3. AIMS AND OBJECTIVES

Alzheimer's disease (AD), the most common type of dementia, is a progressive neurodegenerative disorder prevalent amongst older populations. Almost 50 million people worldwide are suffering from AD, and if no treatment or prevention measures are found soon, the number will rise significantly to 150 million by 2050. The etiology of AD is very intricate; several factors like a low level of ACh, aggregation of Aβ, tau hyperphosphorylation, oxidative stress and dyshomeostasis of biometals are hypothesized to play significant roles in the etiology of AD.

To combat AD-like diseases having a complex etiology, the development of multitarget-directed ligands (MTDLs) is viewed as one of the most assuring drug discovery approaches. Drugs acting on a single target even though having high affinity and selectivity for their targets might not influence the complex etiology of the disease satisfactorily. An MTDL having moderate, but balanced affinities for the targets can still offer more beneficial effects than a mono-targeted molecule. A mild and balanced activity on multiple therapeutic targets might secure higher safety and reduce the risk of therapeutic resistance.

After perusal of current research in this field, we focused our attention on designing new MTDLs as the core objective of anti-AD drug discovery. Despite considerable research on new targets available for AD treatment, the cholinesterase inhibitors still remain the drugs of choice, although they offer only symptomatic and transient benefits to the patients. Several clinical and pre-clinical data indicate that Aβ aggregation and the ROS mechanism also play crucial role in the pathogenesis of AD. However, Aβ aggregation inhibitors or antioxidants all alone might not be sufficient to resist a multifactorial pathological condition like AD. Therefore cholinesterase inhibitors endowed with additional Aβ aggregation inhibitory and antioxidant activities might be a desirable pick to offset the progress of this multifaceted disease.

Heterocyclic compounds with indole and carbazole rings in their structures are prodigiously present in many natural compounds possessing

invaluable medicinal and biological properties. So we planned to use these two active pharmacophoric moieties for the designing of some novel MTDLs. Both of these biologically active moieties were separately fused with other biologically significant pharmacophoric moieties (i.e. 1,2,4-triazine with indole, stilbene and carbohelicene with carbazole) to design the novel scaffolds as shown in **Figure 3.1**. Structural modifications were carried out on these designed scaffolds by incorporating various substituents to obtain some potential leads as anti-AD agents and to establish a meaningful SAR.

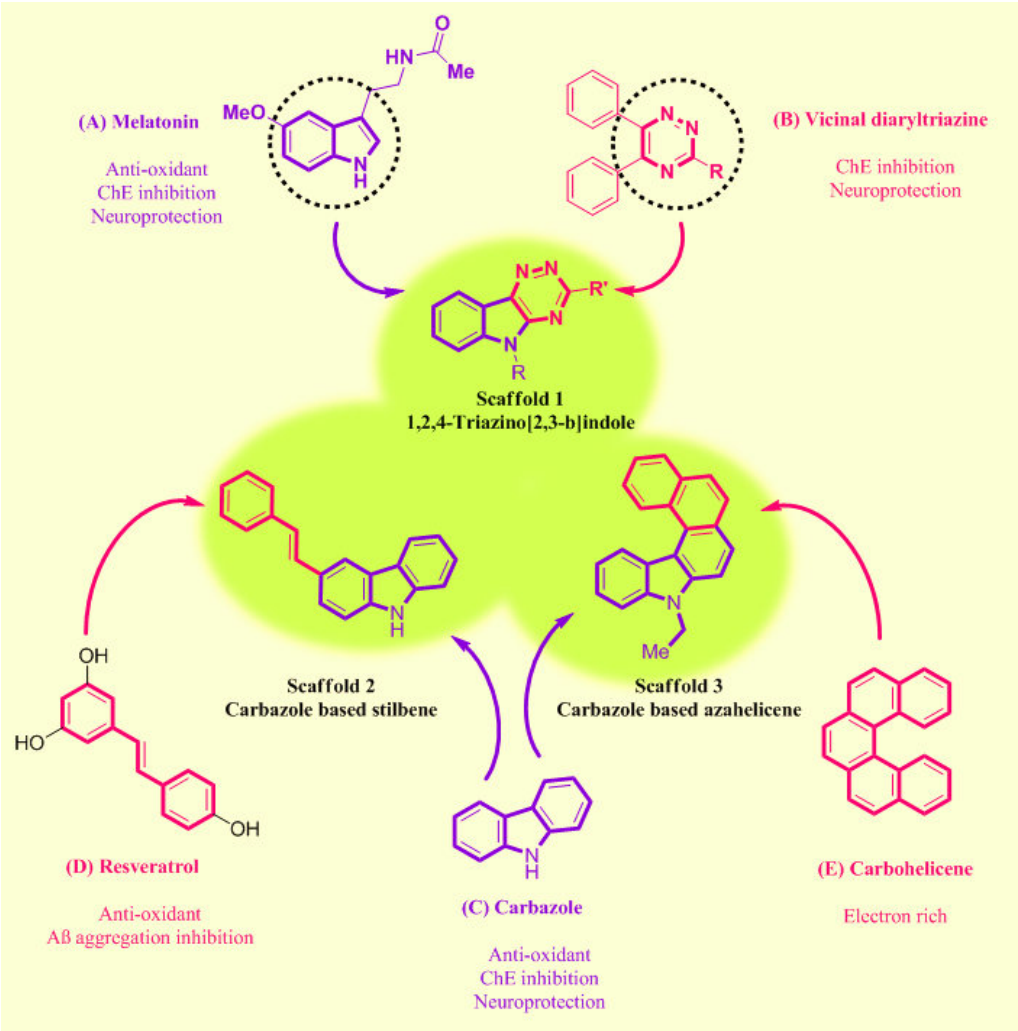

Figure 3.1. Molecular hybridization approach adopted for the development of novel MTDLs as anti-AD agents.

It was envisaged to synthesize the designed compounds and to evaluate them for anti-AD activities. The work carried out for the fulfillment of the proposed plan has been discussed in **Chapter 4**.