LITERATURE REVIEW

- **Basavaraj K. Nanjawade** et al, 2007 had studied the effect of Insitu-forming hydrogels is liquid upon instillation and undergoes phase transition in the ocular cul-de-sac to form visco-elastic gel and this 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 sustain ophthalmic drug delivery.

- **Katarina Edsman** et al, 1998 had studied on the rheological measurements and a small in vivo study of ocular residence times in humans were used to evaluate poloxamer as an ocular vehicle. An increasing concentration of poloxamer resulted in a slightly increasing elasticity of the gels and a decreasing sol–gel transition temperature.

- **Veena S.Belgamwar** et al, 2009 worked on Nasal drug delivery has a variety of advantages. Drugs can be rapidly absorbed through the nasal mucosa, giving rapid onset of action, and avoiding presystemic metabolism. In present study; the nasal mucoadhesive in situ gels of anti-emetic drug Dimenhydrinate were formulated using Gellan gum and Carbopol 934P. The in situ gels so prepared were characterized for gelation, viscosity, gel strength, mucoadhesion, drug content, drug diffusion, ex vivo permeation and histopathological studies. The optimized formulation passing from above tests was further subjected to accelerated stability study. It retained the good stability over the period of 90 days. From the overall performance this in situ gel seems to be an effective delivery system for the nasal route.

- **ZAKI Noha M** et al, 2007 studied on in situ gelation upon contact with nasal mucosa was conferred via the use of the thermo gelling poloxamer 407 whereas mucoadhesion and drug release enhancement were modulated via the use of mucoadhesive and polyethylene glycol (PEG) polymers respectively. The results revealed that the different mucoadhesives augmented the gel viscosity but reduced its sol-gel transition temperatures (T_{sol-gel}) and the drug release. The inclusion of PEG counteracted the effect of the mucoadhesive polymers whereby it decreased the gel consistency and increased the T_{sol-gel} as well as the in vitro drug release. The formulations with favorable sol-gel transition temperatures (25-32°C) and high in vitro drug release (100% release in 60 min) were also rheologically stable upon storage.
Miyazaki S. et al., 2001 has studied the thermo reversible gels formed in situ by aqueous solutions of an enzyme-degraded xyloglucan polysaccharide were evaluated as sustained release vehicles for the ocular delivery of pilocarpine hydrochloride. In vitro release of pilocarpine from gels formed by warming xyloglucan sols (1.0, 1.5 and 2.0% w/w) to 34 degrees C followed root-time kinetics over a period of 6 h. The miotic responses in rabbit following administration of xyloglucan sols were compared with those from in situ gelling Pluronic F127 sols and from an aqueous buffer solution containing the same drug concentration. Sustained release of pilocarpine was observed with all gels, the duration of miotic response increasing with increase of xyloglucan concentration. The degree of enhancement of miotic response following sustained release of pilocarpine from the 1.5% w/w xyloglucan gel was similar to that from a 25% w/w Pluronic F127 gel.

Lin HR et al., 2000 studied on the rheological properties, in vitro release as well as in vivo pharmacological response of various polymer solutions, including Carbopol, Pluronic and Carbopol+Pluronic solution, were evaluated. It was found that the optimum concentration of Carbopol solution for the in situ gel forming delivery systems was 0.3% (w/w), and that for Pluronic solution was 14% (w/w). The mixture of 0.3% Carbopol and 14% Pluronic solutions showed a significant enhancement in gel strength in the physiological condition; this gel mixture was also found to be free flowing at pH 4.0 and 25 degrees C.

Mayol L. et al., 2008 the influence of hyaluronic acid (HA) on the gelation properties of poloxamer blend has been studied with the aim of engineering thermo sensitive and mucoadhesive polymeric platforms for drug delivery. The gelation temperature, viscoelastic properties and mucoadhesive force of the systems were investigated and optimized by means of rheological analyses. By formulating Poloxamer/HA platforms, at specific concentrations, it was possible to obtain a thermo reversible gel with a T (gel) close to body temperature. The addition of HA did not hamper the self assembling process of Poloxamer just delaying the gelation temperature of few Celsius degrees. Furthermore, HA presence led to a strong increase of the Poloxamer rheological properties thus indicating possible HA interactions with micelles through secondary bonds, such as hydrogen ones, which reinforce the gel structure.
Zhidong Liu. 2006 observed that the poor bioavailability and therapeutic response exhibited by conventional ophthalmic solutions due to rapid pre-corneal elimination of the drug may be overcome by the use of in situ gel-forming systems that are instilled as drops into the eye and then undergo a sol–gel transition in the cul-de-sac. Alginate (Kelton®) was used as the gelling agent in combination with HPMC (Methocel E50Lv) which acted as a viscosity-enhancing agent.

Samdar Cohen et.al, 1997 studied on bioavailability can be increased of ophthalmic solution avoiding them to release from lacrimal drainage. They demonstrate that an aqueous solution of sodium alginate (G content) can gel in the eye without addition of external calcium ions or other bivalent/polyvalent cations. He carried his work on Pilocarpine drug and extended the release of drug they also signified that extended the duration of the pressure reducing effect of Pilocarpine; the overall study indicates that the in-situ gelling system based on polymer with high G content is an excellent for the prolonged delivery of pilocarpine.

Jitendra shinde et.al, 2008 had worked on prolonged residence of drug Metoclopramide HCl formulation in nasal cavity by formulating it with Poloxamer and sodium alginate which helped in reduced nasal mucocilliary clearance in order to improve bioavailability.

Kun Na et.al, 1997 studied the pH sensitive Indomethacin delivery system using pullulan. Also carried out formulation using pullulan acetate and measured swelling capacity at different pH.

Yoshie Maitani et.al, 1997 worked on a modeling analysis is presented of drug or peptide absorption and administration via the ocular, nasolacrimal duct and nasal route. This method accounts for fast absorption and retention of drug in the blood after administration. The parameters were calculated based on fitting experimental based on first order absorption processes.

Indu Pal Kaur et.al, 2002 studied on ophthalmic formulations containing bioadhesive or penetration enhancers is commercially available in the market. The use of bioadhesive considerably prolongs the corneal contact time whereas the absorption promoters increase the rate and amount of drug transport. Combining the two approaches would theoretically increase assure an increase in bioavailability.
FV Manvi et.al, 1997 prepared circular ocular inserts by solvent casting, using cellulose acetate as polymer with PEG 6000 and DEP as plasticers. They worked on Timolol Maleate an anti glaucoma drug to sustained the delivery and reduce the possible side effects.

Jennifer J.Kang et.al, 2008 had worked on proteins that were encapsulated into hydro gels and the release was adjusted by varying degree of cross-linker. The use of thermo sensitive polymer for phase transition and release of drug was studied.

Deepika Aggarwal et.al, 2005 presented study on coated niosomal Timolol Maleate by reverse phase evaporation and compared to Timolol solution in terms of IOP lowering effect. Chitosan and Carbopol were used for coating. It was concluded that Chitosan coated formulation was significantly lowering the IOP in the contralateral eye. (20-40%) as compared with the Timolol solution.

Suketu D.Desai et.al, 1998 developed Pluronic F127 containing formulations of Pilocarpine HCl for controlled release ocular delivery. Additives such as PEG4600,PVP10000,PVA 10000,MC 15cp and HPMC 80-120cp.25% concentration of PF127 was effective with 3% HPMC or 5% MC gave promising dissolution results.

Sankar Chelladurai et.al, 2008 developed a gelling system of ketorolac tromethamine which act as non narcotic analgesic. Chitosan and pectin were used as gelling system with optimized concentric range. They concluded the formulation prepared was able to provide better deposition, distribution and residency properties.

J.Balasubramaniam et.al, 2003 studied on Indomethacin as NSAID was developed on the concept of ion activated in situ gelation. Gelrite gum, a novel ophthalmic vehicle which gel s in the presence of mono and divalent cations present in the lacrimal fluid. The formulated system provides sustained release of the drug over 8 hours. The ease of administration coupled with its ability to provide sustained release could probably result in less frequent administration thus enhancing patient compliance.

J.Varshosaz et.al, 2008 studied to increase the low bioavailability and short ocular residence time of ciprofloxacin eye drops, aqueous solutions of drug in Chitosan and Pluronic were prepared to identify suitable composition with regards to gel forming properties and drug release. The membrane less dissolution studies were carried out and release behavior was found till 8 hours.
▸ Witold Musial⁴¹ 2007 studied the effect of various acrylic acid polymers, in composition with methylcellulose on Metronidazole release rate from hydrogels proposed for treatment of acne rosacea. Use of excipient like Carbopol and methylcellulose vealed an increase in viscosity.

▸ Armand B. Pepperman⁴² et.al, 1991 studied on release rates of Metribuzin from various alginates-clay formulations. Several grades and types of sodium alginates when formulated at 1% concentration gave similar release rates of Metribuzin. Author stated that varying the order and manner of mixing ingredient s of the formulation did not improve release rate. The uses of 1% charcoal in place of part of the clay moderate the release of Metribuzin with less than 10% irreversible adsorption.

▸ A.H.El-Kamel⁴³ et.al, 2002 developed Pluronic F 127 based formulation of Timolol Maleate aimed at enhancing its ocular bioavailability. The effect of isotonic agent on PF was carried out and their rheological properties were studied. TM formulation containing 3%methylcellose and low concentration of PF127 showed potential for use as delivery system with improved ocular bioavailability.

▸ Yanxia Cao⁴⁴ et.al, 2007 observed that a novel copolymer was formulated, poly (N-isopropylacrylamide)-Chitosan (PNIPAAm-CS) was investigated for its thermosensitive in situ gel forming properties and potential utilization for ocular delivery. Low critical solution temperature was determined by the cloud point method. The copolymer had a LCST of 32⁰c which is close to eye temperature according to author. The copolymer had little cytotoxicity of PNIPAAm-CS copolymer.

▸ Kouji Nakamura⁴⁵ et.al, 1999 studied and investigate the uptake and release kinetics of Budesonide from P (MAA-g-EG) invitro as well as the pharmacokinetic following nasal administration of the copolymer contained Budesonide. The copolymer exhibit pH and mucoadhesive properties. The drug release from the rug added polymer exhibit classical fickian kinetics showing an initial burst.

▸ Sandeep Kumar⁴⁶ et.al, 1995 the study was to use an aqueous solution containing a viscosity enhancing polymer. The rheological characterization and invitro TM release profile demonstrates the HPMC-PAA solutions have suitable properties as in situ gelling drug delivery system.
➤ **Tanaji Nandgude** et al., 2008 prepared nasal solution of Salbutamol sulphate was prepared for sustained its release and improving its bioavailability. Carbopol was used as a key ingredient to affect pH induced sol to gel conversion of the formulation. The rheological properties were determined and drug release was determined. The final formulation was optimized with specific concentration of Carbopol 934 and HPMC showed pH induced sol-gel conversion, sustained release and higher bioavailability.

➤ **Yeshwant D. Sanzgiri** et al., 1993 they studied on MP ester of Gellan seems to present a suitable means of sustained MP delivery to the eye as well as a model for ophthalmic application of other polymeric prodrugs. The prepared Gellan eye drops seem to provide a simple and effective way to improve on conventional therapy using ophthalmic solutions and suspensions.