Molecular docking and Molecular dynamics simulations on various Marine Bioactive compounds against Neuro Degenerative Disorders

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Abstract

Neurodegenerative diseases (NDDs) are pathologies characterized by the irreversible destruction of certain neurons, which causes the progressive and spiking loss of certain functions of the nervous system. In worldwide, it is the major cause for the dementia. Recent studies reported that as of now, in worldwide 35.6 million and 9.9 million European people are affected by dementia. The neurodegenerative diseases (NDDs) include Alzheimer's (AD) and Parkinson's (PD) diseases. Recently, marine bioactive compounds have attracted the attention of scientists worldwide and these compounds have been found to have several biological activities. Currently, many of the marine derived drugs are available in the market which are approved by the Food and Drug Administration (FDA). Macro algae derived compounds were reported for their neuroprotective activity to treat neurodegenerative diseases (NDDs) such as AD and PD. In the present study, we have carried out molecular docking studies (Induced Fit Docking- IFD) with Alzheimer's disease related target proteins such as Acetylcholinesterase [PDB id: 4M0E], Beta-secretase (BACE-1) [PDB id: 2FDP], Butyrylcholinesterase [PDB id: 4TPK], Glycogen synthase kinase - beta (GSK-3β) [PDB id: 3GB2], p38 alpha MAP kinase [PDB id: 4R3C] and Cyclin-dependent kinase 5 (CDK5-p25) [PDB id: 1UNG] with the bioactive compounds from the macro algae seaweeds of Phaeophyceae, (brown algae) , Rhodophyta (red algae) and Chlorophyta (green algae) which were reported for these activities. Further, the docking results indicate that bioactive phlorotannin compounds Bieckol: -18.20 kcal/mol (AChE), Fucophlorethol A: -17.27 kcal/mol (BACE1), Fucotriphlorethol A: -15.89 kcal/mol (BChE), Phlorofucofuroeckol A: -13.5 kcal/mol7 (GSK-3β) and Fucoidan: -8.21 kcal/mol (p38α-MAP), Spiralisone A: -8.06 kcal/mol (CDK5-p25) have exhibited good docking scores and docking energies with respective target proteins. The above seaweed bioactive compounds showed strong binding affinities and important Hydrogen bond interactions with key catalytic amino acid residues at the active site of the target proteins. Further, the best docked complexes were subjected to molecular dynamics simulations for understanding the stability of binding in protein-ligand complexes.

Keywords: Neurodegenerative Diseases, Alzheimer’s disease, Marine bioactive compounds, Induced Fit Docking, Molecular dynamics simulations