https://doi.org/doi.org/10.5114/oku/203386 (Research Paper)
Received: 15.11.2024 Accepted: 02.12.2024

Eyelid Skin Disorders and Their Impact on the Ocular Surface

Ewa Mrukwa-Kominek[1,2]

[1] Department of Ophthalmology, Faculty of Medical Sciences in Katowice, Medical University of Silesia in Katowice, Poland
Head: Prof. Dorota Wyględowska-Promieńska, PhD, MD
[2] Kornel Gibiński University Clinical Center, Medical University of Silesia in Katowice, Poland
Head: Prof. Dorota Wyględowska-Promieńska, PhD, MD

Summary: The skin is a barrier between the body and the external environment, it is the largest human organ. Healthy skin microbiota is harmless and beneficial to the skin. As a microbiological barrier, it protects against harmful microorganisms.
In turn, the eyelids protect the surface of the eyeball from the adverse effects of external factors. The skin of the eyelids is the thinnest skin in the human body, it is extremely delicate, and does not have subcutaneous fat. The paper discusses eyelid disorders, symptoms accompanying eyelid disorders, including: dry and rough eyelid skin, redness of the eye, a burning/stinging sensation, irritation with a feeling of a foreign body, and others.
The author draws attention to the fact that problems with the skin of the eyelids begin when the protective barrier of the skin is breached, which causes an imbalance in the skin microbiota, and the processes that occur then may contribute to the development of skin diseases.
The paper discusses the influence of cosmetics on the condition of the eyelid skin, and thus the eye surface, and the importance of trehalose 3%, hyaluronic acid 0.15% and Ophiopogon japonicus 0.3% as ingredients of a cream for the treatment of eyelid skin disorders. The paper discusses the case of a 78-year-old patient treated for many years for glaucoma, with chronic eye surface disorders of a toxic-allergic etiology to the drug reaction, which was treated with the use of the newest three-component cream.

Key words: microbiota, eyelid skin, ocular surface, hyaluronic acid, trehaloze, *Ophiopogon japonicus.*

Skin and its functions

The skin, the largest organ in the human body, serves as a crucial barrier between the body and the external environment. In addition to maintaining the body's structure, it performs a variety of essential functions, including protection, temperature regulation, and sensory perception. The skin is also involved in metabolic processes, such as vitamin D synthesis, and in the secretion of sebum, sweat, and pheromones. However, its primary role is protecting the body from microorganisms, dehydration, mechanical damage, and UV radiation. Also, the perception of pain, temperature, touch, and deep sensation originates in the skin.

The skin is composed of three layers [1, 3]: the outermost layer, called the epidermis (containing keratinocytes and melanocytes); the middle layer, the dermis, which consists of collagen and elastic tissue and houses nerves, blood vessels, and sensory receptors; and the innermost layer, the subcutaneous tissue, made up of adipose and connective tissues.

It is worth mentioning that the skin varies in color, thickness, and structure across different areas of the body, depending on specific functional needs [3]. For example, the skin of the eyelids is soft and covered with fine hair, while the skin around the eyebrows is thicker and has coarser hair [4].

Skin microbiota

The skin microbiota is unique to each individual. It consists of millions of microorganisms including bacteria, fungi, and viruses; and the process of skin colonization continues throughout every person's life. The diversity of the microbiota is influenced by host-related factors (genetics, age, gender, hormones, and the immune system) as well as external factors (lifestyle and environment), including diet, UV radiation exposure, environmental pollution, the use of skin care products, treatment with antibiotics and other medications (preservatives), and skin hygiene.

A healthy skin microbiota is not only harmless but also beneficial to the skin [1, 5]. It serves as a microbiological barrier, defending against harmful microorganisms. Certain bacterial species serve as protectors of the skin microbiota by regulating the growth of pathogenic microorganisms. In addition, the skin microbiota acts as an immunological barrier by stimulating the immune system, such as through the induction of interleukins and other immune mediators. As a chemical barrier, it helps reduce skin inflammation for example by secreting anti-inflammatory cytokines.

While a healthy skin microbiota is harmless and beneficial, disruptions in the skin barrier and microbiome (dysbiosis) can lead to various skin conditions, including acne, eczema, and non-healing wounds [6].

Many authors have highlighted that high microbial diversity is linked to a healthy skin microbiome [7]. Skin homeostasis, in turn, plays an important role in human health by preventing colonization by pathogenic microorganisms and supporting the proper functioning of the immune system. Therefore, maintaining the balance of the skin's 'microbial community' is considered essential for healthy skin [1].

At this point, attention should be given to the skin of the eyelids, as it significantly influences the health of the surrounding environment, including the ocular surface. Pathologies affecting the eyelid area can contribute to disorders of the ocular surface. Studies have shown that up to 78% of patients seeking ophthalmic care present with eyelid-related issues.

Eyelids and eyelid-related conditions

Eyelids (Latin: *palpebrae*) shield the surface of the eye from harmful external factors. The skin of the eyelids is the thinnest in the human body [8]. It is exceptionally delicate, lacks subcutaneous fat, and varies in thickness from 0.3 mm at the ciliary margin to 1.1 mm on the upper eyelid [9]. It is smooth, soft, and highly

ISSN 1505-2753

flexible [10]; these characteristics facilitate blinking and play a role in the distribution and drainage of tears. The eyelids protect the eyes from excessive light, trauma, and harmful external factors.

Symptoms associated with eyelid disorders include dry and rough eyelid skin (affecting up to 93% of patients), eye redness, a burning or stinging sensation, irritation with a foreign body sensation, itching, watery eyes (which may occur in the morning or throughout the day), dry eye, light sensitivity, discomfort when opening or closing the eyelids, and blurred vision.

Doan reports a significant association between eyelid disorders and conditions such as rosacea, atopic dermatitis (AD), seborrheic dermatitis, dry eye syndrome (DES), Meibomian gland dysfunction (MGD), allergies, diabetes, and even cataract [11]. Ocular surface lesions may be present in 58% of patients with rosacea. Allergic contact dermatitis, the leading cause of eyelid dermatitis, affects 30–77% of patients. Contact dermatitis resulting from eye drops or cosmetics is the most frequently reported. Atopic dermatitis [12], in contrast, is a chronic inflammatory skin condition [13] affecting 1–10% of adults globally and 15 20% of children. It is marked by eyelid skin dysfunction, chronic inflammation, and an imbalance in the skin microbiota. Eye involvement is reported in 85% of patients with AD [8], with 64% presenting symptoms of DES, 42% – conjunctivitis, and 31% – blepharitis.

Eyelid skin issues arise when the skin's protective barrier is disrupted, leading to an imbalance in the skin's microbiota. This imbalance weakens the skin's immune response and reduces its defense against microorganisms, making it more prone to inflammation or infections. Such conditions can contribute to the development of skin diseases, including AD.

The delicate nature of the eyelid skin makes it particularly vulnerable to various skin conditions. Common symptoms of skin pathologies include itching, burning, irritation, dryness, redness, and inflammation [11]. Eyelid skin requires attention when it becomes dry, sensitive, irritated, red, prone to atopy, swollen, or itchy. These pathologies can result in disturbances to the ocular surface.

The condition of the eyelid skin directly affects the health of the ocular surface [1], which, in turn, influences the outcomes of surgeries involving not just the eyelids [2], but also those targeting the anterior and posterior segments of the eye.

Effects of cosmetics on eyelid skin

Cosmetics applied to the eyelid skin can adversely affect the skin microbiota. This impact may result from active ingredients or components of cosmetic products, such as preservatives and emulsifiers, which, when left on the skin's surface, disrupt its microbial community [10, 11].

Cosmetics and eyelid skin

What makes an ideal cosmetic for the eyelids and surrounding eye area?

Such a product should strengthen the skin's protective barrier, provide adequate hydration, prevent transdermal water loss, be 'microbiota-friendly' (i.e., not disrupt the skin's natural microbiome), be free from preservatives and fragrances, and have a 'short' composition required for the cream formulation, i.e. contain a small number of ingredients [11, 12, 14].

It appears that these qualities can be found in the preparation containing an innovative trio of natural ingredients: 3% trehalose, 0.15% hyaluronic acid (HA), and 0.3% dwarf lilyturf (*Ophiopogon japonicus*), a sterile cream developed in collaboration with ophthalmologists and dermatologists, with a simple formulation designed to protect the highly sensitive skin of the eyelids while minimizing the risk of adverse effects.

Hyaluronic acid is a deeply hydrating biopolymer with long-lasting moisturizing effects. It consists of repetitive disaccharide units of N-acetylglucosamine and glucuronic acid. Naturally present in the human body, it is found in connective tissue, joints, the eye (vitreous body, aqueous humor, and corneal stroma), and the skin. The skin is the largest reservoir of hyaluronic acid in the body, containing approximately 50% of the total body HA content. HA plays an important role in skin healing, hydration, and maintaining skin elasticity. The skin's hyaluronic acid levels naturally decline with age as cells gradually lose their ability to produce it, making supplementation essential. For this reason, HA is a key ingredient in cosmetology. Thanks to its ability to bind and retain water, it deeply hydrates the skin, enhances its radiance and firmness, softens the appearance of wrinkles, and helps reduce skin irritation. This anti-aging effect is especially beneficial for eyelid skin care.

Trehalose is a naturally occurring disaccharide produced by a wide range of living organisms, including bacteria, yeast, fungi, algae, plants, insects, and invertebrates [15, 16]. However, it is not synthesized in mammals. In the human body, trehalose is synthesized as a stress response factor when cells are exposed to environmental challenges such as heat, cold, oxidation, and dehydration. Essentially, trehalose plays a role in regenerating and protecting the skin barrier, preserving cell integrity [15, 17], and maintaining optimal water content, which is important for proper skin hydration. It acts as the skin's protective barrier, shielding skin cells from dehydration and UVB radiation damage.

Ophiopogon japonicus reinforces the skin barrier and helps retain moisture while preserving the balance of the microbiota. *Ophiopogon japonicus* root extract is used to address common skin sensitivity issues.

Ophiopogon japonicus 0.3% strengthens the skin barrier by promoting epidermal differentiation and cohesion, and optimizing lipid organization and conformation. It hydrates the skin by restoring natural moisturizing factors and balancing water content. Additionally, it helps restore microbiota balance by limiting the adhesion of bacteria (such as *Staphylococcus aureus*) on the skin, and inhibits inflammatory reactions by reducing allergen synthesis [18].

Ophiopogon japonicus is a rhizomatous, tufted perennial reaching 10–20 cm in height, with linear, slightly arching leaves resembling grass. Depending on the species and variety, the leaves, which are the plant's main ornamental feature, can range in color from very dark, almost black, to green, silvery-green, or white. From July to September, fragrant, bell-shaped flowers in shades of white to purple emerge among the leaves, followed by round, blue-black fruit. *Ophiopogon japonicus*, native to China, India, Japan, Nepal, and Vietnam, is an easy-to-grow plant. It thrives in moist, fertile, humus-rich, and slightly acidic soil, preferably in sheltered spots with moderate sunlight or partial shade.

The value of the *Ophiopogon japonicus* root extract should be properly recognized. The extract can be used as a vitamin E supplement and a remedy for lowering blood pressure and blood lipid levels. It supports blood circulation by preventing oxidation and scavenging free radicals. Additionally, it may help protect against pathological changes in the main artery and assist in the treatment of atherosclerosis [18, 19].

Ophiopogon japonicus root extract restores the skin microbiota, strengthening the skin barrier, inhibiting inflammatory reactions, hydrating the skin, and promoting microbiota balance. Clinical studies have confirmed its suitability for sensitive eyes, delicate skin, and atopy-prone skin [19]. It is also safe for contact lens wearers.

The cream with these three ingredients works in multiple ways: it soothes, hydrates, protects, regenerates, and reduces swelling. It is free from preservatives and fragrances, and it is designed for sensitive, dry, irritated, and atopy-prone skin. It can be applied to the eyelids, the area around the eyes, and the entire

face. The cream is suitable for all skin types. It can be used by contact lens wearers [17–20]. The inclusion of *Ophiopogon japonicus* root extract enhances the properties of the cream and improves its effectiveness when applied to the delicate eyelid skin.

A preparation containing 3% trehalose, 0.15% hyaluronic acid (HA), and 0.3% *Ophiopogon japonicus* was assessed in clinical trials for its tolerance and effectiveness. The trials evaluated its impact on transepidermal water loss, long-lasting moisturizing and soothing effects, as well as safety. The results of this evaluation enabled the cream to be registered as a medical product [21–25].

Case report

A 78-year-old woman presented for an ophthalmological consultation with significantly reduced visual acuity and subjective complaints. She had cataract surgery in both eyes with the implantation of a monofocal intraocular lens in 2017 and 2018 (no documentation available). The patient had been treated for glaucoma for 15 years. She has been using latanoprost, bimatoprost, and a combination of timolol and dorzolamide, which led to a significant allergic reaction on the periorbital skin and eyelids, along with disruption of the ocular surface. She described the symptoms as tearing, burning and stinging sensation, itching, and severe photophobia, accompanied by pain when opening the eyelids, reading, or watching TV.

Due to poor visual acuity in the right eye (RE) and left eye (LE) (VRE CF loc (+), VLE 0.5/50), the patient had difficulty moving around independently when subjective symptoms developed. An examination revealed the following intraocular pressure (IOP) values: RE = 32 mmHg, LE = 28 mmHg.

Slit-lamp examination revealed edema and redness of eyelid skin in both eyes (Fig. 1) along with blepharitis with accompanying Meibomian gland dysfunction (MGD). The anterior segment showed significant irritation, with marked conjunctival hyperemia and punctate corneal epithelial defects. The iris was calm, and the anterior chamber was clean and deep. The artificial intraocular lens was properly positioned.

The posterior segment was difficult to assess due to significant blepharospasm. However, in the area accessible for examination after pupil dilation, numerous veil-like floaters were observed in the vitreous body. The optic nerve (CN II) disc exhibited a myopic cone, peripapillary atrophy, and degenerative retinal changes in the papillomacular bundle. Significant thinning of the peripheral retina was also noted. The findings were consistent with high myopia. B-mode ultrasound confirmed the presence of floaters in the vitreous body, with the entire retina remaining attached.

Due to significantly elevated intraocular pressure, the patient was administered 2 tablets of Diuramid (acetazolamide) and Kalipoz (potassium chloride) on an as-needed basis. Thirty minutes after drug administration, the IOP was 22 mmHg in the OD and 20 mmHg in the OS.

A bacteriological culture from the conjunctival sac was conducted to identify aerobic bacteria.

The patient was instructed to discontinue all topical medications containing preservatives. Intensive moisturizing was initiated using preservative-free drops containing hyaluronic acid and trehalose. Additionally, a cream containing *Ophiopogon japonicus* was recommended for the eyelids, initially applied twice a day for 7 days, followed by nightly application for the next 21 days. Eyelid margin hygiene using specialized wipes was recommended.

In addition, due to high IOP levels and the discontinuation of preservative-containing topical medications, systemic treatment was introduced: Diuramid tablets twice daily and Kalipoz twice daily for 7 days, with IOP monitoring.

After one week of the aforementioned therapy, the decision was made to discontinue systemic treatment with a carbonic anhydrase inhibitor and to initiate topical IOP-lowering treatment in both eyes. This included a beta-blocker and a carbonic anhydrase inhibitor in preservative-free eye drops, administered twice daily, along with an additional dose of preservative-free carbonic anhydrase inhibitor at noon. By the 7th day after modifying the topical treatment and starting systemic therapy, an improvement in the eye condition was observed, including reduced edema and redness of the eyelid skin, less conjunctival hyperemia, and a decrease in corneal epithelial defects. After 4 weeks of treatment, a noticeable improvement was seen, with the swelling and redness of the eyelid skin resolving, along with a reduction in blepharitis symptoms. The anterior segment was quiet, with no corneal epithelial defects.

Fig. 1. The patient's eyelid skin on the day of the first visit – before the change in treatment.

Visual acuity in the LE improved to 1/50, while IOP was 17 mmHg in the RE and 18 mmHg in the LE.

Fig. 2. The patient's eyelids 3 months after initiating treatment with a cream containing trehalose 3%, HA 0.15% and *Ophiopogon japonicus* 0.3% and intensive regeneration of the eye surface.

The results of a follow-up examination conducted 3 months after the treatment change showed no deterioration in the local condition. The patient regularly applies intensive moisturizers to the ocular surface, along with ensuring eyelid margin hygiene, and uses a cream containing 3% trehalose, 0.15% hyaluronic acid (HA), and 0.3% O*phiopogon japonicus* to the eyelids twice daily. The patient's satisfaction and sense of well-being improved significantly despite her poor visual acuity (Fig. 2.).

Conclusions

It is essential to take a broader view when assessing ophthalmic patients. The eye is more than just the eyeball; it also includes the eyelids and surrounding structures. Pathologies affecting the eyelids can lead to ocular surface disorders, which are a frequent concern among patients seeking ophthalmological care.

The cream containing 3% trehalose, 0.15% hyaluronic acid, and 0.3% O*phiopogon japonicus* is highly regarded for its beneficial properties and effectiveness. It is very well-tolerated by the delicate skin of the eyelids and the eye area, and does not cause irritation or allergies. The cream can assist in alleviating allergic reactions to chemicals and medications, and aid in restoring the skin's natural microbiota.

Disclosure
Conflict of interests: none declared
Funding: no external funding
Ethics approval: Not applicable.

References:

1. Carvalho MJ, Oliveira AS, Santos Pedrosa S, et al.: *Skin Microbiota and the Cosmetic Industry*. Microb Ecol. 2022 Jul, Forthcoming.
2. Lopez-Ojeda W, Pandey A, Alhajj M, et al.: In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. 2022 Oct 17., et al.: *Anatomy, Skin (Integument)* - StatPearls - NCBI Bookshelf (nih.gov). Last Update October 17th 2022.
3. Arda O, Göksügür N, Tüzün Y: *Basic histological structure and functions of facial skin*. Clinics in Dermatology. 2014; 32: 3–13. DOI: 10.1016/j.clindermatol.2013.05.021.
4. Byrd AL, Belkaid Y, Segre JA: *The Human skin microbiome*. Nature Reviews Microbiology. 2018; 16: 143–155.
5. Harris-Tyrin TA, Grice EA: *Microbiota and maintenance of skin barrier function*. Science. 2022; 376: 940–945.
6. Baldwin HE, Bhatia ND, Friedman A, et al.: *The Role of Cutaneous Microbiota Harmony in Maintaining a Functional Skin Barrier*. Journal of Drugs in Dermatology. 2017 Jan 1; 16(1): 12–18.
7. Wallen-Russell C, Wallen-Russell S: *Meta analysis of skin microbiome: new link between skin microbiota diversity and skin health with proposal to use this as a future mechanism to determine whether cosmetic products damage the skin*. Cosmetics. 2017; 4: 1–19.
8. Cochran ML, Lopez MJ, Czyz CN: *Anatomy, Head and Neck: Eyelid*. StatPearls Publishing. 2023. PMID: 29493929 Bookshelf ID: NBK482304.
9. Hwang K, Kim DJ, Se Ho Hwang SH: *Thickness of Korean Upper Eyelid Skin at Different levels*. Journal of Carniofacila Surgery. 2006 January 17; 1: 54–56.
10. Pratchyapruit W, Kikuchi K, Gritiyarangasan P, et al.: *Functional analyses of the eyelid skin constituting the most soft and smooth area on the face: contribution of its remarkably large superficial corneocytes to effective water-holding capacity of the stratum corneum*. Skin Res Technol. 2007 May 13; 2: 169–175.
11. Doan S, Zagórski Z, Palmares J, et al.: *Eyelid Disorders in Ophthalmology Practice: Results from a Large International Epidemiological Study in Eleven Countries*. Ophthalmology and Therapy. 2020; 9(3): 597–608. doi: 10.1007/s40123-020-00268-4.
12. Németh D, Temesvári E, Holló P, et al.: *Preservative Contact Hypersensitivity among Adult Atopic Dermatitis Patients*. Life. 2022; 12(5): 715.
13. Wolf R, Orion E, Tüzün Y: *Periorbital (eyelid) dermatides*. Clinics in Dermatology. 2014; 32: 131–140.
14. Tavassoli S, Wong N, Chanet E: *Ocular manifestations of rosacea: A clinical review*. Clin Exp Ophthalmol. 2021 Mar; 49(2): 104–117.
15. Laihia J, Kaarniranta K: *Trehalose for Ocular Surface Health*. Biomolecules. 2020 May 25; 10(5), 809: 3–15.
16. Ohtake S, Wang YJ: *Trehalose: Current Use and Future Applications*. J Pharm Sci. 100: 2020–2053, 2011: 4–16.
17. Li L, Chen H, Chen X, Chen S, et al.: *Trehalose Protects Keratinocytes against Ultraviolet B Radiation by Activating Autophagy via Regulating TIMP3 and ATG9*. AOxid Med Cell Longev. 2022; 9366494, 6–17.
18. Messaraa C, Drevet J, Jameson D, et al.: *Can Performance and Gentleness Be Reconciled? A Skin Care Approach for Sensitive Skin*. Cosmetics. 2022; 9: 34. https://doi.org/10.3390/cosmetics9020034.
19. Chen M-H, Chen X-J, Wang M, et al.: O*phiopogon Japonicus ---A phytochemical, ethnomedicinal and pharmacological review*. J Ethnopharmacol. 2016; 181: 193–213.
20. Valeille A, Ouilhon C, Hacard F, et al.: *Evaluation ophtalmologique complète dans la DA: identification des critères d'orientation en ophtalmologie*. Revue Française d'Allergologie. 2021; 61, 4: 259.
21. *Kliniczna ocena tolerancji i skuteczności BLEPHADERM® w pielęgnacji skóry atopowej przez skórę i oczy*. Badanie 22E-1350.
22. *Ocena efektu przeznaskórkowej utraty wody i długotrwałego działania nawilżającego BLEPHADERM®*. Studium 22 E-1351.
23. *Kliniczna ocena tolerancji i skuteczności BLEPHADERM® przez skórę i oczy*. Badanie 18E-2458.
24. *Kliniczna ocena natychmiastowego łagodzącego działania produktu kosmetycznego BLEPHADERM® metodą testu pieczenia*. Badanie 22E-1374.
25. *Ocena potencjału uczulającego produktu kosmetycznego: końcowy test bezpieczeństwa klinicznego pod kontrolą dermatologiczną*. Badanie 18E-3120.

Reprint requests to:
Professor Ewa Mrukwa-Kominek, PhD, MD (e-mail: emrowka@poczta.onet.pl)
Department of Ophthalmology, Faculty of Medical Sciences in Katowice,
Medical University of Silesia in Katowice, Poland
Ceglana 35, 40-514 Katowice