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Resumo	Background: Alzheimer's Disease (AD), the most common cause of dementia, is characterized by the amyloid plaques accumulation, generated after the APP cleavage by enzymes, being the most important the beta-secretase-1 (BACE1). Small-molecule BACE1 inhibitors reduced the production of amyloid-β peptide, but clinical trials have demonstrated some adverse effects, although non-progressive and reversible, which indicates that BACE1 inhibition should be better investigated. Peptides are molecules few explored in the drug development field, but have several advantages, such as specificity, bioavailability and ability to cross the brain-blood barrier (BBB). Marine animals are a rich source of peptides, some of them already used in the clinics. Thus, the objective of this work was to find new BACE1 inhibitor peptides from Macrorhynchia philippina venom, a Brazilian marine animal. Method: M. philippina venom was obtained by methanol/acetic acid extraction and tested in SH-SY5Y neurons for toxicity evaluation. The extract was analyzed by mass spectrometry for peptides identification and sequencing, and had their secondary structure determined and prepared for molecular docking with BACE1 (PDB code 2VKM), conducted by MDockPep serve (Xu and Zou, 2020). Results were analyzed by UCSFChimera, and molecules were selected according to their positioning in the enzyme active site, with distance lower than 3 Å between atoms. Selected molecules were also analyzed by ProtParam tool (Gasteiger et al., 2005) for determining physico-chemical properties, BBB permeability and stability. Result: Nineteen peptides were obtained, and none of them have already been described, according to similarity analysis by BLAST algorithm. None of them caused significant cytotoxicity for neurons. From that, 10 were positioned in the BACE1 active site after a global docking analysis, in the same place than a known inhibitor (Ki 1.8 nM). One of them was stable, according to algorithms created from known peptides and high aliphatic index. Moreover, the peptide had high hydrophobicity, according to GRAVY index, indicating high BBB permeation. Conclusion: One new peptide was obtained with potential activity on BACE1 inhibition, with suitable characteristics for a drug. The bioactive peptide represents a good alternative for AD treatment.
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