Hormetic Nutrition in Antiaging Medicine: From bench to Clinics

Calabrese V

Department of Biomedical and Biotechnological Sciences, School of Medicine, University of Catania

Abstract

Human life develops and expands not only in time and space, but also in the retrograde permanent recollection and interweaving of memories. Therefore, individual human identity depends fully on a proper access to the autobiographical memory. Such access is hindered or lost under pathological conditions such as Alzheimer's disease (AD), including recently associated oxidant pathologies, such as neural degeneration occurring in Parkinson's disease (PD) or neurosensorial degeneration occurring in Menière's disease. Oxidative stress and altered antioxidant systems have been suggested to play a role in the aetiology of major neurodegenerative disorders, and altered expression of genes sensing oxidative stress, as well as decreased cellular stress response mechanisms could synergistically contribute to the course of these oxidant disorders. Mushrooms have been used in traditional medicine for thousands of years [1-4]. In our recent study we evaluated the effects of *Hericium erinaceus*, a nutritional mushroom with important antioxidant effects, in a rat model of AD. *Hericium erinaceus* administration reduced behavioral changes and hippocampal neuronal degeneration. Additionally, it reduced phosphorylated-Tau levels and aberrant APP overexpression and β-amyloid accumulation. Moreover, *Hericium erinaceus* decreased the prooxidative and pro-inflammatory hippocampal alterations induced by AD. In particular, it reduced the activation of the NLRP3 inflammasome components, usually activated by increased oxidative stress during the AD. Collectively, our results showed that *Hericium erinaceus* has protective effects on the behavioral alteration and histological modification associated with the AD acting by the modulation of the oxidative and inflammatory pathways, as well as regulating brain cellular stress. Herein, we discuss cellular mechanisms underlying AD neuroinflammatory pathogenesis that are contributory to Alzheimer's disease. We describe endogenous cellular defence mechanism modulation and neurohormesis as a potentially innovative approach to therapeutics for AD and other neurodegenerative conditions that are associated with mitochondrial dysfunction and neuroinflammation, including Meniere disease patients as a measurable model of neurodegenerative neuro-cochleosensory system. Particularly, we consider the emerging role of Vitagenes as an important component of the neuroprotective network, as well as the importance of Coriolus and Hericium nutritional mushrooms in redox stress responsive mechanisms and neuroprotection [5]. In addition, we have explored the development of PD-related pathology in the context of an experimental model of Traumatic brain injury (TBI) and the potential ability of Coriolus versicolor and Hericium erinaceus to prevent neuro-degenerative processes. A growing number of studies have demonstrated that dietary interventions regulate mitochondrial ROS production, detoxification and oxidative damage repair. Many (but not all) of these nutritional interventions are related with extension of lifespan, or protection against diseases related with age, in mammals. Emerging nutraceuticals are today showing promise as modulators of mitochondrial redox metabolism capable of eliciting beneficial outcomes. Mushrooms, known for their strong antioxidant properties, have attracted interest due to their potential in neuroprotection, antioxidant, and anti-inflammatory effects, as well as in proteome and

mitochondrial homeostasis restoration as a basic mechanism to withstand mitochondrial dysfunction-associated neuroinflammatory disorders [1-5].

References

1. D'Amico R, et al., Antioxidants 2021 Jun 2;10(6):898.
2. Trovato A, et al., Neurotoxicology. 53:350-358.
3. Trovato A, et al., Immun Ageing. 2016 13:23. doi: 10.1186/s12979-016-0078-8.
4. Amara I, et al., Cell Stress Chaperones. 2020 25(6):919-928.
5. Scuto M, et al., Int J Mol Sci. 2019 Dec 31;21(1). pii: E284. doi: 10.3390/ijms21010284.