# The rational design of the new anti-alzheimer drugs via *in-silico* approach

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**Abstract:** *In-silico* drug design and discovery studies can be performed by using molecular docking simulation. In this approach, a lead compound is proposed and is developed from the discovery stage to the clinical usage [1]. Amyloid beta (Aß) protein is a desired target for anti-alzheimer drugs in the brain, which plays a crucial role to inhibit the alzheimer disease [2]. The structure of this protein consists of two peptides $Aß_{1-40}$ and $Aß_{1-42}$. The $Aß_{1-42}$ peptide, compared to the $Aß_{1-40}$ peptide displays the faster effect on inhibiting the alzheimer disease [3]. So, the $Aß_{1-42}$ peptide can be applied as a promising target for the treatment of alzheimer. The rational design of drugs is a vital challenge in Pharmaceutical sciences. In this study, the molecular docking simulation is applied for recognition of lead compound by utilizing the interaction of the two anti-alzheimer drugs (rivastigmine and memantine) with $Aß_{1-42}$ peptide. Then, using the lead molecule, five new compounds are proposed. The interactions of the new compounds are investigated with $Aß_{1-42}$ peptide to select the best compound, which offers the high stable interaction energy and high ligand efficienty. Afterwards, the pharmaceutical properties and toxicity of these new compounds are estimated by using OSIRIS DataWarrior software. Employing molecular docking simulation along with the prediction of their pharmaceutical properties helps to discover the new potential drugs. Docking results indicated rivastigmine compared to the memantine offers not only more stable interaction energy (-80.13 vs -58.01 kcal/mol), but also shows higher ligand efficiency (-3.67 vs -3.25). So, rivastigmine is selected as a lead molecule owing to the interaction energy. Moreover, docking results show that the interactions energy of the new compounds A, B, C, D, E are equal to -89.72, -72.00, -86.00, -88.87, -72.42 kcal/mol, respectively. Among the new compounds, compound A represents more stable interaction energy and ligand efficienty (-3.72). On the other hand, OSIRIS DataWarrior results illustrated that the compound A lacks the effects of mutagenic, tumorigenic, sterility and irritant. Moreover, for this compound, clogP, drug likeness and drug score are equal to 2.999, 3.537 and 0.859, respectively. So, based on the aformantioned results, compound A in terms of computational results can be applied as a potential drug. But to ensure the medicinal effect of this compound, the biological and laboratory tests should be performed.

**Keywords:** In-silico method; Molecular docking simulation; OSIRIS DataWarrior software; Anti-alzheimer drugs

**References**

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