth of new blood vessels, which are common in DED. In pathological conditions like corneal neovascularization, VEGF is increased by inflammatory cytokines (e.g., IL-6, IL-8) and hypoxia, which further destabilize the ocular surface (38). EGCG is the main active catechin in green tea and has been shown to strongly prevent blood vessel growth by reducing VEGF signaling. Studies show that EGCG lowers VEGF production and release in corneal and tumor models (39, 40), prevents VEGF from causing endothelial cells to proliferate, migrate, and tube formate, which are important steps in creating new blood vessels (39, 41), and reduces VEGFR-2 (Flk-1/KDR) and other receptors that promote blood vessel growth, limiting abnormal blood vessel growth in the cornea (40, 41).

Also, new evidence suggests EGCG may help corneal nerve function, which is often damaged in severe DED. While there aren't many direct studies on corneal nerves, EGCG has shown a neuroprotective effect in other parts of the body by controlling oxidative stress and inflammation, which are involved in nerve damage (41, 42), and by improving neuron survival and function through pathways involving VEGF and other growth factors (42, 43).

### **The Gut-Eye Axis: A Novel Perspective on Matcha's Systemic Benefits**

The connection between the gut and the eye is a new area of study. It explores how inflammation in the body and imbalances in gut bacteria affect the health of the eye's surface. Studies suggest that matcha polyphenols may help with DED indirectly by changing the composition of gut bacteria and reducing inflammation in the body (44).

For instance, EGCG has been shown to improve the gut's protective barrier and lower the amount of lipopolysaccharides (LPS) in the bloodstream. High levels of LPS are known to cause inflammation on the eye's surface (45). Also, matcha acts as a prebiotic, encouraging the growth of good bacteria like *Bifidobacterium* spp. These bacteria produce short-chain fatty acids (SCFAs) that fight inflammation (46). These SCFAs, especially butyrate, have been shown to reduce the death of cells on the cornea and improve how the tear glands work in animals (47). More research is needed to fully understand how this works. However, the gut-eye connection gives us a good way to see how oral matcha supplementation could help the health of the eye's surface throughout the body.



### Potential limitations and future directions

Despite promising evidence, some limitations must be addressed. The optimal dosage and delivery method (oral vs. topical) of matcha polyphenols for DED remain unclear (6, 15). Furthermore, long-term studies are needed to evaluate the safety and efficacy of these compounds, particularly in individuals with severe DED or comorbid conditions such as autoimmune disorders. (5, 15).

Given the promising mechanisms, matcha could be used to manage DED in a few different ways. Dietary Supplementation: Drinking matcha regularly might help the whole body by providing antioxidants that support healthy eyes. Topical Formulations: Eye drops or gels containing matcha extracts could deliver polyphenols directly to the cornea. Combination Therapies: Matcha could be used with other treatments that are already available, like omega-3 fatty acids, which also help reduce inflammation (46). Future clinical trials should study the best doses, how safe it is to use for a long time, and how well matcha works compared to other antioxidants for people with DED.

### Summary and Conclusions

Dry eye disease is a complex condition caused by oxidative stress and inflammation, remaining a significant public health concern (1).

Matcha, especially from the first harvest, represents strong antioxidant, anti-inflammatory, and tear film-stabilizing properties. It has a lot of polyphenols, especially EGCG, which may help the eyes stay moist and the tear film stable (4, 15).

Preclinical and clinical studies support the role of green tea polyphenols in improving ocular surface health (3, 14), and matcha's superior bioavailability suggests enhanced benefits (5). Most of the current evidence comes from green tea studies, but because matcha enhanced bioavailability and unique composition, it could be a helpful dietary or treatment option for DED prevention. Further research is needed to validate its efficacy in clinical settings and should focus on topical formulations and gut-microbiota interactions, but the existing data support its potential as a natural adjunct in dry eye management.

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