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In-Situ Gelling System: A Review

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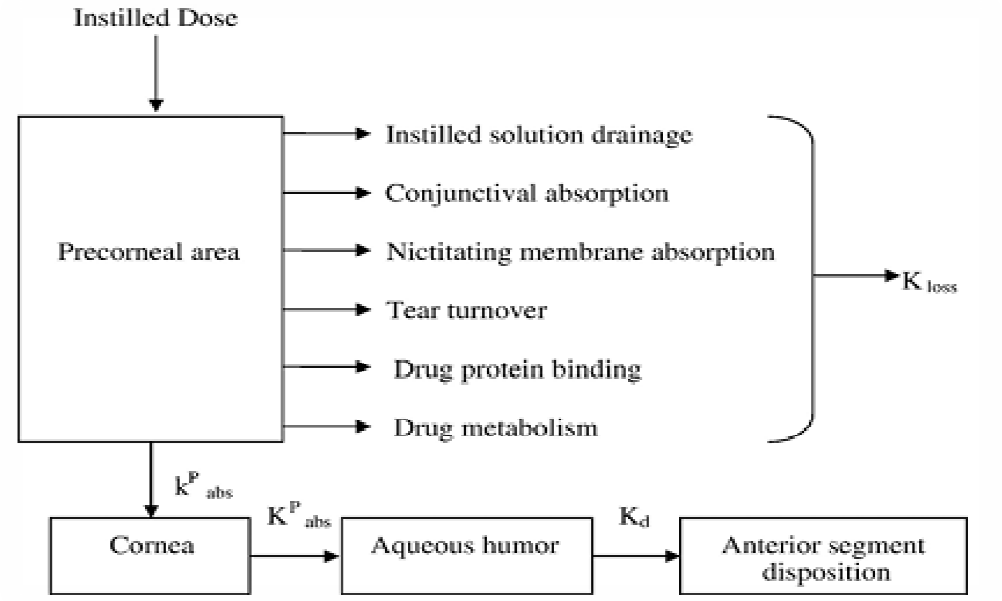
ABSTRACT

Ophthalmic drug delivery is one of the most interesting and challenging endeavors facing the pharmaceutical scientists, the major problem encountered to pharmaceutical scientist is rapid precorneal elimination of the drug, resulting in poor bioavailability and therapeutic response, because of high tear fluid turnover and dynamics. This interest has been sparked by the advantages shown by in situ forming polymeric delivery systems such as ease of administration and reduced frequency of administration, improved patient compliance and comfort. The formation of gels depends on factors like temperature modulation, pH change, presence of ions and ultra violet irradiation, from which the drug gets released in a sustained and controlled manner In situ-forming gels are liquid upon instillation and undergo phase transition in the ocular cul de-sac to form visco-elastic gel and these gels provides a response to environmental changes. In the past few years, an impressive number of novel temperature, pH, and ion induced in situ-forming systems have been reported for sustained ophthalmic drug delivery. Each system has its own advantages and drawbacks. The choice of a particular gel depends on its intrinsic properties and envisaged therapeutic use. Now a days in situ gel have been used as vehicles for the delivery of drugs for both local treatment and systemic effects. In this review basic about in situ gel system covered. From a manufacturing point of view, the production of such devices is less complex and thus lowers the investment and manufacturing cost.

Key words: In-Situ Gel, poor bioavability, pH dependent, controlled release.

INTRODUCTION

The main aim of pharmacotherapeutics is the attainment of effective drug concentration at the intended site of action for a sufficient period of time to elicit the response. A major problem being faced in ocular therapeutics is the attainment of optimal concentration the site of action. Poor bioavailability of drugs from ocular dosage forms is mainly due to the tear production, transient residence time, and impermeability of corneal epithelium.



Model depicting precorneal and intraocular drug movement from topical dosing.

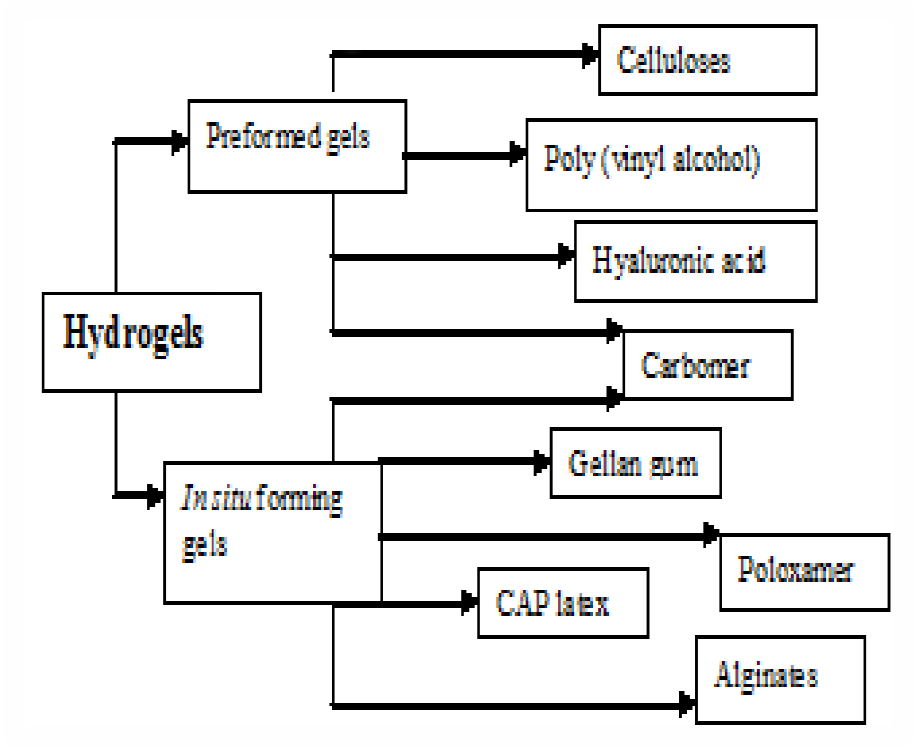
The poor bioavailability and therapeutic response exhibited by conventional ophthalmic solutions due to rapid precorneal elimination of the drug may be overcome by the use of a gel system that are instilled as drops into the eye and undergo a sol-gel transition from the instilled dose

The following characteristics are required to optimize ocular drug delivery systems.

- A good corneal penetration.
- A prolonged contact time with corneal tissue.
- Simplicity of installation for the patient.
- A non-irritative and comfortable form (the viscous solution should not provoke lachrymation and reflex blinking).
- Appropriate rheological properties and concentration of viscolyzer.

These systems have the advantages:

- Prolonged drug release
- Reduced systemic side effects
- Reduced number of applications
- Better patient compliance.
- Generally more comfortable than insoluble or soluble insertion. Less blurred vision as compared to ointment



Conventional ophthalmic dosage forms

DOSAGE FROM	BENEFIT	CONSTRAINTS
Solutions	Convenient	Rapid precorneal elimination. Loss of drug by drainage. Non-sustained action.
Suspensions	Patient compliance. Best for drug with slow dissolution	Drug properties decide Performance. Loss of both solution & Suspended solid.
Emulsions	Prolonged release of drug from vehicle	Blurred vision. Patient's non-compliance. Possible oil entrapment.
Ointments	Flexibility in drug choice. Improved drug stability. Inhibition of dilution by tears. Resistance to nasolacrimal drainage	Sticking of eyelids. Blurred vision. Poor patient compliance. Drug choice limited by partition coefficient.
Gels	Comfortable. Less blurred vision.	Matted eyelids after use. No rate control on diffusion.

➢ **TYPE OF INSITU GEL:**

1. Thermo reversible in situ gels
2. pH sensitive in situ gels
3. Ion sensitive in situ gel
4. Electrical signal sensitive hydrogels

➢ **Importance of in situ gel systems**

The major importance is the possibility of administrating accurate and reproducible quantities compared to already formed gel. It is conveniently dropped as a solution into the conjunctival

sac, enhancing patient compliance and minimizing interference with blinking. It increases the contact time of drug with the mucus at the site of absorption and has better bioavailability.

- **Mechanism of in situ hydrogel in sustained ophthalmic drug delivery**

Many mechanisms have been employed to cause reversible sol-gel phase transition, ie. In situ gel forming system by different environmental conditions. The stimuli that induces various Responses to form hydrogels includes: physical stimuli such as change in temperature, electric Fields, light, pressure, sound and magnetic fields; chemical stimuli such as change in pH and ion activation from biological fluids; and biological or biochemical stimuli such as change in glucose level. Out of these different environmental conditions only pH, ion activated and temperature stimuli are used for ophthalmic drug delivery.

RECENT ADVANCES

One of the challenges facing today's pharmaceutical industry centers on coming up with efficient treatment options that are readily acceptable to physicians and patients. Delivery systems must also contribute to a better therapeutic outcome if they are going to provide viable alternatives to pharmaceuticals currently delivered by other routes. In situ gel formulations are one of the challenging drug delivery systems. Various biodegradable polymers are used for formulation of in situ gels, but there are fabrication problems, difficult process ability, use of organic solvents for their preparation (especially for synthetic polymer based systems), burst effect and irreproducible drug release kinetics. Natural polymers satisfy the characteristics of an ideal polymer but batch to batch reproducibility is difficult therefore synthetic polymers are used. The recent advancement of biotechnologies has led to the development of labile macromolecular therapeutic agents that require complex formulations for their efficient administration N-stearoyl L-alanine (m) ethyl esters when mixed with a vegetable oil and a biocompatible hydrophilic solvent led to the formation of injectable, in situ forming organ gel. Following subcutaneous injection, leuprolide-loaded organ gel degraded and gradually released leuprolide for 14 to 25d

CONCLUSION

In conclusion, in situ gels offer the primary requirement of a successful controlled release product that is increasing patient compliance. Exploitation of polymeric in situ gels for controlled release of various drugs provides a number of advantages over conventional dosage forms. Sustained and prolonged release of the drug, good stability and biocompatibility characteristics make the in situ gel dosage forms very reliable. In situ activated gel forming systems seem to be preferred as they can be administered in drop form and create significantly less problems with vision. Moreover, they provide good sustained release properties. Over the last decades, an impressive number of novel temperature, pH, and ion induced in-situ forming solutions have been described in the literature. Each system has its own advantages and drawbacks. The choice of a particular hydrogel depends on its intrinsic properties and envisaged therapeutic use. Future use of biodegradable and water soluble polymers for the in situ gel formulations can make them more acceptable and excellent drug delivery systems

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