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Hydrogel Based Formulations in Treatment of Glaucoma

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Abstract

Glaucoma is a leading cause of vision impairment, which subsequently leads to loss of eyesight. Various treatment modalities such as topical and systemic medications, laser trabeculoplasty and surgery for the treatment of glaucoma are available; but it is most widely treated with topical eye drops due to self-administration. However, eye drops suffer from poor bioavailability and frequent administration. Hydrogel is a promising drug delivery system which can be administered both topically and injected and deliver the drug for extended period of time. This mini review focuses on published work on hydrogel use in glaucoma treatment.

Keywords: Glaucoma; Hydrogel; Intraocular pressure; Timolol Maleate

Abbreviations: IOP: Intraocular Pressure Measurements; EL: Elastin-like; SEL: Silk Elastin-like; CUR: Curcumin

Introduction

Glaucoma is a group of conditions that leads to damaging of optic nerve and is often associated with high intraocular pressure (IOP) [1,2]. The glaucoma is widely treated with topical eye drops containing antihypertensive drugs such as Timolol Maleate, Xalatan, Pilocarpine, carbonic anhydrase inhibitors, prostaglandin analogue latanoprost [3,4]. However, the adherence to eye drop application schedule is as low as 30% which often results in the progression of the disease which subsequently lead to vision loss and blindness [5,6]. The poor adherence is largely due to the frequent administration. Also, with eye drops, less than 5% of the administered dose is available for therapeutic effect as majority of the drug is cleared either by overflow or vent into nasolacrimal drainage system [7]. To overcome drawbacks associated with eye drops various approaches for sustained local drug delivery are explored such as hydrogels, viscosity modifiers, soft contact lenses, ocular inserts, injections [8-11].

Hydrogels

Hydrogel is a three-dimensional structure with cross-linked networks of either synthetic or natural water-soluble polymers with great potential as an ocular drug delivery system [12]. Hydrogels offers various advantages in ocular drug delivery such as decrease dose amount and dosing frequency thus increase in patient compliance, more convenient than ocular inserts, enhanced bioavailability due to high precorneal residence time and lower nasolacrimal drainage of the drug, reduce systemic toxicity, simple and less costly manufacturing [13] . However, as with every system, hydrogel also has some drawbacks like blurred vision and tufty eyelids.

Depends on the purpose, hydrogels are cross-linked either covalently or non-covalently. Covalently cross-linked hydrogels non-biodegradable are having high cross-linking density and mainly used in contact lenses. While non-colavently cross-linked hydrogels are administered as topical eye drops, subconjunctival injection, and intravitreal injections and cross-linking usually occurs in situ due to various stimulators such as change in pH, presence of ions, pressure, biological changes like enzymes, antibodies and glucose concentrations present in ocular fluids [14].

Hydrogel based formulations for treatment of glaucoma

Both synthetic and natural polymer-based hydrogels have been studies. A controlled-release ocular films of timolol maleate using natural hydrogel from Tamarindus indica seeds showed good film stability with no irritancy to eye and were able to reduce the intraocular pressure for 24 h [15]. A Timolol Maleate loaded thermoresponsive hydrogel based on PNIPAAm–chitosan copolymer with a lower than physiological temperature critical solution temperature (32°C) was prepared [16]. This hydrogel showed a great potential to extend the drug released into a

glaucomatous eye and more effectively reduce intraocular pressure (IOP) compared to conventional eye drops with minimum toxicity demonstrated in 0.5–400 g/mL concentration of polymers by MTT assay. In another study, PNIPAAm-gelatin hydrogel for the intracameral administration of pilocarpine showed a high drug encapsulation (~62%) and cumulative release ratio (~95%) with superior thermal gelation and adhesion and was biodegradable in the presence of an enzyme [17]. This hydrogel was found to be more effective in extending the reduction of IOP and pharmacological responses related to reduced-IOP, such as miotic action and stable corneal endothelium density in comparison to traditional eye drops and injection of free drug.

Gelatin and chitosan were crosslinked with genipin which was tested for controlled intraocular delivery of controlled Timolol Maleate [18]. Similarly, alginate was also employed as a rapidly forming injectable hydrogel for extended delivery of pilocarpine and Kelton LV [19]. A colloidal chitosan-based thermogel with a shear-reversible nature was developed to improve release duration of latanoprost showed lowering of IOP for 40 days in a rabbit glaucoma model with low cytotoxicity in MTT assay and excellent biocompatibility [20]. In a similar study, after topical application of latanoprost-loaded hydrogel, IOP was significantly decreased within 7 days and remained at a normal level for the following 21 days in a triamcinolone acetonide-induced elevated IOP in rabbits [21].

To further extend the release of the drugs, drugs are first loaded in a colloidal carrier before incorporating in a hydrogel. effectively lowers the IOP for 40 days in a rabbit glaucoma model. Linear PNIPAAm and crosslinked PNIAAm nanoparticles containing epinephrine were evaluated for the IOP-lowering effect in rabbits. The decreased IOP response was lasted for six-times and eight-times for linear PNIPAAm and formulation based on the mixture of linear PNIPAAm and crosslinked nanoparticles respectively compared to conventional eye drop [22].

The impairment of aqueous humor drainage via the outflow pathway is mainly responsible for the elevated IOP in glaucoma. This aqueous humor drainage occurs via the trabecular outflow and the uveoscleral outflow pathways. The oxidative stress in the trabecular meshwork often play an important role in the pathogenesis of impaired trabecular outflow facility and therefore, polyphenolic compounds from plant like Curcumin (CUR) with anti-inflammatory and anti-oxidative properties are beneficial. A thermosensitive chitosan-gelatin-based hydrogel containing CUR-NPs and latanoprost was developed as a dual-drug delivery system showed prolonged therapeutic effect over an extended period of time [23]. Self-assembling elastin-like (EL) and silk-elastin-like (SEL) hydrogels containing timolol maleate as antiglaucoma formulation was developed and adhesion tests and intraocular pressure measurements (IOP) were performed in New Zealand rabbits and results suggest potential of this system for the development of antiglaucoma formulation [24].

Conclusion

Glaucoma is a leading cause of vision impairment, which subsequently leads to blindness. Even though various treatment modalities such as topical and systemic medications, laser trabeculoplasty and surgery, improved therapeutic options are still needed. Hydrogel is a promising drug delivery system for the treatment of glaucoma and can be administered both topically and injected. New approaches combining benefits of hydrogels with colloidal drug carriers will further provides improved benefits for the glaucoma patients.

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