Title:
Evaluating the Effect of Lion's Mane Mushroom on Cognitive Function, Stress, Depression, and Mood: A Systematic Review, Meta-Analysis, and Network Pharmacology Study

Rationale and Background:
Lion's Mane mushroom is a natural supplement that may support brain health and emotional well-being. Early studies suggest it can enhance memory, alleviate stress, and reduce symptoms of depression and anxiety. These potential benefits are believed to stem from its ability to stimulate nerve growth and mitigate neuroinflammation. However, no meta-analysis has yet synthesized the available clinical evidence to comprehensively evaluate the effects of Lion's Mane. This review seeks to address that gap by conducting the first meta-analysis assessing its impact on cognitive function, mood, stress, and depression. In addition, a network pharmacology analysis will be performed to explore the underlying mechanisms of action of Lion's Mane bioactive compounds.

Objectives:
This review aims to evaluate the effect of lion's mane mushroom on cognitive function, stress, depression and mood.

Eligibility Criteria:
- **Population:** Participants of any age, sex, or health status (including healthy individuals and clinical populations)
- **Intervention:** Lion's mane mushroom
- **Comparator:** Placebo or pre-intervention
- **Outcomes:** Cognitive function (MMSE scales), stress levels (VAS or DASS-21), depression (BDI), mood (POMS)
- **Study Design:** Randomized and non-randomized study
- **Time frame:** No restriction

Information Sources:
Searches will be conducted in:
- PubMed
- Scopus
- Cochrane
- EBSCO
- ProQuest
- Scilit
- Web of Science

Search Strategy:
Search terms will include combinations of:
("Mane Mushroom" OR "Hericium erinaceus" OR "Lion's Mane") AND (Cognitive OR Cognition OR Stress* OR Depression OR Depressive OR Mood OR Emotion)
Search strategy will be adapted per database.

Data Management and Study Selection:
All identified records will be imported into a Rayyan.ai. Two independent reviewers will screen titles and abstracts, followed by full-text reviews. Disagreements will be resolved by the third author.

Data Extraction:
Data will be extracted using a standardized form, including:

- Study characteristics (author, year, country)
- Population details (age, sex, baseline condition)
- Intervention details (form, dose, duration)
- Comparator
- Outcome measures: Cognitive function (MMSE scales), stress levels (VAS or DASS-21), depression (BDI), mood (POMS)
- Follow-up duration
- Results (means, SD, effect size)

Risk of Bias Assessment:
Risk of bias will be assessed using the Cochrane RoB 2.0 tool for RCTs and ROBINS-I for Non-RCTs.

Data Synthesis:
Data from eligible studies will be combined using meta-analysis. For continuous outcomes (e.g., cognitive test scores,depression or stress scale scores), we will calculate either mean differences (MD) or standardized mean differences (SMD) with 95% confidence intervals, depending on the measurement scales used across studies. A random-effects model will be used to account for expected clinical and methodological heterogeneity. Heterogeneity will be assessed using the I^2 statistic.

Subgroup and Sensitivity Analysis:
If sufficient data are available, subgroup analyses will be performed by:

- Characteristic of population
- Dose/form of intervention
- Study duration

Sensitivity analysis will be conducted to assess the robustness of the results by excluding studies that contribute substantially to heterogeneity.

Certainty of Evidence:
GRADE analysis will be used to assess the certainty of evidence for each outcome.

Ethics and Dissemination:
Ethical approval is not required for this review. The results will be disseminated through peer-reviewed publication.

Registration:
This protocol is registered in PROSPERO.

Funding and Conflicts of Interest:
Review has no specific/external funding but is supported by guarantor/review team. The authors declare no conflict of interest.