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Neuritogenic and in vitro antioxidant activities of Malaysian *Gracilaria manilaensis* Yamamoto & Trono

Jun-Rui Pang[1] · Veronica Ming-Jun Goh[1] · Cheng-Yau Tan[2] · Siew-Moi Phang[2] · Kah-Hui Wong[3] · Yoon-Yen Yow[1]

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Abstract

Numerous marine-based compounds have been identified as having diverse biological activities. *Gracilaria manilaensis* Yamamoto & Trono is a red agarophyte endemic to the Malaysia coastal area. It is used as a gelling and thickening agent for food industries. In this study, the rat pheochromocytoma cell line (PC-12Adh) was employed as in vitro model to investigate the neuritogenic activities in hot aqueous, methanol, and ethanol extracts of *G. manilaensis*. Phytochemical contents and in vitro antioxidant activities of the extracts were also determined. All *G. manilaensis* extracts were found to increase the percentage of neurite-bearing cells and upregulated the neuronal cytoskeleton of PC-12Adh cells with no inhibition across the tested concentration range (0–0.15 mg mL^{-1}). The methanol and ethanol extracts had higher phenolic and flavonoid contents than the hot aqueous extract. They also showed higher antioxidant activities against 2,2-diphenyl-1-pircryhydrazyl (DPPH) and 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) free radicals and higher reducing power compared to the hot aqueous extract. It is believed that *G. manilaensis* may possess potent bioactive compounds that mimic the neuroactivity of the nerve growth factor (NGF) for neuronal survival, development, and differentiation. It has been suggested that agar producer *G. manilaensis* might be a promising dietary supplement for cognitive health in the prevention of neurological disorders.

Keywords *Gracilaria manilaensis* · PC-12Adh · Neuritogenesis · Antioxidant · Phytochemicals

Introduction

Changes in lifestyle patterns, chronic non-communicable diseases such as diabetes, cardiovascular diseases, chronic respiratory diseases, and cancers are becoming increasingly significant causes of disability and premature death. Seaweeds appear to have a close relationship to the prevention of neurodegenerative diseases. This phenomenon is supported by the Japan population who uses seaweeds as part of their pivotal food source; they are lower in risk of dementia and Alzheimer's (Hu et al. 2013; Ozawa et al. 2013). Seaweeds are good sources of antioxidant and anti-inflammation to reduce the burden of chronic illness (Heo et al. 2006; Pangestuti and Kim 2011; Farasat et al. 2014). They contain minerals and nutrients such as iodine, iron, and vitamins, as well as producing phytochemicals and biochemical compounds like carotenoids and polysaccharides for primary consumers of the food chain (de Almeida et al. 2011; Gupta and Abu-Ghannam 2011), and they produce secondary metabolites such as antioxidants (Wells et al. 2017).

Much research shows that seaweeds contain potential phytochemicals which may have a role in therapies against neurodegenerative diseases (Alghazwi et al. 2016). For instance, *Sargassum macrocarpum* contains sargaquinoic acid (MC14) (Tsang and Kamei 2004) and sargachromenol (Tsang and Kamei 2004; Tsang et al. 2005) both of which have antioxidant and neurite outgrowth promoting activity on PC-12Adh cells. The PC-12Adh cell line is derived from pheochromocytoma of *Rattus norvegicus* (Greene and Tischler 1976) and has been improved by the American Type Culture Collection (ATCC) for adherent ability (Wang et al. 2015). It is used as the in vitro model of neuritogenesis due to their morphological, physiological, and biochemical patterns which represent

✉ Yoon-Yen Yow
yoonyeny@sunway.edu.my

[1] Department of Biological Sciences, School of Science & Technology, Sunway University, 47500 Bandar Sunway, Selangor Darul Ehsan, Malaysia

[2] Institute of Ocean and Earth Sciences, University of Malaya, 50603 Kuala Lumpur, Malaysia

[3] Department of Anatomy, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

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