

"Advancements in Ocular Drug Delivery: Exploring the Potential of Oleogel-Based Systems"

^[1*]Archana Dangi, ^[2]Dr. Aakash Singh Panwar

^[1]Research Scholar, Institute of Pharmaceutical Sciences, SAGE University Indore MP. Mob: 9340911399

^[2] Professor, Institute of Pharmaceutical Sciences. SAGE University Indore MP. Mob: 9893093497.
Email: ^[1]archanadangi9@gmail.com, ^[2]aakashsingh.panwar@gmail.com

Abstract: Ocular drug delivery systems are crucial for the effective treatment of various ocular diseases. However, the limited bioavailability and poor penetration of drugs into ocular tissues pose significant challenges. In recent years, oleogel-based systems have emerged as a promising approach to enhance drug delivery to the eye. Oleogels are unique gels composed primarily of a liquid component and an added gelator, resulting in the formation of a stabilized three-dimensional matrix. These gels offer several advantages, including cost-effectiveness, biocompatibility, extended shelf life, resistance to microbial contamination, and thermoreversibility. Additionally, oleogels exhibit non-Newtonian behavior, displaying shear thinning properties that make them ideal for controlled release formulations in ophthalmic applications, both for the front and back of the eye. The treatment of diseases in the posterior segment of the eye, such as macular degeneration, diabetic retinopathy, and glaucoma, presents challenges due to barriers that hinder drug delivery to the back of the eye. Oleogels, particularly vegetable oil-based oleogels, have shown promise as potential vehicles for targeted delivery of hydrophobic or hydrophilic drugs. The applications of oleogels span various fields, including chemistry, pharmaceuticals, cosmetics, biotechnology, and food technology. In pharmacology, oleogels are utilized as drug and vaccine delivery platforms for active ingredients through diverse routes such as transdermal, oral, and parenteral administration. This comprehensive review paper aims to provide an in-depth overview of the utilization of oleogels in ocular drug delivery systems. It discusses the formulation aspects, advantages, and challenges associated with oleogel-based systems, shedding light on their potential to revolutionize ocular drug delivery. The paper delves into the various strategies employed to optimize drug release and enhance ocular bioavailability using oleogels. It explores how oleogels can improve drug solubility, prolong drug release, and enhance drug permeation across ocular barriers. The influence of different oleogel components, such as oils, gelling agents, and additives, on the performance of ocular drug delivery systems is thoroughly examined. Furthermore, the review paper discusses the compatibility of oleogels with different drug classes, including hydrophilic and lipophilic drugs. It also explores the in vitro and in vivo evaluation methods used to assess the efficacy and safety of oleogel-based ocular drug delivery systems, providing valuable insights into their performance. The paper goes beyond the basics and highlights recent advancements and future prospects in the field of oleogel-based ocular drug delivery. It explores the incorporation of nanotechnology and the development of stimuli-responsive oleogels, showcasing the potential for further innovation and improvement. Overall, this review paper serves as a comprehensive resource for researchers, clinicians, and pharmaceutical scientists interested in developing innovative and effective ocular drug delivery strategies. By providing a detailed analysis of oleogel-based systems, it aims to inspire further research and development in this promising field, ultimately leading to improved treatments for ocular diseases.

Keywords: Oleogels, biogel, organogelator, drug delivery, characterization, semi-solid dosage form

Introduction:

Ocular drug delivery systems play a critical role in the treatment of various ocular diseases by ensuring the effective delivery of therapeutic agents to the target tissues. However, the unique anatomy and physiology of the eye present significant challenges for drug delivery, including limited bioavailability and poor penetration of drugs into ocular tissues. Over the years, researchers have explored various strategies to overcome these challenges and enhance the efficacy of ocular drug delivery.

One promising approach that has gained considerable attention is the use of oleogel-based systems. Oleogels are gels composed primarily of a liquid component and an added gelator, resulting in the formation of a stabilized three-dimensional matrix. These gels possess several desirable properties, including cost-

effectiveness, biocompatibility, extended shelf life, resistance to microbial contamination, and thermoreversibility. Moreover, oleogels exhibit non-Newtonian behavior, displaying shear thinning properties that make them suitable for controlled release formulations.

The treatment of diseases in the posterior segment of the eye, such as macular degeneration, diabetic retinopathy, and glaucoma, poses a significant challenge due to the presence of various barriers that hinder drug delivery to the back of the eye. Oleogels, particularly those based on vegetable oils, have shown promise as potential vehicles for targeted delivery of both hydrophobic and hydrophilic drugs. Their unique properties and versatility make them attractive candidates for ocular drug delivery applications.

In addition to ocular drug delivery, oleogels find applications in various fields, including chemistry, pharmaceuticals, cosmetics, biotechnology, and food technology. In pharmacology, oleogels have been utilized as drug and vaccine delivery platforms for active ingredients through diverse routes such as transdermal, oral, and parenteral administration. The versatility and potential of oleogels in controlled drug delivery have sparked significant interest among researchers and scientists.

This review paper aims to provide a comprehensive overview of the utilization of oleogels in ocular drug delivery systems. It will delve into the formulation aspects, advantages, and challenges associated with oleogel-based systems. The paper will explore the strategies employed to optimize drug release and enhance ocular bioavailability using oleogels. Furthermore, it will discuss the compatibility of oleogels with different drug classes and examine the *in vitro* and *in vivo* evaluation methods used to assess their efficacy and safety.

The review will also highlight recent advancements and future prospects in the field of oleogel-based ocular drug delivery, including the incorporation of nanotechnology and the development of stimuli-responsive oleogels. By providing a comprehensive analysis of oleogel-based systems, this review paper aims to serve as a valuable resource for researchers, clinicians, and pharmaceutical scientists interested in developing innovative and effective ocular drug delivery strategies. Ultimately, the advancements in oleogel-based ocular drug delivery systems have the potential to revolutionize the treatment of ocular diseases and improve patient outcomes.

A. Importance of Ocular Drug Delivery Systems: Ocular drug delivery systems are of paramount importance in the treatment of ocular diseases and conditions. These systems are designed to deliver drugs to the eye in a controlled and targeted manner, addressing the unique challenges of ocular drug delivery. They enhance drug bioavailability by overcoming barriers to drug absorption on the ocular surface, ensuring optimal therapeutic outcomes. Moreover, ocular drug delivery systems enable targeted delivery of drugs to specific ocular tissues or compartments, such as the anterior or posterior segment of the eye, improving treatment efficacy while minimizing systemic side effects. They also offer the advantage of prolonged drug release, reducing the frequency of administration and enhancing patient compliance. Additionally, these systems protect drugs from degradation and enhance their stability, ensuring that the drug retains its therapeutic activity until it reaches the target site. This not only improves treatment outcomes but also provides convenience and comfort to patients by reducing the need for frequent administration of eye drops or injections. Overall, ocular drug delivery systems play a vital role in optimizing ocular drug therapy and improving patient care [1].

B. Challenges in Ocular Drug Delivery: Ocular drug delivery faces several challenges due to the unique characteristics of the eye. The ocular barriers, such as the cornea and conjunctiva, limit drug absorption, while the rapid clearance mechanisms, including tears and blinking, quickly remove drugs from the ocular surface. Additionally, the limited permeability of the cornea and the presence of metabolic enzymes and efflux transporters in the eye further hinder effective drug delivery. The anatomical barriers, such as the blood-ocular barrier, restrict the entry of drugs into the posterior segment of the eye. These challenges not only affect the bioavailability and therapeutic efficacy of ocular drugs but also pose difficulties in patient compliance due to the need for frequent administration. Overcoming these challenges requires innovative strategies and technologies to enhance drug penetration, prolong drug residence time, and improve patient comfort. Addressing these challenges is crucial for the development of effective ocular drug delivery systems and the successful treatment of ocular diseases [2-3].

C. Introduction to Oleogel-Based Systems: Oleogels have emerged as a promising drug delivery system, offering advantages such as biocompatibility and the ability to encapsulate hydrophobic active pharmaceutical ingredients (APIs). They can serve as injectable drug depots, providing long-term drug release

without the need for surgical procedures. Researchers are exploring the potential of oleogels for targeted and sustained drug delivery in various pharmaceutical treatments. In the context of retinal diseases, which can cause severe vision loss, the delivery of drugs to the back of the eye poses a challenge. Current approaches, such as intravitreal injections, have limitations in terms of frequency, patient discomfort, and potential complications. Researchers are investigating alternative methods, including ocular inserts and implants, to improve drug delivery to the retina and reduce the need for frequent injections [4, 5]. The development of innovative drug delivery systems, such as oleogel-based formulations, holds promise for enhancing treatment outcomes and patient comfort in the management of retinal diseases.

D. Significance of Exploring the Potential of Oleogel-Based Systems in Ocular Drug Delivery:

Ocular drug delivery is a challenging task due to the unique anatomy and physiology of the eye. Traditional drug delivery systems such as eye drops and ointments have several limitations such as low bioavailability, short residence time, and poor patient compliance. In recent years, oleogel-based systems have emerged as a promising alternative for ocular drug delivery. Oleogels are semisolid systems that consist of a lipophilic phase and a gelling agent. They have several advantages such as improved drug solubility, enhanced drug stability, and prolonged drug release [6].

Several studies have investigated the potential of oleogel-based systems for ocular drug delivery. For example, one study demonstrated that oleogel-based systems can improve the bioavailability of cyclosporine, a commonly used drug for treating dry eye syndrome. Another study showed that oleogel-based systems can enhance the ocular penetration of dexamethasone, a steroid used for treating ocular inflammation. In conclusion, exploring the potential of oleogel-based systems in ocular drug delivery is of great significance and has the potential to revolutionize the field of ophthalmology [7].

Formulation Aspects of Oleogel-Based Systems:

Oleogel-based systems offer unique formulation aspects that make them attractive for drug delivery applications. The selection of gelators, such as low molecular mass organic gelators (LMOGs) or high-molecular-weight oleogelators (HMOGs), plays a crucial role in creating the gel network and stabilizing the formulation. The choice of oil phase is important to ensure compatibility with the gelator and desired drug solubility. Oleogel-based systems can accommodate both hydrophilic and hydrophobic drugs, with hydrophobic drugs being easily incorporated within the oil phase and hydrophilic drugs being encapsulated within the gel network or loaded onto the gelator molecules' surface. The rheological properties of oleogels, including viscosity, shear-thinning behavior, and gel strength, can be tailored by adjusting the gelator and oil phase concentrations, allowing for controlled drug release and ease of administration. Stability and shelf-life are critical considerations, and factors such as gelator concentration, temperature, and storage conditions must be taken into account to maintain the integrity and performance of the formulation [8].

Table 1: Meior steps in the process of development of oleogel

Process	Description
Gelator Selection	Choice of low molecular mass organic gelators (LMOGs) or high-molecular-weight oleogelators (HMOGs) to structure oils and create the gel network.
Oil Selection	Selection of compatible oil phase based on physicochemical properties and desired drug solubility. Options include mineral oils, vegetable oils, or synthetic oils.
Drug Incorporation	Accommodation of both hydrophilic and hydrophobic drugs. Hydrophobic drugs can be incorporated within the oil phase, while hydrophilic drugs can be encapsulated within the gel network or loaded onto the gelator molecules' surface.
Rheological Properties	Tailoring of rheological properties, such as viscosity, shear-thinning behavior, and gel strength, by adjusting gelator and oil phase concentrations. These properties impact ease of administration, stability, and controlled drug release.
Stability and Shelf-life	Consideration of factors like gelator concentration, temperature, and storage conditions to ensure formulation stability and shelf-life. Proper formulation design and packaging are crucial for maintaining integrity and performance.

A. Composition of Oleogels

Table. 2: Important compounds used to prepare oleogel and their role, description, and example

Component	Description	Example	Role
Gelator	Low molecular mass organic gelators (LMOGs) or high-molecular-weight oleogelators (HMOGs)	Ethyl cellulose Beeswax	Forms the gel network and provides structural integrity
Oil Phase	Mineral oils, vegetable oils, or synthetic oils	Mineral oil	Serves as the continuous phase and provides the desired properties to the formulation [8].
Active Ingredient	Hydrophobic or hydrophilic drugs	Ibuprofen (hydrophobic) Insulin (hydrophilic)	Provides the therapeutic effect
Co-solvent	Optional component to enhance drug solubility	Ethanol	Enhances drug solubility
Surfactant	Optional component to stabilize the system	Span 80	Stabilizes the formulation and prevents phase separation
Antioxidant	Optional component to enhance stability	Vitamin E	Protects the formulation from oxidation
Other Additives	Optional components for specific purposes	Menthol (cooling effect)	Provides additional properties or effects as desired [8].

In addition to synthetic organogelators, biomolecules like lecithin, derived from soybean and egg yolks, are extensively used as organogelators due to their high biocompatibility and amphiphilic nature. Lecithin-based oleogels have been studied for various applications, including ophthalmic formulations and transdermal drug delivery.

The choice of solvent in oleogel formulations is crucial. Commonly used solvents include alkanes, mineral oils, and vegetable oils. More recent pharmaceutical formulations utilize biocompatible solvents such as sunflower oil, soybean oil, isopropyl myristate, medium-chain triglycerides, and AOT. Polar solvents like water, ethanol, butanol, polyethylene glycol, propylene glycol, and hydroxyethyl-lactamide can also be used as co-solvents, expanding the range of drugs that can be entrapped within an oleogel. Overall, the combination of organogelators and suitable solvents allows for the formation of oleogels, providing a versatile platform for drug delivery applications.

B. Stabilization of Three-Dimensional Matrix: "In the context of ocular drug delivery, understanding the mechanism behind stabilizing the three-dimensional matrix within oleogel-based systems is of paramount importance. The three-dimensional matrix, often formed by gelling the oil phase, serves as the carrier for the drug, facilitating controlled release into the eye. To enhance the stability of this matrix, several mechanisms come into play.

Firstly, the choice of gelling agents is crucial. Hydrogels or organogels are commonly used to form this matrix. These gelling agents create a network that encapsulates the oil phase, preventing unwanted leakage or disintegration within the eye. Secondly, the optimization of the oleogel's rheological properties plays a significant role. A balanced viscosity and consistency ensure that the matrix retains its structural integrity even in the dynamic environment of the eye, where blinking and tear flow can challenge its stability.

Furthermore, understanding the intermolecular interactions within the oleogel is vital. Ensuring compatibility between the oil phase and gelling agent, and achieving a homogenous distribution of drug molecules, is crucial for sustained and controlled drug release. Lastly, the use of additives or stabilizers, such as antioxidants or preservatives, can further fortify the oleogel matrix against degradation and enhance its overall stability. the mechanism for stabilizing the three-dimensional matrix within oleogel-based systems for ocular drug delivery involves the selection of appropriate gelling agents, optimization of rheological properties,

attention to intermolecular interactions, and the incorporation of additives. These measures collectively enhance the matrix's structural integrity, ensuring the effective and safe delivery of drugs to the eye, ultimately advancing the field of ocular drug delivery [17]."

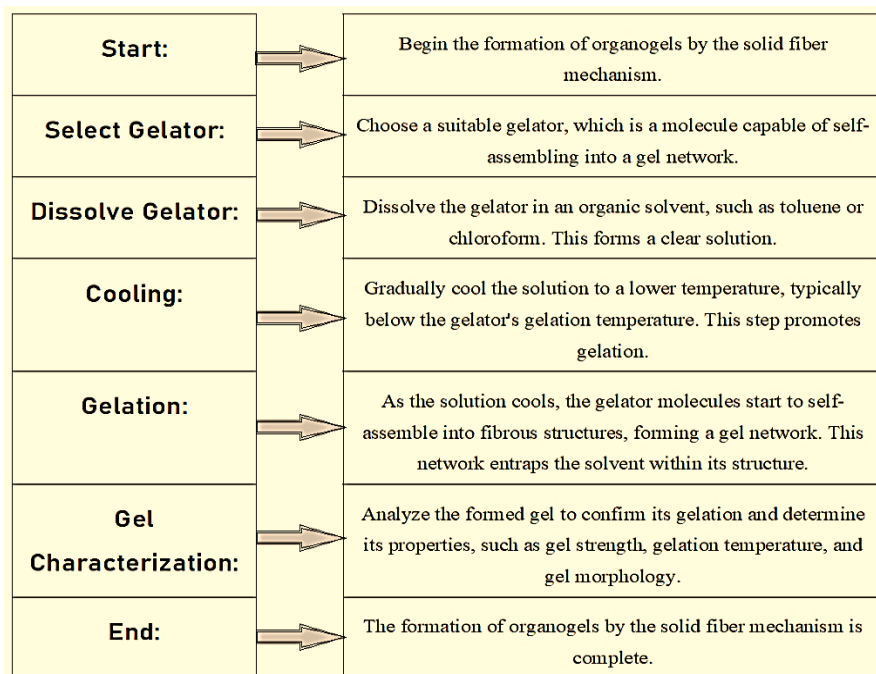


Figure 1. Method of formation of organogels by solid fiber mechanism

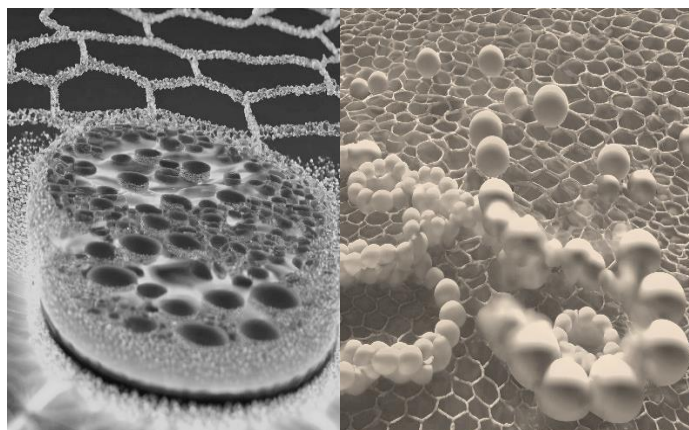


Figure 2. 3D Schematic representation of the interaction between two colloidal silica particles (top), the formation of chain structure

III. Advantages and Characteristics of Oleogel-Based Systems

- A. Cost-effectiveness
- B. Biocompatibility
- C. Extended shelf life
- D. Resistance to microbial contamination
- E. Thermoreversibility

IV. Applications of oleogel-based systems in ocular drug delivery

Table. 3: Applications of oleogel in different fields.

Application	Description
Ophthalmic Formulations	Oleogel-based systems have been studied for ophthalmic drug delivery, including the delivery of drugs to the anterior and posterior segments of the eye.
Transdermal Drug Delivery	Oleogel-based systems have been used for transdermal drug delivery, allowing for controlled release of drugs through the skin.
Injectable Drug Delivery	Oleogel-based formulations have been investigated for injectable drug delivery, including intravitreal injections for targeted drug delivery to the back of the eye.
Subcutaneous Injections	Oleogel-based formulations can be used for subcutaneous injections, enabling the delivery of medications to various body parts [9].

Table. 4: Various dosage forms using oleogel preparation we can make.

Dosage Form	Marketed Formulations
Eye Drops	Oleogel-based eye drops containing cyclosporine for the treatment of dry eye syndrome. Oleogel-based eye drops containing dexamethasone for the treatment of ocular inflammation.
Ocular Inserts	Oleogel-based ocular inserts for sustained release of glaucoma medications. Oleogel-based ocular inserts containing antibiotics for the treatment of eye infections.
Ophthalmic Ointments	Oleogel-based ophthalmic ointments for the treatment of dry eye syndrome. Oleogel-based ophthalmic ointments containing corticosteroids for ocular inflammation [8].

A. Other Applications of Oleogel:

Improving Drug Solubility: Oleogels are a type of semi-solid formulation that are made up of an oil phase and a gelling agent. They have the unique ability to improve the solubility of drugs, especially for hydrophobic drugs that have poor solubility in water-based solutions. This is because incorporating hydrophobic drugs within the oleogel matrix allows for improved drug dissolution and solubilization in the oily phase. Furthermore, the gel network in oleogels helps to stabilize drug molecules, preventing their aggregation and promoting their dispersion throughout the formulation. This leads to improved drug solubility, which in turn can enhance drug bioavailability and therapeutic efficacy. oleogels are a promising tool for enhancing the solubility of hydrophobic drugs, which can lead to more effective drug delivery and improved patient outcomes [8].

Prolonging Drug Release: The concept of oleogels as a drug delivery system is gaining popularity in the pharmaceutical industry due to its ability to provide prolonged drug release, which leads to sustained therapeutic effects. This is particularly useful for medications that require a consistent concentration in the bloodstream or affected area to maintain their efficacy. The gel network in the oleogel acts as a barrier that controls the diffusion of drugs from the oily phase, allowing for a controlled release of the drug over time. This gradual release of drugs from the oleogel matrix occurs due to the rheological properties of oleogels, such as their pseudoplastic behavior and gel strength. These properties influence the rate of drug diffusion, and therefore, the rate of drug release from the oleogel. By adjusting the formulation parameters of the oleogel such as the concentration of gelators and the oil phase, the drug release kinetics can be customized to meet specific therapeutic requirements. This means the release profile can be tailored to provide a desired therapeutic effect, such as a consistent concentration of drug in the bloodstream or affected area, over an extended period of time. oleogels have many advantages as a drug delivery system, including prolonged drug release, controlled release profiles, and the ability to tailor drug release kinetics to meet specific therapeutic requirements [8].

3. Enhancing Drug Permeation Across Ocular Barriers: The advantage of enhancing drug permeation across ocular barriers is that it allows for more effective treatment of various eye diseases and conditions. This includes conditions such as glaucoma, dry eye syndrome, and macular degeneration. When drugs can more easily penetrate the ocular barriers, they can reach the intended target within the eye more efficiently, resulting in better therapeutic outcomes for patients. This can also lead to a reduction in the amount

of medication needed, as well as potential side effects that may occur with higher doses [9]. Ultimately, improving drug permeation can lead to better quality of life for patients with eye conditions.

B. Potential of Oleogels for Targeted Delivery Delivering drugs to the posterior segment of the eye poses several challenges due to anatomical barriers and limited drug permeability. The nature of the corneal epithelium, the blood-aqueous barrier, and the blood-retinal barrier hinder effective drug delivery to the back of the eye. However, oleogels show great potential for targeted delivery in ocular drug delivery. Oleogels can accommodate both hydrophobic and hydrophilic drugs, making them versatile for a wide range of therapeutic agents. The shear-thinning properties of oleogels allow for easy application, either topically or through medical syringes. By designing oleogel-based formulations for delivery to the back of the eye, drugs can be injected into the vitreous, where the high viscosity of the gel helps retain its shape while gradually releasing the drug. The sustained release profiles of oleogels make them promising for controlled release of ophthalmic formulations, addressing the need for long-term drug delivery in the eye. Studies have shown the potential of oleogels in delivering hydrophobic drugs, such as dexamethasone, over extended periods of time, comparable to commercialized implants. Furthermore, oleogels offer the advantage of biocompatibility, as the components used in their formulation have been previously used in biomedical applications [10]. Overall, oleogels hold promise as a novel drug delivery system for targeted and sustained delivery of both hydrophobic and hydrophilic drugs to the posterior segment of the eye, overcoming the challenges associated with ocular drug delivery.

VII. Recent Advancements and Future Prospects

A. Incorporation of Nanotechnology in Oleogel-Based Systems: Recent advancements in the field of nanotechnology have opened up new possibilities for enhancing the performance of oleogel-based drug delivery systems [11]. Nanoparticles, such as superparamagnetic iron oxide nanoparticles (SPIONs), can be incorporated into oleogels to impart additional functionalities. For example, SPION-loaded oleogels have been used to formulate in situ implants for the minimally invasive treatment of cancer lesions. These implants can be guided and monitored using magnetic fields, allowing for targeted drug delivery and real-time imaging. The incorporation of nanotechnology into oleogel-based systems offers opportunities for improved drug loading, controlled release, and targeted delivery to specific sites.

B Stimuli-Responsive Oleogels: Stimuli-responsive oleogels are a rapidly developing area of research in drug delivery. These systems are designed to respond to specific triggers, such as changes in temperature, pH, or enzyme activity, to achieve controlled drug release. For example, pH-sensitive oleogels can release drugs in response to the acidic environment of diseased tissues, while temperature-sensitive oleogels can release drugs when exposed to elevated temperatures associated with inflammation or infection. Stimuli-responsive oleogels offer the potential for on-demand drug release, improved therapeutic efficacy, and reduced side effects [12].

C. Potential for Targeted and Controlled Drug Delivery: Oleogels have shown great potential for targeted and controlled drug delivery. Their high viscosity allows for localized drug delivery, minimizing systemic exposure and reducing side effects. The sustained release profiles of oleogels enable long-term drug delivery, eliminating the need for frequent dosing. Additionally, the versatility of oleogels in accommodating both hydrophobic and hydrophilic drugs expand their applicability to a wide range of therapeutic agents. By designing oleogel-based formulations for specific routes of administration, such as intravitreal or transnasal delivery, targeted drug delivery to the desired site can be achieved [13, 14].

D. Opportunities for Further Innovation and Improvement: While oleogels have shown promise in drug delivery, there are still opportunities for further innovation and improvement. Research efforts can focus on optimizing the formulation of oleogels to enhance drug loading capacity, stability, and release kinetics. The development of novel gelators and the incorporation of functional additives, such as nanoparticles or bioactive molecules, can further enhance the performance of oleogel-based systems. Additionally, exploring new routes of administration and investigating the potential of combination therapies can expand the applications of oleogels in various disease treatments. Continued research and collaboration between scientists, engineers, and clinicians will drive further innovation in oleogel-based drug delivery systems [15].

Combination Therapies: Oleogel-based drug delivery systems provide opportunities for combination therapies, where multiple drugs or therapeutic agents can be incorporated into a single formulation. This

approach allows for synergistic effects and improved therapeutic outcomes. For example, combining an antimicrobial agent with an anti-inflammatory drug in an oleogel can provide a comprehensive treatment for infections [16].

f. Targeted Delivery to Specific Sites: Oleogels can be designed to target specific sites in the body, such as the eye, skin, or gastrointestinal tract. By tailoring the formulation and administration route, drugs can be delivered directly to the desired site, minimizing systemic exposure and improving treatment efficacy.

g. Biocompatibility and Safety: Oleogels are generally considered biocompatible and safe for use in drug delivery applications. The components used in oleogel formulations, such as oils and gelators, have been extensively studied and approved for biomedical use. This enhances the potential for clinical translation and commercialization of oleogel-based drug delivery systems. Further advancements and research in oleogel-based drug delivery systems are expected. This includes exploring new gelators and additives to improve the performance and stability of oleogels, optimizing drug loading and release profiles, and investigating novel routes of administration. Additionally, the integration of advanced technologies, such as 3D printing and microfluidics, may enable the fabrication of customized oleogel-based drug delivery systems with precise control over drug release kinetics and spatial distribution [17].

VIII. Conclusion

A. Summary of the Advancements in Ocular Drug Delivery Using Oleogel-Based Systems:

Oleogel-based systems have emerged as a promising platform for ocular drug delivery. These systems offer targeted and sustained drug release to the back of the eye, overcoming the limitations of traditional delivery methods. The incorporation of hydrophobic and hydrophilic drugs in oleogels, along with their high viscosity and stability, makes them suitable for long-term drug delivery. Advancements in nanotechnology have further enhanced the performance of oleogel-based systems by enabling improved drug loading, controlled release, and targeted delivery to specific sites.

B. Potential Impact on Ocular Disease Treatment:

The advancements in oleogel-based systems have the potential to revolutionize the treatment of ocular diseases. By providing targeted and sustained drug delivery to the back of the eye, oleogels can improve treatment efficacy and patient comfort. They can be used for various ocular conditions, including retinal diseases, glaucoma, and ocular infections. The ability to deliver a combination of drugs in a single formulation opens up possibilities for synergistic effects and improved therapeutic outcomes. Oleogel-based systems also offer the advantage of biocompatibility and safety, making them suitable for clinical translation and commercialization.

C. Importance of Continued Research and Development in this Field:

Continued research and development in oleogel-based drug delivery systems for ocular applications are crucial. Further optimization of formulation parameters, such as gelator selection, drug loading, and release kinetics, can enhance the performance and stability of oleogels. Exploring new routes of administration, investigating the potential of combination therapies, and addressing regulatory considerations will contribute to the successful translation of oleogel-based systems into clinical practice. Collaboration between researchers, clinicians, and industry stakeholders is essential to drive innovation and bring these advancements to patients in need. Continued research and development will pave the way for improved therapeutic outcomes, better management of ocular diseases, and ultimately, improved quality of life for patients.

Reference:

- [1] Gaudana, R., Ananthula, H. K., Parenky, A., Mitra, A. K. (2010). Ocular drug delivery. *AAPS Journal*, 12(3), 348-360.
- [2] Gaudana R, Jwala J, Boddu SHS. Ocular drug delivery: current challenges and strategies. *Journal of Pharmacy & Pharmaceutical Sciences*. 2010;13(3): 411-448.
- [3] Sahoo SK, Dilnawaz F, Krishnakumar S. Nanotechnology in ocular drug delivery. *Drug Discovery Today*. 2008; 13(3-4):144-151.

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- [4] Ahuja M, Dhake AS, Sharma SK, Majumdar DK. Topical ocular delivery of NSAIDs. *AAPS Journal*. 2008; 10(2):229-241.
- [5] Sánchez-López E, Esteruelas G, Ortiz A, et al. Nanoparticulate systems for drug delivery: a review. *Nanomaterials*. 2020;10(5): 1-37.
- [6] Mitra AK, Anand BS. Ocular pharmacokinetics. In: Mitra AK, Anand BS, eds. *Ophthalmic Drug Delivery Systems*. Marcel Dekker, Inc.; 2003: 45-73.
- [7] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7752843/> II. Formulation aspects of oleogel-based systems.
- [8] Patel, A., & Patel, M. (2021). Oleogels: A promising platform for drug delivery. *Journal of Drug Delivery Science and Technology*, 66, 102800.
- [9] Tian J, Liu J, Liu X, Xiao Y, Tang L., “ Intravitreal infusion: A novel approach for intraocular drug delivery.” *Scientific Reports*.(2016) 6: 37676. doi: 10.1038/srep37676. 37
- [10] Falavaijani K., “ Implantable Posterior Segment Drug Delivery Devices; Novel Alternatives to Currently Available Treatments.” *Journal of Ophthalmic & Vision Research*. (2009) 4, 3: 191–193.
- [11] Sullivan C, Barbut S, Marangoni A . “Edible oleogels for the oral delivery of lipid soluble molecules: Composition and structural design considerations.” *Trends in Food Science & Technology* (2016) 57:59–73.
- [12] Mishra M. “Handbook of encapsulation and controlled release.” Boca Raton: CRC Press/Taylor & Francis Group, 2016. 1035–1060.45
- [13] M. Mishra, *Handbook of Encapsulation and Controlled Release*, CRC Press/ Taylor & Francis Group, Boca Raton, 2016, pp. 1035–1060. Print.
- [14] K. Rehman, M. Zulfakar, Recent advances in gel technologies for topical and transdermal drug delivery, *Drug Dev. Ind. Pharm.* 40 (4) (2014) 433–440.
- [15] R. Swati, K. Ankaj, P. Vinay, Organogels: novel delivery systems, *World J.Pharm. Pharm. Sci.* 4 (1) (2014) 455–471
- [16] Lau P, Jenkins K, Layton C, “Current Evidence for the Prevention of Endophthalmitis in Anti-VEGF Intravitreal Injections.” *Journal of Ophthalmology*. (2018) 18,8567912. doi:10.1155/2018/8567912.
- [17] Raj Kapoor Balasubramanian, Abdussalam A Sughir, Goupale “Oleogel: A promising base for transdermal formulations” *Asian Journal of Pharmaceutics* - January-March 2012 page 1-9.