PREFACE

The thesis describes factorial and formulation studies carried out on the effects of cyclodextrins and surfactant in enhancing the solubility, dissolution rate and bioavailability of efavirenz and ritonavir, two BCS class II drugs. The thesis consists of 11 Chapters with 258 references.

Efavirenz and ritonavir widely prescribed anti-retroviral drugs belong to class II under BCS and exhibit low and variable oral bioavailability due to their poor aqueous solubility and they requires enhancement in solubility and dissolution rate for increasing their oral bioavailability. Among the various approaches complexation with cyclodextrins and use of surfactants have gained good acceptance in recent years in industry for enhancing the solubility and dissolution rate of poorly soluble drugs. Though cyclodextrin complexation and use of surfactants for enhancing the solubility and dissolution rate of poorly soluble drugs have been investigated individually, no reports are available on their combined use in enhancing the solubility and dissolution rate.

The combined use of cyclodextrins (βCD and HPβCD) and surfactant Solutol HS15 is an innovative and novel approach for enhancing the solubility, dissolution rate and bioavailability of poorly soluble drugs. Solutol HS15, a non ionic surfactant has not been studied alone or in combination with cyclodextrins for enhancing the solubility, dissolution rate and bioavailability of BCS class II drugs. A systematic investigation in the present work revealed that the individual main effects as well as combined effects of CDs (βCD and HPβCD) and surfactant,Solutol HS15 in enhancing the solubility and dissolution rate (K1) of Efavirenz and Ritonavir are highly significant ( P< 0.01 ). Combination of Solutol HS15 with CDs ( βCD and HPβCD ) resulted in a much higher enhancement in the solubility and dissolution
rate \( (K_1) \) of efavirenz and ritonavir than is possible with CDs and Solutol HS15 alone. βCD- Solutol HS15 gave 54.43 and 28.97 fold increase in the solubility of efavirenz and ritonavir respectively. βCD- Solutol HS15 also gave a 5.95 and 3.81 fold increase in the dissolution rate \( (K_1) \) of solid inclusion complex of efavirenz and ritonavir respectively. FTIR studies indicated no physical and chemical interaction between the selected drugs with CDs and Solutol HS15.

Drug-CD-Solutol HS15 inclusion complexes could be formulated in to tablets by wet granulation method and the resulting tablets also exhibited rapid and higher dissolution rate \( (K_1) \) and dissolution efficiency \( (DE_{30}) \) values when compared to plain tablets and tablets containing CDs alone. Efavirenz tablets formulated employing drug- βCD- Solutol HS15 gave a 42.5 fold increase in the dissolution rate of efavirenz when compared to plain tablets. Ritonavir tablets formulated employing drug-βCD- Solutol HS15 gave 21.35 fold increases in the dissolution rate of ritonavir when compared to plain tablets. In the \textit{in vivo} pharmacokinetic evaluation, efavirenz - βCD-Solutol HS15 inclusion complex exhibited a 4.92 fold increase in the absorption rate \( (K_a) \) and 1.85 fold increase in the \((AUC)_0^\infty\) when compared to efavirenz pure drug. Tablets formulated employing drug-CD-Solutol HS15 inclusion complexes were also quite stable with regard to fast dissolution rate characteristics during stability studies.

**Hence a combination of cyclodextrins (βCD and HPβCD) and Solutol HS15 is recommended for enhancing the solubility, dissolution rate and bioavailability of efavirenz and retinovir, also formulation of their tablets with fast dissolution rate characteristics.**