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Neurotrophic Properties of the Lion's Mane Medicinal Mushroom, *Hericium erinaceus* (Higher Basidiomycetes) from Malaysia

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ABSTRACT: Neurotrophic factors are important in promoting the growth and differentiation of neurons. Nerve growth factor (NGF) is essential for the maintenance of the basal forebrain cholinergic system. Hericenones and erinacines isolated from the medicinal mushroom *Hericium erinaceus* can induce NGF synthesis in nerve cells. In this study, we evaluated the synergistic interaction between *H. erinaceus* aqueous extract and exogenous NGF on the neurite outgrowth stimulation of neuroblastoma-glioma cell NG108-15. The neuroprotective effect of the mushroom extract toward oxidative stress was also studied. Aqueous extract of *H. erinaceus* was shown to be non-cytotoxic to human lung fibroblast MRC-5 and NG108-15 cells. The combination of 10 ng/mL NGF with 1 µg/mL mushroom extract yielded the highest percentage increase of 60.6% neurite outgrowth. The extract contained neuroactive compounds that induced the secretion of extracellular NGF in NG108-15 cells, thereby promoting neurite outgrowth activity. However, the *H. erinaceus* extract failed to protect NG108-15 cells subjected to oxidative stress when applied in pre-treatment and co-treatment modes. In conclusion, the aqueous extract of *H. erinaceus* contained neuroactive compounds which induced NGF-synthesis and promoted neurite outgrowth in NG108-15 cells. The extract also enhanced the neurite outgrowth stimulation activity of NGF when applied in combination. The aqueous preparation of *H. erinaceus* had neurotrophic but not neuroprotective activities.

KEY WORDS: medicinal mushrooms, combination, cytotoxicity, enhancement, extracellular NGF, medicinal mushroom, neurite outgrowth, neurofilament, oxidative stress

ABBREVIATIONS: Bfgf, basic fibroblast growth factor; BDNF, brain-derived neurotrophic factor; DMSO, dimethyl sulfoxide; GDNF, glial cell line-derived neurotrophic factor; H₂O₂, hydrogen peroxide; MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide; NGF, nerve growth factor; NT-3, neurotrophin-3; PBS, phosphate-buffered saline; RMP, resting membrane potential; TUNEL: terminal deoxynucleotidyl transferase-mediated dUTP nick-end labelling