An overview of the cutting-edge Ocular in-situ Gel method for treating bacterial infections.

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***Abstract*—** Ocular delivery system is a challenging drug delivery system. Various types of conventional ocular therapies are present in our market for treating various types of bacterial infections. But these ocular therapies have many drawbacks, like drainage of the instilled solutions, lacrimation, tear turn over, tear evaporation, metabolism, limited corneal area binding by the lacrimal proteins, haziness of eyes etc. These problems can be overcome by using ocular In-situ gel formulation which is sol to gel conversion due to temperature change, pH change and ion activated systems. Various polymers (temperature sensitive, pH sensitive & ion sensitive polymers) are used to form in-situ gel formulation. This novel formulation promotes easy and convenience administration, deliver at the proper dose as well as prolong residence time.

Key words- Ocular, In-situ, Polymer, Temperature, pH, Ion.

INTRODUCTION*:* The eye is a special organ both physically and physiologically, with a variety of physiologically diverse structures and functions that make the organ extremely resistant to external chemicals. Around the world, bacteria are the main cause of ocular illnesses. If untreated, ocular infections can harm the structures of the eye, leading to potential blindness and visual impairments. A few variables, such as contact lenses, trauma, surgery, age, dry eye condition, chronic nasolacrimal duct obstruction, and prior ocular infections [1][2][3], can cause mono- or poly-microbial infections. Numerous types of ocular infections, including conjunctivitis, keratitis, endophthalmitis, blepharitis, orbital cellulitis, and symptoms of dacryocystitis, are typically caused by bacteria [4].
'In position' is the literal translation of the Latin phrase 'In-situ. Drug delivery methods known as in-situ gels undergo in-situ gelation to transform from a solution to a gel after being injected into the body.

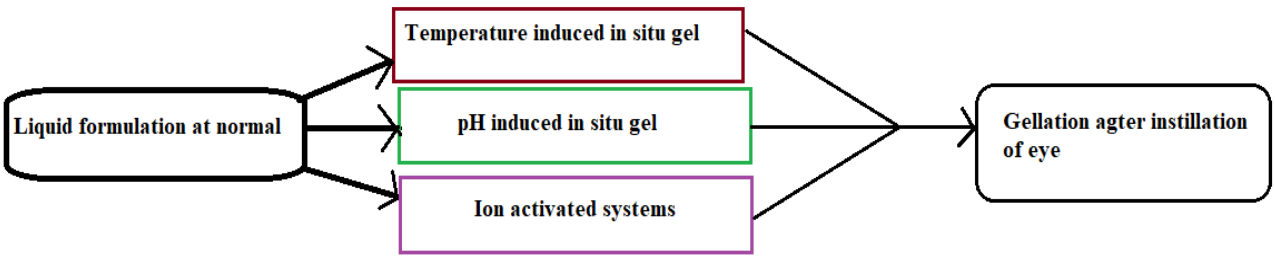

Fig 1: Schematic overview of in situ gel [9]

ADVANTAGES OF OCULAR IN-SITU GEL [10,11,12,13]:

a. Less blurred vision as compared to ointment.
b. Decreased nasolacrimal drainage of the drug which may causes undesirable side effects due to systemic absorption (i.e., reduced systemic side effects).
c. The ability to provide precise and repeatable dosages, as opposed to formulations that have already gelled, while also encouraging precorneal retention.
d. Sustained, Prolonged drug release and maintaining relatively constant plasma profile.
e. Reduced dosing frequency compared to preformed gel. Reduced frequency/number of applications leads to increased patient comfort and compliance.
f. Generally, more comfortable than insoluble or soluble insertion.
g. Increased bioavailability due to increased precorneal residence time and absorption.
h. Avoidance of hepatic first pass.

Type of In Situ Gelling System	Name of Polymers
In Temperature Sensitive In Situ Gelling System:	POLOXAMER/ PLURONICS, CELLULOSE DERIVATIVES (Methyl Cellulose, Hydroxy Propyl Methyl Cellulose, Ethyl Hydroxy Ethyl Cellulose)
In pH Sensitive In Situ Gelling System:	CARBOPOL, POLYCARBOPHILS
In Ion Sensitive In Situ Gelling System:	GELLAN GUM/GELRITE, ALGINATES, XANTHAN GUM

Table No. 1: Polymers used as in-situ gelling agents. [14, 15]

DRUGS THAT MAY BE USED IN IN- SITU TECHNOLOGY FOR OCULAR DELIVERY SYSTEM [16]:

1. Naphazoline HCL TI-allergic, 2. Ofloxacin, 3. Chloramphenicol, 4. Gentamycin antibiotics, 5. Dexamethasone, 6. Prednisolone, 7. Tobramycin with steroid, 8. Brimonidine Tartrate, 9. Pilocarpine,10. Pilocarpine Nitrate ophthalmic solution 2% w/v 5ml, 11. Timolol gents for glaucoma, 12. Ketorolac tromethamine anti-inflammatory – NSAID, 13. Clotrimazole , 14. Econazole, 15. Lignocaine HCL, 16. Proparacaine HCl CAL anesthetics, 17. Atropine sulfate, 18. Cyclopentolate, 19. Phenylephrine Hcl, 20. Prednisolone, 21. Triamcinolone Acetonide.

LITERATURE REVIEW:

Dol H. et al. found that In-situ hydrogels are administered as drops into the eye, where they undergo a sol to gel transition. By prolonging their contact with corneal tissue, they improve ocular bioavailability and need less frequent administration. The goal of the research was to create a pH-triggered ocular drug delivery system employing a mix of gelling chemicals with various in situ gelation mechanisms for the fluoroquinolone antibiotic Moxifloxacin hydrochloride. In situ gels were made using the simple dispersion method with carbopol and HPMC in a factorial design, and they were subsequently assessed for pH, gelling capacity, drug content, rheology, gel strength, and in-vitro diffusion studies, as well as statistical studies and comparison with commercial eye drop formulations. The created formulations offered continuous release, were stable, and were therapeutically effective.[17]

Patil S. et al. found that patients with chronic conjunctivitis or ocular irritation may use norfloxacin ophthalmic solution because it has been demonstrated to be useful in treating ocular infections. To prepared the Norfloxacin in situ gel various concentrations of polymers are used, such as Carbopol-940 (0.1, 0.2, 0.3 0.4, 0.5% w/v). Also used HPMC-E50LV (1.5% w/v), HPMC E4M (0.6% w/v) and HPMC K4M (0.5% w/v). These all are uesd as a pH triggered gelling system, with the objectives of increasing contact time, achieving controlled release, reducing the frequency of administration and obtaining greater therapeutic efficacy of the drug. Following preparation, the in situ gels were analysed for visual appeal, clarity, pH, drug content, and in situ gelation. Additionally, sterility tests, texture analysis, rheological research, and in vitro drug release experiments were conducted. By these tests it was clear to us that, the polymeric in situ gels generated were transparent and clear and had a good gelling capacity. The drug contents of all optimized formulations were found to range between 98.30- 99.97%. The formulations of our in situ gels may have exhibited pseudoplastic behaviour traits. The formulations that were created were light yellow in colour, therapeutically effective, stable, and non-irritating. They also offered sustained drug release for up to eight hours. [18]

Saini R. et al. explains that there was a need to design an enhanced drug delivery system because the traditional ocular drug administration methods, such as solutions, suspensions, and ointments, have limitations such precorneal removal was enhanced, efficiency varied significantly, and vision was obscured. To address the limitations of conventional medication therapy, in situ forming polymeric formulations were created. Before being injected to the body, these formulations are in solution form, but once there, they undergo gelation. Changes in a particular physico-chemical parameter (such as pH, temperature, or ion sensitivity) that regulate the drug's prolonged and controlled release are among the factors that affect gel formation.[19]

Sharadha M et al. found that in situ hydrogel composed of chitosan, sodium glycero-phosphate, benzalkonium chloride loaded with Ofloxacin to extend the drug delivery in the ocular socket using a suitable transporter. The dispersion approach was employed to create the in situ gel. The developed delivery system decreases the side effects, improves the efficiency and patient compliance. The prepared formulation was characterized by FT-IR, DSC and evaluated for gelation temperature, gelation capacity, viscosity, content uniformity, sterility and in vitro release. Gel viscosity rises with temperature and polymer concentration; medication concentration has minimal to no impact on formulation viscosity. As there was no bacterial development even after 14 days, it was ensured that all formulations were sterile. The ideal formulation exhibited good rheological and gelling characteristics. According to in vitro release experiments, the F5 optimised in situ gel had a better ability to maintain the medication than other formulations. As a result, the newly created in situ gel formulation of Ofloxacin was successful in treating conjunctivitis.[20]

CONCLUSION: The conventional ocular formulations have various types of drawbacks like ocular drainage, blurred vision, poor bioavailability, frequent doing of instillation which has lower patient compliance, tear turn over etc. On the other hand, there are

various advantages are present in case of ocular in-situ gel formulations like less blurred vision, increased bioavailability, prolong drug release due to use of various polymers, reduced doing frequency which provides good patient compliance. So, it can be concluded that, this ocular in-situ gel is a novel drug delivery system which has many advantages, which are very useful for treatment of ocular diseases in this modern world.

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