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| Resumo | Background; One cause of the Alzheimer's disease (AD) is the amyloid plaques accumulation, generated after an endoproteolytic cleavage of APP by secretases (WAKABAYASHI; STROOPER, 2008). Secretase inhibitors have been studied, but failed in clinical trials due to high toxicity and/or efficacy (HUNG; FU, 2017). So far, the main clinical treatment for AD is the administration of cholinesterase inhibitors that only increases the patient's survival in a few years (GAN et al., 2004). Molecules from natural products have been used as prototypes in the development of new drugs, and species from marine habitat have provided compounds of therapeutic interest, none of them applied to AD (MALVE, 2016). Thus, the objective of this work was to find new druggable β-secretase (BACE1) inhibitors among molecules described from marine animals, aiming a new prototype for amyloid plaques decrease.<br>Method: Molecules from marine animals were searched in scientific articles and prepared for docking, conducted by Swiss Dock server, to predict molecular interaction with BACE1 (PDB code 2VKM). Results were analyzed by UCSF Chimera, and molecules were selected if they were positioned in the enzyme active site, with distance lower than 3 Å and binding energy lower than -6 kcal/mol. Selected molecules were analyzed for their pharmacokinetics properties (PK) and druggability using the SwissADME server.<br>Result: From 48 molecules, 3 were selected by molecular docking. Psammaplin A (PsA) is one of them, extracted from the poriferous Aplysin and known for its antibacterial and antitumor activities (SELEGHIM et al, 2007). It had favorable binding energy (−9.71 kcal/mol) and short distance between the ligand and the protein (1,923 and 2,615 Å2); however, its PK was not suitable for a drug. On the other hand, 1H-Benzo[de][1,6]naphthyridine and Sebastianine A had lower binding energy as well (−6.76 and −6,98 kcal/mol, respectively) and favorable PK: logP ~2.5, high gastrointestinal absorption, brain-blood barrier permeant, low ability to inhibit liver enzymes and no violation of the Lipinski's rules, characteristics to be druggable.<br>Conclusion: Using molecular docking, 3 molecules were selected as potential inhibitors of BACE1, being two of them druggable and good prototypes for the treatment of AD. |
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