Novel Drug Delivery System Applied On Dry Eye Disease

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Abstract ; Dry eye disease (DED) is a prevalent, multifactorial ocular surface disorder characterized by tear film instability, hyperosmolarity, inflammation, and neurosensory abnormalities, leading to discomfort, visual disturbance, and reduced quality of life. Conventional therapeutic options such as artificial tears, lubricating gels, and ointments are limited by rapid precorneal clearance, poor ocular bioavailability, and the requirement for frequent administration, which compromise treatment efficacy and patient compliance. To overcome these drawbacks, novel drug delivery systems (NDDS) have emerged as promising strategies in the management of DED. Various NDDS platforms have been developed to enhance drug solubility, stability, ocular penetration, and sustained release. Nanoparticles, including liposomes, micelles, dendrimers, and polymeric carriers, provide targeted and prolonged therapeutic action. Lipid-based systems such as solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) improve corneal absorption and protect drugs from degradation. In-situ gelling systems, ocular inserts, and biodegradable films prolong retention time on the ocular surface, reducing dosing frequency. Contact lens-mediated delivery offers continuous, controlled release of drugs, while hydrogel-based formulations not only deliver therapeutic agents but also mimic the natural tear film to provide lubrication. These advanced systems collectively address the limitations of conventional formulations by improving pharmacokinetics, minimizing systemic absorption, and reducing local side effects. Furthermore, patient compliance and therapeutic outcomes are significantly enhanced due to reduced dosing frequency and improved drug efficacy.

Keywords : Dry eye Disease, novel Drug Delivery System.

1. Introduction

Novel Drug Delivery Systems (NDDS) are advanced pharmaceutical technologies designed to deliver therapeutic agents in a controlled, targeted, and sustained manner, improving drug bioavailability, efficacy, and patient compliance while minimizing side effects. These systems utilize innovative carriers such as nanoparticles, liposomes, hydrogels, ocular inserts, and in-situ gels to overcome the limitations of conventional drug delivery methods. Dry eye disease (DED) is a common ocular disorder associated with tear film instability, inflammation, and ocular surface damage, which significantly affects vision and comfort. Traditional eye drops and lubricants have limited effectiveness due to rapid elimination and poor absorption, while novel drug delivery systems (NDDS) are being developed to enhance drug residence, provide sustained release, and improve overall therapeutic efficiency. Biomaterials are increasingly being explored for the treatment of dry eye disease due to their ability to restore tear film stability, reduce inflammation, and enhance ocular surface repair. Current research focuses on innovative materials that provide sustained drug delivery, improved lubrication, and better patient outcomes, with future developments aiming to further optimize safety and therapeutic efficacy. Retinal diseases, including age-related macular degeneration, diabetic retinopathy, and retinal vein occlusion, remain leading causes of irreversible vision loss worldwide. Conventional treatment approaches, such as intravitreal injections and systemic therapies, are often limited by short drug half-life, poor bioavailability, patient non-compliance, and the invasive nature of repeated administrations. To overcome these challenges, novel drug delivery systems (NDDS) have emerged as promising strategies, offering targeted, sustained, and minimally invasive delivery of therapeutic agents to the posterior segment of the eye. Advances in nanotechnology, biomaterials, and sustained-release formulations are reshaping ocular pharmacotherapy and hold great potential to improve therapeutic efficacy while reducing treatment burden in retinal disorders. The human eye is a highly complex and well protected organ, where physiological and anatomical barriers often limit the effective delivery of therapeutic agents. Conventional ocular dosage forms such as eye drops, ointments, and systemic medications frequently suffer from drawbacks including poor bioavailability, rapid drug elimination, and the need for frequent administration. These limitations not only reduce therapeutic efficacy but also affect patient compliance in long-term treatments. To address these challenges, novel ocular drug delivery systems have been developed, providing innovative approaches for targeted, sustained, and efficient drug transport to both the anterior and posterior segments of the eye. Advances in nanotechnology, hydrogels, in-situ gels, implants, and other controlledrelease platforms are opening new possibilities for improving treatment outcomes, reducing side effects, and enhancing patient quality of life. Thus, novel ocular drug delivery represents a new vision in ophthalmic therapeutics, bridging the gap between conventional formulations and future personalized eye care.

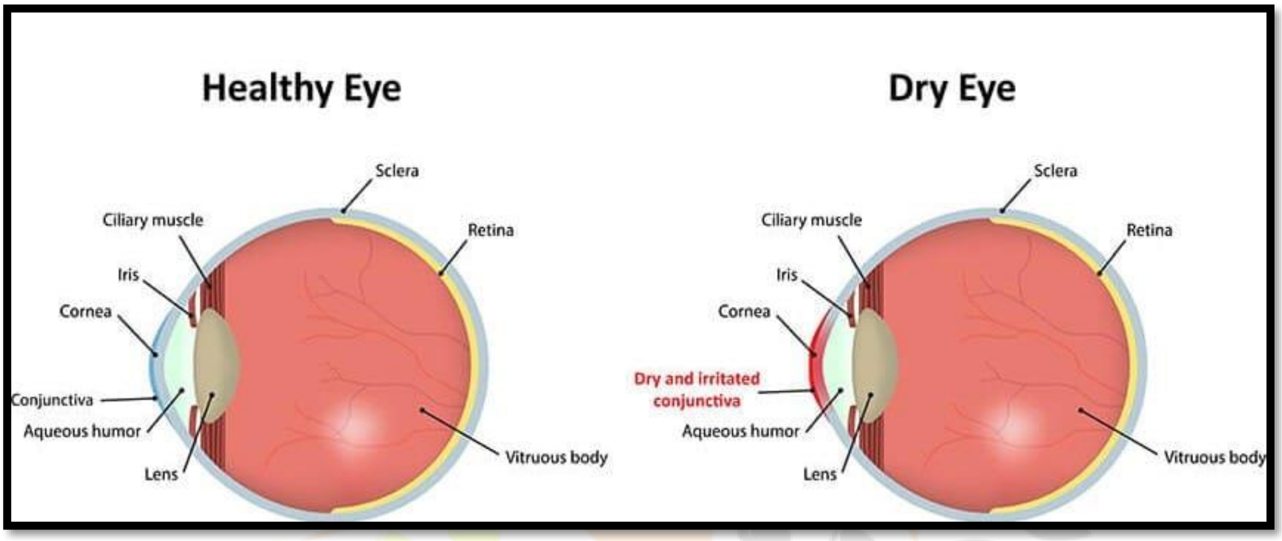

Figure 1 : Healthy Eye / Dry Eye

2. Pathophysiology of dry eye disease

1) Tear film Dysfunction: The defining characteristic of dry eye disease (DED) is increased tear film osmolarity, which can harm the ocular surface both directly and indirectly through mechanisms such as inflammation, tear film instability, epithelial damage, and altered neurosensory function of the ocular surface. These inflammatory events compromise ocular surface integrity and further destabilize the tear film, creating a self-sustaining vicious cycle of disease progression. In addition to hyperosmolarity, factors such as ocular surface inflammation from allergic eye conditions, preservative-induced toxicity, or xerophthalmia can also initiate and aggravate this pathological cycle.

2) Inflammation: Dry eye disease (DED) is a widespread condition, affecting an estimated 5% to 34% of the global population. The disease is thought to arise from mechanisms such as increased tear film osmolarity and inflammation of both the ocular surface and lacrimal glands. Clinically, DED is categorized into two main types: aqueous-deficient DED, characterized by reduced tear production, and evaporative DED, marked by excessive tear evaporation. These changes, including increased tear osmolarity, activate stress signaling pathways in ocular surface cells, leading to the release of innate inflammatory mediators. This, in turn, can recruit and activate CD4+ T cells, which secrete cytokines that contribute to damage of the corneal, conjunctival, and lacrimal gland epithelium. The ocular surface Is a highly specialized exposed mucosa, lined with stratified epithelium that acts as a protective barrier against environmental, microbial, and inflammatory insults. The conjunctival epithelium, second only to the intestine, contains a high density of mucus-secreting goblet cells. It also hosts a diverse array of resident immune cells, including natural killer cells, dendritic cells, macrophages, γδ T cells, and CD4+ and CD8+ T cells, which normally play a role in antimicrobial defense but may also contribute to the development of dry eye disease.

3) Meibomian Gland Dysfunction: The meibomian glands, located along the eyelid margins, produce lipids that form the outermost layer of the tear film, helping to minimize tear evaporation. Dysfunction of these glands can result from reduced secretion due to atrophy, gland dropout, or blockage of the gland openings. Besides meibomian gland issues, other significant contributors to excessive tear evaporation include infrequent or incomplete blinking, eyelid malposition, vitamin A deficiency, contact lens wear, and environmental influences such as dry air or strong airflow. When the meibomian glands do not work properly (a condition called Meibomian Gland Dysfunction, MGD), the oily layer is reduced or altered. This can cause faster tear evaporation, leading to dry eye disease, irritation, redness, or blurry vision. Common causes of gland dysfunction include blockage of the gland openings, aging, inflammation, and long-term contact lens use.

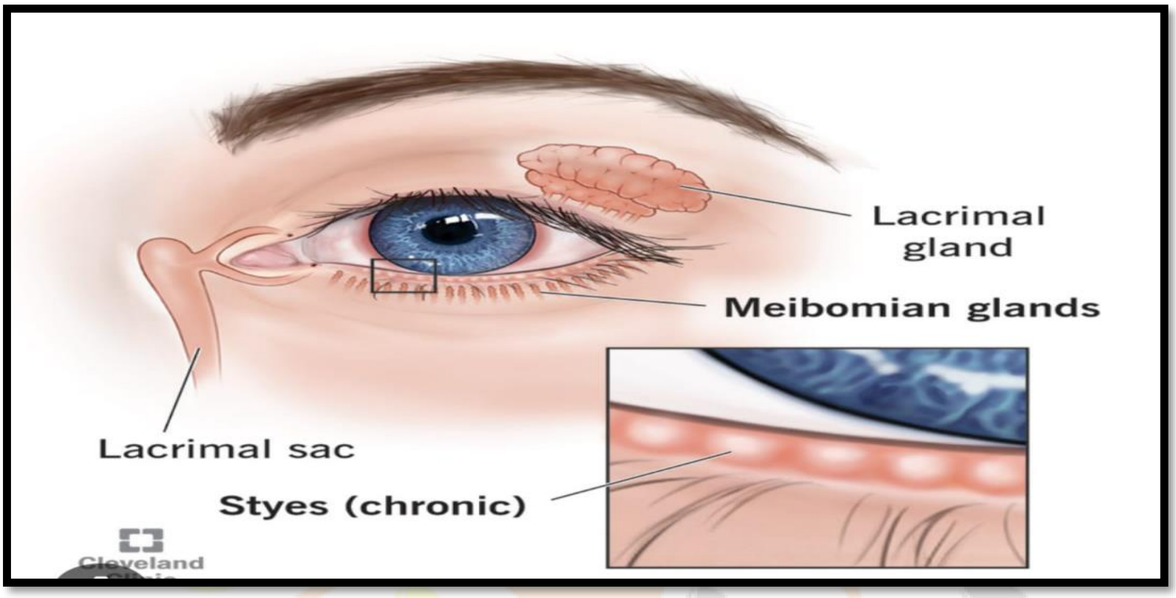

Figure 2 : Meibomian Gland Dysfunction

4) Oxidative Stress: Oxidative stress arises when there is an imbalance between the production of reactive oxygen species (ROS) and the cell's antioxidant defense systems. The eye is particularly vulnerable to oxidative damage due to constant exposure to light and the high metabolic activity of its tissues. The anterior segment of the eye, being directly exposed to ultraviolet (UV) radiation, relies on a complex antioxidant system to protect the retina from UV-induced damage. Meanwhile, the posterior segment has a high metabolic rate and oxygen consumption, which leads to elevated ROS generation. Additional factors such as inflammation, aging, genetic predisposition, and environmental pollutants further increase ROS production and compromise antioxidant defenses, creating conditions favorable for oxidative stress. Disruption of the redox balance has been implicated in the development of multiple ocular diseases affecting both the anterior and posterior segments. This review aims to provide an updated understanding of oxidative stress mechanisms in ocular diseases and explores potential therapeutic strategies to mitigate oxidative damage in the eye.

3. Limitations of Conventional Therapies

1) Poor Bioavailability: Dry eye disease (DED) is usually managed with a combination of therapeutic approaches to achieve effective symptom control. Artificial tear formulations are often prescribed as the first-line option, followed by medicated topical eye drops when needed. However, conventional eye drops have limited bioavailability because the eye's natural protective barriers cause rapid clearance from the precorneal area, which restricts drug absorption and therapeutic action. In addition, certain excipients included in these formulations may cause ocular irritation or toxicity, potentially worsening DED manifestations. These factors make the development of effective topical eye drops particularly complex. This review outlines the major challenges in eye drop formulation for DED, beginning with an overview of commonly available artificial tears, their mechanisms, and clinical use. It also discusses different

formulation strategies aimed at improving ocular drug delivery, highlighting their benefits, drawbacks, and role in marketed products for DED management.

2) Potential Side Effects: Long-term use of anti-inflammatory medications in dry eye management is associated with adverse effects such as cataract formation and increased intraocular pressure leading to glaucoma. Similarly, immunomodulatory agents often require extended periods before showing therapeutic benefits, and their tolerability issues can negatively impact patient compliance. Surgical interventions—including punctal occlusion, salivary gland transplantation, tarsorrhaphy, and amniotic membrane application—are available alternatives, but they fail to provide a permanent solution.

3) Slow Onset of Action: Artificial tears remain the cornerstone of dry eye disease (DED) therapy, offering short-term relief of symptoms without targeting the underlying disease mechanisms. Pharmacological options that do address the pathophysiology often require several months typically 3 to 6 to achieve noticeable benefits, and in many cases, patients may encounter tolerability concerns. These limitations underscore the demand for newer agents that act more rapidly while maintaining a favorable safety profile. In managing DED, patient education plays a crucial role. Practitioners must emphasize the chronic, multifactorial nature of the condition and set realistic expectations, making clear that consistent treatment is essential and that therapeutic benefits may not be immediate. This review discusses current approaches to DED management, with particular attention to pharmacologic strategies, and provides guidance for eye care professionals in fostering patient adherence and optimizing treatment outcomes.

4) Symptomatic Treatment Only: Traditional therapies for dry eye disease, such as artificial tears and lubricating drops, primarily provide symptomatic relief rather than addressing the underlying causes of the condition. While these treatments can temporarily alleviate discomforts like dryness, irritation, and burning, they do not specifically interact with the core mechanisms contributing to dry eye disease, including inflammation, oxidative stress, and meibomian gland dysfunction. Consequently, these therapies may not effectively modify the disease course or provide long-term relief. This limitation underscores the need for novel therapeutic approaches that not only alleviate symptoms but also target the underlying pathophysiological processes, aiming for more sustained and effective management of dry eye disease.

5) Needs of Frequent Dosing: Frequent dosing is a major factor influencing patient adherence in the management of dry eye disease. Many conventional eyes drop and lubricants require multiple applications per day to maintain symptomatic relief, which can be burdensome for patients. The article highlights that patients generally prefer medications that minimize dosing frequency, as high-frequency regimens are associated with decreased compliance and lower treatment effectiveness. This emphasizes the need for developing therapies with longer ocular residence times or sustained-release formulations to reduce the number of daily administrations, thereby improving adherence, patient satisfaction, and overall treatment outcomes.

6) Variability in Patients Response: Dry eye disease (DED) presents with significant variability in both symptoms and clinical signs, complicating diagnosis and treatment. Patients often report non-specific symptoms such as visual disturbance, photophobia, and ocular discomfort, including foreign body sensation, grittiness, and burning. Paradoxically, there may be excessive tearing, as discomfort triggers reflex tearing. The severity of symptoms does not always correlate well with the severity of signs observed during clinical examination. This discrepancy can arise from factors like a low pain threshold, where symptoms exceed signs, or reduced corneal sensation, where signs exceed symptoms. Such variability underscores the complexity of DED and the challenges in predicting patient responses to treatment.

4. Needs for novel drug delivery system

1) Improve Bioavailability: Enhancing bioavailability is a major requirement in novel drug delivery systems (NDDS), particularly for drugs that are poorly soluble in water or prone to instability, as these factors limit absorption at the intended site of action. Traditional drug formulations often face rapid degradation, quick clearance from the body, or insufficient tissue accumulation, which can reduce their therapeutic efficacy.

2) Targeted Drug Delivery System: Novel drug delivery systems (NDDS) are essential for addressing several limitations of conventional therapies. One of the main needs is precise targeting, as traditional

drugs often disperse throughout the body, causing side effects and reducing efficacy. NDDS can deliver therapeutic agents specifically to diseased tissues or cells, enhancing treatment outcomes. Additionally, many drugs, particularly biologics, are unstable and prone to degradation in the body; encapsulation within NDDS protects these drugs and prolongs their activity. Controlled or sustained release is another requirement, as it helps maintain consistent drug levels over time, improving efficacy and reducing dosing frequency. Finally, NDDS must overcome physiological barriers, such as the blood-brain barrier, to ensure drugs reach their intended targets effectively, thereby maximizing therapeutic benefit while minimizing systemic toxicity.

3) Control/sustained Release: Traditional drug formulations often require frequent dosing to maintain effective therapeutic levels, which can negatively impact patient compliance. Controlled or sustained release delivery systems are designed to overcome this drawback by releasing drugs gradually over an extended duration. This slow and consistent release helps maintain steady plasma concentrations, reduces fluctuations in drug levels, lowers the frequency of administration, and ultimately enhances treatment adherence while minimizing side effects.

4) Protect Drug from Degradation: Many therapeutic molecules such as proteins, peptides, and nucleic acids are inherently unstable in the biological environment. They are prone to chemical breakdown (e.g. hydrolysis, oxidation), or degradation by enzymes before they reach their intended site of action. Novel Drug Delivery Systems (NDDS) are engineered to overcome these vulnerabilities by encapsulating or complexing the drug with protective carrier materials. These carriers shield the drug from enzymatic attack and harsh chemical conditions, delay its exposure to degradative factors, and deliver it more intact to the target site. In many cases, this also extends the drug’s half-life in circulation, improves its bioavailability, and enhances efficacy while reducing required doses and side effects.

5) Reduce Side Effects: Drugs delivered by conventional methods often spread throughout the body, affecting both diseased and healthy tissues. This non-specific distribution can cause adverse effects in organs or cells that are not meant to interact with the drug. Novel Drug Delivery Systems (NDDS) help minimize these unwanted side effects by directing the drug more precisely to the target site or controlling the release over time. When a drug is encapsulated in targeted carriers (such as ligands, antibodies, or cell-membrane decorations), or when release is triggered only under specific stimuli (such as pH, enzymes, redox conditions), the healthy tissues are better protected. Such systems allow for lower total doses, fewer systemic exposures, and better safety profiles, all of which improve patient outcomes and reduce risks associated with treatment.

5. Diagnosis for DED

1. Tear film stability

1.1 Fluorescein Break-Up Time (BUT): The tear film break-up time test is a simple and rapid procedure performed after instilling fluorescein dye into the eye. The patient is instructed to keep their eyes open without blinking, and the corneal surface is then examined under cobalt blue illumination. The interval between the last blink and the first appearance of a dry spot, where fluorescein no longer coats the cornea, is measured in seconds. A longer BUT indicates greater tear film stability, with values above 8–10 seconds generally regarded as normal.

1.2 Non-Invasive Break-Up Time (NIBUT): Since fluorescein dye can itself alter tear film stability, non-invasive methods for assessing tear break-up time have gained increasing use with recent technological developments. In this approach, specialized software automatically detects tear film disruption by analyzing reflections from the ocular surface, typically using grid patterns or Placido disk images. The program evaluates various zones of the cornea, identifying distortions or breaks in the reflected mires to determine tear film stability.

2. Ocular surface

2.1 Fluorescein Staining: Fluorescein staining is a common method to assess corneal damage in dry eye disease. A moistened sterile fluorescein strip or fluoresceincontaining eye drops, sometimes combined with a topical anaesthetic, are applied to the lower eyelid. While strips may cause mild irritation and drops may briefly burn, damaged or missing epithelial cells on the cornea absorb the dye and appear bright green under cobalt blue light. These stained areas indicate epithelial compromise, helping to evaluate the severity and pattern of dry eye and guide appropriate management.

2.2 Lissamine Green Staining: Lissamine green is a vital dye used to evaluate the ocular surface, especially the conjunctiva, in dry eye disease. It stains degenerating or devitalized epithelial cells and areas of mucin deficiency, helping to detect early ocular surface damage that may not be visible with fluorescein. The dye is applied as eye drops and is generally well tolerated, causing minimal irritation compared to rose bengal. Under slit-lamp examination, stained areas appear green, allowing clinicians to assess the extent and pattern of ocular surface compromise and guide dry eye management.

3. Tear volume and production

3.1 Schirmer's Test: Schirmer's test assesses tear production using a small paper strip marked with a ruler. The folded end of the strip is placed inside the inferior conjunctival fornix at the temporal one-third of the lower eyelid. After 5 minutes, the strip is removed, and the extent of wetting is measured in millimeters. The test can be performed with or without topical anesthesia. Tear production of less than 10 mm in 5 minutes is generally considered indicative of reduced tear secretion, suggestive of dry eye.

3.2 Tear Meniscus Assessment: After fluorescein dye instillation, the tear meniscus is visible along the lower eyelid margin when viewed under a cobalt blue filter. Its height may be approximately judged by comparing it with the height of the slit lamp beam, though this technique lacks consistency and reproducibility. A more precise evaluation can be obtained using anterior segment OCT, which allows objective measurement of tear meniscus height. However, the accuracy of this method depends on the imaging system, the analysis software, and the examiner's expertise.

4. Biochemical markers

4.1 Tear Osmolarity: Tear osmolarity testing is a simple, minimally invasive, and rapid procedure that can be carried out by trained ophthalmic personnel. According to the TFOS DEWS II report, elevated osmolarity is a hallmark indicator of dry eye disease. The TearLab osmometer, based on lab-on-a-chip technology, allows measurement with minimal operator dependency. The disposable test card is positioned at the lower tear meniscus, requiring less than 100 nanoliters of sample, which makes it suitable even in cases of severe aqueous deficiency. A tear osmolarity value below 300 mOsm/L with an inter eye difference of less than 8 mOsm/L is considered normal. Readings above 300 mOsm/L are associated with dry eye, with severity graded as mild (300 320 mOsm/L), moderate (320–340 mOsm/L), and severe (> 340 mOsm/L).

4.2 Tear osmolarity refers to the quantitative evaluation of the concentration of dissolved salts present in the tear fluid. Elevated or abnormal values are indicative of disturbances in tear film homeostasis and may signal underlying ocular surface disease. [38] Lactoferrin Test: Lactoferrin, a protein secreted by the acinar cells of the lacrimal gland, is naturally present in tears. It possesses both antimicrobial and anti-inflammatory functions. Reduced levels of lactoferrin have been reported in individuals with dry eye disease, correlating with impaired aqueous tear secretion. The TearScan 270 MicroAssay System (Advance Tear Diagnostic, Birmingham, AL) serves as a point-ofcare device that measures tear lactoferrin concentration using only 0.5 microliters of tear sample.

6. NDDS in dry eye disease

Liposomes: Liposomes are spherical vesicles ranging from 25 nm to 10 µm in size, composed of a phospholipid bilayer. These vesicles can adhere to the cornea either by being coated with an adhesive polymer or dispersed in an adhesive gel, which helps in the effective delivery of water-soluble drugs. Positively charged liposomes, in particular, can interact strongly with the negatively charged mucin on the corneal epithelium, further enhancing drug delivery. Liposomal formulations used for managing dry eye disease (DED) are available as lipid containing eye drops, including Vyseo®, Clarimist®, Tears Again®, ActiMistTM, and OptrexTM, which are beneficial for patients with mild to moderate evaporative DED. Studies have shown that these lipid-based eye drops are more effective at stabilizing tear fluid and reducing tear osmolarity compared to formulations containing hydroxypropyl methylcellulose or sodium hyaluronate. Additionally, liposomal sirolimus has been developed and is under investigation for DED treatment. Overall, liposomes help alleviate DED symptoms and improve tear film structure and stability. Nonetheless, challenges such as manufacturing scale-up and stability issues limit their widespread clinical use, and ongoing research is expected to address these limitations.

Nanomicells: Nanomicelles are colloidal carriers with sizes between 5 nm and 200 nm, formed by the self-assembly of block copolymers or surfactants in aqueous solutions. Polymeric nanomicelles are generated from block copolymers containing both hydrophobic and hydrophilic monomers, while surfactant nanomicelles are composed of amphiphilic molecules with hydrophilic head groups (anionic, cationic, zwitterionic, or nonionic) and hydrophobic tails. Both types of nanomicelles have been explored for the treatment of dry eye disease (DED). Polymeric nanomicelles show great promise as drug delivery systems for DED. Methoxy poly (ethylene glycol)-hexyl substituted poly (lactides) (MPEGhexPLA) nanomicelles loaded with cyclosporine A (CsA) have demonstrated biocompatibility in human corneal epithelial cells and effectiveness in DED therapy. In animal studies, MPEG-hexPLA micelles enhanced pre-corneal residence of CsA (327 ng/mL in rabbits) compared to Restasis® (142 ng/mL), and corneal tissue concentrations were significantly higher (1540 ng/g vs).

Nanoparticles: Nanoparticles (NPs) have emerged as versatile carriers for ocular drug delivery in dry eye disease, owing to their small size (10–300 nm) and ability to encapsulate therapeutic agents. By shielding drugs from rapid clearance through tear turnover and enzymatic degradation, NPs enhance solubility, prolong residence time on the ocular surface, and enable controlled or sustained drug release. Polymeric nanoparticles, such as those fabricated from PLGA, chitosan, or polycaprolactone, gradually release their cargo via polymer erosion and diffusion, while lipid-based carriers—including solid lipid nanoparticles, nanostructured lipid carriers, and nanoemulsions—are particularly effective at solubilizing hydrophobic molecules and improving their ocular bioavailability. In the context of DED, lipid-based systems have been investigated to replenish the lipid component of the tear film and to facilitate delivery of immunomodulators like cyclosporine and tacrolimus, whereas polymeric nanoparticles have been explored for administering anti-inflammatory drugs and mucin stabilizing agents in preclinical settings.

In Setu Gels: Hydrogels and in-situ gelling systems represent an important class of ocular drug delivery platforms that take advantage of their unique physicochemical properties to improve therapeutic outcomes in dry eye disease. Hydrogels are three-dimensional polymeric networks with a high-water content, closely mimicking the hydrated environment of natural ocular tissues. This structure not only provides soothing lubrication but also serves as a reservoir for controlled drug release. In-situ gels are particularly attractive for ocular use, as they are instilled as low-viscosity eye drops and subsequently undergo a sol-to-gel transition once exposed to physiological triggers such as temperature, pH, or ionic composition of tears.

Implants/Ocular Insert: Ocular inserts and implants, including punctal plugs, are solid or semisolid drug delivery systems designed to be placed in the conjunctival sac or lacrimal punctum, where they release therapeutic agents in a controlled manner over extended periods ranging from days to months. These devices can be bioerodible, degrading naturally without intervention, or non-erodible, requiring manual removal, and they are engineered to deliver drugs through matrix diffusion, reservoir release, or polymer degradation. In the context of dry eye disease, drug-eluting punctal plugs carrying cyclosporine or corticosteroids and dissolvable inserts releasing lubricants or anti-inflammatory agents have been explored to provide sustained ocular surface therapy, improve tear retention, and reduce systemic side effects. The key advantages of these systems include prolonged duration of action, achievement of higher local drug concentrations, reduced dosing frequency, and improved patient adherence compared to conventional eye drops. However, limitations remain, such as foreign-body sensation, risk of extrusion or spontaneous loss, the need for removal in non-erodible designs, and possible device-related complications including irritation, inflammation, or infection.

Mucoadhesive System: Mucoadhesive systems represent an advanced ocular drug delivery strategy that exploits the ability of certain polymers to adhere to the mucin layer covering the ocular surface, thereby resisting the rapid clearance caused by blinking and tear turnover. These systems typically incorporate mucoadhesive polymers such as chitosan, hyaluronic acid, and carbomers, which form noncovalent interactions like hydrogen bonding, electrostatic attraction, or hydrophobic forces with mucins, prolonging the contact time of the formulation with the corneal and conjunctival epithelium. By increasing residence time, they enhance drug absorption and bioavailability, overcoming one of the major limitations of conventional eye drops. Mucoadhesive approaches can be applied in multiple formats, including polymer coatings on nanoparticles and liposomes, incorporation into hydrogel matrices, or as surface modifications that improve ocular retention of nanocarriers.

Biomaterials-based System: Biomaterials-based systems represent a broad and versatile class of novel ocular drug delivery and therapeutic platforms that build upon advanced material science to address the multifactorial nature of dry eye disease (DED). These systems encompass a wide range of engineered materials, including synthetic and natural polymers, dendrimers, bioactive scaffolds, peptide-based structures, and hybrid composites, all of which can be designed to interact with the ocular surface in highly specific ways. Their functionality extends beyond drug delivery, as biomaterials can be engineered to restore or mimic the natural tear film components, provide lubrication, act as scaffolds for ocular surface healing, or even serve as carriers for biologics and regenerative therapies.

Dentrimers: Dendrimers are novel polymers characterized by a radially branched, treelike structure that usually forms a three-dimensional architecture around a central core. Their internal cavities enable them to function as nanocapsules capable of encapsulating therapeutic agents. Additionally, their surfaces can be easily engineered by attaching biocompatible polymers or functional groups, making them versatile carriers. These properties, along with their high-water solubility, make dendrimers promising candidates for managing dry eye disease (DED).

7. Summary

Dry Eye Disease (DED) is a multifactorial ocular surface disorder caused by tear film instability, hyperosmolarity, inflammation, and neurosensory dysfunction, leading to discomfort and impaired vision. Conventional treatments such as artificial tears and lubricants provide only temporary relief due to poor bioavailability, rapid clearance, and frequent dosing requirements. To overcome these limitations, Novel Drug Delivery Systems (NDDS) have been developed. These include nanoparticles, liposomes, nanomicelles, in-situ gels, ocular inserts, contact lenses, mucoadhesive systems, hydrogels, dendrimers, and biomaterials-based systems. NDDS improve solubility, enhance corneal penetration, prolong ocular retention, and allow targeted and sustained drug release. They also reduce side effects, improve patient compliance, and enhance overall therapeutic efficacy. Diagnostic tools such as fluorescein/NIBUT, Schirmer's test, osmolarity tests, and biochemical markers are used to assess DED. NDDS platforms like lipid-based carriers, polymeric nanoparticles, hydrogels, and drug-eluting devices significantly advance DED management by mimicking tear film, reducing inflammation, and improving lubrication. Emerging technologies such as neuro-stimulators, scleral lenses, and Aero Pump spray devices further support novel therapeutic strategies.

8. Conclusion

Novel Drug Delivery Systems (NDDS) represent a promising advancement in the management of Dry Eye Disease. By overcoming the challenges of conventional therapies such as short drug residence time, poor bioavailability, and symptomatic treatment only NDDS enable sustained, controlled, and targeted drug delivery with fewer side effects. Systems like liposomes, nanoparticles, hydrogels, and dendrimers not only improve drug retention and therapeutic outcomes but also enhance patient compliance by reducing dosing frequency. Future perspectives focus on biomaterials, regenerative approaches, and personalized ocular therapy, which could provide long-term solutions by addressing the underlying pathophysiology of DED rather than just offering symptomatic relief. Although challenges such as manufacturing, stability, and regulatory approval remain, NDDS hold great potential to revolutionize ocular drug delivery and improve the quality of life for patients with Dry Eye Disease.

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