CHAPTER VI. CONCLUDING REMARKS

The main interest of the investigations gathered here was in pursuit of developing a topical dosage form of a suitable antivitiligo agent. As many as 65 million world population suffers from this skin disease. In Vitiligo, white blood cells attack and destroy pigment cells in discrete areas of the skin. It is called an auto-immune disorder, because the pigment cells become regarded by the body as "foreign" and are therefore rejected. Attempts in classifying Vitiligo has two approaches. In one approach Vitiligo is classified as segmental Vitiligo and non-segmental Vitiligo. Yet another approach three types are identified i.e., localized, generalized and universal Vitiligo. Localized Vitiligo is further classified into focal and segmental : generalized into acrofacial , vulgaris and mixed subtypes. When it is understood that, the conventional treatments were followed by several unwanted but unavoidable side effects, a group of scientists had a ground breaking discovery that piperine an alkaloid extracted from *Piper nigrum* (black pepper) could regenerate pigmental cells, melanin which is responsible for the skin and hair colour. According to them piperine was found not only to stimulate the replication of melanocytes but also induces the formation of melanocytes dendrites.

Here piperine was considered as the payload drug. Thus pilot scale extraction and isolation of piperine by soxhlation and refluxation method were done and the former method gave comparatively better yield. Standardization of pepper and piperine were done and the later was compared with the commercial piperine. Since the results were very much comparable, for scale up soxhlation was considered.

For achieving the aim, development of conventional and non conventional dosage forms were taken into consideration. To meet the large quantity of dosage forms and consistency modified diffusion cell and consistency tester were designed and fabricated. The optimization of the formulation was done based on the ability of the formulation to tailor the drug in the dermal region were melanocytes are located. Under conventional formulations ointment and cream was considered and under novel dosage forms phytosomes, transfersomes and cubical nano particles. Ointment because of the occlusive nature drug was not sufficiently penetrating the stratum corneum, even in presence of urea employed as
penetration enhancer. Cream gave a much better tissue bioavailability. In both cases the drug was compatible with the excipients.

Pharmacological studies revealed that the group which was subjected to the topical cream therapy was found to commence repigmentation within 59 days and the group subjected to cream and UV therapy was found to repigment by three weeks but repigmentation was spotted scatter (patchy) type whereas in the former group it was found to be homogenous. Almost complete pigmentation was achieved for the first and second group towards 59 and 50 days respectively.

Phytosomes were considered because of its unique ability of bonding together with the phyto- constituent as its integral part. Such a complex is obtained by reaction of stoichiometric amounts of phospholipid and the substrate in an appropriate solvent. Phytosomal cream was prepared and slight increase in the tissue retention of piperine in the dermis when compared to cream was observed.

In transfersomes, retention and was observed with span 80 incorporated transfersomes which also showed more entrapment efficiency compared to its comparable tween 80 formulation. This was observed when span 80 (TS1) was used and when phosphatidyl choline concentration was kept low. Under external pressure the vesicles were able to extrude through a pore size lower than its size and regain its shape. This indicates the ultraflexible nature of the vesicles which truly deserve the term “transfersomes”. The kinetics, efficiency and the transfersome mediated transport can be tailored for trans-epidermal, deep tissues and systemic depending on the vesicular composition, dose and form.

To enhance the tissue piperine bioavailability the work was further explored in the fabrication of nano sized cubosomes and appraised. TEM pictures proved cubosomes its nano size and drug quantification palpably proved the maximum drug targeting in the dermis with minimal buffer diffusion and unpenetration. Thus it has to be suggested that cubosomes drug: GMO was 1:1 and poloxamer 407 when kept at 9% with respect to drug-GMO was able to tailor the drug maximum at the dermal region when compared to other intra and inter formulation variables awarding this as the optimised formulation.

The fascinating insights can be comprehensively compared for all formulations as tissue drug concentration, drug diffused into the buffer and that left unpenetrated on the dorsal surface of the skin. The main challenge of the aim was that the drug must penetrate the
tough Stratum corneum, but rather without getting down into the blood stream and undergo sink conditions, the drug must retain in the deep dermal layers.

Summarizing the tissue drug bioavailability for each optimized formulations, drug tailored in the dermal region was in the descending order: ointment > cream > phytosomes > transfersomes > cubosomes.

Drug quantification from each optimized formulations diffused into the buffer was phytosomes > transfersomes > cream > ointment > cubosomes.

Drug left over the dorsal skin surface of each optimized formulation in the descending order was ointment > cream > phytosomes > cubosomes > transfersomes.

Out of all formulations cubosomes were shown the maximum dermal drug tailoring when compared to transfersomes, phytosomes, cream and ointment. It can be concluded that the kinetics, efficiency and the derug transport can be tailored for trans-epidermal, deep tissues and systemic depending on the formulation composition, dose and form. It has to be added that the fabricated students diffusion cell and consistency tester.

The story of a simple pepper to the world of nanotechnology was truly sensational indeed!