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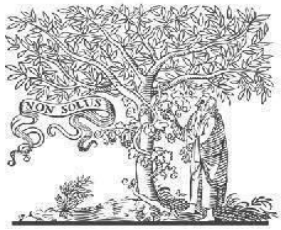

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DEVELOPMENT AND EVALUATION OF OCULAR IN SITU GELLING SYSTEMS CONTAINING CIPROFLOXACIN HYDROCHLORIDE

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Abstract:

The current review on in situ gelling systems focuses on polymeric formulations that initially exist in solution form but transform into gels under physiological conditions. Designing ocular drug delivery systems presents a significant challenge for pharmaceutical scientists, especially given the eye's sensitivity. Topical administration of ophthalmic drugs aims to alleviate symptoms and signs of ocular surface inflammatory disorders, treat infections, manage glaucoma, and address intraocular inflammation. Our objective is to formulate an ocular delivery system for Ciprofloxacin. In situ gels, known for their elastic properties, resist drainage from the eye, thereby prolonging contact time with the ocular surface. The transition from solution to gel phase depends on various stimuli such as pH changes, temperature modulation, solvent exchange, ultraviolet irradiation, and the presence of specific ions or molecules. Drug delivery systems with these properties are valuable for preparing sustained-release formulations of bioactive molecules. In situ gel-forming polymeric formulations are administered via various routes including oral, ocular, rectal, vaginal, injectable, and intraperitoneal routes. They offer several advantages over conventional drug delivery systems, including sustained and prolonged action.

Keywords: Gels, in-situ gel, ophthalmic drugs, glaucoma, bioactive molecules, sustained release, polymers, and drug delivery systems.

Introduction:

Ophthalmic drug delivery stands as one of the most compelling challenges for pharmaceutical scientists today. Ophthalmic preparations, whether in liquid, semi-solid, or solid forms, contain active pharmaceutical ingredients intended for application to the conjunctiva, conjunctival sac, or eyelids. These preparations are designed for courses of treatment that may span several days, although they include preservatives, there remains a risk of microbial contamination once the sterile seal is broken during use. The eye is a vital and unique organ situated within the orbital cavity of the skull, protected by its bony walls. It houses muscles of the eyeball, their nerves, blood vessels, and the lacrimal gland. Beyond providing vision, the eye enables organisms to receive and process visual detail and perform various light-sensitive

functions independent of vision. Drug delivery to the eye is challenging due to its anatomical structure, which limits drug absorption into deeper tissues.

The eye's structure can be categorized into anterior and posterior segments. The anterior segment, visible from the outside, includes the cornea, conjunctiva, aqueous humor, iris, ciliary body, and lens. The posterior segment, constituting the inner two-thirds of the eye, comprises the vitreous humor, retina, choroid, and optic nerve. Several conventional ophthalmic drug delivery systems exist, such as eye drops, ointments, lotions, and suspensions.

Optimizing ophthalmic drug delivery systems requires specific characteristics:

- Sterility
- Isotonicity
- Effective corneal penetration
- Minimal protein binding
- Reduced drainage tendency
- Ease of application and removal

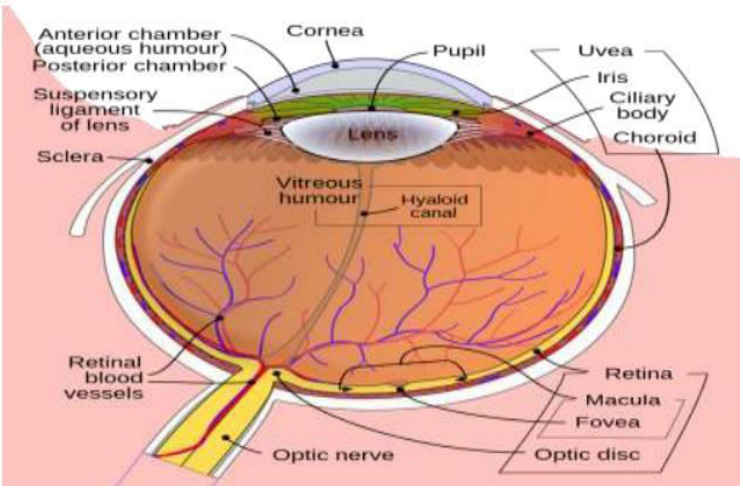

Figure 1.1: Schematic diagram of the human eye

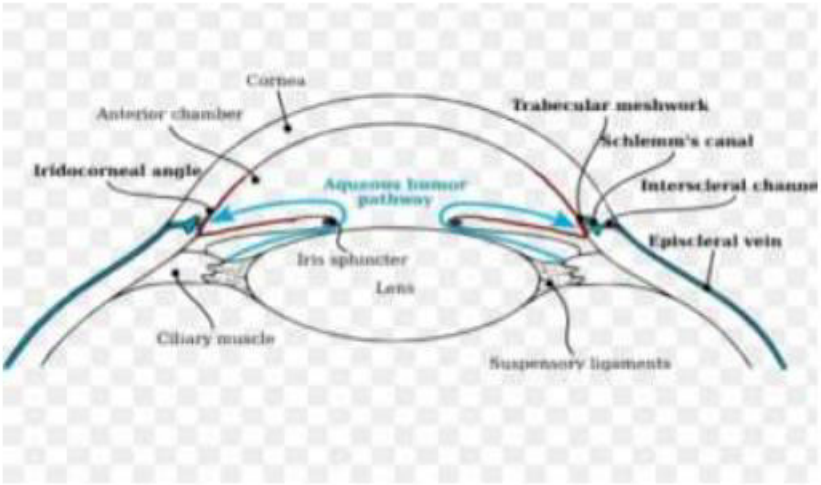

Figure1.2: Aqueous humour pathway

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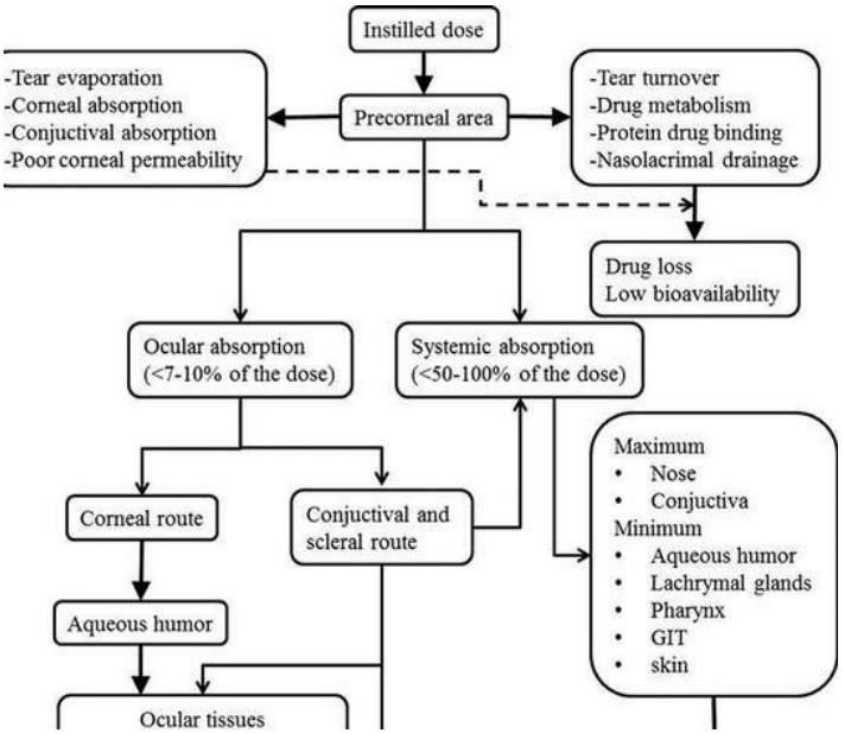

Figure 1.3: Absorption of the drug from the eye

1.4 Glaucoma: Glaucoma is not a single disease but rather a group of disorders characterized by elevated intraocular pressure (IOP), which leads to optic nerve atrophy and peripheral visual field loss. It is an eye condition where the IOP exceeds normal levels (above 25 mm Hg). Maintaining a proper balance between aqueous humor production and reabsorption is crucial to keep IOP within normal limits. When the production rate exceeds reabsorption, IOP can rise, potentially causing permanent vision loss if left untreated. Untreated glaucoma can result in irreversible damage to the optic nerve.

1.5 TYPES: a) **Open-angle glaucoma:** Typically affects both eyes, with one eye often more severely affected. The angle of the anterior chamber remains open and appears normal. This type of glaucoma develops slowly and painlessly, often without initial symptoms. If left untreated, peripheral vision loss occurs gradually. It commonly affects older individuals (aged over 50). While there is no cure, early detection and treatment can slow its progression and preserve eyesight through medication or surgery.

b) **Angle-closure glaucoma:** Occurs due to obstruction in the outflow of aqueous humor, typically caused by partial or complete closure of the angle between the iris and the trabecular meshwork. This obstruction leads to a rapid increase in IOP, sometimes within hours. It is less common than open-angle glaucoma, which progresses more gradually over time.

c) **Low-tension glaucoma:** Also known as normal-tension glaucoma, this type is less common. Despite normal eye pressure, damage to the optic nerve still occurs. The exact mechanism of this damage is not fully understood.

1.6 CAUSES AND RISK FACTORS:

- **Age:** Advanced age is a significant risk factor for glaucoma.
- **Genetics:** Family history of glaucoma increases the likelihood of developing the condition.

- **Medical Conditions:** Conditions such as diabetes mellitus and cardiovascular disease can predispose individuals to glaucoma.
- **Ocular Hypertension:** High pressure within the eye, known as intraocular pressure (IOP), can lead to glaucoma or permanent vision loss by damaging the optic nerve.
- **Physical Injuries:** Trauma to the eye, often caused by blunt force like head injuries or direct impact to the eye, can elevate eye pressure and potentially damage the optic nerve.
- **Severe Myopia:** High degrees of nearsightedness increase the risk of glaucoma and other serious eye complications.
- **Ocular Surgery:** Procedures such as cataract surgery can sometimes cause temporary spikes in eye pressure, which can usually be managed with medication.
- **Migraine:** Prolonged increases in eye pressure associated with migraines can lead to vision loss if not promptly addressed.
- **Corticosteroid Use:** Long-term use of topical or systemic steroids can induce secondary open-angle glaucoma, similar to chronic simple glaucoma. While the increased eye pressure from steroid therapy is reversible, any resulting damage to the optic nerve is usually permanent.

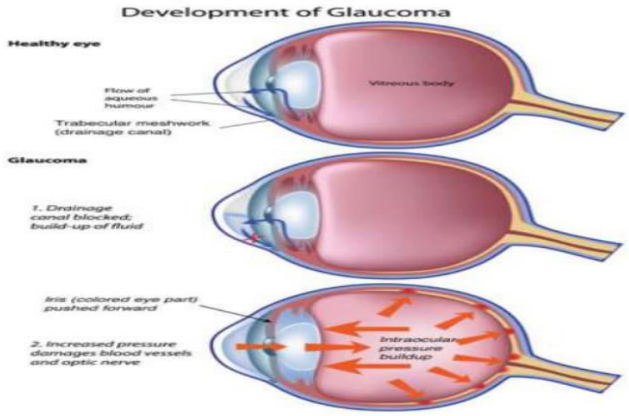

Figure1.4: Structure of Normal Eye and Glaucoma Eye

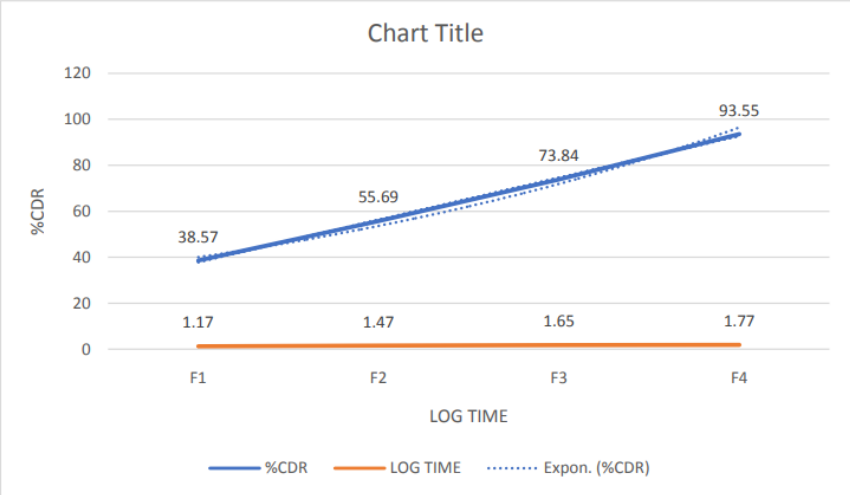

Figure 1.5: Standard Curve of F4 showing Korsmeyer–Peppas model release

Conclusion:

Ciprofloxacin, a broad-spectrum antibacterial agent used to treat ocular infections, was successfully formulated into in-situ gel-forming eye drops. Sodium alginate served as the gelling agent, with HPMC enhancing viscosity. This formulation presents a viable alternative to conventional eye drops, offering enhanced bioavailability due to prolonged precorneal residence time and sustained drug release. Its ease of administration and reduced frequency of use contribute to improved patient acceptance. The formulation exhibited robust gelation and favorable rheological properties, effectively retaining the drug. Notably, formulation F4 demonstrated 93.55% cumulative drug release, surpassing limitations of conventional ocular dosage forms. This approach enhances patient compliance through easy application, improved ocular bioavailability, prolonged corneal contact time, and reduced dosing frequency.

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