Preface

Alzheimer's disease is a progressive neurodegenerative disease most frequently associated with memory deficits and cognitive decline with less prevalent clinical manifestations increasingly being recognized. Amyloid plaques and neurofibrillary tangles make up the cardinal pathological biomarkers of this disease. Eventually, the cognitive decline starts to affect behavior, speech, visuospatial orientation as well as the motor system, other causing dementia, thereby, making it impossible for the patient to accomplish daily tasks.

Acetylcholinesterase (AChE), β-secretase-1 (BACE 1), phosphodiesterase 9A (PDE-9A), matrix metalloproteases (MMPs), glycogen synthase kinase 3β (GSK3β), monoamine oxidase B (MAO-B), N-methyl D-aspartate (NMDA) receptors, tau kinase etc form the chief therapeutic targets for AD therapy. Inhibition of cholinesterase enzymes remains one of the main goals of anti-AD medication in order to alleviate symptoms.

Multidisciplinary synthetic approaches are in considerable demand in the field of modern drug development. A crucial step in the development of multi-target directed Ligands (MTDL) for drug discovery is the design and creation of unique chemical entities that can operate concurrently at several molecular targets. Given the complicated etiology of AD and the drawbacks of single-target medications, MTDL approaches are becoming more and more recognised as effective AD treatments. In the current work, different kinds of MTDL scaffolds are investigated using modern drug discovery methodologies.

The work embodied in this thesis has been presented under the following chapters:

Chapter 1: The chapter provides an introduction to AD and deals with details regarding background, pathophysiology and available therapeutics for the treatment of AD. Further, the various approaches involved in drug design are also described.

Chapter 2: The chapter deals with the literature background related to targets involved in the several hypotheses of interest.

Chapter 3: In this chapter, the objectives of the study and plan of work are incorporated.

Chapter 4: The chapter deals with the development of Multifunctional hybrid sulfonamides as novel therapeutic agents for Alzheimer's disease.

Chapter 5: The chapter deals with *in silico* identification of the potential PDE-9A inhibitors through computational techniques.

Chapter 6: The development multi-target *N-benzyl piperazinyl sulfonamide* derivatives for the management of AD is presented in the chapter. It describes the methodology used for design, synthesis, characterization, *in vitro*, *in silico* and *in vivo* evaluations of sulfonamides of N-benzyl piperazinyl followed by results and discussion.

Chapter 7: This chapter outlines the summary and conclusions of the research work undertaken.

Chapter 8: The references, used to carry out the research work, are presented in the chapter.

An appendix consisting of the additional supporting information and a list of publications during the course of the Ph.D. are included.