RESEARCH ARTICLE

Uridine from *Pleurotus giganteus* and Its Neurite Outgrowth Stimulatory Effects with Underlying Mechanism

Chia-Wei Phan1,2,*, Pamela David1,2, Kah-Huii Wong1,3, Murali Naidu1,3, Vikineswary Sabaratnam1,4,*

1 Mushroom Research Centre, Institute of Biological Sciences, Faculty of Science, University of Malaya, 50603 Kuala Lumpur, Malaysia, 2 Centre of Excellence for Learning and Teaching, UCSI University, No. 1, Jalan Menara Gading, UCSI Heights, 56000 Cheras, Kuala Lumpur, Malaysia, 3 Department of Anatomy, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, 4 Institute of Biological Sciences, Faculty of Science, University of Malaya, Kuala Lumpur, Malaysia

* phancw@ucsiuniversity.edu.my (CWP); vikl@um.edu.my (VS)

Abstract

Neurodegenerative diseases are linked to neuronal cell death and impairment of neurite outgrowth. An edible mushroom, *Pleurotus giganteus* was found to stimulate neurite outgrowth *in vitro* but the chemical constituents and the underlying mechanism is yet to be elucidated. The chemical constituents of *P. giganteus* (linoleic acid, oleic acid, cinnamic acid, caffeic acid, *p*-coumaric acid, succinic acid, benzoic acid, and uridine) were tested for neurite outgrowth activity. Uridine (100 μM) was found to increase the percentage of neurite-bearing cells of differentiating neuroblastoma (N2a) cells by 43.1±0.5%, which was 1.8-fold higher than NGF (50 ng/mL)-treated cells. Uridine which was present in *P. giganteus* (1.80 ±0.03 g/100g mushroom extract) increased the phosphorylation of extracellular-signal regulated kinases (ERKs) and protein kinase B (Akt). Further, phosphorylation of the mammalian target of rapamycin (mTOR) was also increased. MEK/ERK and PI3K-Akt-mTOR further induced phosphorylation of CAMP-response element binding protein (CREB) and expression of growth associated protein 43 (GAP43); all of which promoted neurite outgrowth of N2a cells. This study demonstrated that *P. giganteus* may enhance neurite outgrowth and one of the key bioactive molecules responsible for neurite outgrowth is uridine.

Introduction

The economic burden of neurodegenerative disease is enormous and is expected to grow rapidly as more people live longer. Current drug therapy for neurodegenerative diseases is ineffective with many side effects and it only provides a short term delay in the progression of the disease. Further, the drug development pipeline is drying up and the number of drugs reaching the market has lagged behind the growing need for such drugs. It is therefore of utmost importance to find appropriate solutions to prevent, or perhaps impede, the development of neurodegenerative diseases.