ID651 | Antioxidant and Neuroprotective Potential of Mushroom Biomass: Effects on ROS Production in Human Microglial Cell Line (HMC3) and Alzheimer's Disease Caenorhabditis elegans Models

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Background: Mushrooms exhibit diverse bioactive compounds with prebiotic, immunomodulatory, antioxidant, and neuroprotective effects. These benefits may arise from direct metabolite absorption and gut microbiota modulation, a key regulator of brain health through the gut-brain axis1. This study explored the neuroprotective potential of macromolecules from the mushroom biomass (MB) from Trametes versicolor (TV), Hericium erinaceus (HE), and Pleurotus ostreatus (PO) before and after gastrointestinal digestion (GID), together with microbiota-derived metabolites. Their effects were evaluated in the human microglial cells (HMC3) by ROS measurement and in transgenic Caenorhabditis elegans Alzheimer's disease (AD) models by chemotaxis and paralysis assays.

Methods: Bioactive compounds in MBs were quantified by enzymatic assays, HPLC, and spectrophotometric methods. GID was simulated by the INFOGEST standardized method, and the microbiota-derived metabolites were determined by human fecal fermentation. Intracellular ROS in HMC3 cells were measured using a fluorescent probe. Transgenic C. elegans AD models were used for chemotaxis and paralysis assays.

Results: Biochemical characterization of MBs confirmed the presence of bioactive compounds with antioxidant potential. TV showed higher levels of γ-aminobutyric acid (GABA; 125.99 mg/100 g), ergosterol (8.97 mg/100 g), ascorbic acid (3.31 mg/100 g), carotenoids (18.05 mg/100 g), and free phenolic compounds (113.31 mg GAE/100 g). HE possessed higher tocopherol levels (816.74 µg/100 g), while PO was richer in zinc content (2.37 mg/100 g). Total glucan content (76.15-80.45%) and selenium content (87.68–93.04 µg/100 g) were similar across species. All biomass species inhibited ROS production in microglia (15.35–21.29%) at 0.63–1.25 mg/mL. Digestive fractions of all mushroom species significantly improved chemosensory responses in the BR5270 strain, which expresses the hyperphosphorylated tau protein in neurons. TV, HE, and PO also significantly delayed paralysis progression in the CL4176 strain. Moreover, butyric acid and GABA restored chemotaxis deficits in CL2355 and delayed progressive paralysis in CL4176, both strains with amyloid beta peptide expression, indicating protective effects against amyloid-induced neuronal dysfunction.

Conclusions: Mushroom biomass-derived compounds and microbiota metabolites show neuroprotective potential, mitigating Aβ- and Tau-induced toxicity, two of the main hallmarks of AD.