

List of Table

| | | |
|------------|---|----|
| Table 2.1 | Patented Products of Modafinil | 15 |
| Table 2.2 | Clinical Trial in Dyslexia and ADHD | 20 |
| Table 2.3 | Properties of type I, II, III and IV lipid formulations | 23 |
| Table 2.4 | Marketed formulation of SMEDDS | 30 |
| Table 2.5 | Structural sections of nasal cavity and their impact on permeability | 32 |
| Table 2.6 | Theory of Mucoadhesion | 36 |
| Table 2.7 | List of patented microemulsion product | 43 |
| Table 3.1 | Physico-chemical property of Modafinil | 55 |
| Table 3.2 | Pharmacokinetic Profile of Modafinil | 57 |
| Table 3.3 | Drug-Drug interaction for Modafinil | 58 |
| Table 3.4 | Physico-chemical property of Vinpocetine | 58 |
| Table 3.5 | Pharmacokinetic profile of Vinpocetine | 61 |
| Table 3.6 | Drug-Drug interaction for Vinpocetine | 62 |
| Table 3.7 | Pharmaceutical specification for Clove Oil | 63 |
| Table 3.8 | Pharmaceutical specification for Capmul MCM C8 | 64 |
| Table 3.9 | Pharmaceutical Specification of Tween-80 | 65 |
| Table 3.10 | Pharmaceutical Specification for PEG-400 | 66 |
| Table 3.11 | Pharmaceutical specification for Chitosan | 67 |
| Table 4.1 | List of Material | 71 |
| Table 4.2 | List of Instruments | 71 |
| Table 4.3 | Parameters for RP-HPLC method | 77 |
| Table 4.4 | Absorbance for the calibration plot of Modafinil in ACN: Water (35:65) by (1st order derivative)UV Spectrometer | 80 |
| Table 4.5 | Linearity of method of analysis of Modafinil in ACN: Water (35:65) by UV Spectrometer | 81 |
| Table 4.6 | Accuracy of the UV method for Modafinil | 81 |
| Table 4.7 | Intraday precision analysis of Modafinil estimated by UV method | 81 |
| Table 4.8 | Interday precision analysis of UV method for Modafinil | 81 |
| Table 4.9 | Stability analysis of UV method for Modafinil | 82 |

| | | |
|------------|---|-----|
| Table 4.10 | Area for the Calibration Plot of Modafinil by HPLC | 84 |
| Table 4.11 | Linearity of the calibration plot for Modafinil by HPLC | 84 |
| Table 4.12 | Accuracy of the HPLC method for Modafinil | 85 |
| Table 4.13 | Intraday precision analysis of HPLC method for Modafinil | 85 |
| Table 4.14 | Interday precision analysis of HPLC method for Modafinil | 86 |
| Table 4.15 | Solution Stability analysis of HPLC method for Modafinil | 86 |
| Table 4.16 | Area for the calibration plot of Modafinil by HPLC in Plasma | 88 |
| Table 4.17 | Linearity of the Calibration Plot for Modafinil in Plasma by HPLC | 88 |
| Table 4.18 | List of Material | 89 |
| Table 4.19 | List of Instruments | 89 |
| Table 4.20 | Parameters for HPLC method | 91 |
| Table 4.21 | Absorbance for the calibration plot of Vinpocetine at 314 nm in methanol by UV Spectrometer | 95 |
| Table 4.22 | Linearity of method of analysis of Vinpocetine in methanol by UV | 96 |
| Table 4.23 | Recovery study for accuracy of Vinpocetine estimated by UV method | 96 |
| Table 4.24 | Intraday and Interday precision analysis of Vinpocetine estimated by UV method | 97 |
| Table 4.25 | Stability analysis of UV method for Vinpocetine | 97 |
| Table 4.26 | Absorbance of Vinpocetine at 314 nm in diffusion media | 98 |
| Table 4.27 | Linearity of analytical method of Vinpocetine in diffusion media | 99 |
| Table 4.28 | Calibration plot of Vinpocetine by HPLC | 99 |
| Table 4.29 | Linearity of method of analysis of Vinpocetine by HPLC | 100 |
| Table 4.30 | Accuracy of the HPLC method for Vinpocetine | 101 |
| Table 4.31 | Intraday precision analysis of HPLC method for Vinpocetine | 101 |
| Table 4.32 | Interday precision analysis of HPLC method for Vinpocetine | 101 |
| Table 4.33 | Solution Stability analysis of HPLC method for Vinpocetine | 102 |
| Table 4.34 | Calibration plot of Vinpocetine by HPLC | 103 |
| Table 4.35 | Linearity of method of analysis of Vinpocetine by HPLC | 103 |
| Table 4.36 | Calibration plot of Vinpocetine in plasma by HPLC | 104 |
| Table 4.37 | Linearity of method of analysis of Vinpocetine in Plasmaby HPLC | 104 |

| | | |
|------------|--|-----|
| Table 4.38 | Area for the calibration plot of Vinpocetine in Plasmaby HPLC | 105 |
| Table 4.39 | Linearity of method of analysis of Vinpocetine in Plasma by HPLC | 106 |
| Table 4.40 | Area for the calibration plot of Vinpocetine in Brain Homogenate | 106 |
| Table 4.41 | Linearity of method of analysis of Vinpocetine in Brain Homogenate by HPLC | 107 |
| Table 5.1 | List of Drug and Excipients | 111 |
| Table 5.2 | List of Equipments | 112 |
| Table 5.3 | Variables with Desired Criteria of Dependable variable | 117 |
| Table 5.4 | Characteristic Peaks of FT-IR Spectra of Modafinil | 120 |
| Table 5.5 | Melting Point of Modafinil using Different Methods | 120 |
| Table 5.6 | Solubility of Modafinil in Different Oils | 122 |
| Table 5.7 | Solubility of Modafinil in Different Surfactants | 123 |
| Table 5.8 | Solubility of Modafinil in different Co-surfactants | 124 |
| Table 5.9 | Emulsification Efficiency | 125 |
| Table 5.10 | Drug Loading Capacity in Different Smix/Km Ratio | 128 |
| Table 5.11 | Concentration Range of the Ingredients from Preliminary Trial | 129 |
| Table 5.12 | Levels of Independent factors in Experimental Design | 129 |
| Table 5.13 | D-Optimal Mixture Design for the Optimization of SMEDDS | 130 |
| Table 5.14 | Selection of the Model for Globule Size Analysis (Statistical Analysis) | 131 |
| Table 5.15 | ANOVA Analysis of Experimental Design for Globule Size Analysis | 131 |
| Table 5.16 | ANOVA Study Results for Globule Size Analysis | 132 |
| Table 5.17 | Selection of the model for % Transmittance Analysis (Statistical analysis) | 134 |
| Table 5.18 | ANOVA Analysis of Experimental Design for % Transmittance Analysis | 135 |
| Table 5.19 | ANOVA study Results for % Transmittance Analysis | 136 |
| Table 5.20 | Constraints Applied for Selection of Optimized Batch | 138 |
| Table 5.21 | Formulation Parameters Based On Desirability | 138 |
| Table 5.22 | Suitability of Predicted Desirability Plot for Optimized Formulation | 139 |
| Table 5.23 | Predicted Batch of Analysis for the SMEDDS within Desirable Area | 140 |
| Table 5.24 | Concentration of the Ingredients for Optimized Batch | 140 |

| | | |
|------------|--|-----|
| Table 5.25 | List of Drug and Excipients | 143 |
| Table 5.26 | Variables with Desired Criteria of Dependable variable | 146 |
| Table 5.27 | Characteristic peaks of FT-IR spectra of Vinpocetine | 148 |
| Table 5.28 | Melting point of drug using different methods | 149 |
| Table 5.29 | Solubility of Vinpocetine in Different Oils | 149 |
| Table 5.30 | Emulsification efficiency of surfactant and co surfactant | 151 |
| Table 5.31 | Concentration range for the optimization of Microemulsion | 154 |
| Table 5.32 | Levels of Independent factors in Experimental Design | 155 |
| Table 5.33 | D- Optimal Mixture Design for the Optimization of Microemulsion | 156 |
| Table 5.34 | Selection of the model for Globule Size Analysis (Statistical analysis) | 157 |
| Table 5.35 | ANOVA analysis of experimental design for Globule size Analysis | 157 |
| Table 5.36 | ANOVA study Results for Globule size Analysis | 158 |
| Table 5.37 | Selection of the model for % Transmittance Analysis (Statistical analysis) | 160 |
| Table 5.38 | ANOVA analysis of experimental design for % Transmittance Analysis | 160 |
| Table 5.39 | ANOVA study Results for % Transmittance Analysis | 161 |
| Table 5.40 | Constraints Applied For Selection Of Optimized Batch | 163 |
| Table 5.41 | Formulation Parameters Based on Desirability | 163 |
| Table 5.42 | Suitability of Predicted Desirability Plot for Optimized Formulation | 164 |
| Table 5.43 | Concentration of the Ingredients for optimized batch | 165 |
| Table 5.44 | Effect of drug loading on stability of the microemulsion system | 166 |
| Table 5.45 | Optimization of chitosan concentration | 167 |
| Table 5.46 | Optimized formula for microemulsion and mucoadhesive microemulsion | 167 |
| Table 6.1 | Classification of SMEDDS based on dispersibility | 173 |
| Table 6.2 | Thermodynamic stability testing for SMEDDS | 176 |
| Table 6.3 | Effect of dilution medium (Dilution Factor 100) on SMEDDS | 177 |
| Table 6.4 | Percentage Transmittance of diluted SMEDDS with distilled water | 179 |
| Table 6.5 | Viscosity of the SMEDDS before and after dilution with distilled water | 179 |
| Table 6.6 | Thermodynamic stability testing for Microemulsion systems | 185 |

| | | |
|------------|---|-----|
| Table 6.7 | Effect of dilution medium (Dilution Factor 100) on microemulsion systems | 186 |
| Table 6.8 | Percentage Transmittance for 100 times diluted microemulsion systems | 189 |
| Table 6.9 | Viscosity of the ME and MME before and after dilution | 189 |
| Table 7.1 | List of Material and Reagents | 196 |
| Table 7.2 | List of Equipments | 196 |
| Table 7.3 | In vitro dissolution profile of Modafinil loaded SMEDDS,pure drug and Marketed formulation(in 0.1N HCL with 0.5 % SLS) | 199 |
| Table 7.4 | Effect of pH on dissolution profile of SMEDDS | 200 |
| Table 7.5 | In vitro drug diffusion profile for SMEDDS and suspension of Modafinil | 201 |
| Table 7.6 | Ex vivo permeability study of optimized SMEDDS formulation and drug suspension from Stomach | 202 |
| Table 7.7 | Ex vivo permeability study of optimized SMEDDS formulation and drug suspension from Intestine | 203 |
| Table 7.8 | List of Materials and Reagents | 207 |
| Table 7.9 | List of Equipments | 207 |
| Table 7.10 | In vitro diffusion profile of Vinpocetine loaded ME, MME and Suspension | 210 |
| Table 7.11 | Ex vivo drug permeation study for Vinpocetine loaded ME, MME and Suspension | 211 |
| Table 7.12 | Diffusion Co-Efficient | 211 |
| Table 8.1 | List of materials, Glassware and Instruments used for In-vivo study | 216 |
| Table 8.2 | Groups of animal model for pharmacokinetic study | 217 |
| Table 8.3 | Basic information regarding drug administration | 217 |
| Table 8.4 | Plasma Drug Concentration | 219 |
| Table 8.5 | Pharmacokinetic parameters for various formulations of Modafinil after orally administered (10.278 mg/kg) into healthy rats | 220 |
| Table 8.6 | List of materials, Glassware and Instruments used for In-vivo study | 222 |
| Table 8.7 | Groups of animal model for pharmacokinetic study | 223 |
| Table 8.8 | Plasma drug concentration at predetermined time intervals | 225 |

| | | |
|-------------|---|-----|
| Table 8.9 | Brain drug concentration at predetermined time intervals | 225 |
| Table 8.10 | Plasma Pharmacokinetic parameters of Vinpocetine for various formulations after administered (0.514 mg/kg) into rats (n = 3, mean \pm SD) | 226 |
| Table 8.11 | Brain Pharmacokinetic parameters of Vinpocetine for various formulations after administered (0.514 mg/kg) into rats | 227 |
| Table 9.1 | Stability Study for SMEDDS at RT and Accelerated conditions | 232 |
| Table 9.2 | Stability Study at Room Temperature and Accelerated conditions for ME | 237 |
| Table 9.3 | Stability Study at Room Temperature and Accelerated conditions for Mucoadhesive Microemulsion (MME) | 239 |
| Table 10.1 | Learning and Intact Reference Memory | 247 |
| Table 10.2 | Short Term Working Memory | 248 |
| Table 10.3 | Percentage time spent in each quadrant on Day 6 | 249 |
| Table 10.4 | Percentage time spent in each quadrant on Day 7 | 250 |
| Table 10.5 | Percentage time spent in each quadrant on Day 8 | 251 |
| Table 10.6 | Learning and Intact Reference Memory | 253 |
| Table 10.7 | Short Term Working Memory | 254 |
| Table 10.8 | Percentage time spent in each quadrant on Day 6 | 255 |
| Table 10.9 | Percentage time spent in each quadrant on Day 7 | 256 |
| Table 10.10 | Percentage time spent in each quadrant on Day 8 | 257 |