Journal of
Chemical Biology & Pharmaceutical Chemistry

Abstract

Development of heterocyclic analogs of curcumin for Alzheimer's disease

Ms. Puja Mishra
Dr. B.C. Roy College of Pharmacy & Allied Health Sciemces, Durgapur, India

Abstract:

Amyloid β (Aβ) peptide monomers polymerizes to form insoluble amyloid fibril aggregates and accumulates as senile plaques which eventually leads to cognitive impair- ment. Modulating abnormal amyloid aggregation can be considered as a therapeutic target for Alzheimer's disease. Recent studies supports that Curcumin interferes with larger protein aggregate formation by destabilizing the salt bridge (Asp 23-Lys 28) of Aβ protein. Anti-amyloid compounds must inhibit such accumulation by stabilizing soluble Aβ oligomers by forming hydrogen bonds and π-π stacking. Docking scores of such modifications mostly ranged in between -5.9 to -7.1 Kcal/mol which is even more than that of standard curcumin (-5.5 Kcal/mol). In silico docking studies of compound (1) with both Aβ protein and β-secretase enzyme (BACE1) was found to be-

6.4 Kcal/mol and -8.7 Kcal/mol respectively which is higher than that of standard. Compound 1 interacts with KLVFFAE fragment (Lys16-Glu22) which is essential for dimerization of the monomers by π-π stacking with Phe A:19. Ala21 in the salt bridge also exerts π-made interac- tions with the central isoxazole ring as well as the terminal phenyl ring.

The compound (1) exhibit hydrogen bond- ing interaction with Thr232 which is located in S3 pocket of BACE1 making compound binding stable within the pocket. De novo ligand design generated best suitable de- rivative of the selected lead by iterations. Both compounds (1) and de novo designed lead offspring reached the bind- ing pocket of both the proteins, passed Lipinski's rule of five and in silico toxicity testing by admetSAR.

Biography:

Ms.Puja Mishra has completed her Master's degree in Pharmacy from IIT BHU. She is pursuing PhD from MAKAUT university and working as an Assistant profes- sor in Durgapur, W.B.

Webinar on Computer Aided Drug Design | December 04, 2020 | London , UK

Citation: Ms. Puja Mishra; Development of heterocyclic analogs of curcumin for Alzheimer's disease; CADD 2020 ; December 04, 2020; London , UK.