Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/bysse721

"EFFECTS OF HYPERTONIC SALTWATER WASH ON OCULAR SURFACE SENSITIVITY"

Abdul Qadeem Soomro[1], Fayaz Ahmed Soomro*[2], Abdul Sattar[3], Shoaib Ahmed Shaikh[4], Syed Saifullah Shah[5], Abdullah Laghari[6], Hina Khan[7]

[1]Consultant Ophthalmologist, Alibrahim EYE Hospital, Isra Postgraduate Institution of Ophthalmology Malir, Karachi
Email: DRQADEEM@YAHOO.COM
[*2]Consultant Ophthalmologist, Institute Al Ibrahim EYE Hospital Isra Postgraduate Institute of Ophthalmology Karachi
Email: DRFAYAZSOOMRO@YAHOO
[3]Consultant Ophthalmologist, Institute Al Ibrahim EYE Hospital Isra Postgraduate Institute of Ophthalmology Karachi
Email: sattarazad123@gmail.com
[4]Consultant Ophthalmologist, Institute Al Ibrahim EYE Hospital Isra Postgraduate Institute of Ophthalmology Karachi
Email: evermore_majestic_bojee@hotmail.com
[5]Consultant Ophthalmologist, Institute Al Ibrahim EYE Hospital Isra Postgraduate Institute of Ophthalmology Karachi
Email: saifulshah083@gmail.com
[6]Optometrist, Institute Al Ibrahim EYE Hospital Isra Postgraduate Institute of Ophthalmology Karachi
Email: LAGHARI08@GMAIL.COM
[7]Professor, Deputy Director Research and Postgraduate Affairs

***Corresponding Author:** Fayaz Ahmed Soomro,
Email: DRFAYAZSOOMRO@YAHOO

ABSTRACT

Background: Ocular surface is very important in retaining sensory acuity and visual acuity. With ocular disruption caused by epithelial cell disruption, tear film instability, or osmotic imbalance, changes in the sensitivity of the ocular surface may result in discomfort and ocular dysfunction. The osmotic and epithelial protective effects of hypertonic saline have been well investigated, however, little has been conducted on the sensitivity of the ocular surface.

Purpose: The study aimed to assess the outcomes of hypertonic salt water wash on ocular surface sensitivity, tear film stability and patient-reported comfort.

Methods: This was a prospective interventional study that took place at Isra Postgraduate institute of ophthalmology Al Ibrahim Eye Hospital, Pakistan between March, 2024 and March, 2025. One hundred and twenty individuals whose skin encountered discomfort were enrolled. The sensitivity of the ocular surface was measured by a Cochet-Bonnet esthesiometer, tear breakup time (TBUT) was used to determine the stability of the tear film and the Ocular Surface Disease Index (OSDI) was applied to assess the symptoms. The participants were given sterile 5% hypertonic saline wash twice a day during a four-week period. The baseline, 2-week and 4-week assessments were done.

Findings: Corneal sensitivity increased significantly between 42.8 +- 6.4 mm at the beginning of the study and 54.2 +- 5.1 mm at four weeks ($p < 0.001$). Tear breakup time went up to 12.1 +- 1.5 seconds as compared to 7.9 +- 1.8 ($p < 0.001$). The scores of OSDI were lower (19.4 +- 5.9) as compared to 38.5 +- 7.2 ($p < 0.001$), which showed a better patient comfort score. No serious adverse effect was observed and mild transient irritation was reported in 7.5% of participants.
Conclusion: Hypertonic salt water wash has a significant effect on the ocular surface sensitivity, stability of the tear film, and comfort of the patient. It is a safe, efficient and readily available therapeutic method of enhancing the health of the ocular surface.

Keywords: Hypertonic saline, ocular surface sensitivity, tear film stability, corneal sensitivity, dry eye, ocular surface disease, hyperosmolarity, saline wash.

INTRODUCTION

The ocular surface is a highly specialized a sensory protective interface which preserves optical clarity and tear film stability as well as defense against environmental stress. It consists of the cornea, conjunctiva, tear film, and the related neural networks that all maintain the visual functionality and homeostasis. Any kind of interference in such a sensitive system will make a big difference in the sensitivity of the ocular surface, causing discomfort, inflammation and vision loss. Hypertonic saline solutions have found extensive application in ophthalmology owing to their osmotic nature, which aids the flow of fluids across the corneal tissues and aids in restoring the integrity of the epithelia. Clinical trials have also proved that hypertonic saline is an effective way to decrease corneal edema by removing excessive fluid within the stroma and thus increasing the corneal transparency and decreasing the stress of the epithelials (1). Saline-based therapies have been shown to be useful in mucosal systems (e.g. nasal and respiratory epithelium) as well as ophthalmic applications, and have been shown to benefit barrier function and decrease inflammatory response, thus, it has been proposed that saline-based therapies can be used to regulate the ocular surface (2). Moreover, saline solutions have been identified to have cleansing and protective actions in mucosal hygiene, such as the ocular rinsing, where it is useful in removing debris and potentially harmful substances and epithelial surfaces of the sensitive tissue (3). Recent discoveries in ocular surface biology have designated the need to preserve epithelial barrier integrity as an approach to averting inflammation, oxidative stress, and mitochondrial malfunction, which may compromise ocular sensitivity and nerve functioning (4). Corneal nerves mediate ocular surface sensitivity and they are some of the densely innervated body structures in the human body. These neurons are extremely important in the sense of mechanical, thermal, and chemical stimulation, thus ensuring the reflex tearing and the well-being of the epithelial. Interfering with ocular surface homeostasis as a result of environmental, chemical, or osmotic stress may modify neural sensibility and lead to the development of abnormal sensitivity or ocular discomfort. New treatment modalities have been directed towards stabilizing the goggles and safeguarding the viability of the nerves with new biomaterials and drugs. Indicatively, recent studies have shown that ocular surgery can be done using antioxidant hydrogels to restore the epithelial health and enhance ocular surface functioning through suppression of oxidative damage and inflammation (5). Direct influences of corneal sensory nerves by chemical exposures and osmotic imbalances cause continued pain and changes in sensitivity, indicating the need to stabilize the extracellular environment (6). The processes of inflammation are key to ocular surface disorders, with inflammatory mediators capable of interfering with the integrity of the epithelium and sensitizing nociceptive nerve endings leading to the development of chronic ocular discomfort and hypersensitivity (7). Precise methods of quantifying drug delivery, such as topical therapeutic agents have demonstrated positive outcomes in the domain of healing the eye skin, as well as with the operation of the ocular surface, by promoting epithelial recovery and diminishing inflammatory actions (8).

Hyperosmolarity has been known to be a key issue affecting the ocular surface physiology and sensitivity. High levels of osmotic stress may trigger inflammation, apoptosis of cells and disruption of corneal epithelial cells and nerve function and tear stability. Research has demonstrated that

hyperosmolar states are capable of triggering immune responses, such as macrophage-based inflammatory mechanisms, which lead to epithelial damage and sensory adaptation (9). Moreover, the extreme stress of the ocular surface has the ability to deteriorate the limbal stem cell activity, which is vital to the regeneration and maintenance of corneal epithelial tissues, thereby worsening ocular surface dysfunction and sensitivity changes (10). Chemical irritants and toxic agents can be responsible of such pathological alterations as epithelial damage, inflammation, and neural dysfunction, and it is important to maintain the best osmotic pressure at the ocular surface (11). The use of protective formulations and osmotic agents as part of the osmoprotective strategies has been seen as a possible therapeutic intervention to address the stabilization of ocular surface cells and maintenance of sensory functions in osmotic stress environments (12).

The inflammation and oxidative stress are the major processes involved in the altered ocular surface sensitivity. These mechanisms have the potential to alter tear film composition, compromise epithelial regeneration, sensitize cornea nerves, and cause pain. The most recent developments in ocular therapies have been on anti-inflammatory and protective therapy to interrupt the cascade of epithelial damage and neural sensitization. The use of nanozyme-based therapeutic eye drops has demonstrated the capability to decrease inflammation and reclaim ocular surface condition through the regulation of cellular stress reaction and tissue recovery (13). Equally, hyaluronic acids have been broadly utilized to stabilize tear films and promote better epithelial repair to the benefit of superior ocular comfort and sensitivity regulation (14). Neural sensitization is an essential element of ocular surface diseases and also pharmacological treatment on neural pathways has proved to be effective in alleviating corneal pain and enhancing the sensory balance (15). These results indicate that the interplay between epithelial integrity, inflammation, and neural sensitivity in ocular surface homeostasis is a complex affair (16).

The treatment strategies, which enhance epithelial repair and neural recovery, are crucial in the restoration of ocular surface sensitivity. Therapies based on growth factors have been reported to augment epithelial repair as well as augment the stability of tear films, which results in better performance of the ocular surface and decreased sensitivity malformations (17). Moreover, neuromodulatory therapies were also shown to decrease ocular pain and enhance tears secretion, meaning that they can restore neural and epithelial homeostasis (18). The osmotic effects of hypertonic saline have also made it a prospective resource in treatment beyond the reduction of corneal edema and have been suggested to affect ocular surface sensitivity through the impact of the osmotic environment and epithelial repair. Nevertheless, although hypertonic saline has been found to be beneficial in oedema of the cornea and the repair of the epithelium, its direct impact on the ocular surface sensitivity has not been adequately examined. Knowledge of the impact of hypertonic saltwater wash on ocular surface sensitivity is hence crucial in streamlining treatment interventions that tend to enhance ocular comfort, healing of the epithelial integrity and maintenance of corneal neural activity.

Objective: To evaluate the effects of hypertonic salt water wash on ocular surface sensitivity, tear stability, and patient comfort, and to determine its safety and therapeutic potential in improving ocular surface function.

MATERIALS AND METHODS

Study Design: This prospective, interventional, hospital-based clinical study was conducted to evaluate the effects of hypertonic salt water wash on ocular surface sensitivity.

Study Setting: Isra Postgraduate institute of ophthalmology Al Ibrahim Eye Hospital, Pakistan.
Duration of Study: March, 2024 and March, 2025.

Sample Size: A total of 120 participants were enrolled using non-probability consecutive sampling. The sample size was calculated based on expected changes in ocular surface sensitivity with a confidence level of 95% and power of 80%.

Inclusion Criteria: The inclusion criteria were participants between 18-65 years who produced symptoms of ocular surface discomfort, dryness or lower ocular surface sensitivity. Patients who had clinically stable ocular surface, mild to moderate cases of dry eye, or corneal epithelial irregularities were allowed to join. The inclusion of patients who had normal intraocular pressure levels and did not have an active ocular infection was also included. They had to ensure that they did not undergo any ocular surgery within six months and that they did not take hypertonic saline therapy in the last three months. Male and female patients willing to take part in study procedures and follow-up visits were recruited.

Exclusion Criteria: Patients were to be excluded with severe ocular surface disease, active infection of the eye, corneal ulcer, glaucoma, and history of ocular trauma. Patients with systemic diseases that interfere with ocular sensitivity like diabetes mellitus that is not controlled, autoimmune diseases, or neurological diseases were not involved. Patients on topical ocular therapy other than artificial tears and hypersensitive to saline solutions were excluded. Pregnant or lactating women were excluded because of possible physiological differences that might exist on the ocular surface sensitivity. Patients who had received previous corneal transplantation or refractive surgery, or who have a deficiency of limbal stem cells were also excluded to eliminate confounding factors of ocular surface sensitivity.

Methods

Ocular surface sensitivity of the baseline was determined by means of a Cochet Bonnet esthesiometer, where sensitivity of the cornea is assessed by providing controlled mechanical stimulation of its central cornea. Tear breakup time (TBUT) was used to determine tear film stability and Ocular Surface Disease Index (OSDI) questionnaire was used to assess ocular discomfort. The subjects were subjected to hypertonic salt water wash with sterile 5% hypertonic saline solution used twice a day in four weeks. Every wash was performed using sterile conditions of gently ocular irrigation with 10 mL of hypertonic saline. Two weeks and four weeks post-initiation of treatment were used as the follow-up periods. Alterations on the ocular surface sensitivity, tear stability and patient-reported comfort were noted and evaluated. The safety was considered through the observation of adverse effects that included irritation, redness or epithelial damage. All measures were taken by trained ophthalmologists to produce uniformity and consistency of measurements.

Results

The study enrolled 120 participants of which 120 pass through to the full duration of the study which was four weeks. The average age of the respondents was 41.69812.3 and the sample size was 120 (56.7) and 120 (43.3) men and women respectively. Most of the participants were aged 31-50 years of age and this group forms the most frequent population with regards to ocular surface discomfort and sensitivity changes.

Table 1: Demographic Characteristics of Participants (n = 120)

Variable	Frequency (n)	Percentage (%)
Age (years)		
18–30	28	23.3
31–40	34	28.3
41–50	32	26.7
51–65	26	21.7
Gender		
Male	68	56.7
Female	52	43.3

Such findings show equal representation in the adult age groups with a little bit more males. The study population had lower sensitivity on the baseline ocular surface sensitivity when measured by the Cochet-Bonnet esthesiometer. Moderate improvement was seen after two weeks of hypertonic salt water wash and improvement was noted substantially after four weeks.

Table 2: Comparison of Ocular Surface Sensitivity Scores

Time Interval	Mean Sensitivity (mm)	Standard Deviation	p-value
Baseline	42.8	6.4	—
2 weeks	48.6	5.8	<0.001
4 weeks	54.2	5.1	<0.001

There was a statistically significant improvement in ocular surface sensitivity over time ($p < 0.001$), indicating therapeutic effectiveness of hypertonic saline wash.
Tear film stability, assessed using tear breakup time (TBUT), also improved significantly following treatment.

Table 3: Tear Breakup Time (TBUT) Comparison

Time Interval	Mean TBUT (seconds)	Standard Deviation	p-value
Baseline	7.9	1.8	—
2 weeks	9.8	1.6	<0.001
4 weeks	12.1	1.5	<0.001

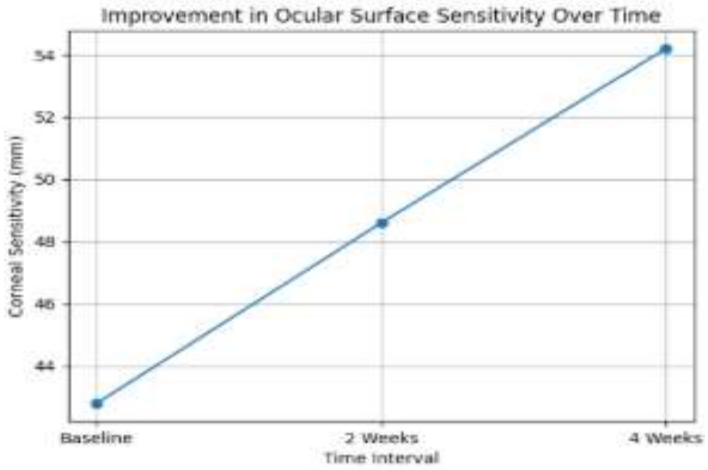
The improvement in TBUT indicates enhanced tear film stability and improved ocular surface health. Patient-reported symptoms assessed using the Ocular Surface Disease Index (OSDI) showed significant reduction in discomfort scores.

Table 4: Ocular Surface Disease Index (OSDI) Scores

Time Interval	Mean OSDI Score	Standard Deviation	p-value
Baseline	38.5	7.2	—
2 weeks	28.7	6.5	<0.001
4 weeks	19.4	5.9	<0.001

The progressive reduction in OSDI scores demonstrates significant improvement in subjective ocular comfort.

Graph 1: Improvement in Ocular Surface Sensitivity Over Time



The chart diagram shows that sensitivity of the ocular surface increases steadily throughout the treatment period. There were no severe negative effects during the research. Minor temporary irritation occurred in 9 participants (7.5%), and this went unresolved so the treatment could not be stopped in the first week. Thus, hypertonic salt water wash led to statistically and clinically significant recovery in the ocular surface sensitivity, tear film stability, and patient comfort. The results indicate its efficacy as a harmless and effective therapeutic method to enhance the ocular surface functioning.

Discussion

The current research assessed the impact of hypertonic salt water wash on the ocular surface sensitivity, the stability of the tear film and patient comfort. These results showed great improvement in corneal sensitivity, tear breakup and subjective symptom improvement after 4 weeks of treatment. These findings indicate that hypertonic saline has a positive effect on the reestablishment of homeostasis at the ocular surface and neural functionality. Hypertonic saline has been known to possess the osmotic properties in drawing excessive fluid out of corneal tissues to enhance the integrity and transparency of epithelial cells (1). This osmotic process is likely to have been a cause of the observed ocular surface sensitivity improvement by restoring the health of the epithelia and decreasing stromal edema. Other studies have demonstrated the efficacy of similar osmotic treatments in mucosal tissues; hypertonic saline enhances epithelial barrier activity and alleviates inflammation, which further indicates the potential of hypertonic saline in the regulation of the ocular surface (2). Also there has been evidence of removal of irritants and inflammatory mediators of epithelial surfaces induced by saline-based cleansing therapies which are likely to reduce neural irritation and enhance sensory recovery (3). Epithelial barrier repair is of significance in preserving corneal nerve activity and ocular surface sensitivity in general, especially in disease processes that are linked to epithelial perturbation and inflammation (4).

The increase in ocular surface sensitivity that was experienced in the study can be explained as the increase in the recovery of the epithelium and the minimization of the stress caused by inflammation. The corneal nerves are extremely sensitive to osmotic changes, inflammatory changes and a derailment of the epithelial integrity may have an adverse effect on the neural functioning. New developments in ocular surface therapeutics highlight the need to mitigate oxidative stress and inflammation to heal epithelial and neural conditions (5). Cornel neurons can also be greatly damaged by environmental and chemical stress factors, which lead to changes in sensitivity and persistent pain (6). Released inflammatory mediators at the time of ocular surface stress have the potential to sensitize nerve endings resulting in abnormal sensory responses. Thus, the therapeutic measures aiming at decreasing inflammation and stabilizing the epithelial cells are crucial in restoring the normal ocular sensitivity (7). Epithelial repair and inflammatory drug delivery strategies have also proved to be effective in enhancing corneal health, and neural responsiveness, which is similar to the observed improvement in the current research (8).

Hyperosmolar stress is a long-known cause of damage and change in ocular surfaces and changes in sensitivity. Hyperosmolarity may cause epithelial apoptosis, inflammatory signaling and immune activation that results in impairment of corneal sensory function (9). In extreme situations, chronic osmotic stress may result in failure of the limbal stem cell that is vital to epithelial healing as well as the integrity of the ocular surface (10). Similar pathological changes, such as epithelial injury and neural dysfunction, can be obtained when exposed to toxic agents and other environmental irritants, which makes it essential to maintain osmotic equilibrium at the ocular surface (11). The controlled therapeutic dosage of hypertonic saline can be used to restore the osmotic balance and promote epithelial healing without damaging the cells. Osmoprotective treatments have shown the capacity to stabilize epithelial cells and prevent osmotic stress, which can be used to support the therapeutic rationale of hypertonic saline application in enhancing the sensitivity of the ocular surface (12).

The increase in stability of tear film in this research also helps to favor positively the effect of hypertonic saline therapy. The stability of tear films is vital to the preservation of epithelial hydration, minimization of friction and shielding of corneal nerves. The inflammatory processes may interfere with the composition of the tear films and lead to the damage of the epithelia and neural sensitization.

Recent treatment methods such as nanozyme-based therapy have shown to be effective in suppressing the inflammation and restoring tears film stability, indicating that inflammation is a significant factor to consider when it comes to ocular surface diseases (13). Hyaluronic acids have been also found to be of great value in terms of enhancing tear film stability and epithelial processes which also helped in restoration of ocular surface sensitivity by protecting the epithelial layer (14). One of the major contributors to ocular surface disorders is neural sensitization, which can be enhanced to a considerable extent by interventions aimed at improving the health of epithelial cells and consequently enhance sensory functions and decrease discomfort (15). The results can be attributed to the findings in the present study showing an increase in tear film stability and sensitivity, which indicate the role of hypertonic saline in the restoration of the epithelial and neural homeostasis (16).

The other notable result of this study was a drastic change in subjective discomfort as indicated by better scores on Ocular Surface Disease Index. Close correlates of epithelial damage, tear film instability and neural dysfunction are ocular discomfort. Examples of therapeutic interventions that enhance epithelial regeneration include therapeutic interventions that enhance tear film stability and reduce neural irritation. Therapies based on growth factors have been shown to be effective in stimulating epithelial repair and in ocular surface well-being (17). Promising outcomes have also been experienced with neuromodulatory therapies in the reduction of pain in the eyes and enhancement of tear secretions, which implies the need to recover neural balance in conditions of the ocular surfaces (18). Hypertonic saline can also play its role in such effects by enhancing the hydration of the epithelium, decreasing the stress of inflammation, and stimulating neural recovery.

Conclusion

This research revealed that hypertonic salt water wash has a major positive impact on ocular surface sensitivity, tear film stability, and patient report comfort. The results reveal that hypertonic saline can facilitate recovery of epithelial integrity, improve corneal nerve activity as well as better the tear film dynamics that are vital in ensuring ocular surface homeostasis. Its efficacy of the treatment is confirmed by significant changes in the corneal sensitivity measurements, tear breakup time, and symptom scores. The hypertonic saline osmotic effect probably helps in the commandment of fluids, alleviates stress in the epithelium and assists in the recuperation of neurons, which leads to an enhanced ocular surface functioning. Notably, the intervention demonstrated a good safety profile, and the level of irritation was mild and temporary with a few participants experiencing the same. These findings indicate that hyper tonic salt water wash is safe, effective and accessible therapeutic form of ocular surface sensitivity. The introduction of hypertonic saline treatment into the clinical setting has the potential to optimize the treatment of ocular surface diseases, as well as the overall patient outcome.

References

1. Agrawal S, Gupta S, Gupta N, Vanathi M, Tandon R. Efficacy of hypertonic saline in treatment of corneal edema: A randomized crossover trial. *Medical Journal Armed Forces India.* 2024;80(5):522–527.
2. Štanfel D, Kalogjera L, Ryazantsev SV, Hlača K, Radtsig EY, Teimuraz R, Hrabač P. The role of seawater and saline solutions in treatment of upper respiratory conditions. *Marine Drugs.* 2022;20(5):330.
3. Parviz S, Duncan L, Rabago D. Soap and water to hands and face-eye rinse, nasal irrigation and gargling with saline for COVID-19 with anecdotal evidence. *Rhinology.* 2021;4:185–193.
4. Xia Y, Zhang Y, Du Y, Wang Z, Cheng L, Du Z. Comprehensive dry eye therapy: overcoming ocular surface barrier and combating inflammation, oxidation, and mitochondrial damage. *Journal of Nanobiotechnology.* 2024;22(1):233.
5. Yang M, Chen X, Chen Z, Zhao N, Zeng Z, Huang X, Li Z, Li J, Zhao G, Deng M, Zou Z. Thermoresponsive antioxidant metal-free carbon nanodot hydrogel: An effective therapeutic approach for ocular surface disease. *Science Advances.* 2025;11(30):eadt8775.

6. Graca M, Sarantopoulos K, Horn DB. Chemical toxic exposures and chronic ocular pain. *Frontiers in Toxicology.* 2023;5:1188152.
7. Chen T, Zhou N, Liang Q, Li Q, Li B, Chu Y, Zhang D, Chen Z, Tsao JR, Feng X, Hu K. Biochanin A: Disrupting the inflammatory vicious cycle for dry eye disease. *European Journal of Pharmacology.* 2024;977:176583.
8. Ma B, Pang L, Huang P, Bai J, Zhang Z, Wu H, Cai M, Yang J, Xu Y, Yin X, Qu C. Topical delivery of levocarnitine to the cornea and anterior eye by thermosensitive in-situ gel for dry eye disease. *Drug Design, Development and Therapy.* 2021;15:2357–2373.
9. Han Y, Zhang Y, Yuan K, Wu Y, Jin X, Huang X. Hyperosmolarity promotes macrophage pyroptosis by driving the glycolytic reprogramming of corneal epithelial cells in dry eye disease. *Frontiers of Medicine.* 2023;17(4):781–795.
10. Lin S, Cai M, Zhang L, Mao Y, Wu H, Liu X, Li Y, Liang M, Cheng X, Yu F, He H. Limbal stem cell dysfunction induced by severe dry eye via activation of the p38 MAPK signaling pathway. *The American Journal of Pathology.* 2023;193(11):1863–1878.
11. Quiroga-Garza ME, Ruiz-Lozano RE, Azar NS, Mousa HM, Komai S, Sevilla-Llorca JL, Perez VL. Noxious effects of riot control agents on the ocular surface: Pathogenic mechanisms and management. *Frontiers in Toxicology.* 2023;5:1118731.
12. González-Cela-Casamayor MA, López-Cano JJ, Bravo-Osuna I, Andrés-Guerrero V, Vicario-de-la-Torre M, Guzmán-Navarro M, Benítez-del-Castillo JM, Herrero-Vanrell R, Molina-Martínez IT. Novel osmoprotective DOPC-DMPC liposomes loaded with antihypertensive drugs as potential strategy for glaucoma treatment. *Pharmaceutics.* 2022;14(7):1405.
13. Chu D, Zhao M, Rong S, Jhe W, Cai X, Xiao Y, Zhang W, Geng X, Li Z, Zhang X, Li J. Dual-atom nanozyme eye drops attenuate inflammation and break the vicious cycle in dry eye disease. *Nano-Micro Letters.* 2024;16(1):120.
14. Hynnekleiv L, Magno M, Vernhardsdottir RR, Moschowits E, Tønseth KA, Dartt DA, Vehof J, Utheim TP. Hyaluronic acid in the treatment of dry eye disease. *Acta Ophthalmologica.* 2022;100(8):844–860.
15. Fakih D, Guerrero-Moreno A, Baudouin C, Réaux-Le Goazigo A, Parsadaniantz SM. Capsazepine decreases corneal pain syndrome in severe dry eye disease. *Journal of Neuroinflammation.* 2021;18(1):111.
16. Fakih D, Guerrero-Moreno A, Baudouin C, Réaux-Le Goazigo A, Parsadaniantz SM. Capsazepine decreases corneal pain syndrome in severe dry eye disease. *Journal of Neuroinflammation.* 2021;18(1):111.
17. Fan L, He T, Shi J, Ke X, Lu X. Effects of recombinant human epidermal growth factor eye drops combined with phacoemulsification on visual acuity recovery and dry eye complications. *Computational and Mathematical Methods in Medicine.* 2022;2022:1041558.
18. Cammalleri M, Amato R, Olivieri M, Pezzino S, Bagnoli P, Dal Monte M, Rusciano D. Effects of topical gabapentin on ocular pain and tear secretion. *Frontiers in Pharmacology.* 2021;12:671238.