

IN-SITU OCULAR GEL - A NOVEL APPROACH TOWARDS OCULAR DRUG DELIVERY

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ABSTRACT

Conventional ocular drug delivery like ointments, eye drops, suspensions has many disadvantages of lacrimation, blurred vision and most important rapid precorneal elimination. So in order to overcome these drawbacks various novel approaches were developed such as insitu gel, ocusert, minidisc, collagen shield, nanosuspension, ocular film, nanoparticulate system, ocular iontophoresis, niosomes liposomes, dendrimers, etc. . In situ ocular gel is a recent advancement in ocular drug delivery system. In situ ocular gel system comprise delivery vehicle composed of polymers (natural, semi synthetic or synthetic) which has a special property of sol-gel conversion when influenced by some biological stimulus such as pH, temperature and ions. In situ ocular gels are evaluated for various parameters such as physical appearance, pH, clarity, gelling capacity, drug content, isotonicity evaluation, in vitro drug release studies, viscosity, sterility testing , accelerated studies, texture analysis and irritancy test.

KEYWORDS: In situ ocular gel, Novel ocular dry delivery

INTRODUCTION

Eye is considered as very sensitive organ. Perfect vision and ocular functionalities of eyes are generally performed by the cells in eyes and transparent tissues due to tight cellular membrane and barriers which control the fluid and solvent.[1] The delivery and targeting of ocular therapeutics is generally hindered by some barriers. The lachrymal flow and blinking reflex help in maintaining a good environment and remove foreign material from the eye.

The hindrance by barriers and tear flow lead to drainage of drug from the eye when instilled into it. This leads to poor bioavailability of drug, thus decreasing the desired therapeutic effect of the drug.[2] But one of the advantage of ocular route is that drug enter to the systemic circulation by eliminating hepatic first pass metabolism[3].

Conventional ocular drug delivery generally consists of eye drops as the principal and widely used formulation. Eye drop can be manufactured easily and have better patient compliance but their poor bioavailability is the major problem, which arises due to certain factors mentioned below:

- Lacrimation
- Non-productive absorption
- Drainage of instilled solution
- Tear evaporation and permeability
- Limited corneal area and poor corneal metabolism[4]

Ointments, suspensions and aqueous gels are few other conventional ophthalmic formulations developed to enhance ophthalmic bioavailability, but certain drawbacks of these formulations are:

- Poor patient compliance,
- Blurred vision,
- Difficulty in self-insertion,
- Premature release of drug, and
- Instability of the formulation[4-6]

***In situ*ocular gels (Novel Drug Delivery System)**

To overcome problems of acquiring and retention of optimum drug concentration at the site of action in the eye, various approaches of novel ocular drug delivery were studied. In situ ocular gel is considered to be one of the novel ocular drug delivery system.

In situ gel system comprise delivery vehicle composed of polymers (natural, semi synthetic or synthetic) which has a special property of sol-gel conversion when influenced by some biological stimulus[7].

The few advantage of in situ ocular drug delivery includes:

- Easy administration like a conventional eye drop formulation,
- Ease of fabrication,
- Patient compliance,
- Sustained and controlled drug release due to formation of gel network,
- Enhancement of drug bioavailability, and
- Prolonged retentivity at the site of action[8-10]

Mechanism of in situ gels

***In situ* formation based on physical mechanism**

Swelling

When polymer absorbs water from surrounding environment and expand to desired space, In situgelformation occurred. There are certain polymers that swells in water to form lyotropic liquid crystal.

Diffusion

In this method the precipitation or solidification of polymers may occur due to diffusion of solvent from polymer solution to surrounding tissue. The useful solvent for such system is N-methyl pyrrolidone (NMP)[11].

In situformation based on chemical reactions mechanism

In situgels formed by chemical reaction involves precipitation of inorganic solid from supersaturated ionic solutions, enzymatic processes, and photo-initiated processes[12].

Various Approaches To *In Situ* Gelation

As discussed earlier, In situ gel system shows phase transition from sol to gel upon getting biological stimulus. Three types of biological stimulus are presented by ocular route viz Temperature, pH and ions that are present in the lachrymal fluid[7].

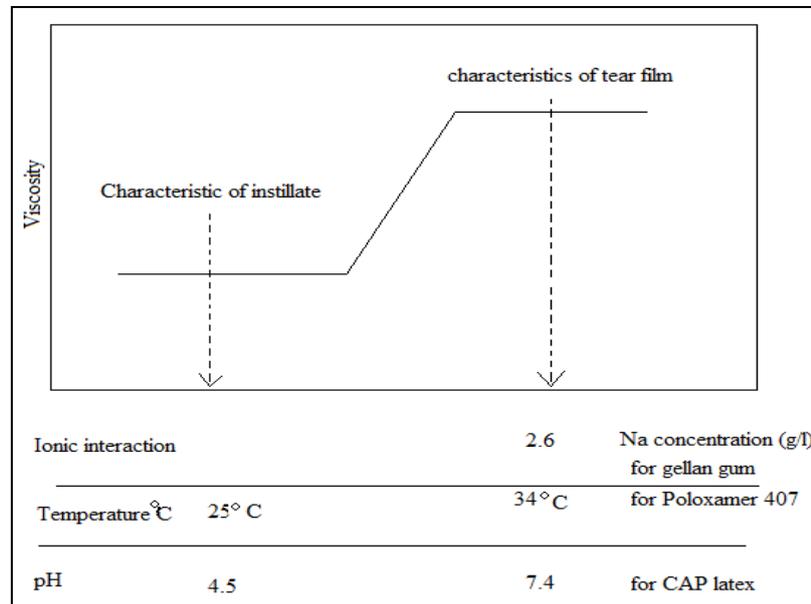


Figure 1: Scheme representing viscosity change on the ocular surface when using ophthalmic *in situ* gelling system [4]

Temperature triggered *In-situ* gel

Temperature sensitive *in situ* gelling system or temperature triggered *in situ* gel is considered to be the most commonly studied class of stimulus-sensitive polymer system in drug delivery research [13]. In this system at a specific temperature sol gel transitions occur, and this temperature is called as ‘low critical solution temperature (LCST)’. The main reason (assumed) for the sol to gel conversion is the difference in the solubility at different temperature. When the temperature is below LCST, the hydrogen bonding between the hydrophilic group on polymeric surface and water molecule favours enhanced dissolution of polymer chain and the system remain in the form of solution. But when the system is placed in temperature greater than LCST, the hydrogen bond corrupts. Thus the hydrophobic interaction is increased, there by facilitating sol-gel transformation[14].

The polymers that shows temperature induced Gelation are Poloxamer or pluronics, cellulose derivatives (methyl cellulose, HPMC, EGEC) and xyloglucanetc[7, 8].

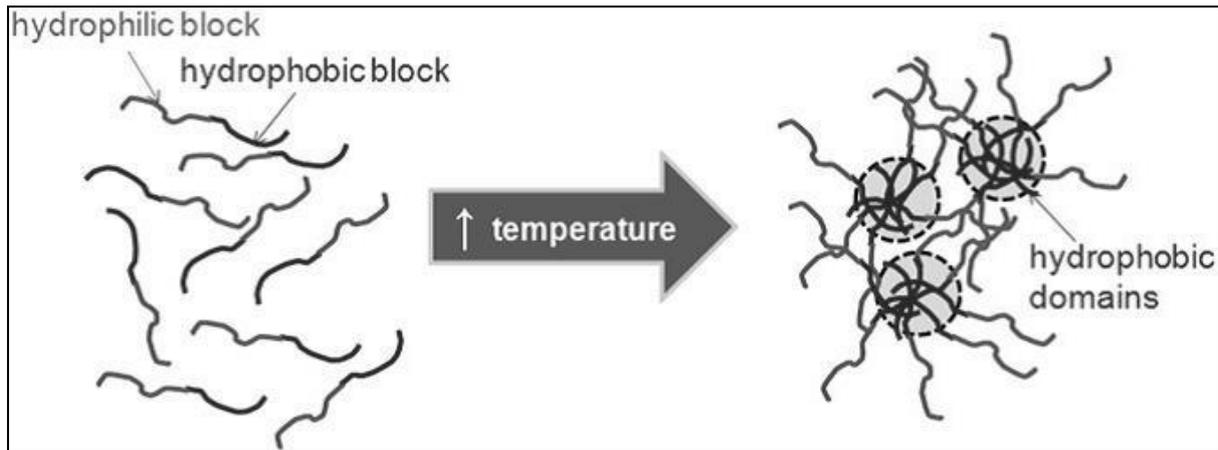


Figure 2: Mechanism of temperature sensitive system[15]

pH triggered *In-situ* gel

pH is considered to be the important biological parameter present at ocular site and instantaneously forms gel formation upon getting bio-stimulus. The change in the pH is responsible for the gelling of the system. At pH 4.4 the formulation is a free –running solution which coagulates when the pH is raised by the tear fluid to pH 7.4. So the pH change is about 2.8 units after instillation of the formulation (at pH 4.4) into the tear film leads to almost instantaneous transformation of the highly fluid latex into viscous gel[8].

The few advantages of pH sensitive in situ gelling system include; increase in therapeutic efficacy, stability, and patient compliance. Temperature triggered in situ gel also provides sustained release of drug for longer period of time than conventional eye drop [7]

The polymers that show pH induced/ triggered Gelation are Chitosan, Carbopol, and HPMC etc. The pH sensitivity of these polymers is due to the presence of ionisable groups present on the polymer surface that exhibit a sharp change in the degree of ionization and water solubility at specific pH (pKa)[16].

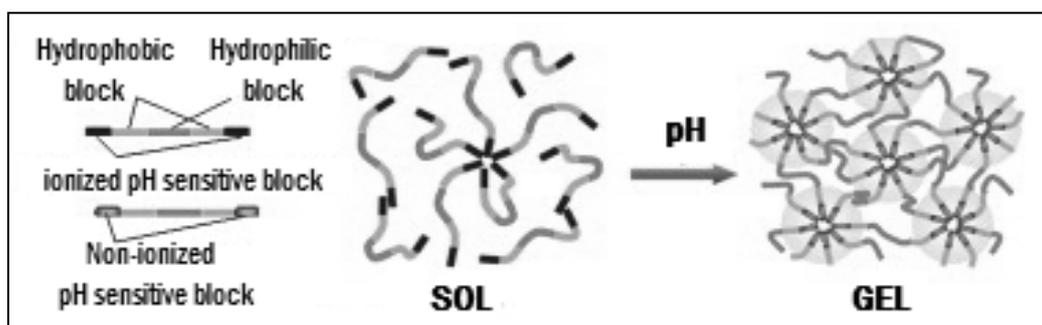


Figure 3: pH sensitive system[17]

The polymers with a large number of ionisable groups are known as polyelectrolyte. In the case of weakly acidic (anionic) groups, swelling of hydrogel increases with the increase in external pH, but decreases in the case of weakly basic (cationic) group[18].

Ion activated *In-situ* Gelation

Ion-sensitive gelling system or ion activated *in-situ* Gelation is the process in which Gelation of the solution instilled is triggered by the change in ionic strength. It is assumed that the osmotic gradient across the surface of the gel is responsible for the gelation. The aqueous polymer solution forms a clear gel in the presence of mono or divalent cations typically found in the tear fluids. The initiation of Gelation process of the polymer is stimulated by electrolyte of the tear fluid especially Na^+ , Ca^{2+} and Mg^{2+} cations when liquid solution is instilled in the conjunctival cul-de-sac[19].

The polymers that show ion activated Gelation are Gellan Gum, Alginates and Carrageenan etc.

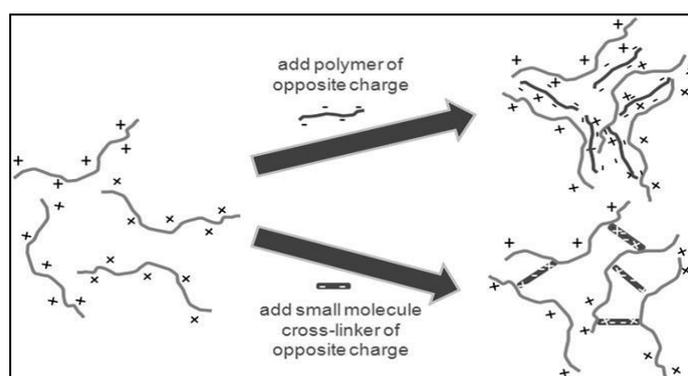


Figure 4: Mechanism showing Ion activated In-situ Gelation [17]

WORK REVISED IN THE FIELD OF *IN SITU* OCULAR GEL

Shashank N. Nayak et al (2017) carried out their work on pH triggered *in situ* ophthalmic gel of Moxifloxacin hydrochloride and Ketorolac tromethamine combination. *In situ* gels were prepared using carbopol 934 as gelling agent and Carboxy tamarind kernel powder and hydroxy propyl methyl cellulose K15M as viscosity enhancing agent and controlling polymer. The formulations were evaluated for various parameters like appearance, clarity, pH, gelling capacity, drug content, antimicrobial studies, sterility studies and *in vitro* diffusion studies. From the *in vitro* diffusion studies it was found that the release pattern of

the best formulation indicated that drug shows zero order release pattern for a period of 12 hours, thus increasing the contact time of drug with ocular tissues and reducing the nasolacrimal drainage. Hence it can be concluded that *in situ* ophthalmic of moxifloxacin HCL and ketorolac tromethamine combination can be a boon to ophthalmic drug delivery and replacement of conventional eye drop. [20]

Makwana S.B. et.al (2015), formulated and evaluated pH responsive in-situ ocular gel using ciprofloxacin hydrochloride as API. Sodium alginate was used as gelling agent along with Hydroxy propyl methyl cellulose (HPMC) as viscosity enhancer to facilitate sustained release of drug. The four different formulations were formulated using different concentration of sodium alginate and HPMC and evaluated for clarity, gelling capacity, pH measurement, drug content, rheological study and in vitro drug release. The results obtained indicated that among the four developed formulation the formulation having the concentration of sodium alginate and HPMC in 3:1 gives better result and found to be an optimized batch. Thus this developed formulation can also be considered as a viable alternative to conventional eye drop [21].

SainiRamanjit et.al (2015) provided an overview of in situ ocular gels, their mechanism , approaches of in situ gelation along with advantages and disadvantage of conventional and novel in situ gel ophthalmic formulations and also gave a detailed information about the evaluation of in situ ocular gels[17]

Patil S.K. et.al (2015) developed and optimized in situ gels of Norfloxacin for the treatment of conjunctivitis. Norfloxacin in situ ocular gels were prepared as pH triggered gelling system using different concentrations of polymers. 12 different batches of formulation were prepared using Carbopol-940 (0.2, 0.3, 0.4 and 0.5% w/v) whereas three different grades of HPMC; E50LV, E4M and K4M were used in concentration of 1.5%, 0.6% and 0.5% w/v respectively. The formulation was designed to achieve controlled release of drug along with increase in contact time and therapeutic efficacy. The prepared in situ ocular gels of Norfloxacin were evaluated for their physical appearance, pH, clarity, in situ gelation and drug content. Also, the sterility testing, rheological studies, texture analysis and in vitro drug release studies of prepared formulations were also carried out. The prepared in situ gels possess pseudoplastic behaviour and drug content ranges between 98.3 -99.97%. The developed formulation was

found to stable, non irritant, therapeutically efficacious and also provides sustained release of drug up to 8 hrs[22]

Puranik K.M. et.al (2015), developed and evaluated sol to gel transition system for the ocular delivery of an antifungal drug, Voriconazole. The formulation was designed to deliver drug to eye through ion activated system, by using sodium alginate as cross linker and HPMC K15M as viscosity enhancer. Addition of polymer and co polymer enhanced the bioavailability and reduced dose frequency. It was studied that Voriconazole is a hydrophobic drug so complex of drug was made by using β -CD in 1:3 by kneading method to enhance water solubility of Voriconazole. The nine different batches of the voriconazole in-situ gel were prepared using different concentrations of sodium alginate and HPMC K15M. The variables of prepared formulation were optimized using 3^2 factorial designs. The formulation prepared was also evaluated for pH measurement, gelling capacity, clarity, in vitro drug release, sterility testing, drug content, sterility testing and isotonic studies. The ex vivo drug penetration was also studied using goat corneas. The sustained release of drug up to 8 hrs was seen in the prepared formulation[23].

Preethi G B et.al (2015) formulate and evaluate in situ mocoadhesive ophthalmic hydrogel for sustained delivery of PerfloracinMesylate based on the concept of ion activated gelation for the prolonged precorneal residence time. Formulations were prepared using sodium alginate as a gelling agent and hydroxy methyl cellulose as mocoadhesive agent. Formulated gels were evaluated for gelling capacity, bio adhesive forces, rheological property, ex vivo and in vitro release profile for the selection of optimized formulation. From the results it was concluded that prepared formulations can be conveniently administer in drop form that undergo a phase transition in the ocular cul-de-sac to form a viscoelastic gel which increases the corneal residence time and sustain the drug for the longer period of time.[24]

Rathod K.B. et.al (2014), prepared and evaluated controlled release in- situ gel of Norfloxacin for drug delivery to eye. The objective of developing the formulation was to achieve controlled release of the drug and also to increase the contact time. Around five formulations were prepared by taking different concentrations of Carbopol-934 and HPMC K4, using pH triggered gelation system. The developed in-situ gels of Norfloxacin were then evaluated for various parameters such as visual appearance, pH, clarity, drug content, gelling capacity, sterility testing, in vitro drug release studies and rheological studies. From the studies it was concluded that all the five developed formulations are light yellow in colour,

having pH between 6 to 6.5 and 97% as average drug content. The prepared formulation possesses significant viscosity after gelation with satisfactory gelling capacity. The formulated pH triggered system provides 8 hrs in vitro sustained release of drug and also found that it was devoid of any deleterious effect on ocular tissue [25].

SampathiSunitha (2014) formulates and evaluates polymeric ocular in situ gel system of Lomefloxacin hydrochloride. The main aim of the work is to improve the bioavailability of the drug by using in situ polymers that exhibit reversible liquid gel phase transitions. Poloxamer 407 and HPMC were used in different ratios to prepare in situ gels. FT-IR spectroscopy was used to know the drug and polymer incompatibilities. The developed in situ gels were also evaluated for gelation temperature, drug content, clarity, pH, viscosity, in vitro drug release and ex-vivo studies. The prepared in situ gels formulations provide a sustained release up to 10hrs with cumulative drug release ranging from 91.025 to 98.31%. Formulation having concentration of 16%w/v poloxamer 407 and 1%w/v HPMC was found to be optimized formulation, having optimum pH and gelation temperature which is required for an in situ gel drug delivery system. The results indicated that the extent of gelation and release of drug depended on the concentration of polymers used [26].

KashikarS.Vrushali et.al (2013) formulates and evaluates temperature and ion-activated in situ ocular gel system of ofloxacin. For temperature triggered in situ gelation system, Pluronic F-127 and Pluronic F-68 were used in combination along with chitosan which act as a permeation enhancer; whereas for ion activated in situ gelling only Gellan gum was used. Firstly the different combinations of placebo formulations were developed and suitable composition for use as in situ gelling system was identified by evaluating clarity and gelling capacity of formulation. The in situ ocular gels of ofloxacin were then evaluated for Drug-polymer interaction study, in vitro drug release study, in vitro transcorneal permeation study, ocular irritation study, Gamma scintigraphy and ocular pharmacokinetic study. From the gamma scintigraphy, it was concluded that precorneal drainage is significantly controlled by in situ gel forming ability of the developed system. Thus, ocular bioavailability of the drug will increase due to increase in residence time in eye. From pharmacokinetic studies it was concluded that C_{max} of in situ gelling formulation was found to be 1.4 times higher than marketed eye drops solution at the similar $T_{1/2}$ of 1hr[27].

Shetgaoncar N.N et.al (2013) develop an ophthalmic drug delivery system of Perfloxacinmesylate for in situ gelling system using Gelrite as ion sensitive gelling agent and

HPMC K4M as viscofying agent. The formulations were optimized by 2^2 factorial design using Design expert software 8.0 versions. Factorial batches of in situ pefloxacinmesylate ophthalmic gel release were evaluated for the *in-vitro* drug release and viscosity by its regression analysis. The optimized formulations show release profiles and responses which were close to predicted responses. From the optimization results, it was observed that Gelrite and HPMC K4M is an excellent gelling agent and viscofying agent in combination for the preparation of *in situ* ophthalmic gel. [28]

Agarwal A.K et.al (2012) gave the brief information about the latest developments in in-situ ocular gel drug delivery along with the information related to mechanism of ocular absorption and different types of polymers used as an ocular vehicle for in situ ocular gel drug delivery system. [9]

MandalSonjoy et.al (2012) formulated and evaluated an in situ gel forming ophthalmic formulation of Mociboxacin. Sodium alginate was used as a moco adhesive polymer and HPMC as viscosity enhancer. Sodium alginate gets converted into gel under the influence of divalent cations (Ca^{2+}) present in the lachrymal fluid. Six different batches of formulation were prepared with different concentration of sodium alginate and HPMC. The pH of formulation was adjusted to 6.5 by addition of suitable concentration of buffering agent. The formulations were sterilized in an autoclave at 121°C for 15 minutes and evaluated for clarity, pH measurement, rheological behaviour, gelling capacity, drug content, in vitro diffusion study, antimicrobial activity, isotonicity and eye irritation study. The eye irritation test was performed on albino rats (males). The developed formulation found to exhibit sustained release of drug up to a period of 10 hours. The formulation was also found to be non irritating with no ocular damage. Thus from result it was concluded that in situ gelling system containing gums can be used as a viable alternative to conventional ocular drugs delivery system. [29]

Nayak N Shashank et.al (2012) prepares and evaluates pH triggered in situ ophthalmic gels of moxifloxacin hydrochloride. Carbopol 934 was used as gelling agent along with hydroxy propyl methyl cellulose (HPMC K15M) as viscosity enhancer. The developed formulations were evaluated for visual appearance, pH measurement, clarity, gelling capacity, drug content, sterility studies, in vitro diffusion studies along with microbiological and stability studies. Sustained release of 8 hrs was shown by selected formulation. Draize eye test was also carried out and optimized formulation was found to be non irritant to rabbit eyes. The

results conclude that formulation with 0.5% w/v Carbopol 934 and 0.3% w/v HPMC K15M was found to be optimized formulation which shows pseudoplastic behaviour in solution as well as gel forms. [30]

Cao Feng et.al (2010) focused on preparation and evaluation of thermo sensitive and mocoadhesive in situ gelling ophthalmic system of azithromycin. Poloxamer 407 and poloxamer 188 were used as gelling agent. Carbopol 947P was also added to the gelling system so as to increase the solubility of azithromycin by salt effect and thus help in enhancing the mocoadhesive property of the system. The in situ gels were evaluated for gelation temperature, rheological studies, measurement of mocoadhesive forces, in vitro release studies and in vivo resident studies. Gelation temperature of these systems ranged from 31.21–36.31°C depending on the ratio of P407 and P188. Mucoadhesion force of the system composed of Poloxamer 407/Poloxamer 188/Carbopol 974P (21/5/0.3%, w/v) was 2.3-fold that without carbopol 974P. Viscosity of the formulation was in a suitable range at 25°C and pseudoplastic behaviour was observed at 35°C. The formulation exhibited a 24-h sustained release of azithromycin. In vivo resident experiments showed AUC_{0–12} of drug in rabbit tears increased by 1.78-fold for in situ gel compared with eye drop. At 12 h, tear concentrations exceeded minimum inhibitory concentration (MIC) breakpoint for the most common causative pathogens of bacterial conjunctivitis by 2.8-fold. Results in vitro and in vivo indicated that this droppable gel performed better than azithromycin eye drop did [31].

GratieriTais et.al (2010) worked to obtain an ophthalmic delivery system with improved mechanical and mocoadhesive properties that could provide prolonged retention time for the treatment of ocular diseases. They prepared in situ forming gels having combination of a thermosetting polymer (PEO-PPO-PEO, poloxamer) with a mocoadhesive agent (chitosan). Different polymer rations were evaluated by oscillatory rheology, texture and mocoadhesive profile. Retention time of the formulation was verified by conducting scinitigraphy studies in human. The results showed that chitosan improves the mechanical strength and texture properties of poloxamer formulations and also confers mocoadhesive properties in a concentration-dependent manner. After a 10-min instillation of the poloxamer/chitosan 16:1 formulation in human eyes, 50–60% of the gel was still in contact with the cornea surface, which represents a fourfold increased retention in comparison with a conventional solution. Therefore, the developed formulation presented adequate mechanical and sensorial properties and remained in contact with the eye surface for a prolonged time [32].

Mohan E.C. et.al (2009) prepared and evaluated in situ gel of Ciprofloxacin HCl for ocular drug delivery. The main aim of formulation was to overcome the rapid precorneal elimination of the drug, thus increased bioavailability and therapeutic response of the drug. For the pH triggered in situ ocular gel, Carbopol 940 was used as gelling agent along with HPMC which act as a viscosity enhancer. 14%w/v of Pluronic F-127 and 1.55w/v of HPMC was used in combination as gelling agent for thermo reversible gelation. Gellan gum (Geltrine) is an anionic exocellular polysaccharide has a property of cation induced gelation, thus 0.6% w/v of Gellan gum was used as a polymer in the formulation of ion activated in situ ocular gels. The three prepared formulations were evaluated for clarity, visual appearance, pH, drug content and rheological studies. In vitro release profile of drug and stability testing at 25⁰C and 40⁰C were also carried out. Antimicrobial activity of the formulation was also studied using cup plate technique. From the results it was concluded that the formulation were at liquid at pH 6.4-7.1 and undergo sol-gel transition at pH7.4 and temperature 37⁰C. the formulations prepared were found to be stable, therapeutically efficacious, non irritant and provide sustain release of drug up to 6 hrs, but formulated ion activated in situ ocular gel shows long duration of release followed by pH triggered in situ ocular gel and thermo reversible in situ ocular gel.[33]

Nanjwade K. Basavaraj et.al (2009) presents their work preparation and evaluation of an ophthalmic delivery system for a nonsteroidal anti-inflammatory drug, ketorolac tromethamine, based upon the concept of pH triggered in situ gelation. Carbopol 934 and Methocel K4M were used in preparation of in situ gels. Compatibility studies of the drug excipients were carried out using differential scanning calorimetry (DSC). The prepared formulations were characterized for clarity, pH, drug content, sol-to-gel transition by scanning electron microscopy (SEM), in vitro and in vivo drug release, ocular irritation and stability. The clarity, pH and drug content of the developed formulation were found to be satisfactory. The developed formulation was found to be therapeutically efficacious, stable, non-irritant, and an and drug shows sustained release up to 8 hours. [34]

Mansour Mai et.al (2008) prepared and evaluated ocular poloxamer based Ciprofloxacin HCl in situ forming gels with an aim of prolonging corneal contact time, enhancing ocular bioavailability, controlling drug release and improving patient compliance. Around 14 in situ gels were prepared using different concentration of Poloxamer 188(P188) and

Poloxamer407(P407). The bioadhesive property of gel was enhanced by adding different concentration of HPMC and hydroxyethyl cellulose (HEC) as mocoadhesive. The formulations prepared were evaluated for drug release, rheological behaviour, sol-gel transition temperature, and mocoadhesive forces. The in vivo antimicrobial efficacy of formulations was compared with marketed conventional eye drop by using rabbit eyes. The results concluded that gelation temperature was found to ranged between 28⁰C to 34.03⁰C. It was also concluded that with the increase in the concentration of P407, HPMC and HEC, the viscosity and mocoadhesive forces of the in situ ocular gels were also increased but in vitro drug release decreased. The formulation having composition of P407, HPMC and HEC as 18%, 13% and 1.5% w/w respectively and P407, HPMC and HEC as 18%, 13% and 0.5% w/w respectively were found to have optimum release and mocoadhesive properties. These formulations found to have improved ocular bioavailability with enhance therapeutic response as compared to marketed conventional eye drops [58].

Srividya B. et.al (2000) formulates and evaluates an ophthalmic delivery system of an antibacterial agent, ofloxacin, based on the concept of pH triggered in situ gelation. The formulations were prepared using different concentrations of Carbopol 934 and HPMC. Three different grades of HPMC i.e E4M, K4M and E50LV were used for rheological evaluation. The prepared formulations were evaluated for rheological studies, in vitro release studies, antimicrobial efficacy studies, ocular irritation studies and accelerated stability studies. The results conclude that the developed formulations were therapeutically efficacious, stable, non irritant and provide sustained release of the drug over an 8 hr period. Thus the developed system is considered as a viable alternative to conventional eye drop. [35]

EdsmanKatarian et.al (1998) performed the rheological measurements to study the gel and sol-gel transition of an in situ ocular gel of Poloxamer 407. Poloxamer was evaluated as an ocular vehicle by studying rheological behaviour and performing in vivo study of ocular residence in human volunteer. It was concluded from the rheological studies that increase in the concentration of poloxamer lead to increase in the elasticity of gel while sol-gel transition temperature gets decreased. The contact time also increased with the increase in concentration poloxamer and maximum contact time of prepared in situ ocular gel was found to be 1 hour. The poloxamer system was not found to be a better ophthalmic in situ gel due to strong concentration dependence of sol-gel transition temperature when combined with dilution that occur in the eye.[2]

Carlfors Johan et.al (1998) studied the rheological behaviour of the in situ ocular gels using Gelrite as polymer. Different formulations were prepared using different concentration of Gelrite (0.4%, 0.5%, 0.6% and 0.7%w/v) and precorneal contact time was studied on two human volunteers and six New Zealand White rabbits. The rheological properties of solution and gels were measured using a Bohlin VOR rheometer. The results concluded that with the increase in the concentration of electrolyte the elastic moduli of the gel increased. The elasticity of the gels was independent of Gelrite concentration at physiological concentration of electrolyte. Results also concluded that decrease in the osmolarity of the formulation lead to increase in human precorneal contact time up to 20 hours. Thus the result indicated that a high rate of sol-gel transition results in long precorneal contact time.[36]

CONCLUSION

In situ ocular gel system is the new novel approach 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.

Thus in situ ocular gels are found to a viable alternative to conventional eye drops.

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