PREFACE

New drug discovery and development is a highly interactive process, which involves a number of scientists of different disciplines. At the centre of the process of drug discovery are the components of drug design. Drug design is not merely the design of the prototype molecule, but is a process which starts with the crucial decision to investigate a particular group of compounds, which is then followed by constant inputs from the chemists and the biologists with continuous interaction which guide the course of drug discovery and development to the stage when the product is introduced into clinical practice. Drug discovery basically encompasses lead identification, design of the prototype structure based on the lead thus identified followed by lead optimization. It is very rarely that the drug which ultimately finds use in clinical practice is originally planned to be made. Practically all the successful drugs have evolved as the result of a process of continuous modification and improvement of some basic structural type with which the investigation started.

The process of drug design, however continues even after the final selection of a candidate drug after optimisation of the therapeutic index. Modification may be needed to develop new dosage forms, or new delivery forms or prodrugs for modifying the physical or pharmacokinetic character of the candidate molecules. Elements of drug designs thus guide the course of drug development from lead identification right through to clinical application.

The more important sources of leads, approaches to drug design and methods available for lead optimisation are listed below.
A. Sources of Leads

* Ethno-therapeutic leads
* Knowledge of the structure, mode of action, side effects of known drugs.
* Structure of receptors/enzymes
* Biochemical leads
* Biological screening results

B. Design of Prototype Structures

* Substructure analysis of known drugs and design of prototypes based on concepts of:
  - bioisosterism
  - grafting of pharmacophores on carrier systems.
* Building of active structures into molecules with constrained or enhanced conformational mobility.

C. Lead Optimisation

* QSAR studies; computational methods.
* Computer aided molecular modelling.

These approaches are not exclusive of each other and quite often more than one of these approaches may need to be used in the development of a product or one set of compounds. The present thesis is based on the identification of N-phenylpiperazine containing/carrying molecules as a group of drugs, with N-phenylpiperazine component as the essential pharmacophore and designing molecules by grafting N-phenylpiperazine pharmacophore on them, followed by biological screening and lead optimisation using QSAR techniques.