

Medicinal mushroom extracts exert differential effects *in vitro* on the release of inflammatory mediators by stimulated peripheral blood mononuclear cells from healthy, older adults

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Medicinal mushrooms contain both water-soluble and insoluble biologically active compounds which are hypothesised to have anti-inflammatory, antioxidant and immunomodulatory properties.⁽¹⁾ However, there is limited quality evidence both *in vitro* and *in vivo* supporting the proposed effects. Further, whether treatment is beneficial in populations where immune function is compromised, such as older adults, is unclear. As such, the aim of this study was to examine the effects of medicinal mushroom extracts on inflammatory mediator release in stimulated peripheral blood mononuclear cells (PBMCs), isolated from healthy subjects aged 50 years and older. Isolated PBMCs were cultured at a density of 2×10^6 cells/mL and treated separately with 1 and 10 mg/mL of extracts (water-ethanol, WE; water-ethanol with Kakadu Plum, KP; water-glycerin, WG; water-glycerin liposomal, WGL) from medicinal mushrooms *Hericium coralloides* (HC) and *Trametes versicolor* (TV) for 3 hours. Following treatment, PBMCs were stimulated, separately, with 1 MOI rhinovirus A1 (RVA1), 0.1 multiplicity of infection (MOI) influenza A/H1N1pdm09 (H1N1), 5 ng/mL lipopolysaccharide (LPS), or 100 µg/mL house dust mite (HDM). Inflammatory mediator concentrations were measured in cell-free supernatants using LEGENDplex™ assay. For RVA1, H1N1: interleukin (IL)-1β, IL-6, IL-8, IL-10, interferon (IFN)-α2, and IFN-γ. For LPS: IL-1β, IL-6, IL-8, IL-10, and tumour necrosis factor (TNF)-α. For HDM: IL-4, IL-5, IL-13, IL-6, IL-10 and TNF-α. Data was analysed using Friedman Test, with Dunn's multiple comparisons where appropriate. In the presence of either RVA1 or H1N1, type I and II IFN was impaired ($p < 0.05$) following treatment with at least one concentration of all extracts compared to untreated cell controls. This was coupled with greater pro-inflammatory cytokines (IL-1β, IL-6, and IL-8). RVA1-induced IL-10 was elevated in HCWG (10 mg/mL, $p < 0.001$) treated cells compared to control. Similarly, H1N1-induced IL-10 was greater following HCWG (1 mg/mL, $p < 0.001$; 10 mg/mL, $p < 0.001$) and TVWE (10 mg/mL, $p = 0.033$), compared to untreated cells. In the presence of LPS, IL-1β was significantly lower with extracts from TV, compared to untreated cells. Following HDM exposure, the concentration of IL-5 was significantly lower with 10 mg/mL HCWG, HCWGL, TVWE, TVWG, and TVWGL extracts, compared to untreated cells. Similarly, at least one dose of all extracts, except KP extracts, had significantly lower HDM-induced IL-13 compared to untreated cells. Following HCWG (1 mg/mL, 10 mg/mL) and HCWE (10mg/mL), this was coupled with greater HDM-induced IL-10 compared to untreated cells. Extracts of medicinal mushrooms exert differential effects on the release of inflammatory and antiviral mediators *in vitro*. The observation of reduced type 2 cytokines in response to HDM, a common allergen, may be beneficial in conditions where allergic inflammation is present including asthma, allergic rhinitis, and eczema. Further research is needed to examine effects of extracts *in vivo*.

References

1. Ślusarczyk J, Adamska E & Czerwik-Marcinkowska J (2021) *Nutrients* 13 (9), 3178.