3. NEED AND OBJECTIVE

Drug carrier can be defined as the administration of drug from natural or synthetic origin, in order to control the \textit{in vivo} availability of drug molecules for pharmacological effects. After the application of dosage, usually a small amount remains available to the sites of interest and major fraction to the unwanted sites giving side effects. Development of drug carrier intended to reach tissues to utilize maximally giving minimum side effects. Drug carrier systems are become more difficult because of the, arrival of low-molecular-weight molecules. Also emergence of bio-macromolecules with poor aq. solubility; tissue permeation and increased use of bio-materials with less understanding of physical properties all limit research in drug carrier systems. Controlled delivery to the eye of drugs is limited by effective protective mechanisms offering by corneal tissues. Good penetration is prerequisite for absorption of drugs to the eyes and more contact time. One of the way of optimization of drug carrier system to eye is by improving precorneal drug retention. To optimize drug carrier, the various characteristics are required such as, good precorneal penetration, improved contact time, ease of instillation, non-irritative and comfortable form and optimum viscosity.

An ultimate ocular carrier system would be designed as in the form of drops with no blurred vision/irritation. This would need one to three applications a day. The usefulness to patient is simplicity, a reduced frequency of instillation, minimum toxicity and untoward effects. Still existing most carrier systems are, “superficially primitive and less effective” However, one of the most facilitating and difficult target facing by the researchers is drug delivery to eye.
The present investigation involves formulation development of the IS hydrogel of FQ and BCS Class I drugs, to increase residence and bioavailability. Different gelling systems viz. pH sensitive, ion sensitive and temperature sensitive are used. To develop the ISG ophthalmic solutions of FQ drugs viz. LFX, OFX and NFX, equivalent to 0.5%, 0.3% and 0.3% w/v respectively.

- **Phase transition based on temperature:** Combinations of PXM 407 and PXM 188 which undergoes transition from liquid to gel at eye temperature (33-34°C) were selected to form ISG ophthalmic solutions with the aid of mucoadhesive polymer, HPMC K4M and chitosan as a penetration enhancer.

- **Phase transition based on ion:** Alginates and gellan gum are known to undergo transition from liquid to gel in presence of cations in tear fluid (Ca$^{2+}$, Na$^+$), hence selected to form ISG ophthalmic solutions with the aid of mucoadhesive polymers.

- **Phase transition based on pH:** CP are known to undergo transition from liquid to gel in the presence of higher pH of tear fluid, hence were selected to form ISG ophthalmic solutions with the aid of mucoadhesive polymer, HPMC K4M. CP 974P was used as it is a benzene free grade of CP.

  ➤ Evaluation of developed ISG formulations for appearance, clarity, gelation temperature, gelling capacity, pH, drug content, *in vitro* drug release, transcorneal permeation study, mucoadhesion, antimicrobial efficacy and isotonicity.

  ➤ Further, evaluation of optimized formulations for ocular irritation, ocular pharmacokinetic study, precorneal clearance study using gamma scintigraphy using rabbit as animal model and stability study.
3.1 PLAN OF WORK

I) Literature survey

II) Collection of drug, polymers and other excipients

III) Preformulation studies
   - Characterization of drugs and polymers
   - Selection of vehicle
   - Formulation developments

IV) Evaluation
   ✓ Appearance and clarity
   ✓ pH
   ✓ Gelation temperature
   ✓ Gelling capacity
   ✓ Drug content
   ✓ Mucoadhesion test
   ✓ *In vitro* drug release studies
   ✓ Rheological behavior
   ✓ Transcorneal penetration studies
   ✓ Drug polymer interaction studies
   ✓ Antimicrobial efficacy studies
   ✓ Isotonicity
   ✓ Precorneal clearance study using gamma scintigraphy
   ✓ Ocular irritation studies
   ✓ Ocular pharmacokinetic study by HPLC
   ✓ Stability studies