



Cholinesterase inhibitory activities of neuroprotective fraction derived from red alga *Gracilaria manilaensis*

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Abstract

Anti-cholinesterase (ChE)s are commonly prescribed as the symptomatic treatment of Alzheimer's disease. They are applied to prevent the breakdown of neurotransmitter acetylcholine (ACh) that bind to muscarinic and nicotinic receptors in the synaptic cleft. Seaweeds are one of the richest sources of bioactive compounds for both nutraceuticals and pharmacognosy applications. This study aimed to determine the anti-ChEs activity of *Gracilaria manilaensis*, one of the red seaweeds notables for its economic importance as food and raw materials for agar production. Methanol extracts (GMM) of *G. manilaensis* were prepared through maceration, and further purified with column chromatography into a semi-pure fraction. Ellman assay was carried out to determine the anti-acetylcholinesterase (AChE) and anti-butyrylcholinesterase (BuChE) activities of extracts and fractions. Lineweaver-Burk plot analysis was carried out to determine the inhibition kinetic of potent extract and fraction. Major compound(s) from the most potent fraction was determined by liquid chromatography-mass spectrometry (LCMS). GMM and fraction G (GMMG) showed significant inhibitory activity AChE with EC_{50} of 2.6 mg/mL and 2.3 mg/mL respectively. GMM and GMMG exhibit mixed-inhibition and uncompetitive inhibition respectively against AChE. GMMG possesses neuroprotective compounds such as cynerine A, graveoline, militarinone A, eplerenone and curumenol. These findings showed a promising insight of *G. manilaensis* to be served as a nutraceutical for neuronal health care in the future.

Keywords: *Gracilaria manilaensis*, Alzheimer's disease, Graveoline, Mixed-inhibition, Uncompetitive inhibition, Cholinesterases

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