PREFACE

The study of heterocycles as an evergreen field in the branch of organic chemistry and always attracts the attention of scientists working not only in the area of natural products but also in the synthetic organic chemistry. Moreover, many useful drugs have emerged from the successful investigations carried out in this branch. Besides, spectacular advances have been made to furtherance the knowledge of relationship between chemical structure and biological activity. In fact, this tendency is reflected by the voluminous data available in literature on heterocyclic chemistry. Thus, the successful applications in various fields ensure a limitless scope for the development of structurally novel compounds of this type with a wide range of physico-chemical and biological properties.

The work presented in this thesis entitled “Design, Synthesis and Pharmacological Screening of Substituted Tetrahydropyridines and Piperidine Derivatives” have been divided into five chapters. The piperidine scaffold as wide-ranging in its therapeutic uses as it is ubiquitously found in drugs. It is a key structural component of successful anti-Parkinson’s drugs and displays antipsychotic, antiviral, metabolic, antimicrobial, antidepressants, acetylcholinesterase inhibitors, antimalarial activity and anticonvulsants. Highly functionalized pyridines including aryl and heteroaryl-substituted derivatives are wide spread in the pharmaceutical and agrochemical sectors. Efficient methodology for the synthesis of new derivatives, with broad functional group capability, is, therefore, of considerably current interest. The basic studies gave us interesting information about tetrahydropyridines has been useful in the search for the synthesis and biological evaluation of desired derivatives.

Chapter I gives general background on piperidines and tetrahydropyridines covering the literature survey for different methods used in the synthesis of piperidines and tetrahydropyridines and their pharmacological importance. From the past literature survey of interesting biological activity for these classes of derivatives prompted us to synthesize piperidine and tetrahydropyridine derivatives and investigate their biological importance.

Chapter II explains the synthesis, characterization of tetrahydropyridine derivatives via Suzuki coupling as acetylcholinesterase inhibitors against different sources.
Alzheimer's disease (AD) is an irreversible, progressive neurodegenerative disorder that occurs gradually and results in memory loss, unusual behavior, personality changes and a decline in thinking abilities. Taking into account the increase in life expectancy, the fact that the incidence of AD increases with advancing age, and the devastating effects of this illness, nowadays AD represents a major public health problem and will presumably be the most important pathology of the 21st century in the developed countries. To date the cholinesterase inhibitors have been shown to improve some aspects of cognitive performance, however efficacy has been poor and side effects are problematic. The use of catalytic cross coupling protocols for preparing aryl-functionalised heterocycles is very topical and in this context heterocyclic boronic acids are emerging as important reagents for Suzuki-Miyaura Reactions. From basic knowledge acquired from the previous literature survey, we synthesized tetrahydropyridine derivatives via Suzuki coupling. All the synthesised compounds were characterized by 1H NMR, LC/MS, IR and CHNS analysis. Synthesised novel compounds were evaluated for their efficacy as AChE inhibitors.

Chapter III describes the synthesis, characterization and pharmacological screening of new bioactive 3-(piperidin-4-yl)benzo[d]isoxazole derivatives. Our simple and short and environmentally benign process began with the synthesis of 2,4-difluorobenzoyl-4-(1-formyl)piperidines and it involves the four step. All the synthesised compounds were characterized by 1H NMR, LC/MS, IR and CHNS analysis. 3-(piperidin-4-yl)benzo[d]isoxazole sulphonamide and 3-(piperidin-4-yl)benzo[d]isoxazole urea derivatives were evaluated for their efficacy as PLA2 inhibitors. 3-(piperidin-4-yl)benzo[d]isoxazole carboxamide and 3-(piperidin-4-yl)benzo[d]isoxazole thiourea derivatives were screened for their efficacy as antiproliferative agents against different carcinoma cell lines. X-ray crystal structure analysis of some derivatives presenting the ORTEP diagram, crystal packing, crystal data and structure refinement.

Chapter IV deals with the general approach for the synthesis of the target compound diphenyl(piperidin-4-yl)methanol was discussed and accomplished in high yield by efficient synthetic routes. All the synthesised compounds were characterized by 1H NMR, LC/MS, IR and CHNS analysis. Diphenyl(piperidin-4-yl)methanol sulphonamide and diphenyl(piperidin-4-yl)methanol urea derivatives checked for
their antimicrobial studies against different bacterial strains. Diphenyl(piperidin-4-yl)methanol sulphonamide and diphenyl(piperidin-4-yl)methanol thiourea derivatives were screened for their efficacy as antiproliferative agents against different carcinoma cell lines. X-ray crystal structure analysis of some derivatives has been discussed.

**Chapter V** gives the synthesis, characterization of 2,3-dihydro-5,6-dimethoxy-2-((piperidin-4-yl)methyl)inden-1-one derivatives. All the synthesised compounds were characterized by 1H NMR, LC/MS, IR and CHNS analysis. Among the synthesised compounds 2,3-dihydro-5,6-dimethoxy-2-((piperidin-4-yl)methyl)inden-1-one sulphonamides and 2,3-dihydro-5,6-dimethoxy-2-((piperidin-4-yl)methyl)inden-1-one thiourea were screened for their efficacy as antiproliferative agents against different carcinoma cell lines. 2,3-dihydro-5,6-dimethoxy-2-((piperidin-4-yl)methyl)inden-1-one carboxamide and 2,3-dihydro-5,6-dimethoxy-2-((piperidin-4-yl)methyl)inden-1-one urea derivatives were evaluated for their efficacy as AChE inhibitors.