LIST OF FIGURES

Figure 1: Life style, richness and sex don’t have anything to do with Vitiligo ...(14)

Figure 2: Schematic representation of melanogenic pathway showing major intermediates and enzymes (tyrosinase and tyrocinase related proteins, TRP1, TRP2) involved in the biogenesis of melanin) ... (20)

Figure 3: Flow chart illustrating neurochemical melanocytic degradation leading to vitiligo due to accumulation of norepinephrine, defective recycling of 6BH4, concomitant release of \( \text{H}_2\text{O}_2 \) along with other factors... (21)

Figure 4: Cross section of skin demonstrating various anatomical features... (27)

Figure 5: Various mechanisms proposed in material transport across the skin membrane... (32)

Figure 6: Thermodynamic cycle of micelle formation. The process of assembling \( n \) separated amphiphiles (a) to a micelle (d) can be performed in three steps: (1) Creating a cavity in the solvent (light gray) (b); (2) Transferring the hydrophobic chains (dark gray) from the aqueous solution into the cavity (c); (3) Distributing the polar units (gray) over the surface of the cavity and reconnecting them to the hydrophobic groups (d)... (43)

Figure 7: Representation of typical geometry for a vesicle formation, \( P = V/\alpha_0 I_c \)

Figure 8: A) \( P= 1/3 \), micelle formation B) \( P =1/ 2 \), cylindrical micelle C) \( P= 1 \), planar bilayer D) \( P > 1 \), inverted micelle... (44)

Figure 9: Structural representation of one transfersome unit... (45)

Figure 10: The wide spectra of established “Somes”: (A) Organization of the Phytosome molecular complex (B) Colloidosomes (C) Ethosomes (D) Cubosomes (E) Liposomes (F) Niosomes (G) Differentiation of Phytosome and Liposome... (51)

Figure 11: Hypothetical structure of cubosome... (64)

Figure 12: Theoretical diagram explaining the core of cubosomes lodging the drug... (66)

Figure 13: Representation of nodal surface variations in cubosomes... (67)
Figure 14: Schematic diagram of preparation methods for cubosomes–Top- down approach...(70)

Figure 15: Schematic diagram of preparation methods for cubosomes - Bottom- up approach...(71)

Figure 16: (A) Pepper before ripening (B) High resolution picture of Peppercorn (C) Black and white peppercorns...(74)

Figure 17: From left to right: ripened pepper, green pepper, white pepper, powdered pepper...(75)

Figure 18: Molecular Structure of Piperine…(82)

Figure 19: Molecular structure of Phosphotidyl choline...(84)

Figure 20: Molecular structure of glyceryl monooleate...(85)

Figure 21: chemical structure of polaxamer 407...(86)

Figure 22: Molecular structure of acrilic acid monomer in carbomer resin...(87)

Figure 23: Indigenously designed (left) and fabricated (right) Students diffusion cell (SDC-1T09) in its final shape...(93)

Figure 24: Indigenously designed (left) fabricated (right) Consistency tester CT1-10 in its final shape...(95)

Figure 25: Standard calibration curves for Piperine at $\lambda_{max}$ 344nm in ethanol, (left) and right (buffer pH 6.6) n=6…(102)

Figure 26: Beautiful golden yellow needle shaped (acicular) piperine crystals...(103)

Figure 27: TLC of Piperine in UV chamber viewed at 254nm: Solvent front (SF), distance travelled by spot (DT), point of application of spot (PA)...(105)

Figure 28: Histogram of particle size distribution of Piperine crystals...(106)

Figure 29: Absorption maximum of Piperine...(108)

Figure 30: FTIR Spectra of Piperine...(109)
**Figure 31:** X-ray Diffractograms of Piperine powder before and after sonication...(110)

**Figure 32:** SEM studies on piperine crystals before (L) and after (R) sonication. The reduction in size and unorganized morphology in the later is evident...(111)

**Figure 33:** Flow chart demonstrating pharmacological studies of the optimised conventional dosage form for Vitiligo...(116)

**Figure 34:** SEM of cream (left) and phase contrast microphotograph (200X) of ointment (right)...(118)

**Figure 35:** Drug diffusion profile from cream and ointment with and without urea into buffer pH6.6 which was detected at 344 nm...(118)

**Figure 36:** Microscopic pictures of Globules as a part of stability studies at 1st week (A) 2nd week (B) 3rd week (C) 4th week (D)...(119)

**Figure 37:** TLC of piperine alone and the formulated cream when observed under UV. Spots are showing similar Rf value which suggests drug is intact in the formulation...(120)

**Figure 38:** Skin irritation test of optimised formulation on rabbits...(122)

**Figure 39:** Chronological arrangement of pictorial representation of New Zealand (OB) brown rabbits subjected to antivitiligo experimental therapy by piperine-cubosomal hydrogel. The animal groups were G1 (control), G2 (treatment with piperine-cubosomal hydrogel), G3 (UVR + treatment with piperine-cubosomal hydrogel). Defoliation followed by follicular depigmentation (bleaching) was observed in 35 days while recovery period of antivitiligo activity was observed in almost 60 days...(124)

**Figure 40:** Flow chart representing fabrication of phytosomes which was incorporated into cream...(126)

**Figure 41:** FTIR reports: (a) piperine (b) phosphatidyl choline (c) physical mixture (d) complex ...(129)

**Figure 42:** SEM pictures of (a) piperine crystals (b) piperine after sonication (c) phosphatidyl choline (d) piperine – phosphatidyl choline complex (e) Digital microphotograph piperine-phospholipid complex...(132)
Figure 43: Cumulative drug release profile of piperine from phytosomal cream formulations (P1, P2, P3) diffused into buffer solution of pH6.6 detected at 344 nm...(134)

Figure 44: Plots of log % drug concentration V_s time for different temperatures...(135)

Figure 45: Plot of log k V_s 1 / T to determine k at T25°C...(136)

Figure 46: Design of Indigenously fabricated diffusion cell for collecting large sample volume (A) separating pig skin from ear pinna cartilage (B)...(139)

Figure 47: FTIR Spectra of pure drug piperine (A) and PM of piperine + phosphatidyl choline (B)...(141)

Figure 48: Phase contrast photomicrographs taken by camera Lucida of transfersomes with (a) before and (b) after filtration under external pressure...(142)

Figure 49: TEM picture (L) and SEM (R) of transfersomes which shows flexible nature (A) while squeezing through the membrane and regains the shape (B)...(143)

Figure 50: representation of vesicular size and entrapment efficiency of transfersomes...(143)

Figure 51: Drug diffusion profile into buffer pH 6.6 from transfersomes of different variables- TT1 ( ) TT2 ( ) TT3 ( ) TS1 ( ) TS2 ( ) TS3...(144)

Figure 52: Flow chart describing the procedure of fabricating cubosomes...(147)

Figure 53: Hypothetical diagram demonstrating the part of the skin and the technique employed...(151)

Figure 54: Hypothetical diagram exhibiting CAM and ISM...(152)

Figure 55: Rabbits who have to be exposed to UVR were offered new special dress which protected them especially their eyes...(153)

Figure 56: FTIR of pure drug (A) and its physical mixture with GMO (B), Poloxamer 407 (C) and (D)...(156)

Figure 57: TEM pictures of cubosome samples taken during its manufacture before agitation and at 5min, 10min and 15 min of sonication (please consider the flow chart of preparation).
Before and after sonication it is clearly evident that the particles not only reduced its size but also are almost homogenous...(157)

**Figure 58:** Cumulative percentage drug release from cubosomes into buffer pH 6.6 detected at 344 nm...(158)

**Figure 59:** Encapsulation efficiency of cubosomes-C1,C2,C3...(159)

**Figure 60:** Pie diagram representing tissue drug bioavailability report of cubosomes incorporated hydrogels C1,C2,C3 and drug alone in hydrogel...(159)

**Figure 61:** Clockwise from top left: (A) Micropipette loaded with the formulation being introduced through the keyhole window. (B) Carefully, the formulation is instilling over the CAM. (C) Keyhole being sealed (D) after 24 hrs the window was opened, it is evident that there was robust proliferation of blood capillaries but no atypical growth...(160)

**Figure 62:** Chronological arrangement of pictorial representation of New Zealand (OB) black rabbits subjected to antivitiligo experimental therapy by piperine-cubosomal hydrogel. The animal groups were G1( control ), G2 (treatment with piperine-cubosomal hydrogel ), G3 ( UVR + treatment with piperine-cubosomal hydrogel ). Defoliation followed by follicular depigmentation (bleaching) was observed in 60 days while recovery period of antivitiligo activity was observed in almost 90 days...(162)

**Figure 63:** Confocal images of excised pig skin tissue taken at excitation, 543 nm; emission: 592 nm by using rodoxine dye taken at periodical time intervals. (A) untreated skin (B) 1 h after treatment (C) 3 h (D) 6 h: SC-stratum corneum, DE-dermis, AB-air bubble, CU-cubosomes, HF-hair follicle...(163)

**Figure 64:** DSC thermograms of formulation treated (T) and untreated (UT) pig skin epidermis...(164)

**Figure 65:** Multicompartment skin irritation for all cubosomes C1-C3 (test) and C0 (placebo) to check irritation if any is because of API or excipients. It is evident that during the period of 72 h the study there is no irritation...(165)