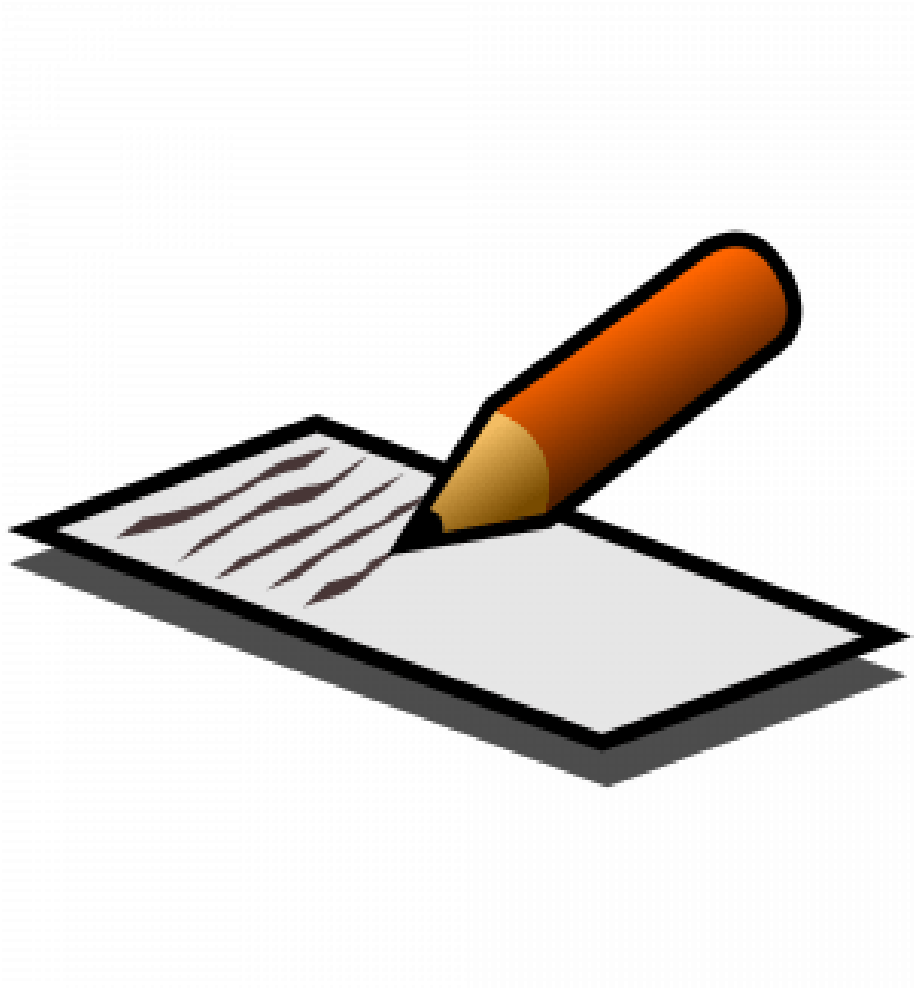
CHAPTER 6

CONCLUSIONS AND FUTURE PROSPECTS



- Conclusions
- Future prospects

6.1. Conclusions

Advantages of topical therapy over phototherapy and systemic therapy are well established. The marketed products available as OTC products are conventional preparations (gels, creams, ointments, etc.) that exhibits lower efficacy and cause local toxicity due to rapid loco-regional drug release and systemic toxicity as a result of systemic leaching of the drug. In order to address these challenges, the focus has been switched to nanotherapeutics. There are several reports claiming that nano-carriers are preferred for their promising delivery of therapeutic agents to localized skin surface due to their smaller size, greater permeation through biological barriers, better surface properties, high skin deposition and sustained drug release properties, they were able to prove advantageous in treating psoriasis. These nano-systems include both lipidic and polymeric nano-carriers. These nano-systems offer many benefits over conventional delivery systems as discussed abovehowever certain disadvantages are also associated with these systems. Lipidic nano-systems are associated with the limitations including burst release, limited opportunities for chemical modifications, instability and high polydispersity index, drug partitioning, drug expulsion, etc. Polymeric nano-systems are associated with disadvantages such as lower drug entrapment, multiple steps that are involved in the preparation method, use of large quantities of organic solvents, scalability and cost of manufacturing.

In order to get benefits of both systems, lipid-polymer hybrid nano-systems have been developed that combines advantages of both lipidic and polymeric nano-carriers resulting into good drug loading capacities, a more controlled drug release, improved cellular uptake and biocompatibility avoiding the disadvantages associated with them. The present research work disclosed development of a scalable monolithic lipid-polymer hybrid nano-carrier based platform

technology for delivering several hydrophobic small molecules including clobetasol propionate, cholecalciferol (Vitamin D) and coenzyme Q10 for treating imiquimod (IMQ) induced psoriasis in *Swiss albino* mice. These LPNs consisted of a solid lipid, liquid lipid and an amphiphilic copolymer, mPEG-PLA. The method of preparation adopted for fabricating these hybrid systems is very simple and could be easily scaled-up at commercial levels as it has employed High Pressure Homogenizer. The LPNs loaded with all the three drug molecules exhibited spherical morphology demonstrating a sustained drug release profile. Further, the nanoparticle loaded gels were stable at 2-8 °C and room temperature for 6 months with no burst effect. *In vitro* assays on HaCaT cells showed significantly higher uptake of LPNs involving lipid-raft mediated and caveole mediated endocytic uptake mechanism with improved cytotoxicity, apoptosis and cell cycle arrest. Further, LPNs penetrated into deeper layers of skin, showed no systemic leaching and enhanced efficacy in IMQ-induced psoriasis-like skin condition in Swiss albino mice. Enhanced efficacy was proved by markedly improved PASI parameters thoroughly supported by histopathology and immunohistochemistry. For all the three drug molecules, their resulting nano-formulation proved therapeutic efficacy at half strength in comparision to their respective conventional gels (reference products) at full strengths demonstrating successful dose reduction. These LPNs could serve as a platform for delivering various hydrophobic potent molecules for skin diseases including cancer, eczema, acne, skin infections, etc and could be translated for clinical evaluation and commercial application.

6.2. Future prospects

In the present work, we have developed scalable monolithic lipid-polymer hybrid nano-carriers for delivering various hydrophobic molecules (such as clobetasol propionate,

cholecalciferol and coenzyme Q10) for ameliorating psoriatic inflammation. There are several facets of the developed formulations and nano-platform that could be investigated in the future to facilitate their clinical translation.

- These developed nano-formulations could be further scale-up using HPH for clinical translation
- Apart from the above-mentioned drug molecules, other potent hydrophobic drugs could be loaded in this platform and could be explored for their anti-psoriatic potential.
- These monolithic LPH nano-systems could be explored for treating several dermal problems e.g. cancer, eczema, acne, skin infections.
- Apart from the treating dermatological problems, these nano-systems could be further explored for cosmetic applications owing to their features of deeper dermal penetration.
- These nano-carriers could also be modified with targeting groups on the hydrophilic block i.e. polyethylene glycol and could be used for active targeting of therapeutic agents.
- The surface chemistry of the nano-hybrid vehicles could be modified for delivering proteins, peptides and oligonucleotides.