Therapeutic potential of culinary-medicinal mushrooms for the management of neurodegenerative diseases: diversity, metabolite, and mechanism

Chia-Wei Phan¹,², Pamela David¹,³, Murali Naidu¹,³, Kah-Hui Wong¹,³, and Vikineswary Sabaratnam¹,²

¹Mushroom Research Centre, Institute of Biological Sciences, Faculty of Science, University of Malaya, Kuala Lumpur, Malaysia, ²Institute of Biological Sciences, Faculty of Science, University of Malaya, Kuala Lumpur, Malaysia, and ³Department of Anatomy, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Abstract
Mushrooms have long been used not only as food but also for the treatment of various ailments. Although at its infancy, accumulated evidence suggested that culinary-medicinal mushrooms may play an important role in the prevention of many age-associated neurological dysfunctions, including Alzheimer’s and Parkinson’s diseases. Therefore, efforts have been devoted to a search for more mushroom species that may improve memory and cognition functions. Such mushrooms include Hericium erinaceus, Ganoderma lucidum, Sarcodon spp., Antrodio camphorata, Pleurotus giganteus, Lignosus rhinocerotis, Grifola frondosa, and many more. Here, we review over 20 different brain-improving culinary-medicinal mushrooms and at least 80 different bioactive secondary metabolites isolated from them. The mushrooms (either extracts from basidiocarps/mycelia or isolated compounds) reduced beta amyloid-induced neurotoxicity and had anti-acetylcholinesterase, neurite outgrowth stimulation, nerve growth factor (NGF) synthesis, neuroprotective, antioxidant, and anti-(neuro)inflammatory effects. The in vitro and in vivo studies on the molecular mechanisms responsible for the bioactive effects of mushrooms are also discussed. Mushrooms can be considered as useful therapeutic agents in the management and/or treatment of neurodegeneration diseases. However, this review focuses on in vitro evidence and clinical trials with humans are needed.

Introduction
Life expectancy of humankind had increased to 50–60 years at the beginning of the twentieth century due to improved medical, dietary, and sanitation conditions. It is, however, foreseen that society will witness an elevated life expectancy of 80–90 years by the twenty-first century (Candore et al., 2006). Nevertheless, ageing is inexorable with an age-associated decline in immune competence and the onset of chronic inflammation leading to neurodegenerative diseases including dementia, Alzheimer’s disease (AD) and Parkinson’s disease (PD); atherosclerosis and stroke; diabetes; sarcopenia; and cancer (Martorana et al., 2012). With the increased lifespan of the world’s population, it is estimated that about 80 million people will suffer from dementia by 2040 whereby AD accounted for almost 60% of dementia cases (Bharadwaj et al., 2010).

The pathological hallmarks of AD are characterised by amyloidogenic processing of amyloid precursor protein (APP) and a subsequent β-amyloid cascade and tau hyperphosphorylation (Claeysen et al., 2012). Other hypotheses of AD pathogenesis include microglial activation associated with neuroinflammation, increased level of acetyl cholinesterase (AChE) activity, and free radical generation (Martorana et al., 2012). Drug therapies for AD include nicotine, melatonin, estrogens (Côté et al., 2012) cholinesterase inhibitors, and an N-methyl-D-aspartate receptor antagonist named memantine (Hong-Qi et al., 2012). However, the current AD drug therapy is ineffective and only provides a short-term delay progression of AD. Moreover, although there was a close association of the use of non-steroidal anti-inflammatory drugs (NSAIDs) and a lower incidence of AD, patients suffered from withdrawal syndrome as a result of gastrointestinal toxicity (Hong-Qi et al., 2012).

There has been a recent upsurge of interest in complementary and alternative medicine, especially dietary supplements and functional foods in delaying the onset of age-associated neurodegenerative diseases. As recently reviewed by Perry & Howes (2011), phyto-chemical approach for dementia and AD treatment includes galantamine from Narcissus sp., lemon balm (Melissa officinalis), and periwinkle (Vinca minor). Other edible “brain food” consists primarily of blueberry, grape seed, pomegranate, and walnut. The polyphenol entities found in the vegetables,