3 CHAPTER 3: AIM, OBJECTIVES & RATIONALE

3.1 RATIONALE

Bacterial conjunctivitis and keratitis are common ocular infections and are mainly caused bacteria such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae* and Coagulase negative *Staphylococci*. Topical antibiotic eye drops are most preferred route of administration. These drops are capable of achieving high tissue levels. However, this route has limitation of frequent dosing usually every half an hour for the first 24 – 36 h. Among topic antibiotics, fluoroquinolones (specifically fourth generation fluoroquinolones) are treatment of choice in both bacterial keratitis & conjunctivitis. It use and effectiveness has been validated by multiple studies.

The medication frequency depends upon the severity of infection. It is usual to start half-hourly drops all through 24 h for most patients. A loading dose of a drop every 5 min for the first 30 min is used in severe ulcers [Bacterial Keratitis: Preferred Practice Pattern, 2018.]. Hence, there has always been focus in reducing dosing frequency and increasing patient compliance, sustained release ocular formulation that provides increased pre-corneal residence time, improved permeability and intra-stromal bioavailability.

Extended release approved formulations in US Besivance® and Moxeza® (US brands) have targeted precorneal residence time using xanthan gum & polycarbophil gel (table 12). However, literature search have shown improved permeability of Moxifloxacin utilizing nano systems.

**Table 12: Commercial extended release formulation**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Indication</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moxeza (Moxifloxacin Hydrochloride)</td>
<td>Ophthalmic</td>
<td>A Xanthan gum base formulation to be instilled in the affected eye(s) 2 times daily for 7 days.</td>
<td>Bacterial conjunctivitis</td>
</tr>
<tr>
<td>Besivance (Besifloxacin Hydrochloride)</td>
<td>Ophthalmic</td>
<td>A Polycarbophil base formulation to be instilled in the affected eye(s) 3 times a day, four to twelve h apart for 7 days</td>
<td>Bacterial conjunctivitis</td>
</tr>
</tbody>
</table>
SLNs delivery systems have been successfully used in other fluoroquinolones such as levofloxacin, ofloxacin and gatifloxacin by researchers [Baig et al, 2016; Ustündağ-Okur et al, 2014; AbulKalam et al, 2013 a&b].

3.2 AIM

Aim of present work is

- Sustained release ocular formulation that provides increased pre-corneal residence time, improved permeability and thereby pharmacodynamic effectiveness in bacterial keratitis & bacterial conjunctivitis rabbit animal model.

- Use on SLNs as probable delivery system for drug in combination with in-situ gel system. Also, impact of each formulation and process components shall be studied in designing such formulation systems.

3.3 OBJECTIVE

The objective of study includes

I. Development of a sustained release ocular delivery of fluoroquinolones that provides extended delivery of drug into the aqueous humour for longer period of time as well maintain therapeutic concentration throughout the dosing regimen.

II. Evaluation of formulation strategy as per QbD principle for optimization of formulation and process components.

III. Establishing the performance of selected formulation based on in vitro characterization in Pharmacodynamic model.