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Review Article

Ocular in Situ Gel: Development, Evaluation, and Advancement

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ABSTRACT

In situ gel refers to a gel that forms when a solution is placed in the eye. The solution undergoes a transformation, typically from a liquid to a gel, in response to environmental conditions (like temperature, pH, or ionic strength). This helps the drug stay in place longer, improving its effectiveness by allowing for sustained release. Antibacterial ophthalmic. This means the formulation is designed for the eye and contains antibacterial agents that target eye infections. These agents are usually intended to treat or prevent bacterial infections like conjunctivitis or corneal ulcers. Such formulations are typically designed to offer controlled drug release, which can improve patient compliance and reduce side effects compared to traditional eye drops. The gel helps the drug remain in contact with the ocular surface for an extended period, while the antibacterial properties target pathogens that may cause infections.

INTRODUCTION

In ophthalmic care, bacterial infections of the eye, such as conjunctivitis or keratitis, require effective and targeted treatment. Traditional eye drops and ointments often fail to provide sustained drug release, resulting in suboptimal therapeutic outcomes. **Improved Drug Retention** is an instillation into the eye, the gel undergoes a phase transition, increasing its viscosity and allowing for prolonged contact time on the ocular surface. This leads to better drug retention and enhanced bioavailability compared to liquid formulations. **Sustained Release** is the in situ gels can be

designed to release the antimicrobial agents slowly over time, ensuring a steady concentration of the drug at the infection site, reducing the frequency of administration and improving patient compliance. Targeted Delivery is the gel formulation can be tailored to deliver antibacterial agents directly to the site of infection, minimizing systemic side effects and improving the effectiveness of the treatment. Minimized Irritation in which Unlike conventional eye drops that may cause irritation due to their frequent application or preservatives, in situ gels are often formulated to be gentle on the delicate ocular

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tissues, reducing irritation and enhancing patient comfort.

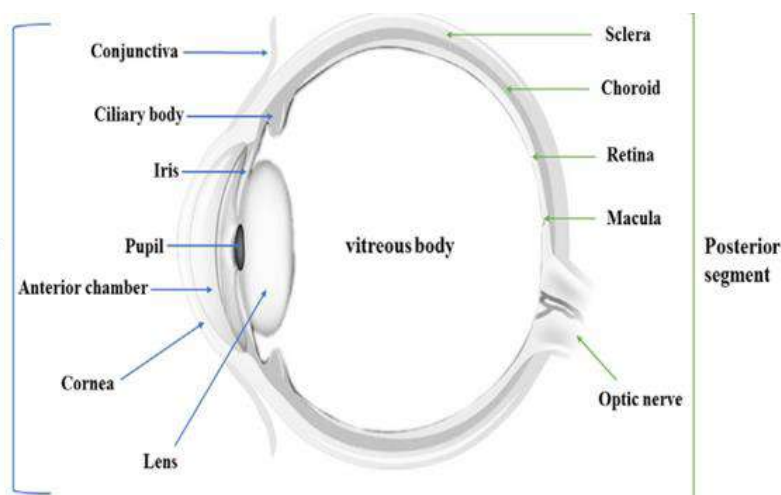


Fig No.1 : Anatomy of the eye(3)

ADVANTAGS OF IN SITU GEL(4)(5)

1. To provide sustained and controlled drug delivery.
2. To increase the ocular bioavailability of drug by increasing the corneal contact time.
3. Drug effect is prolonged hence frequent instillation of drug is not required.
4. For patient compliance and enhance therapeutic performance of drug.

DISADVANTAGES OF IN SITU GEL

1. May not reach deeper eye tissues effectively.
2. Can cause eye discomfort or allergic reactions.
3. Environmental factors can affect gel formation.
4. May require frequent application.
5. Can cause blurring or discomfort if too thick or thin.
6. Difficult to produce stable formulations.

IDEAL CHARACTERISTICS OF IN SITU GEL(4)(6)

1. It should not irritate or harm the sensitive eye tissues.
2. The gel should stay on the eye longer for better drug absorption.

3. It should release the antibacterial medicine slowly over time, reducing the need for frequent use.
4. The gel should help the medicine get absorbed well into the eye.
5. It should change into a gel when applied to the eye, helping it stay in place.

DISEASE OF EYE(1)

Eye diseases can affect different parts of the eye and can cause a range of symptoms, from redness and irritation to pain and vision problems. Conjunctivitis is inflammation of the thin layer of tissue covering the white part of the eye. It's usually caused by a bacterial or viral infection and causes redness, itching, and discharge. It's highly contagious. The inflammation of the eyelids, often due to bacterial infections, causing redness, swelling, and crusting around the eyelashes. It can lead to irritation and discomfort. This is an infection of the cornea, the clear front part of the eye. Bacterial keratitis can cause severe pain, blurred vision, sensitivity to light, and eye redness. It's often seen in people who wear contact lenses. Such infection occurs due to when you live in polluted air, moving in polluted air during road work cement particles and dust particles get into the eye and causes an antibacterial infection.

Fungal eye infection are extremely rare but they causes blindness the most common way to develop a fungal eye infection is as a result of eye injury. Particularly if the injury was caused by plant material such as stick or thorn.

CLASSIFICATION OF OPHTHALMIC IN SITU GEL(7)(5)

They are classified according to the natural polymer and synthetic polymers soluble, Insoluble are classified as follows:

NATURAL POLYMER

Natural polymers are derived from natural sources such as plants, animals, or microorganisms. They are often preferred in ophthalmic drug delivery systems like in situ gels due to their biocompatibility, biodegradability, and low toxicity. They can also be chemically modified to optimize the release profiles of drugs. They polymers are often chosen for their ability to form gels under specific conditions (e.g., pH, temperature, or ionic strength), enabling controlled drug release, enhanced ocular retention, and improved patient compliance. Their mucoadhesive properties further contribute to prolonged contact time with the ocular surface, thereby increasing drug bioavailability.

Synthetic polymers

Synthetic polymers are artificially synthesized macromolecules that are engineered through polymerization processes to achieve specific structural, chemical, and physical properties. These polymers offer a high degree of control over their molecular weight, architecture, and functionality, making them highly versatile in various applications, including drug delivery systems. In ophthalmic formulations, synthetic polymers are utilized to create in situ gel systems that provide controlled or sustained release of therapeutic agents, thereby improving drug bioavailability and enhancing patient compliance.

METHODS OF IN SITU GEL(6)(5)

1. Thermally Triggered System

Temperature-sensitive hydrogels are probably the most commonly studied class of environment-sensitive polymer systems in drug delivery research. The use of biomaterial whose transitions from 'sol to gel' is triggered by increase in temperature is an attractive way to approach in-situ formation. The ideal critical temperature range for such system is ambient and physiologic temperature and no external source other than that of body heat is required to trigger gelation. A useful system should be endurable to account for small differences in local temperature, such as it might be encountered in appendages in the oral cavity

2. pH Triggered Systems :

The second approach of in situ gel formation is based on Change in pH. Certain polymers such as PAA (Carbopol®, carbomer) or its derivatives, polyvinylacetal diethylaminoacetate (AEA), Mixtures of poly (methacrylic acid) (PMA) and poly (ethylene glycol) (PEG) shows change from sol to gel with change of pH. Swelling of hydrogel increases as the external pH increases in the case of weakly acidic (anionic) groups, but decreases if polymer contains weakly basic (cationic) groups.

3. Temperature Triggered system

Temperature is the most widely used stimulus in environmentally responsive polymer systems. The change of temperature is not only relatively easy to control, but also easily applicable both in vitro and in vivo. In this system, gelling of the solution is triggered by change in temperature, thus sustaining the drug release. These hydrogels are liquid at room temperature (20–25 °C) and undergo gelation when in contact with body fluids (35– 37 °C), due to an increase in temperature. The use of biomaterial whose transitions from sol-gel is triggered by increase in temperature is an

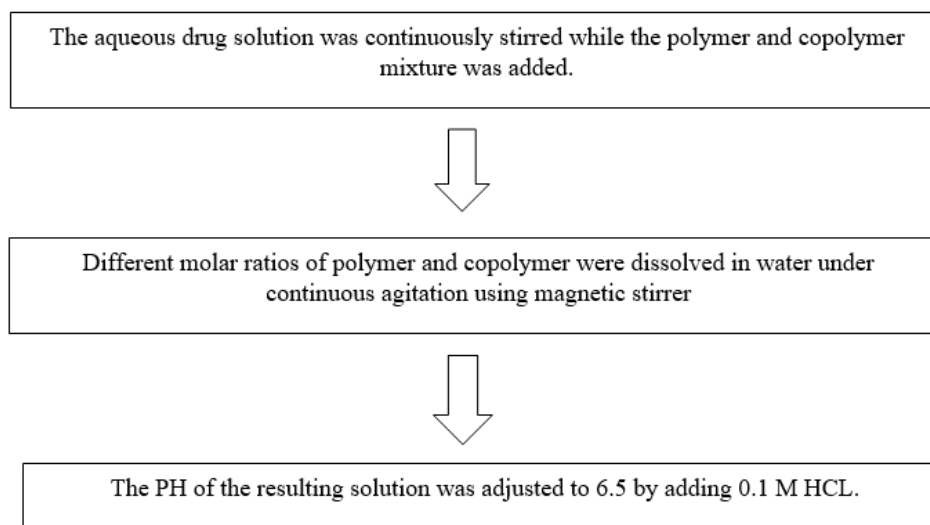


attractive way to approach in situ formation. The polymers which show temperature induced gelation are Poloxamer or pluronics, cellulose derivatives (methyl cellulose, HPMC, ethyl (hydroxyl ethyl) cellulose (EHEC) and xyloglucan etc.

Sr No.	Exipients	Activity
1	API	Antibiotics
2	Sodium Alginate	Polymer
3	HPMC	polymer
4	Water	solvent

Table No.1: Excipient of in situ gel(8)

Preparation– of In Situ gel:(8)



Evaluation test of IN SITU Gel:(9)(10)

1. Clarity

Clarity test was observed by visual inspection under a good light, viewed against a black and white background, with the contents set in motion with a swirling action. Also it was observed for formation of turbidity or any unwanted particles dispersed in the solution.

2. Gelling capacity

The gelling capacity of the prepared formulation was determined by placing a drop of the formulation in a beaker containing 50 ml of freshly prepared concentrated calcium chloride solution and was visually observed for gelling time.

3. Rheological studies

The primitive ophthalmic solution, suspension, and ointment dosage forms are clearly no longer

sufficient to combat these diseases, and current research and development efforts to design better therapeutic systems are the primary focus of this research work. The aim of the present investigation is to formulate an in situ gel and from our prior knowledge we know that gels show thixotropic behaviour, so rheological studies are to be performed.

4. Measurement of pH

Each formulated batch, pH was measured using pH metre which was previously calibrated using standard buffers of pH 4 and pH 7 as per the established procedure.

5. Drug content

1 ml of the developed formulation was dissolved in 100 ml phosphate buffer (pH 7.4) followed by spectrophotometric estimation of the aliquot to determine drug concentration.



6. In vitro dissolution studies

Dissolution studies of samples were performed using Franz diffusion apparatus and phosphate buffer (pH 7.4) as a dissolution medium. Phosphate buffer with pH 7.4 will simulate the lacrimal fluid. The temperature was maintained at 37.0 °C with the speed of rotation maintained at 100 rpm. The samples were withdrawn at various time intervals and analysed spectrophotometrically for the drug content

CONCLUSION :

In situ gel was successfully formulated as in situ gel forming eye drops using sodium alginate and HPMC. The mixture can be used as an in situ gelling vehicle to enhance ocular bioavailability and patient compliance. Physicochemical characterization and in vitro drug release studies indicated that the developed formulation (IG 3) may prove to be a viable alternative to conventional eye drops and ointment in terms of ease of administration with added benefits of sustained drug release which may ultimately result into improved.

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