3. AIMS AND OBJECTIVES

Benzothiazole, a heterocyclic ring, has been widely used in the development of drug candidates.[85] A number of drugs having benzothiazole ring system are used clinically for the management of several central nervous system (CNS) diseases. To name two, riluzole, a benzothiazole derivative, is used in amyotrophic lateral sclerosis (ALS)[86] and ethoxzolamide has been reported to suppress epileptic seizures.[87] Benzothiazole derivatives are used as Alzheimer's brain imaging agents.[88] Thus, benzothiazole is considered as a privileged scaffold having the potential to be used for the development of therapeutics for AD.[89-91] Some diaryl derivatives have been reported as potent neuroprotective agents.[92] This laboratory has been involved in the design and development of diaryltriazines **(XXIII)**[93] as potent multi-targeting ligands for the treatment of AD. It was presumed that the multipotent

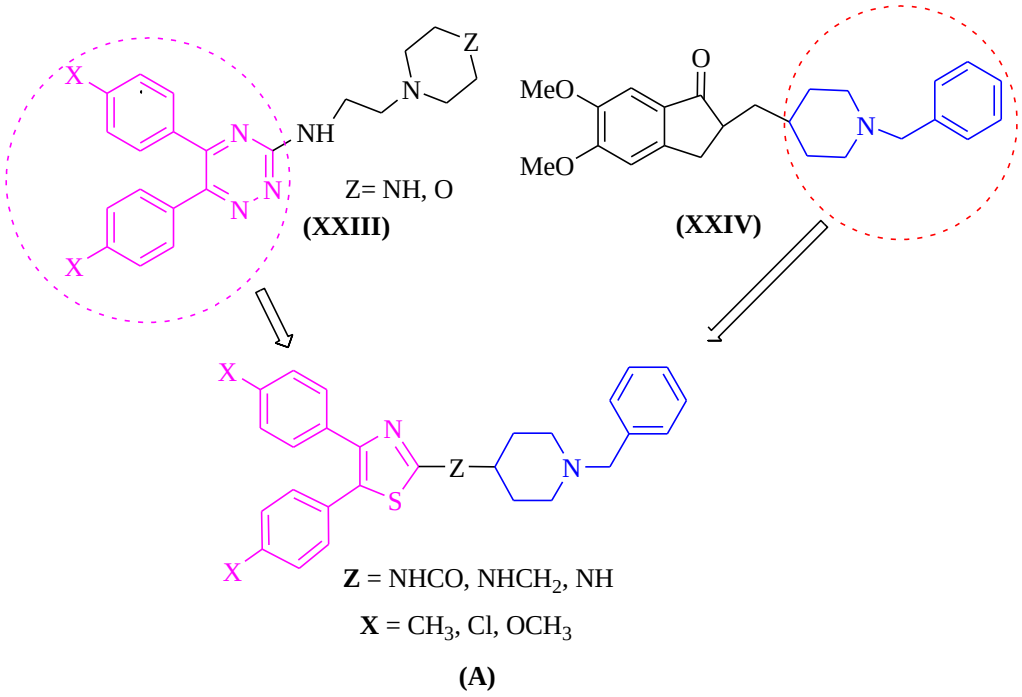

Figure 5: Designing of novel series of compounds as cholinesterase inhibitors

activity of these diaryltriazine **(XXIII)** resided in the diaryltriazine scaffold, not in the morphino/piperiazinoethyl side chain and thiazole ring showing more affinity for CNS targets

could be used to replace the triazine nucleus. Donezepil **(XXIV)** has been endowed with multile favourable activites like cholinesterase inhibitory, Aβ1-42-induced neuroprotective and anti-oxidant, specific pharmacophoric features of donepezile has not been identified with these activites. It was considered worthwhile to design hybrid molecules in which the dimethoxyindanone scaffold of donepezil **(XXIV)** was replaced with diarylthiazole through some linker **(Figure 5.)** to obtain multi-targeting ligands having the potential to be used in the management of AD. Till date vicinal diarylthiazoles have not been reported as AD-responsive agents.

Benzylpiperidine moiety present in donepezil **(XXIV)** is another important AD-responsive pharmacophore. So, we thought it logical to replace the triazine ring present in compounds **(XXIII)** with its bioisostere thiazole in the designed compounds and attach the benzylpiperidine pharmcophore to it through one or two atoms' linker **(Figure 5)**. It was planned that the resulting compounds would be evaluated for their anti-Alzheimer's potential. Thus, it was thought herewith to adopt an approach wherein a diarylthiazole moiety is joined to benzylpiperidine to get novel hybird molecules of type (A) **(Figure 5)** as potential multitargeted anti-Alzheimer's agents.