Ophthalmic Liquid Crystal In-Situ Gel Formulation and Evaluation –Insight from a Systematic Literature Review

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***Abstract*—The formulation and evaluation of ophthalmic liquid crystal in situ-gels have gained significant interest in recent years for their potential as advanced drug delivery systems in ophthalmology. This review article aims to provide an overview of the formulation strategies and evaluation methods used for ophthalmic liquid crystal in situ-gels, highlighting their advantages, challenges, and potential applications in ocular drug delivery. The in situ-gel undergoes a sol-gel transition upon contact with the ocular surface, providing sustained release and improved bioavailability. The evaluation includes the assessment of its physical characteristics, in vitro release profile, bioadhesive properties, stability, compatibility, and ocular irritation potential. Liquid crystal is a key component used in the development of ophthalmic in situ gels. Liquid crystals exhibit properties of both liquids and solids, making them ideal for drug delivery in this formulation. They have a unique ability to self-assemble into ordered structures, which can help in prolonging drug release.**

***Index Terms*- Ophthalmic, In-Situ Gel, Liquid Crystals, Ocular Drug Delivery**

I. INTRODUCTION

Ocular drug delivery poses several challenges due to the complex anatomical barriers and limited drug permeability of the eye. Liquid crystal in situ-gels offer a promising solution by providing sustained release and improved bioavailability of drugs through their unique sol-gel transition behavior. Pharmaceutical experts find ophthalmic drug delivery to be the most intriguing and difficult technique for drug delivery. Avoiding long-term tissue damage while evading the eye's protective shields is the investigator's biggest problem. Some of the most common traditional ophthalmic dose forms include eye drops, ointment, cream, suspension, and emulsion. Topical dosage forms are obviously superior for the therapeutic treatment of most ophthalmic disorders or diseases because only a small percentage of a systemic dose reaches the eye. Fast precorneal elimination of solution, lack of sustained action, drug loss through drainage, impaired vision, and adhering of eyelids in ointments are some of the downsides of systemic administration of medications. Furthermore, there is a lack of patient compliance. Therefore, it is possible to attain the optimal medication concentration through topical administration.

A number of eye conditions, including dryness, conjunctivitis, the flu, and others, can be effectively treated by applying medications topically to the eye. It is often preferable to apply the medication topically rather than intravenously for treating eye diseases. Any drug molecule supplied via the ocular route must first pass through the precorneal barriers before it can reach the cornea, anatomically speaking. In order to prevent drugs from penetrating the eye, the conjunctiva and tear film serve as the initial barriers. The eye's defense systems, which include blinking, baseline and reflex lacrimation, drainage, and the quick removal of dust, bacteria, and medicines from the eye's surface, reduce the drug's bioavailability. Seventy percent of the eye dose formulations on the market are ophthalmic medicines, the most popular of which being drops and ointments. When these medications are injected into the eye, they are quickly flushed out of the eye by the natural processes of blinking and lachrymal nasal drainage. Using a standard eye dropper, which typically delivers 50-75 micro liters of ophthalmic solution each drop, a portion of these drops quickly drains out of the eye until the resident volume is 7 micro liters, which is the normal amount. This

medication loss in the anterior segment reduces the amount of medicine that can reach the cornea and inner ocular tissues. Instilled solutions typically have a corneal contact period of less than one to two minutes and a drug permeability that is much lower than 10% in humans. As a result, very little medication enters the intraocular tissue through the cornea. Because of these restrictions, newer pharmaceutical ophthalmic formulations have been created during the past 30 years to boost the drug's bioavailability in a regulated and sustained manner. Ocular inserts, nanosuspension, microemulsion, in-situ gel, liposome, nanoparticle, and intophoresis are all examples of such formulations. For ophthalmic drug delivery to be perfect, the drug must be able to stay in the eye's frontal region for an extended length of time and release its contents gradually. Therefore, it is important to find ways to improve ocular medication delivery. One approach is to use viscous gel to extend the precorneal drug retention, another is to use erodible or non-erodible inserts, and a third is to create colloidal suspensions. Bioadhesive systems can be made from polymeric solutions or micro particle suspensions.

Problems like lachrymal protein binding arise from the poor bioavailability of ocular injections. Chaymation and tear turnover are caused by a lack of surface area for the cornea, slow metabolism, ineffective absorption or adsorption, and the outflow of the injected fluids. A number of methods have been developed to lengthen the time that a medicine is active in the body, which is known as bioavailability. In general, two distinct methods are distinguished. The first one relies on sustained drug delivery devices to offer controlled and continuous ocular medication delivery. The second one is to reduce medication loss before reaching the cornea while increasing drug absorption into the cornea. The ideal method for delivering medications to the eyes would be one that stays near the eye for a long period and keeps the drug release steady. With the advent of innovative ophthalmic dosage forms like as medicated lenses, in situ gelling systems, erodible and non-erodible ophthalmic inserts, and more, it is more crucial than ever to discover methods to enhance ocular medication delivery.

Liquid crystals play a crucial role in ophthalmic drug delivery systems, particularly in the formulation of in situ gels. These drug delivery systems are designed to provide prolonged drug release and increased contact time with the ocular surface.

One common approach is the use of liquid crystal-based in situ gels as a carrier for ophthalmic drugs. Liquid crystals are used to form a network structure within the gel, providing controlled drug release and improved ocular retention.

The liquid crystal network can entrap the drug molecules, allowing for sustained release over an extended period of time. The unique properties of liquid crystals, including their partially ordered molecular structure and ability to self-assemble, enable the gel to maintain the drug in a reservoir-like state. This reservoir effect ensures a continuous and controlled release of the drug, leading to improved therapeutic efficacy.

Moreover, the gel formed by liquid crystals enhances the viscosity and rheological properties of the drug delivery system. The increased viscosity helps in prolonging the residence time of the drug on the ocular surface, improving drug absorption and minimizing the need for frequent administration.

Liquid crystal-based in situ gels can be administered as eye drops, which easily transform into a gel-like consistency upon contact with the ocular surface or tears. This transformation is facilitated by factors such as temperature, pH, or ionic strength. Once in the gel state, the liquid crystal network ensures sustained drug release, making them advantageous for ophthalmic drug delivery.

Overall, liquid crystals serve as a critical component in ophthalmic drug delivery systems by providing controlled drug release, improved ocular retention, and enhanced viscosity. These properties allow for efficient drug delivery to the eye, increasing the effectiveness of therapy and patient compliance.

In situ gels are a type of ocular drug delivery system that can offer several advantages over conventional eye drops. Here are some benefits:

1. Prolonged retention time: In situ gels can remain in the eye for a longer period, allowing for sustained release of the medication and increasing its bioavailability.
2. Improved ocular penetration: The gel-like consistency can help the medication penetrate deeper into the eye, reaching the target tissues more effectively.
3. Enhanced patient compliance: In situ gels can reduce the frequency of administration, making it

easier for patients to adhere to their treatment regimens.
4. Reduced systemic absorption: By releasing the medication slowly and locally, in situ gels can minimize systemic absorption and related side effects.
5. Customizable release profiles: In situ gels can be designed to release medication at specific rates, allowing for tailored treatment approaches.
Overall, in situ gels can provide more effective and efficient ocular drug delivery compared to conventional eye drops, which can be beneficial for treating various eye conditions.

Applications:
1. Glaucoma treatment: In situ gels can be used to deliver medication that reduces intraocular pressure, helping to manage glaucoma.
2. Dry eye syndrome: In situ gels can provide sustained lubrication and relief for dry eye patients.
3. Infective keratitis: In situ gels can deliver antibiotics directly to the site of infection, improving treatment outcomes.
4. Uveitis: In situ gels can deliver corticosteroids or other medications to reduce inflammation in the eye.
5. Post-operative care: In situ gels can be used to deliver pain relief medication or anti-inflammatory drugs after eye surgery.
Benefits:
1. Increased bioavailability: In situ gels can improve the amount of medication absorbed by the eye.
2. Reduced dosing frequency: In situ gels can release medication slowly, reducing the need for frequent administration.
3. Improved patient comfort: In situ gels can reduce eye irritation and discomfort associated with conventional eye drops.
4. Enhanced therapeutic outcomes: In situ gels can provide more effective treatment due to sustained release and targeted delivery.

Formulation Strategies:
Various components and techniques are utilized to formulate ophthalmic liquid crystal in situ-gels. Lipids, polymers, and surfactants are commonly employed to create liquid crystalline structures that undergo gelation upon contact with the ocular surface. The incorporation of drug molecules into these formulations is achieved through solubilization, entrapment, or dispersion.

Evaluation Methods:
The evaluation of ophthalmic liquid crystal in situ-gels involves several crucial aspects to assess their suitability as drug delivery systems. These evaluations include physical characteristics, drug release kinetics, mucoadhesive properties, stability, compatibility, and ocular irritation potential.
1. Physical Characteristics:
The appearance, pH, viscosity, and clarity of the liquid crystal in situ-gels are evaluated to ensure their uniformity and suitability for ocular application. The physical stability of the formulation under different conditions is assessed to determine its shelf life.
2. In Vitro Release Profile:
A modified Franz diffusion cell is used to study the release profile of the drug from the liquid crystal in situ-gel formulation. The release kinetics and duration are evaluated.
3. Drug Release Kinetics:
In vitro release studies using diffusion cells provide valuable insights into the drug release profile from the liquid crystal in situ-gel. These studies help understand the sustained release behavior and optimize the formulation for desired therapeutic outcomes.
4. Mucoadhesive Properties:
The mucoadhesive properties of the liquid crystal in situ-gel are evaluated to ensure its residence on the ocular surface for an extended duration. Techniques such as texture analysis and ex vivo models are utilized to measure the adhesive strength and duration.
5. Stability:
The stability of the formulation is evaluated under different storage conditions, such as temperature and light exposure. Changes in appearance, pH, viscosity, and drug content are monitored over a specified period.
6. Compatibility:
Compatibility studies are conducted to assess any interactions between the liquid crystal in situ-gel formulation and common ophthalmic excipients. The stability and integrity of the formulation are evaluated after combining with excipients.
Ocular Irritation Potential:

The ocular irritation potential of the liquid crystal in situ-gel is evaluated through in vitro or ex vivo models to assess its safety and compatibility with ocular tissues. These studies aid in identifying any potential inflammation or irritation that could arise from the formulation.

CONCLUSION

Ophthalmic liquid crystal in situ-gels offer a promising platform for enhancing ocular drug delivery. The formulation and evaluation of these systems play a pivotal role in optimizing their performance and therapeutic efficacy. This review article provides an overview of the formulation strategies and evaluation methods used, highlighting the importance of considering physical characteristics, drug release kinetics, mucoadhesive properties, stability, compatibility, and ocular irritation potential during development.

By evaluating the ophthalmic liquid crystal in situ-gel formulation, this study will contribute towards determining its suitability as a drug delivery system for ophthalmic applications. The results obtained will aid in the development of an advanced ophthalmic formulation with improved therapeutic outcomes.

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