NEUROPROTECTIVE EFFECTS OF THE LIPIDIC EXTRACT FROM INTEGUMENT OF SQUID *DOSIDICUS GIGAS*

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Key words: *Dosidicus gigas*, integument, phospholipids, amyloid β-peptide.

ABSTRACT

The integument of the squid *Dosidicus gigas* is an industrial waste and trouble the industrial processing. In this study, we examined the lipid composition and neuroprotective effects of *D. gigas* integument lipidic extract (DGI) in SH-SY5Y neuroblastoma cells which have been exposed to H_2O_2. The results showed that phospholipids, triacylglycerol and cholesterol accounted for 70.90 ± 4.96 (mean ± S.D.), 20.70 ± 3.54 and 8.40 ± 0.28% of DGI, respectively. And the main fatty acids were docosahexaenoic acid (30.53% of total fatty acid), palmitic acid (20.36% of total fatty acid) and eicosapentaenoic acid (11.84% of total fatty acid). DGI at the concentrations of 2, 4 and 8 mg/ml successfully protected SH-SY5Y cells against the cytotoxicity, markedly increased the cell proliferation, antioxidant enzymes of glutathione contents and catalase activities, and inhibited the secretion of amyloid β-peptide 1-42. Our results suggested that DGI may be a possible approach in the prevention of Alzheimer's disease and other neurodegenerative diseases.

I. INTRODUCTION

The first histological clinical report of Alzheimer's disease (AD) is mentioned in 1907 [1]. The observations of patients with clinically developed AD indicate that numerous psychopathological symptoms, including intellectual dysfunctions, orientation dysfunctions, memory dysfunctions, emotional disturbances, motor and psychomotor dysfunctions, etc. [3]. These psychopathological symptoms would make AD patients lose living abilities gradually and depend on families and care-givers severely, and acting like a neonate. Up to 90% of patients with dementia developed significant behavioral problems during the course of their illness [34], however the substantial proportion of patients with AD develop delusions or hallucinations sometimes over the course of their illness [32]. In other words, AD is considered simply as another form of dementia and it is common for aging individuals as well. Amyloid β-peptide (Aβ), an insoluble fibril deposites, is the major component of the senile plaques (SP) that characterize AD brain [15]. It has been demonstrated that Aβ is toxic directly to cultured neuron [37], and Aβ monomers assemble into dimmers, trimmers and higher aggregates, all of which are highly neurotoxic associated with AD [39]. Aβ involved on various neuronal cells surface receptors to generate reactive oxidative species (ROS), and ROS also leads to the hyperphosphorylation of Tau protein that destabilizes microtubules. This process eventually forms intracellular neurofibrillary tangles, one of observable hallmark pathology of AD [45]. In brain tissue, the level of thiobarbituric acid reactive substances (TBARS), superoxide dismutase (SOD) activity and catalase (CAT) activity are significantly decreased in AD temporal cortex when compared to age-matched controls [26]. It was observed that the sites of neurodegeneration and oxidative stress are associated with increased Aβ deposits in AD brain [19]. According to these observations, it is directly responsible for oxidative damage to neuron, leading to subsequent neuronal loss in the AD brain.

The squid *Dosidicus gigas*, also known as jumbo flying squid, is a commonly used by frozen seafood processing companies. Fresh squid *D. gigas* has a sticky consistency and their tissue is chewy. Its integument is separated from the edible part when unfrozen by hot water and treated as a fishery wastes troubling industrial processing [31]. Reportedly the phospholipids is 80-85% of total lipid in squid *Ommastrephes bartrami*, and docosahexaenoic acid (DHA) is a major fatty acid of total compositional fatty acid, moreover eicosapentaenoic acid (EPA) as the second [33, 10]. Numerous studies have reported that dietary DHA is required during development when cellular differentiation [7], enhanced a maze-learning ability in aged mice [24], prevention of AD [8], and reduced fish or DHA intake increases risk for AD [25]. Besides, phospholipids is a potentially useful source of ω-3 polyunsaturated fatty acid, and it has showed that intestinal absorption of phospholipids is followed by preferential uptake of ω-3 polyunsaturated fatty acid by the brain [27]. In animal model,

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