INTISARI

Penyakit Alzheimer berkaitan dengan disfungsi sistem kolinergik akibat degradasi asetilkolin (ACh) yang terlalu cepat oleh enzim asetilkolinesterase (AChE). Inhibitor AChE menjadi target terapeutik penting, namun tantangan utama adalah kemampuan senyawa untuk melewati blood-brain barrier (BBB). Dua kandidat peptida teripang yaitu VLCAGDLR dan SWIGLK telah berhasil di identifikasi. Studi ini bertujuan mendesain peptida bioaktif dari teripang yang memiliki afinitas tinggi terhadap AChE, stabil secara fisik, dan berpotensi menembus BBB. Uji in silico menunjukkan SWIGLK memiliki afinitas pengikatan lebih baik (−10.2 kcal/mol) dibandingkan galantamine sebagai kontrol positif dengan inhibisi 12,11% (0,19 mM) dan memiliki potensi agregasi rendah ketika di evaluasi dengan Congo Red. Pemotongan menghasilkan dua peptida pendek: TP 1.1 (WIGL) dan TP 1.2 (WIG) dengan afinitas masing-masing −11.8 dan −10.8 kcal/mol di sisi PAS AChE. Uji inhibisi menunjukkan aktivitas TP 1.1 sebesar 11,02% (0,19 mM) dan 13,44% (0,29 mM), sedangkan TP 1.2 mencapai 16,96% dan 25,42% pada konsentrasi yang sama. Evaluasi potensi agregasi peptida menggunakan teknik turbidimetri memberikan informasi bahwa TP 1.1 dan TP 1.2 tetap stabil sebagai kandidat terapi Alzheimer berbasis peptida pendek. Temuan ini menunjukkan pendekatan fragmentasi peptida dapat meningkatkan aktivitas inhibisi AChE dan mendukung desain peptida presisi untuk target di otak.

Keyword: Alzheimer, inhibitor AChE, Peptida teripang, Stabilitas peptida

ABSTRACT

Alzheimer's disease is associated with cholinergic system dysfunction due to the rapid degradation of acetylcholine (ACh) by the enzyme acetylcholinesterase (AChE). AChE inhibitors are important therapeutic targets; however, a major challenge lies in the ability of compounds to cross the blood–brain barrier (BBB). Two sea cucumber–derived peptide candidates, VLCAGDLR and SWIGLK, have been successfully identified. This study aimed to design bioactive peptides from sea cucumber with high affinity toward AChE, good physical stability, and potential BBB permeability. *In silico* analysis showed that SWIGLK exhibited a higher binding affinity (−10.2 kcal/mol) than galantamine, the positive control, with 12.11% inhibition at 0.19 mM and low aggregation potential as evaluated by Congo Red staining.Fragmentation of yielded two short peptides: TP 1.1 (WIGL) and TP 1.2 (WIG), with binding affinities of −11.8 and −10.8 kcal/mol, respectively, at the PAS site of AChE. *In vitro* inhibition assays demonstrated that TP 1.2 achieved the highest activity, with 16.96% inhibition at 0.19 mM and 25.42% at 0.29 mM, compared to TP 1.1 which reached only 13.44%. Turbidimetric evaluation confirmed that both short peptides remained physically stable.Overall, these findings indicate that peptide fragmentation can enhance AChE inhibitory activity, with TP 1.2 emerging as the most promising short peptide candidate for Alzheimer's disease therapy due to its superior inhibition performance and stability.

Keywords:
Alzheimer, AChE inhibitor, holothuroidea, peptide stability, blood-brain barrier