

Medicinal mushrooms as multitarget agents against mental fatigue: antioxidant and neuroprotective insights

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INTRODUCTION

Mental fatigue is an increasingly common condition associated with aging, chronic stress, and neurological disorders, which negatively impacts cognitive performance, mood, and physical efficiency [1]. Its multifactorial origin, involving oxidative stress, mitochondrial dysfunction, chronic inflammation, and neuroimmune imbalance, makes it difficult to manage with current therapeutic approaches, whose effectiveness remains limited [2]. Therefore, there is growing interest in identifying safer, multi-target strategies. In this context, medicinal mushrooms emerge as promising natural sources of bioactive compounds with antioxidant, neuroprotective, and immunomodulatory properties. For this reason, the present study investigates *Cordyceps sinensis* (Berk.) Sacc., *Ganoderma lucidum* (Curtis) P. Karst., and *Hericium erinaceus* (Bull.) Pers. to evaluate their potential role in counteracting the mechanisms involved in mental fatigue.

METHODS

Extracts of *C. sinensis*, *G. lucidum*, and *H. erinaceus* were obtained using ultrasound-assisted extraction (UAE), employing different solvents (water and ethanol at various concentrations) and temperatures. Based on a preliminary literature review, the optimal extraction conditions were identified (65 °C, 1 hour). Additional extractions were performed at room temperature to evaluate industrial scalability. Total phenolic content was quantified and antioxidant activity was evaluated using ABTS, DPPH, and FRAP assays. The results were integrated using the Relative Antioxidant Capacity Index (RACI). Neuroprotective potential was evaluated using cell-free *in vitro* assays targeting acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes, with galantamine serving as the reference inhibitor.

CONCLUSIONS

A comparative evaluation of the different extraction conditions confirmed that the composition of the solvent strongly influences the biological activity of all three mushroom species. For *C. sinensis*, the aqueous extracts (particularly the one obtained at room temperature) exhibited the highest antioxidant capacity and the most significant AChE inhibitory effects. Regarding the BChE inhibitory capacity of *C. sinensis*, the CS_E50 extract showed the best activity. *G. lucidum* and *H. erinaceus* achieved better antioxidant performance in ethanol-based extracts (GL_E50, GL_E95, HE_E70), also demonstrating moderate and comparable inhibition of AChE and BChE. The observed cholinesterase inhibitory activity suggests a potential neuroprotective effect, supporting their possible application in the prevention or management of cognitive decline, neurodegenerative disorders, and mental fatigue.

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RESULTS

Bioactivity was strongly influenced by the solvent composition and extraction temperature, highlighting the crucial role of these parameters in determining the recovery of bioactive compounds. As for *C. sinensis*, the aqueous extract (CS_W) exhibited the highest antioxidant capacity according to the RACI index (Fig. 1), suggesting greater efficiency in the extraction of antioxidant compounds. In contrast, *G. lucidum* and *H. erinaceus* exhibited the highest antioxidant activity in ethanol-based extracts, especially at higher concentrations and temperatures (GL_E95, HE_E70), indicating that less polar compounds, such as triterpenoids and phenolic derivatives, contribute significantly to their antioxidant potential.

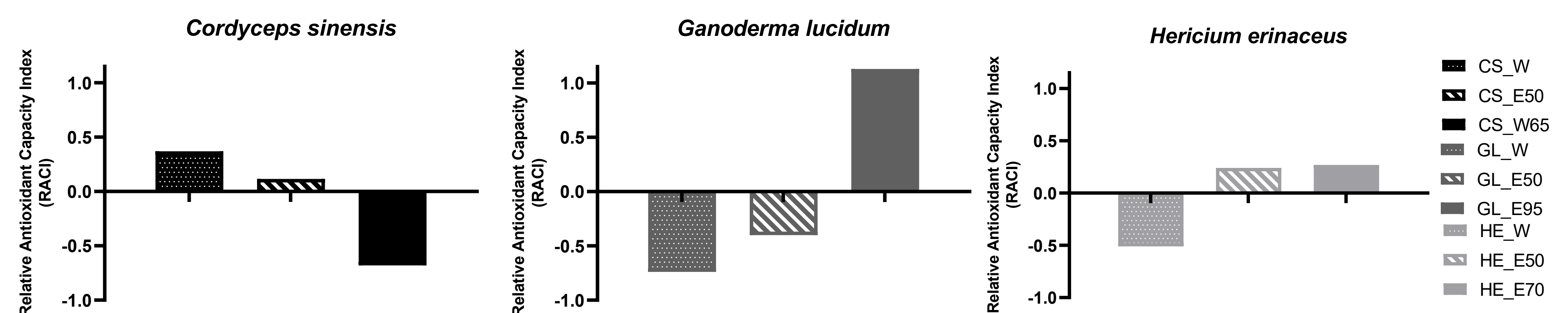


Figure 1. Relative antioxidant capacity index of CS, GL and HE extracts.

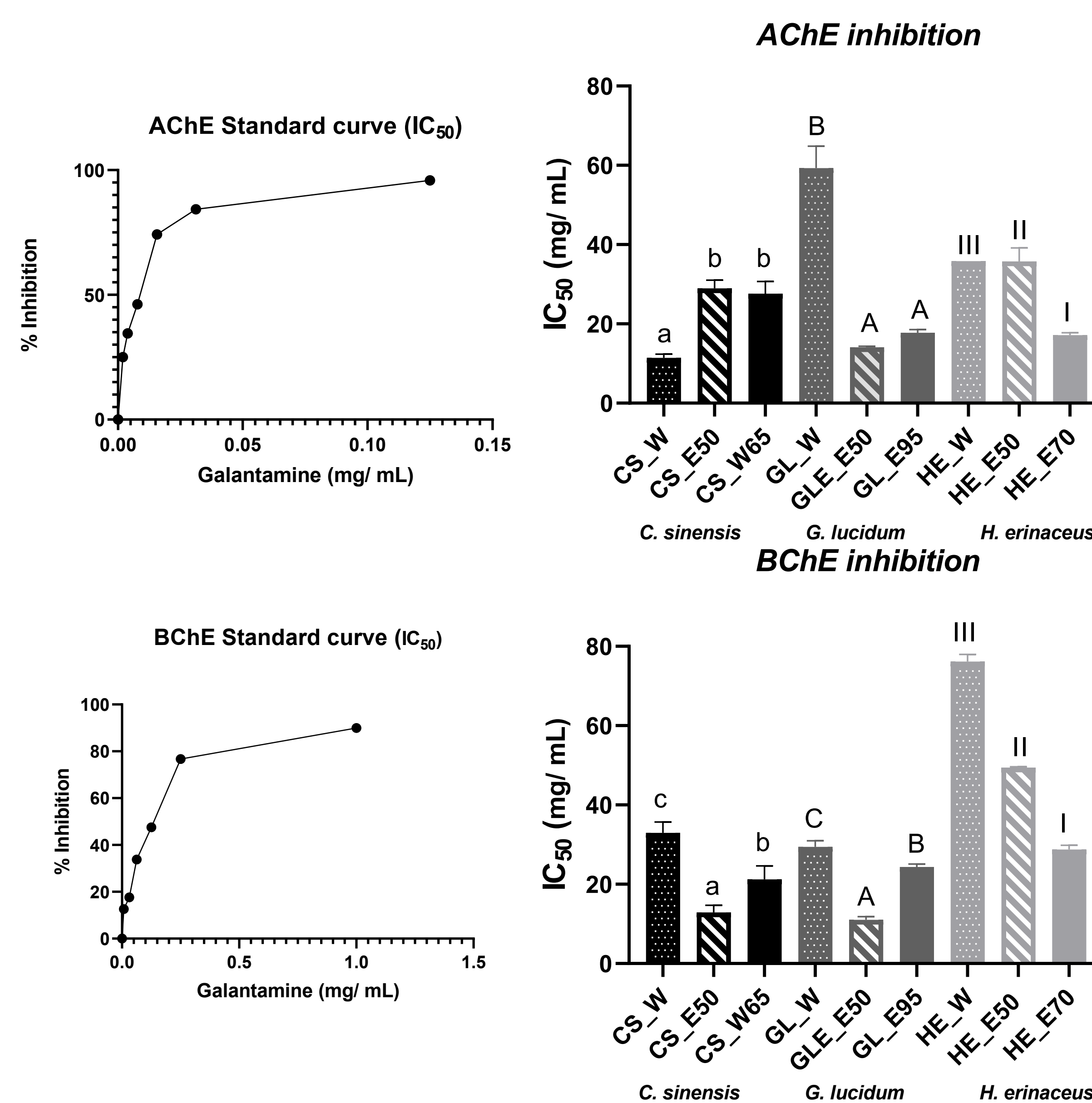


Figure 2. IC₅₀ values are presented as mean ± SD (n = 3), using descriptive statistical analysis. Data are expressed as mean ± SD (n = 3); a, b, c letters indicate significant differences among *C. sinensis* extracts; A, B, C among *G. lucidum* extracts and I, II, III among *H. erinaceus* extracts.

Enzymatic assays demonstrated dose-dependent inhibitory activity against both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes, supporting the neuroprotective potential of the extracts (Fig.2). For AChE inhibition, the aqueous extract of *C. sinensis* (CS_W) showed the highest activity, while ethanol extracts of *G. lucidum* (GL_E50, GL_E95) and *H. erinaceus* (HE_E70) exhibited comparable and pronounced inhibitory effects. Regarding BChE inhibition, the 50% EtOH extract (CS_E50) of *C. sinensis* showed the strongest activity, while the aqueous extract (CS_W65) also demonstrated notable effects. For *G. lucidum*, the 50% EtOH extract (GL_E50) was the most effective, whereas *H. erinaceus* confirmed the highest activity with the 70% EtOH extract (HE_E70), suggesting a multitarget profile and a potential synergistic effect among different classes of bioactive compounds.

REFERENCES

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LEGEND

CS, *Cordyceps sinensis*; GL *Ganoderma lucidum*; HE, *Hericium erinaceus*
CS_W, GL_W, HE_W (WATER, rt), CS_E50, GL_E50, HE_E50 (50%EtOH/H₂O, rt), CS_W65 (WATER, 65°C), GL_E95 (95%EtOH/H₂O, 65°C), HE_E70 (70%EtOH/H₂O, 65°C)