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REVIEW OF SUSTAINED RELEASE ANTIBACTERIAL OCULAR GELS

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ABSTRACT: Most ocular treatment requires the topical administration of ophthalmically active drugs to the tissue around the ocular cavity. Several types of dosage structures can be applied, as the delivery system for the ocular delivery of drugs. The most prescribed dosage structure is the eye drop solution. The present work describes the formulation and evaluation activated of an ophthalmic delivery system of an enemy of bacterial agent-Norfloxacin, based on the concept of Ion activated, pH-triggered and temperature activated in situ gelation. Sodium alginate was used as the gelling agent for Ion activated in situ gel, Polyacrylic corrosive (Carbopol-934) was used as the gelling agent for pH-triggered in situ gel and Poloxamer was used as the gelling agent for temperature activated in situ gel in combination with HPMC K4 M which acted as a consistency enhancing agent.

I. INTRODUCTION

Ophthalmic drug delivery is one of the most interesting and challenging endeavors confronting the pharmaceutical scientists. The life systems, physiology and biochemistry of the eye render this organ exquisitely impervious to foreign substances. The challenging to the formulator is tocircumvent the protective barriers of the eye without causing permanent tissue damage. The development of newer, more sensitive analytic techniques and therapeutics agents renders urgency to the development of successful and advanced ocular drug delivery systems.

The objective of pharmacotherapeutics is the attainment of an effective drug concentration at the intended site of action for a desired length of time. Eye, as an entry for drug delivery is generally used for the neighborhood therapy as against systemic therapy so as to evade the danger of eye damage from high blood concentrations of drug,which are not intended for eye.

The eye drop dosage structure is easy to ingrain however suffers from the inherent downside that the vast majority of the instilled volume is eliminated from the precorneal area resulting in a bioavailability running from 1-10% of complete administrated dose. The fast precorneal elimination of hauls given in eye drops is essentially due to conjunctival absorption, solution drainage by gravity, induced lacrimation and ordinary tear turnover. Because of helpless ocular bioavailability, many ocular drugs are applied in high concentrations. This cause both ocular and systemic side effects, which is often related to high peak drug concentrations in the eye and in systemic circulation. The frequent periodic instillation of eye drops becomes necessary to keep up a persistent sustained level of medication. This gives the eye a massive and unpredictable dose of medication.

The therapeutic efficacy of an ophthalmic drug can be greatly improved by drawing out its contact with the corneal surface. For achieving this purpose, consistency enhancing agents are added to eye drop preparations or the drug is formulated in a water insoluble ointment formulation to support the duration of intimate drug eye contact. Unfortunately, these dosage structures give just possibly maximum sustained drug-eye contact than eye drop solutions and don't yield a steady drug bioavailability. Repeated medications are as yet required for the duration of the day.

OCULAR INSERTS AS CONTROLLED DRUG DELIVERY STSTEMS

Ocular inserts are defined as preparations with a strong or semisolid consistency, whose size and shape are especially designed for ophthalmic application (i.e., bars or shields). These inserts are placed in the lower fornix and, less frequently, in the upper fornix or on the cornea. They are normally composed of a polymeric vehicle containing the drug and are primarily used for topical therapy.

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Advantages

Reduction of systemic absorption (which happens freely with eye drops by means of the naso lacrimal conduit and nasal mucosa)

Accurate dosing in opposition to eye drops that can be improperly instilled by the patient and are somewhat lost after administration, each insert can be made to contain a precise dose which is completely retained at the administration site.

Increased ocular residence, hence a prolonged drug action and a higher bioavailability with respect to standard vehicles.

Disadvantages

The occasional inadvertent misfortune during sleep or while scouring the eyes.

Their movement around the eye, in rare instances, the simple removal is made more troublesome by unwanted migration of the insert to the upper fornix.

A capital disadvantage of ocular inserts resides in their strong consistency, which means that they are perceived by patient as a foreign body in the eye. This may constitute a formidable physical and psychological barrier to user acceptance and compliance.

II. LITERATURE REVIEW

Smadar et al, developed a new in situ gel shaping ocular delivery system of drug from alginate undergoing gelation in the eye. They established that an aqueous solution of sodium alginate may gel in the eye, without including of external calcium ions or additional bivalent/polyvalent cations. Alginate with guluronic corrosive filling of more than 65%, for example, Manugel DMB, at once produced gels leading their accumulation to simulated tear liquid, while those having low glucoronic corrosive contents, for example, Ketton LV, formed weak gels at a relatively slow rate and hence it was indicated that the in situ gelling alginate systems, based on polymers with high guluronic corrosive contents was superior drug carrier for the sustained delivery of pilocarpine.

Ashish et al, in situ gels of optimized Levobunolol Hydrochloride for the therapy of glaucoma. LevobunololHCl in situ gel was formulated utilizing different proportions of polymers, for example, Carbopol 940, HPMC E4M and HPMC E50LV by pH induced gelling system with the point of to enhance the time of contact, to achieve the control release, to decrease the rate of administration better therapeutic efficacy of drug. The formulated in situ gels were subsequently assessed for their visual appearance, pH, clearness, drug content examination, in vitro gelation (Gelling strength), rheological studies, in-vitro drug release studies and sterility testing. The formed polymeric in situ gels were transparent, clear, possessing acceptable gelling strength.

Srividya et al, developed and characterized an ophthalmic drug delivery system of Ofloxacin, based on the idea of pH triggered in situ gelation. Polyacrylic corrosive (Carbopol 940) was utilized as the gel framing agent in a combination with HPMC E50LV which behaved as a thickness increasing agent. The developed formulations was discovered to be therapeutically efficient, non-aggravation, stabilize and provided steady release of the drug over a 8 h period. The formulated system was subsequently a realistic substitute to conventional eye drops.

Balasubramaniam et al, studied an ophthalmic delivery system of indomethacin, based on the assumption of ion activated in situ gelation. Gelrite (gellan gum), a novel ocular medium, which gels in the existence of mono or divalent cations there in the tear liquid, was utilized as the gelling agent. Gellan gum was investigated as a medium for the preparation of eye drops of indomethacin (1% m/V), which experience gelation when instilled into the parkway of the eye and offer steady release of the drug all through the treatment of uveitis. The prepared formulations were therapeutically effective (in a uveitis induced hare eye model) and rendered steady release of the drug over an 8 hour period in vitro and the prepared formulations were devoid of any unsafe consequence on the ocular tissues.

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Wu et al, formulated a pH triggered in situ gelling medium for ocular release of puerarin. The importance of hydroxy propyl-beta-cyclodextrin (HP-beta-CD) on the aqueous dissolvability and in vitro corneal penetration of puerarin was furthermore inquired. The puerarin dissolvability raised linearly and proportionately to the HP-beta-CD concentrations and 5% (w/v) HP-beta-CD improved its ocular permeableness definitely. Carbopol 980NF was utilized as the gelling agent in mixture with HPMC (Methocel E4M) which behaved as a consistency increasing agent. The most selected concentrations of Carbopol 980NF and HPMC E4M for the in situ gel framing delivery systems were 0.1% (w/v) and 0.4% (w/v) respectively. As these two vehicles were compounded, an in situ gel which is having the suitable gel strength and gelling capacity under physiological condition may be obtained. This compounded solution may flow freely under non-physiological condition and depicted the quality of pseudoplastic liquid in both situation.

Shivanand et al, developed a novel in situ gum based ocular drug delivery system of linezolid. Hydroxypropyl guar (HPG) and xanthum (XG) were utilized as gum with the mixture of HEC, carbopol, and sodium alginate as thickness increasing agents. The prepared formulations showed steady release of drug from formulation over a period of 6 h, in this manner enhancing residence time of the drug. The formulations were recognized to be non-aggravating with no ocular damage.

Harish et al, formulated in situ oral topical gels of clotrimazole established on the theory of pH triggered and ion activated systems. A pH triggered system involving Carbopol 934P (0.2-1.4% w/v) and ion triggered system including gellan gum (0.1-0.75% w/v) with HPMC E50LV which was utilized to extend the release of clotrimazole (0.1% w/v). Formulations were assessed for gelling ability, gel strength, consistency, bioadhesive force, spreadability, hostile to microbiological efficacy studies and in vitro drug release. The role of Carbopol as in situ gel shaping system was confirmed by the characteristic to change into powerful gels when the pH was increased while in gellan gum this alteration occurred in the existence of monovalent/divalent cations. Result of calcium carbonate alongside further process parameters modified and established that addition of calcium ions developed stiffer gels. The lucidity, drug content, and pH of the prepared gel were detected to be acceptable. The thickness was detected to be in the range 5 to 85 cPs for the sol, while for the gels it was up to 16000 cPs. The formulation showed pseudo plastic flow with thixotrophy. The highest gel strength (utilizing texture analyzer) in addition to bioadhesion was determined to be up to 6.5 g and 4 g correspondingly. The optimized preparations were capable to release the drug up to 6 h.

Eaga et al, developed ophthalmic delivery of Ciprofloxacin, based on the concepts of pH-triggered, ion activated system and thermo reversible gelation. Poly acrylic corrosive (Carbopol 940) was utilized as the gel framing agent in mixture with HPMC, which behaved as a consistency increasing agent (pH triggered system). Pluronic F-127 (14 %) was employed as the thermal reversible gelation in mixture of HPMC (1.5 %), integration of HPMC was to decrease the concentration of pluronic needed for in situ gelation. Gelrite (Gellan gum) is an anionic exocellular polysaccharide showed characteristic cation-induced gelation (0.6 %). The developed formulations was discovered to be therapeutically efficient, non-aggravation and stable, which offered steady release of the drug over a period of 6 h.

Hanan et al, formulated ophthalmic delivery systems of moxifloxacin, which is established on the idea of temperature activated in situ gelation with Pluronic (PL) and pH triggered in situ gelation with carbopol 934 were prepared. The produced formulae were assessed considering their gelation temperature (for PL systems), gelling ability (for CL systems), rheological features, in vitro release behavior and mucoadhesion limit. Among different formulae examined, P6 and C5 depicted best gelation temperature of 33.9°C subsequent to dilution with simulated tear liquid (STF) and moment gelation that remains for few hours correspondingly. Even however the evaluated index of mucoadhesion was more prominent (7.325 Pa) for C5 compared to (1.947 Pa) for P6, more prominent measure of moxifloxacin was sustained in the aqueous humor area of the eye over 8 h subsequent instillation of P6 with considerable 2.8 overlap increase in the Cmax and AUC(0-∞) compared to C5.

Swati et al, studied on pH triggered in situ gelling system of timolol maleate based on the perception of pH activated in situ gelation. Carbopol was utilized as the gelling agent in admixture with chitosan (amine polysaccharide), which acted as a thickness enhancing agent. Carbopol 0.4% w/v and chitosan 0.5% w/v formulation was in fluid state at room temperature and undergone quick transition into the gooey gel phase at the pH of the tear liquid (lacrimal liquid, pH 7.4). The results from formulation clearly demonstrated that carbopol-chitosan based formulation was therapeutically efficacious and showed a diffusion controlledtype of release behavior over a period of 24 hour.

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Padma et al, formulated and evaluated ocular delivery system of a calming drug diclofenac sodium, based on the idea of pH activated in situ gelation by utilizing sodium alginate, In vitro release studies indicated that the formulation showed better drug release when contacted with STF solution at 8 hrs study period. It showed antimicrobial, antibacterial and antifungal efficacy with selected microorganisms. The results demonstrated that the developed system is an alternative to conventional ophthalmic drops, patient compliance, mechanically oriented and economical.

Basavaraj et al, prepared an ophthalmic delivery system of Ketorolac tromethamine, utilizing Polyacrylic corrosive (Carbopol 934) as gel framing agent in admixture with HPMC K4M which acted as a consistency increasing agent based on the conception of pH activated in situ gelation. The prepared formulations was discovered to be therapeutically effective, stable, non-aggravation, and rendered steady drug release over a 8 h period. The prepared formulation was consequently a viable alternative to conventional eye drops by virtue of its capacity to increase bioavailability through its longer precorneal time of residence and capacity to develop sustained drug release.

Kugalur et al, formulated a pH dependent in situ ophthalmic gels of ketorolac tromethamine utilizing Carbopol 940, which is used as gelling agent in combination with hydroxyl propyl methyl cellulose (HPMC K4M) as a consistency enhancer. Benzalkonium chloride at suitable concentration was used as a preservative. The prepared formulations were evaluated for lucidity, pH measurements, gelling limit, drug content and in vitro diffusion study. Under rheological investigation both solution and gel was discovered to be having pseudo plastic behavior. The selected formulations showed sustained release of drug over a period of 8 h with increased residence time.

Jain et al, formulated an ophthalmic delivery system for Ciprofloxacin hydrochloride for once per day, based on the conception of pH activated in situ gelation. The in situ gelling system involved utilization of polyacrylic corrosive (Carbopol 980NF) as a phase transition polymer, Hydroxypropyl methylcellulose (Methocel K100LV) as a release agent, and ion exchange resin as a complexing agent. The developed formulations were discovered to be stable, non aggravation to bunny eyes and increased residence time of the gel formed in situ alongside its capacity to release drugs in a sustained manner with enhanced bioavailability. Hence it was concluded that in situ gels are a commonsense substitute to conventional eye drops by giving sustained release of medicaments to the eye.

Gonjari et al, prepared thermo reversible mucoadhesive gel of flucanazole. Gels were developed by means of the cool method alongside poloxamer 407 and different mucoadhesive polymers, for example, HPMC K4M, HEC and PVP K30. A customized device (modified K-C diffusion cell utilizing corneal membrane of sheep's eye as a diffusion membrane) was employed for assessment of permeation of drug through corneal membrane of a sheep. The developed gels were clear, homogenous in consistency, and had spreadability with a pH range of 6.8 to 7.3. Adequate bioadhesion on the corneal surface of sheep and better gel strength were additionally noticed. Diffusion studies have revealed that a framework is the best-fit model. As the proportion of mucoadhesive agent is raised, the rate of diffusion decreases. The order of drug diffusion over the membrane was HEC > PVP K30 > HPMC K4M.

Wu et al, studied the relationship among the strength of baicalin and insitupH-triggered gelling system. In vitro and in vivo evaluations were performed utilizing several methods namely rheometry, Gamma scintigraphic technique and miniature dialysis method. The rheological action showed a critical enrichment ingelstrength under physiological conditions, and the formulation rendered consistent release of the drug over a period of 8 hour. In elimination studies, the radioactivity of formulation was constantly superior than that of the control solution. In addition, the AUC and Cmax values were 6.1 foldand 3.6 fold higher than those of the control solution respectively. The results demonstrated that an insitu pH triggered gelling system have better ability to keep up baicalin stable and retain drug release than marketed baicalineyedrops to increase the ocular bioavailability.

III. CONCLUSION

Ocular gel system is the new novel methodology toward ocular drug delivery. Many researches were done on in situ ocular gels. Better patient compliance, enhancement of drug bioavailability, prolonged retentivity at the site of action and controlled release of drug are the advantages on in situ ocular gel over conventional ocular drug delivery system.

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