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Can sesquiterpenes from Persian Gulf sea hare be applied as acetylcholinesterase inhibitors in treatment of Alzheimer symptoms? comparative quantum mechanics and molecular docking study

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Background and Aims: Seven chamigrenes compound 1, acetyldeschloroelatol 2, deschloroelatol 3, acetylelatol 4, elatol 5, 8-acetylcaespitol 6 and caespitol 7 from Persian gulf sea hare: Aplysia dactylomela were studied theoretically to reveal their chemical activity. These compounds also were evaluated as acetylcholine-teras (AChE) inhibitors.
Methods: Sesquiterpenes geometries have been optimized at the density functional level of theory. Vibrational frequencies have been done to confirm all the stationary points correspond to the true minima . In molecular docking study, the complexes of acetylcholinesterase from "Torpedo californica" and huperzineA (HupA), donpezil, kaempferol and galanthamine respectively were brought out by using Autodock 4. Then ligands were separated and the same receptor AChE from Torpedo California with pdb accession code 1VOT was docked with all seven given molecules. Also, PCA was used to acquire the pharmocophoric profile of our investigated sesquiterpenes.
Results: The electronic study reveals those molecules which contain more negative oxygen have higher dipole moment in molecule 2, 4 and 7. Moreover, the charge analysis of systems show that the oxygen of hydroxyl group in molecule 3, 5 and 7 is better hydrogen donor in hydrogen bonds. The docking study of molecules shows molecule 4 is the best inhibitor of TpAChE among the all seven molecules and its docked energy is higher than HupA and Kempferol but less than galanthamine and donpezil. Molecule 4 binds in both the acyl-binding pocket and the choline-binding site. Also, Asp72 has two hydrogen bonds with its acetate group. The PCA shows the HOMO-1 orbital energy, LogP, logS and volume are the most significant properties
Conclusions: These findings can lead to design new molecules with marine origin and pharmacological properties, which may be helpful for treatment of Alzheimer disease.

Keywords: AChE inhibitor; Docking, Binding affinity; Marine sesquiterpens