The areas of current interest in pharmaceutical biotechnology which have a significant impact on clinical therapy are enhancement of dissolution rate and bioavailability of insoluble and poorly soluble drugs and development of controlled release drug delivery systems. Many of the modern drugs belong to the Class II under Biopharmaceutical Classification System (BCS), which are characterized by low solubility and high permeability and exhibit low and variable dissolution and bioavailability and pose problems in the design of controlled release products due to their insoluble character. Sparfloxacain (antibacterial), nifedipine (antianginal and antihypertensive) and nimodipine (antianginal and antihypertensive) belong to BCS-Class II and require enhancement in solubility and dissolution rate for increasing their oral bioavailability and development of controlled release drug delivery systems. The present investigation, biotechnological studies on cyclodextrin complexation, has been undertaken with an objective of studying the complexation between two cyclodextrins, β-cyclodextrin (β CD) and hydroxy propyl β-cyclodextrin (HPβ-CD) and the selected drugs sparfloxacain (SPF), nifedipine (N) and nimodipine (NM). The feasibility of employing cyclodextrin complexation for enhancing the solubility, dissolution rate and bioavailability and for obtaining controlled release of these insoluble drugs was investigated.

Complexation of the selected drugs (SPF, N, NM) with β-CD and HPβ-CD, the effect of CD complexation on the solubility, the type of phase solubility diagram and the stability constant of the CD complexes formed were investigated by phase solubility studies. Solid inclusion complexes of SPF, N and NM with β-CD and HPβ-CD in each case were prepared at 1:1, 1:2 and 1:3 ratios of drug and CD by two methods namely kneading and coevaporation methods. The complexes were evaluated for drug content uniformity, dissolution rate and dissolution efficiency.

Solid inclusion complexes of SPF-βCD (1:3) and SPF-HPβCD (1:3) prepared by kneading method were formulated into tablets by both direct compression and conventional wet granulation method and the resulting tablets were evaluated for drug content, hardness, friability, disintegration time and dissolution characteristics. The stability of the dissolution rate
characteristics of sparfloxacain tablets formulated employing β-CD were evaluated as per ICH guidelines.

In vivo evaluation of sparfloxacain tablet formulations F1 (plain tablets) and F2 (tablets formulated employing SPF-βCD, 1:3 complex) was carried out in human subjects. Serum concentrations of sparfloxacain were determined by the microbiological assay method developed in the present investigation. From the time versus serum concentration data, c_{max}, t_{max}, K_{el}, t_{1/2}, AUC_{0→∞} and K_{a} were calculated.

Controlled release matrix tablets each containing 120 mg of nimodipine were formulated employing nimodipine alone and its CD complexes and using sodium carboxy methyl cellulose (sodium CMC) and hydroxypropyl methyl cellulose (HPMC) as matrix materials. The matrix tablets were prepared by conventional wet granulation method and were evaluated for hardness, friability, drug content, disintegration time and drug release characteristics. Nimodipine release from the matrix tablets was studied in simulated gastro-intestinal fluids for a period of 12 hr. Pharmacokinetic evaluation was done on (i) matrix tablets containing nimodipine alone in sodium CMC matrix (Formulation F4) and (ii) matrix tablets containing nimodipine - βCD complex in sodium CMC matrix (Formulation F5) in healthy human subjects as per a cross-over randomized block design (n = 4).

The results of the present investigation clearly indicated that the solubility and the dissolution rate of sparfloxacain, nifedipine and nimodipine (three drugs belonging to BCS class II category with low solubility) could be greatly enhanced by complexation with β-CD and HPβ-CD. The increase in solubility is due to the formation of stable 1 : 1M complexes between the drug and CD molecules in solution. The solid inclusion complexes of drug and CD exhibited several times higher dissolution rates and dissolution efficiency values than the corresponding uncomplexed drugs.

Sparfloxacain - CD complexes could be formulated into compressed tablets by both direct compression and wet granulation methods and the resulting tablets exhibited rapid and higher dissolution rates and dissolution efficiency values than those formulated employing sparfloxacain as such. The higher dissolution rates of these tablets remained unaltered during
stability studies carried out as per ICH guidelines. Sparfloxaan tablets formulated employing SPF-βCD (1 : 3) inclusion complexes exhibited significantly higher rates of absorption when compared to those formulated with sparfloxaan alone. But the extent of bioavailability remained the same in both the cases.

Matrix tablets formulated employing nimodipine - βCD (1 : 1) inclusion complexes gave slow, controlled and complete release of nimodipine over a period of 12 hr, which was not possible with similar tablets formulated employing nimodipine as such. Matrix tablets formulated employing cyclodextrin complexes exhibited good controlled release characteristics, both in vitro and in vivo.

Basing on the results of the investigation cyclodextrin complexation with β-CD and HPβ-CD is recommended for enhancing the solubility and dissolution rate of sparfloxaan, nifedipine and nimodipine. Cyclodextrin complexes can be formulated into compressed tablets with higher rates of dissolution and absorption by both direct compression and wet granulation techniques. Cyclodextrin complexes can also be used in the design of controlled release matrix tablets of insoluble drugs for obtaining slow, controlled and complete drug release over longer periods of time.

The work carried out on matrix tablets of nimodipine resulted in the development of new technology of enhancing the solubility and dissolution rate of insoluble drugs (such as nimodipine) by cyclodextrin complexation before formulation into controlled release tablets. The cyclodextrin complexes with higher solubility and dissolution rate could be employed in the formulation of matrix tablets for obtaining controlled release of such insoluble drugs.