

## Preface

Alzheimer's Disease (AD) is an age-related neurodegenerative disorder, which accounts for more than 80% of dementia cases worldwide in older people. It is characterized by the deposition of A $\beta$  plaque and neurofibrillary tangles. The disease leads to progressive loss of memory, functional ability to learn and is primarily characterized by the progressive loss of memory associated with other cognitive deficits. Despite decades of study on the etiology of disease and also significant efforts by the pharmaceutical industry to develop therapies, there is no effective treatment available to cure AD or inhibit its progression significantly. However, there are few drugs viz. donepezil, galantamine, and rivastigmine, approved by USFDA, acting on cholinergic pathway and memantine acting on NMDA receptor. Recently, Aducanumab and Lecanemab are approved in the US as disease-modifying agents in AD.

Considering the disease complexity and treatment challenges, naturally obtained leads from medicinal plants were selected for drug development. The plant-based drugs like galantamine, physostigmine, and rivastigmine act as cholinesterase inhibitors and are being used to improve memory in AD patients. Several studies are ongoing for the identification of plant-based medications for the management of AD. In this study, natural products and their semisynthetic derivatives were explored as multitarget drug-directed ligands.

The present study is divided into seven chapters:

**Chapter 1** deals with Alzheimer's disease (AD), its pathophysiology, and current treatments for AD.

**Chapter 2** provides insight into the literature reports related to the relevant work.

**Chapter 3** includes the hypothesis, rationale, and plan of the work.

**Chapter 4** bioactivity guided fractionation, characterization, *in vitro*, *in silico*, and *in vivo* studies of *Adhatoda vasica*.

**Chapter 5** design, synthesis, characterization, *in vitro*, *in silico*, and *in vivo* studies of vasicine derivatives.

**Chapter 6** design, synthesis, characterization, *in vitro*, *in silico*, and *in vivo* studies of piperine derivatives.

**Chapter 7** deals with the conclusion and summary

References used to carry out the research work, are presented. An appendix consisting of the additional supporting information, spectral data of representative compounds, and a list of publications during the Ph.D. are included.