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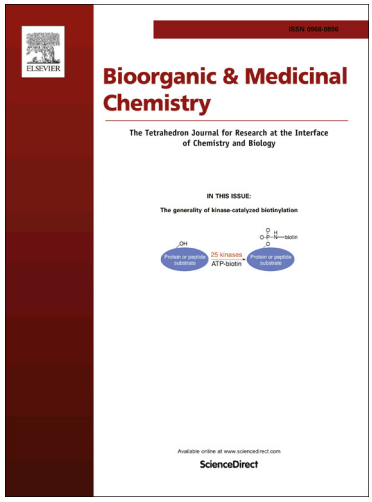

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Synthesis, Anticholinesterase Activity and Molecular Modeling Study of Novel Carbamate-Substituted Thymol/Carvacrol Derivatives

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Abstract

New thymol and carvacrol derivatives with the carbamate moiety were synthesized and their inhibitory effects on acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) were evaluated. 5-isopropyl-2-methylphenyl(3-fluorophenyl)carbamate (**29**) was found to be the most potent AChE inhibitor with IC_{50} values of 2.22 µM, and 5-isopropyl-2-methylphenyl (4-fluorophenyl)carbamate (**30**) exhibited the strongest inhibition against BuChE with IC_{50} value of 0.02 µM. Additionally, the result of H4IIE hepatoma cell toxicity assay for compounds **18, 20, 29, 30** and **35** showed negligible cell death. Moreover in order to better understand the inhibitory profiles of these molecules, molecular modeling studies were applied. Binding poses of studied compounds at the binding pockets of AChE and BuChE targets were determined. Predicted binding energies of these compounds as well as structural and dynamical profiles of molecules at the target sites were estimated using induced fit docking (IFD) algorithms and post-processing molecular dynamics (MD) simulations methods (i.e., Molecular mechanics Poisson–Boltzmann surface area (MM-PBSA) approaches).

Keywords: Thymol, Carvacrol, Carbamate, Alzheimer's Disease, Molecular Docking, Molecular Dynamics (MD) Simulations, MM-PBSA, Induced Fit Docking (IFD)

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