

LIST OF FIGURES

| Sr. No. | Titles | Page No. |
|--|---|----------|
| Chapter 2: Literature Review | | |
| Fig. 2.1 | Pathogenesis of psoriasis | 16 |
| Fig. 2.2 | Types of psoriasis | 18 |
| Fig. 2.3 | Clinical symptoms of Atopic dermatitis | 19 |
| Fig. 2.4 | Pathophysiology of Atopic Dermatitis | 20 |
| Fig. 2.5 | Conventional topical treatments available for Atopic dermatitis | 21 |
| Fig. 2.6 | Different mechanism of actions of Antimicrobial Peptides | 23 |
| Fig. 2.7 | Structure of Omiganan | 24 |
| Fig. 2.8 | Various vital factors which affect the percutaneous absorption of drugs | 28 |
| Fig. 2.9 | Several permeation enhancement techniques employed for drug delivery | 29 |
| Fig. 2.10 | Conventional drug delivery systems used for topical delivery | 30 |
| Fig. 2.11 | Nano-carriers based drug delivery systems for dermal route | 31 |
| Chapter 3: Analytical Method | | |
| Fig. 3.1 | Typical HPLC chromatogram of Omiganan (3 µg/ml) | 57 |
| Fig. 3.2 | Overlay plot of Omiganan by HPLC method | 58 |
| Fig. 3.3 | Calibration plot of Omiganan by HPLC method | 58 |
| Fig. 3.4 | Typical HPLC chromatogram of DPK-060 (1 µg/ml) | 61 |
| Fig. 3.5 | Overlay plot of DPK-060 by HPLC method | 61 |
| Fig. 3.6 | Calibration plot of DPK-060 by HPLC method | 62 |
| Chapter 4: Preformulation study | | |
| Fig. 4.1 | Mass spectra of Omiganan | 70 |
| Fig. 4.2 | Mass spectra of DPK-060 | 70 |
| Fig. 4.3 | Solubility of Omiganan in various excipients | 71 |
| Fig. 4.4 | Solubility of DPK-060 in various excipients | 72 |
| Fig. 4.5 | FT-IR spectra of Omiganan | 73 |

| | | |
|--|---|----|
| Fig. 4.6 | FT-IR spectra of Omiganan + lipids mixture (for liposomes) | 73 |
| Fig. 4.7 | FT-IR spectra of Omiganan + lipids mixture (for NLCs) | 74 |
| Fig. 4.8 | FT-IR spectra of Omiganan and lipids mixture (for lotion) | 74 |
| Fig. 4.9 | FT-IR spectra of DPK-060 | 75 |
| Fig. 4.10 | FT-IR spectra of DPK-060 + lipids mixture (NLCs) | 75 |
| Fig. 4.11 | FT-IR spectra of DPK-060 and lipids mixture (for lotion) | 76 |
| Chapter 5A) Formulation Development: Omiganan Nano-lipid Constructs | | |
| Fig. 5A.1 | Ishikawa diagram showing probable variables that may influence CQA | 85 |
| Fig. 5A.2 | Actual v/s Predicted plot for % Drug entrapment | 88 |
| Fig. 5A.3 | Contour plot (2D) showing the combined effect of lipid concentration and homogenization cycles on % drug entrapment | 90 |
| Fig. 5A.4 | Contour plot (2D) showing the combined effect of lipid concentration and Smix concentration on % drug entrapment | 91 |
| Fig. 5A.5 | Contour plot (2D) showing the combined effect of Smix concentration and Homogenization cycles on % drug entrapment | 91 |
| Fig. 5A.6 | Response surface (3D) showing the combined effect of lipid concentration and Homogenization cycles on % drug entrapment | 92 |
| Fig. 5A.7 | Response surface (3D) showing the combined effect of lipid concentration and Smix concentration on % drug entrapment | 92 |
| Fig. 5A.8 | Response surface (3D) showing the combined effect of Smix concentration and Homogenization cycles on % drug entrapment | 93 |
| Fig. 5A.9 | Actual v/s Predicted plot for Particle size | 95 |
| Fig. 5A.10 | Contour plot (2D) showing the combined effect of lipid concentration and Homogenization cycles on Particle size | 97 |

| | | |
|--|---|-----|
| Fig. 5A.11 | Contour plot (2D) showing the combined effect of lipid concentration and Smix concentration on Particle size | 97 |
| Fig. 5A.12 | Contour plot (2D) showing the combined effect of Smix concentration and Homogenization cycles on Particle size | 98 |
| Fig. 5A.13 | Response surface (3D) showing the combined effect of lipid concentration and Homogenization cycles on Particle size | 98 |
| Fig. 5A.14 | Response surface (3D) showing the combined effect of lipid concentration and Smix concentration on Particle size | 99 |
| Fig. 5A.15 | Response surface (3D) showing the combined effect of Smix concentration and Homogenization cycles on Particle size | 99 |
| Fig. 5A.16 | Desirability plot | 100 |
| Fig. 5A.17 | Overlay plot | 102 |
| Fig. 5A.18 | Zeta potential of the developed Omiganan nano-lipid constructs | 103 |
| Fig. 5A.19 | SEM image of the developed Omiganan loaded nano-lipid | 104 |
| Fig. 5A.20 | Particle size of the optimized Omiganan nano-lipid constructs | 104 |
| Chapter 5B) Formulation Development: Omiganan Liposomes | | |
| Fig. 5B.1 | Ishikawa diagram showing probable variables that may influence CQA | 116 |
| Fig. 5B.2 | Actual v/s Predicted plot for % Drug entrapment | 120 |
| Fig. 5B.3 | Contour plot (2D) showing the combined effect of lipid concentration and sonication amplitude on % drug entrapment | 122 |
| Fig. 5B.4 | Contour plot (2D) showing the combined effect of lipid concentration and sonication time on % drug entrapment | 122 |
| Fig. 5B.5 | Contour plot (2D) showing the combined effect of sonication time and sonication amplitude on % drug entrapment | 123 |

| | | |
|---|--|-----|
| Fig. 5B.6 | Response surface (3D) showing the combined effect of lipid concentration and sonication amplitude on % drug entrapment | 123 |
| Fig. 5B.7 | Response surface (3D) showing the combined effect of lipid concentration and sonication time on % drug entrapment | 124 |
| Fig. 5B.8 | Response surface (3D) showing the combined effect of sonication time and sonication amplitude on % drug entrapment | 124 |
| Fig. 5B.9 | Actual v/s Predicted plot for vesicle size | 126 |
| Fig. 5B.10 | Contour plot (2D) showing the combined effect of lipid concentration and sonication amplitude on vesicle size | 128 |
| Fig. 5B.11 | Contour plot (2D) showing the combined effect of lipid concentration and sonication time on vesicle size | 129 |
| Fig. 5B.12 | Contour plot (2D) showing the combined effect of sonication time and sonication amplitude on vesicle size | 129 |
| Fig. 5B.13 | Response surface (3D) showing the combined effect of lipid concentration and sonication amplitude on vesicle size | 130 |
| Fig. 5B.14 | Response surface (3D) showing the combined effect of lipid concentration and sonication time on vesicle size | 130 |
| Fig. 5B.15 | Response surface (3D) showing the combined effect of sonication time and sonication amplitude on vesicle size | 131 |
| Fig. 5B.16 | Desirability plot | 132 |
| Fig. 5B.17 | Overlay plot | 134 |
| Fig. 5B.18 | Zeta potential of the developed Omiganan liposomes | 135 |
| Fig. 5B.19 | Cryo-TEM images of the developed Omiganan loaded liposomes | 136 |
| Fig. 5B.20 | Vesicle size of the optimized Omiganan liposomes | 136 |
| Chapter 6A) Formulation Development: DPK-060 Nano-lipid Constructs | | |
| Fig. 6A.1 | Ishikawa diagram showing probable variables that may influence CQA | 153 |

| | | |
|------------|--|-----|
| Fig. 6A.2 | Actual v/s Predicted plot for % Drug entrapment | 156 |
| Fig. 6A.3 | Contour plot (2D) showing the combined effect of lipid concentration and homogenization cycles on % drug entrapment | 158 |
| Fig. 6A.4 | Contour plot (2D) showing the combined effect of lipid concentration and Surfactant concentration on % drug entrapment | 159 |
| Fig. 6A.5 | Contour plot (2D) showing the combined effect of Surfactant concentration and Homogenization cycles on % drug entrapment | 159 |
| Fig. 6A.6 | Response surface (3D) showing the combined effect of lipid concentration and Homogenization cycles on % drug entrapment | 160 |
| Fig. 6A.7 | Response surface (3D) showing the combined effect of lipid concentration and Surfactant concentration on % drug entrapment | 160 |
| Fig. 6A.8 | Response surface (3D) showing the combined effect of Surfactant concentration and Homogenization cycles on % drug entrapment | 161 |
| Fig. 6A.9 | Actual v/s Predicted plot for Particle size | 163 |
| Fig. 6A.10 | Contour plot (2D) showing the combined effect of lipid concentration and Homogenization cycles on Particle size | 165 |
| Fig. 6A.11 | Contour plot (2D) showing the combined effect of lipid concentration and Surfactant concentration on Particle size | 165 |
| Fig. 6A.12 | Contour plot (2D) showing the combined effect of Surfactant concentration and Homogenization cycles on Particle size | 166 |
| Fig. 6A.13 | Response surface (3D) showing the combined effect of lipid concentration and Homogenization cycles on Particle size | 166 |
| Fig. 6A.14 | Response surface (3D) showing the combined effect of lipid concentration and Surfactant concentration on Particle | 167 |

| | | |
|---|--|-----|
| | size | |
| Fig. 6A.15 | Response surface (3D) showing the combined effect of Surfactant concentration and Homogenization cycles on Particle size | 167 |
| Fig. 6A.16 | Desirability plot | 169 |
| Fig. 6A.17 | Overlay plot | 171 |
| Fig. 6A.18 | Zeta potential of the developed DPK-060 nano-lipid constructs | 172 |
| Fig. 6A.19 | SEM image of the developed DPK-060 loaded nano-lipid constructs | 173 |
| Fig. 6A.20 | Particle size of the optimized DPK-060 nano-lipid constructs | 173 |
| Chapter 7 <i>In-vitro</i> and <i>ex-vivo</i> studies | | |
| Fig. 7.1 | <i>In-vitro</i> drug release profiles of Omiganan loaded formulations | 191 |
| Fig. 7.2 | <i>In-vitro</i> drug release profiles of DPK 060 loaded formulations | 191 |
| Fig. 7.3 | <i>In-vitro</i> cell viability data for Omiganan formulations in 3T3-fibroblast cells | 195 |
| Fig. 7.4 | <i>In vitro</i> cell viability data for DPK-060 formulations in 3T3-fibroblast cells | 195 |
| Fig. 7.5 | <i>In vitro</i> cell uptake of Omiganan formulations in 3T3-fibroblast cells | 197 |
| Fig. 7.6 | <i>In vitro</i> cell uptake of DPK 060 formulations in 3T3-fibroblast cells | 198 |
| Fig. 7.7 | Results of hemocompatibility study of Omiganan & DPK 060 formulations | 200 |
| Fig. 7.8 | Protease degradation assay of Omiganan loaded formulations | 202 |
| Fig. 7.9 | Protease degradation assay of DPK 060 loaded formulations | 202 |

| | | |
|---|---|-----|
| Fig. 7.10 | Fluorescence microscopic images of mice skin sections after 6 h of treatment with Omiganan formulations | 205 |
| Fig. 7.11 | Fluorescence microscopic images of mice skin sections after 6 h of treatment with DPK 060 formulations | 206 |
| Chapter 8 <i>In-vivo</i> studies | | |
| Fig. 8.1 | Imiquimod induced psoriatic animal model development on the back skin and right ear | 216 |
| Fig. 8.2 | Visual analysis of improvement in psoriatic lesions after treatment; A) Normal control, B) Model control (Only Imiquimod), C) Standard control (Betamethasone Dipropionate gel, Betagel), D) Free Omiganan gel, E) Omiganan lotion, F) Omiganan liposomal gel, G) Omiganan NLC gel | 217 |
| Fig. 8.3 A | Erythema score | 218 |
| Fig. 8.3 B | Scaling score | 218 |
| Fig. 8.3 C | Skin thickening score | 219 |
| Fig. 8.3 D | Total PASI score | 219 |
| Fig. 8.4 | % Change in spleen weight | 220 |
| Fig. 8.5 | Visual analysis and comparison of spleen size after treatment; A) Normal control, B-C) Standard control (Betamethasone Dipropionate gel, Betagel), D) Free Omiganan gel, E) Omiganan lotion, F) Omiganan liposomal gel, G) Omiganan NLC gel, H-I) Model control (Only Imiquimod) | 221 |
| Fig. 8.6 | % Change in body weight | 221 |
| Fig. 8.7 | Histopathological images of mice skin for different animal groups; A) Normal control, B) Model control (Only Imiquimod); Blue arrow indicates hyperkeratosis, black arrow indicates acanthosis, orange arrow indicates the presence of inflammatory cells, C) Free Omiganan gel, D) Omiganan lotion, E) Standard control (Betamethasone Dipropionate gel, Betagel), F) Omiganan liposomal gel, G) | 222 |

| | | |
|-----------|--|-----|
| | Omiganan NLC gel | |
| Fig. 8.8 | IL-6 and TNF- α levels for different animal groups after treatment | 223 |
| Fig. 8.9 | Ovalbumin induced eczema animal model development | 224 |
| Fig. 8.10 | Visual analysis of improvement in eczematic lesions after treatment; A) Normal control, B) Model control (Only Ovalbumin), C) Standard control (Betamethasone Dipropionate gel, Betagel), D) Free Omiganan gel, E) Omiganan lotion, F) Omiganan liposomal gel, G) Omiganan NLC gel, H) Free DPK-060 gel, I) DPK-060 lotion, J) DPK-060 NLC gel | 224 |
| Fig. 8.11 | Histopathological images of mice skin for different animal groups; A) Normal control, B) Model control (Only Ovalbumin), C) Free Omiganan gel, D) Omiganan lotion, E) Omiganan Liposomal gel, F) Omiganan NLC gel, G) Standard control (Betamethasone Dipropionate gel, Betagel), H) Free DPK-060 gel, I) DPK-060 lotion, J) DPK-060 NLC gel | 225 |
| Fig. 8.12 | Skin thickness for different animal groups after treatment | 226 |
| Fig. 8.13 | IL-4 levels for different animal groups after treatment | 227 |
| Fig. 8.14 | TNF- α levels for different animal groups after treatment | 227 |
| Fig. 8.15 | IL-6 levels for different animal groups after treatment | 228 |