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Review Article

A review on ophthalmic in - Situ gel

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ABSTRACT

The field of ocular drug delivery is one of the most interesting and challenging fields for Formulation Scientists or Pharmacists. In ophthalmic in situ gel many polymers are used which form gel by various mechanisms like pH-sensitive gel and thermo sensitive gel. We can make in situ ocular gel instead of an ophthalmic solution to overcome the problem of low bioavailability. Some common diseases which are cured by in situ ocular gel delivery are blepharitis, conjunctivitis, keratitis, trachoma, glaucoma, etc. The major disadvantages of old formulations such as solutions, suspensions, emulsions, ointments, etc. are poor bioavailability, increased pre-corneal elimination, and high variability in efficacy respectively.

1. Introduction

Generally in situ ocular gel is a hydrogel that is made of different types of polymers like Hydroxypropyl Methylcellulose, Gellan gum, Carbomer, and poloxamer. In-situ ocular gel is a solution before application but after administration, it is converted into a gel by a different mechanism.[1–3]

1.1. Advantages of in situ ocular gel

1. Improved Local Bioavailability.
2. Reduced dose frequency.
3. Patient-friendly.
4. Prolonged drug release.[4]
5. Due to gelation precorneal residence time is increased and nasolacrimal drainage is decreased.

1.2. Type of In-situ gelling system used in the ocular system

1. Temperature-induced in situ gel system.
2. pH-induced in situ gel system.
3. Ion induced In situ gel systems.[5,6]

1.3. Temperature-induced in situ gel system

The temperature-induced in situ gel system is a hydrogel that is converted into the gel from sol when temperature increases. The polymer involved in that type of gel is temperature sensitive. The body temperature is sufficient to trigger sol to gel conversion external temperature is required to trigger sol to gel conversion.[7]

2. Example of Polymer- Poloxamer (Kolliphor P 407).

2.1. pH-induced in situ gel system

A pH-induced in situ gel system is a hydrogel that is converted into the gel from sol when pH changes. The polymer involved in that type of gel is pH sensitive. The eye pH is sufficient to trigger sol to gel conversion.[8]

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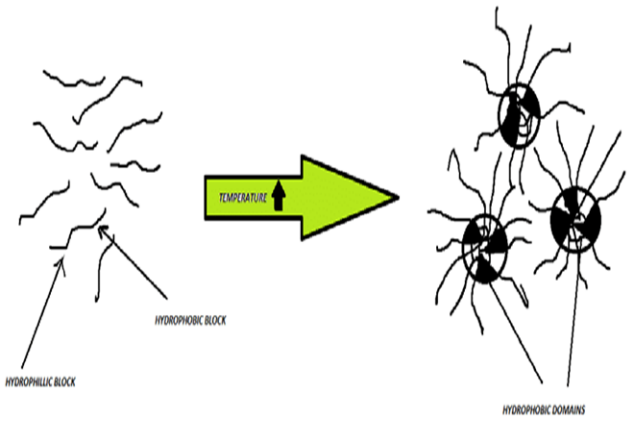

Fig. 1: Mechanism of Temperature triggered in-situ gel.

3. Example of Polymer- Carbomer

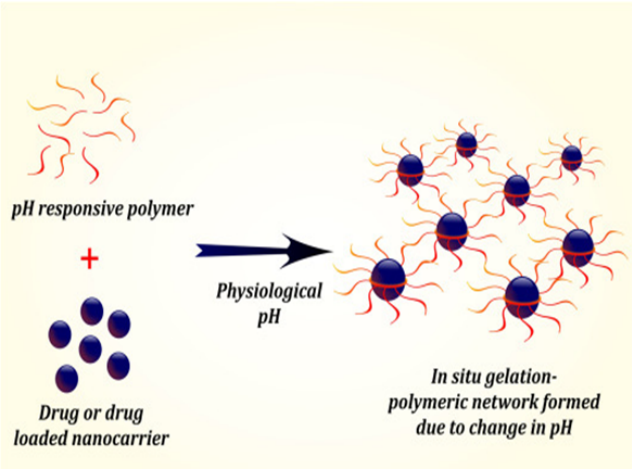

Fig. 2: Mechanism of pH-triggered in-situ gel.

3.1. Ion induced In situ gel systems

Some polymers also convert from sol to gel in presence of various ions. Some polysaccharides come under ion-sensitive polymers. It is assumed that the rate of gelation is depending on the osmotic gradient across the gel surface. The osmolality of the eye solution may influence the sol to gel transition in the eye. In tear fluid generally, mono or divalent cations are present which form a clear gel of aqueous polymer solution. Gellan gum is an anionic polysaccharide that undergoes gelling in presence of mono and a divalent cation. The Na, Ca, and Mg ions that are present in the tear fluid generally initiate the sol to gel transition. In presence of divalent cation (Ca) alginic acid undergoes gelation.[9]

4. Example of Polymer- Gellan gum

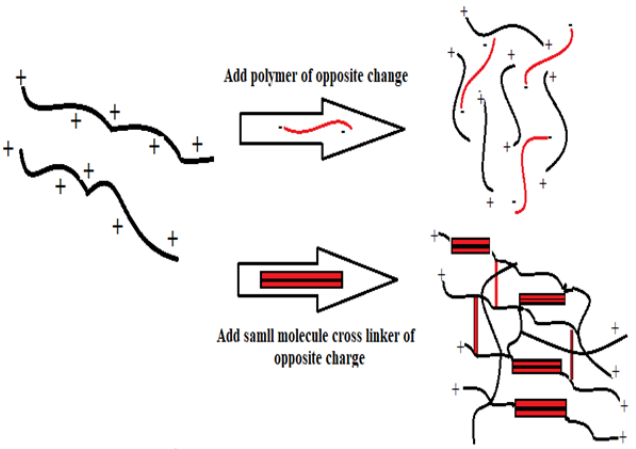

Fig. 3: Mechanism of Ion activatedin-situ gel system.

4.1. Evaluation parameters

1. Appearance and Clarity
2. Sol-gel transition temperature/pH and gelling time
3. In-Vitro Drug Release.
4. Ocular irritancy test
5. Gelling capacity
6. Viscosity testing
7. Sterility testing
8. Drug Content determination

5. Appearance and Clarity

Appearance and Clarity of formulation are visually checked with help of black and white background.

Example- White colored transparent solution and free from a visible particle.[10,11]

5.1. Sol-gel transition temperature and gelling time

This test is used for only thermosensitive gel. 4.6 ml of a formulation is transferred into the Test tube and heated test tube at a specific rate of temperature increase. The conversion in a gel is checked by tilting the test tube, no movement of the sample is seen one can say that gel is formed. Gelling time can be defined as the time required for the first detection of gelation.[12]

6. In-Vitro Drug Release

For In vitro drug release study Franz diffusion cell is used to determine drug release from a gel. There are two compartments present in the Franz diffusion cell one is the donor compartment and the second is the receptor compartment. Both Compartment separated by placing a dialysis membrane in between. The receptor compartment

was filled with simulated tear fluid and formulation was placed in the donor compartment. The temperature of the receptor compartment was maintained at 37°C. Sample withdraws at pre-decided tome point. Analysis of sample is done by suitable analytical method.[13]

6.1. Ocular irritancy test

An ocular irritancy test is performed on male albino rabbits. The formulation is administered in rabbit eyes and irritancy is tested at the time interval of 1hr, 2hr, 48hr, 72hr, and 1 week after administration. Observation is noted for redness, swelling & watering of the eyes.[14]

6.2. Gelling capacity

The gelling capacity was measured by placing a drop of in-situ gel in a vial containing 2 ml of simulated salivary fluid (pH 6.8-7.4) freshly prepared and equilibrated at 37° and visually evaluating the gel formation and noting the time for gelatin and the time taken for the gel formed to dissolve.[15]

6.3. Rheological studies

The viscosity and rheological properties of the in-situ gel are tested using a Brookfield viscometer.[16]

6.4. Sterility testing

The in-situ is applied for 14 days at 30-35 ° C in the liquid thioglycolate medium to detect bacterial growth and at 20-25 ° C in Soya casein digest to detect fungal growth in the product.[17]

6.5. Drug Content determination

The drug content of in-situ gel is determined with help of a UV spectrometer or HPLC or any other suitable method.[18]

7. Conclusion

Ocular drug delivery system is challenging field in which most of the scientists are taking challenges to combat different problems associated to this delivery. Steady advancement in the understanding of mechanism and processes governing ocular drug absorption and disposition and continuing technological advances have surely brought some improvements in the efficacy of Ocular drug delivery system.

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9. Conflict of Interest

The authors declare no relevant conflicts of interest.

10. Source of Funding

None.

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