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REVIEW PAPER

Effects of *Ganoderma lucidum* ("lingzhi") supplementation on blood lipids – a systematic review of clinical trials

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ABSTRACT

Introduction and aim. Impaired blood lipid profile is a major risk factor for cardiovascular disease, the leading cause of mortality worldwide. Supplementation of *Ganoderma lucidum* ("lingzhi") has been postulated to have a positive impact on blood lipids. This review aims to evaluate the evidence on this topic.

Material and methods. A systematic search of Google Scholar, PubMed and clinicaltrials.gov databases was performed to identify randomized clinical trials and cross-over trials which assessed the effects of lingzhi supplementation on blood lipids. The gathered data were reviewed and analyzed in accordance with PRISMA guidelines.

Analysis of the literature. Of the 805 records identified in the initial search, a total of 7 studies met all the inclusion criteria and were qualified for the review. None of them reported a statistically significant change in triglycerides, high-density lipoprotein, or low-density lipoprotein during lingzhi supplementation. Only 2 out of 7 trials showed a moderate decrease in total cholesterol level.

Conclusion. There is no evidence to support any effect of *G. lucidum* supplementation on triglycerides, high-density lipoprotein or low-density lipoprotein. Its influence on total cholesterol also remains highly doubtful based on the present systematic review.

Keywords. cardiovascular disease, cholesterol, *Ganoderma lucidum*, lingzhi, lipids

Introduction

Cardiovascular disease is the leading cause of death worldwide, accounting for 27% of global mortality.[1] Impaired blood lipid profile, especially elevated level of low-density lipoprotein, presents a major, yet potentially modifiable risk factor for its development.[2,3] For this reason, statins – the most common lipid-lowering drugs – play a key role in the primary prevention of cardiovascular disease.[4] However, the use of statins is associated with several side effects, which has stimulated extensive research into alternative therapies.[5]

Ganodrema lucidum (commonly known as "lingzhi" or "reishi") is a mushroom widely used in traditional medicine of many Asian countries, notably in traditional Chinese medicine. It is believed to possess immunomodulating, bacteriostatic, hepatoprotective, and life-prolonging properties.[6] Some research also suggests that *G. lucidum* has a beneficial impact on impaired blood lipid profile and could be used in the cardiovascular disease prevention.[7–9]

Aim

Despite considerable clinical and research interest in this topic, a methodologically rigorous summary of the existing literature is lacking. No up-to-date review has systematically assessed the potential effects of *G. lucidum* supplementation on blood lipids in the general population. This article aims to fill this gap by critically

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analyzing existing clinical trials, including the latest research.

Material and methods

The study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA 2020) statement,[10] but was not prospectively registered. The focus was on the effect of lingzhi supplementation on blood lipids, namely: triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL,) and low-density lipoprotein (LDL).

Search strategy

PubMed and Google Scholar databases were searched using the following phrases: ("Ganoderma lucidum" OR "Reishi" OR "Lingzhi") AND ("Lipids" OR "Cholesterol" OR "Triglycerides" OR "Cardiovascular"). No restrictions regarding language, publication period or publication type were applied. Moreover, ClinicalTrials.gov repository was screened for all studies, which used "Ganoderma" as an intervention/treatment. In addition, reference lists of included articles were manually checked to identify more potentially relevant publications. The final search took place on September 9, 2024.

Study selection

All identified studies were entered into Rayyan software[11] and duplicates manually removed. A single author analyzed each unique study based on title and abstract, and then evaluated the full texts of publications that passed the initial assessment. Studies were considered to be eligible for the review if they fulfilled all of the following criteria: randomized controlled trials or controlled crossover trials; *G. lucidum* in a single-component preparation; changes in TG, TC, HDL, and LDL as an outcome; full text in English language. Conversely, the exclusion criteria were: in vitro studies, animal studies, no-intervention studies, case reports, reviews or meta-analyses; studies lacking randomization or a control group; studies that only administrated *G. lucidum* in combination with other herbal medicine; publications in languages other than English.

Data extraction

Data from all included publications were extracted and analyzed by a single researcher. Extracted information included: first author's last name and publication date; study design; sample size; participants health status; administered dose of *G. lucidum*; duration of the intervention; statistically significant outcomes regarding blood lipids.

Risk of bias assessment

Risk of bias was judged by a single author in accordance with the recommendations of the Cochrane Handbook of Systematic Reviews of Interventions.[12] The applied criteria were: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. Each criterion was rated as "low risk", "unclear risk" or "high risk."

Analysis of the literature

Literature selection

The electronic search yielded 805 records. Of these, 95 were excluded as duplicates, and 695 because they were not relevant to the purpose of the review. In the latter case, the main reasons behind exclusion were: unrelated topic (studies discussing biotechnology, biochemistry or ecology of *G. lucidum*), wrong study type (reviews, laboratory studies or animal studies), non-English language studies. The remaining 15 publications were retrieved and subjected to rigorous evaluation, of which 8 did not meet the inclusion criteria due to wrong outcome (n=3) and flawed study design, i.e. lack of randomization or appropriate control group, (n=5). Ultimately, 7 studies were included in the review (Fig. 1).

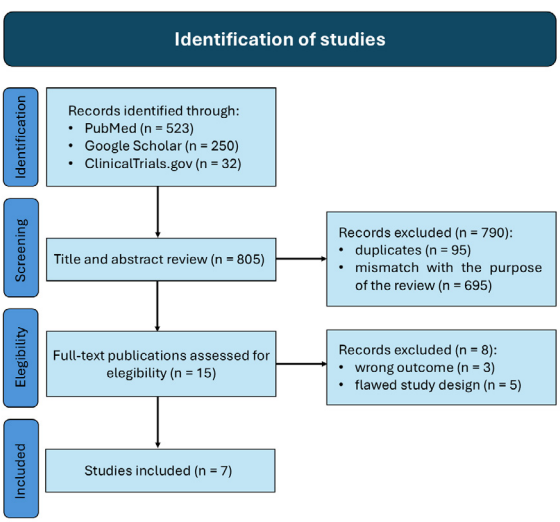

Fig. 1. PRISMA flowchart of this systematic review

Characteristics of the included studies

As the articles included in this study vary greatly in terms of research methodology and data reporting practices, it seems appropriate to discuss them in detail. The Wachtel-Galor 2004a[13] study was a double-blind placebo-controlled crossover trial which enrolled 10 healthy patients. Half of the subjects were non-selectively assigned to begin daily supplementation with 720 mg *G. lucidum*, and another half with suitable placebo. Supplementation lasted 10 days, and after at least two-week-long washout period, patients received the alternative treatment. The obtained data suggested a negligible decline in blood lipids (TG, TC, HDL, LDL) levels after *G. lucidum* supplementation, but the changes were not statistically significant.

Wachtel-Galor 2004b[14] was a follow-up to the above-mentioned study. Its protocol was very similar to Wachter-Galor 2004a, the major differences being the number of participants (n=18), the daily dose of *G. lucidum* (1440mg per day), and the duration of the trial (4 weeks). The authors again reported a slight, statistically insignificant trend towards a decrease in blood lipids levels after *G. lucidum* supplementation.

Gao 2004a[15] was a randomized controlled clinical trial that evaluated the effect of supplementation with 5400 mg *G. lucidum* in patients suffering from type II diabetes mellitus. After 12 weeks, no statistically significant changes were observed in TG, TC, HDL, and LDL levels in either the treated or control groups.

The Gao 2004b[16] study was a double-blind randomized controlled trial conducted among 170 patients with coronary heart disease. Participants received 5400 mg *G. lucidum* daily or placebo for 12 weeks. The authors noted a significant decrease in TC level in the *G. lucidum*-treated group, with no significant change in the control group. Nevertheless, the authors did not present between-groups comparison of these changes. Additionally, no data have been published regarding TG, HDL, and LDL levels.

Chu 2011[17] was another double-blind crossover study conducted to assess whether *G. lucidum* supplementation has any effect on blood lipids levels. It recruited 26 hypertensive and/or dyslipidemic patients, who were randomly allocated to start with 1440 mg *G. lucidum* per day or a placebo. After 12 weeks of supplementation and 4 weeks of a crossover period, participants switched to the corresponding groups and received alternative treatments. The results of Chu 2011 were hard to interpret. A significant crossover effect prevented the authors from conducting a proper analysis of changes in TG and HDL levels. The data obtained from the first treatment period showed a mild decline in TG and a moderate increase in HDL in the *G. lucidum*-treated group, however, comparison of changes between groups did not show statistical significance. No statistically significant differences were also observed between groups in terms of changes in TC and LDL levels based on data from both treatment periods.

During the Klupp 2016 trial, 84 patients with type II diabetes mellitus and metabolic syndrome were randomized into one of three groups to receive either 3000 mg lingzhi, 3000 mg *G. lucidum* plus 1000 mg *Cordyceps sinensis,* or placebo.[18] The supplementation period lasted 16 weeks. Due to the small sample sizes, the authors decided to combine both treatment groups for further analysis. This approach did not reveal any significant changes in any of the blood lipids in the combined-treatment group compared to the control group.

The potential effects of *G. lucidum* supplementation in 72 overweight patients were investigated in the Babamiri 2022 trial.[19] The study was double-blind, randomized, and placebo-controlled, with each participant receiving 750 mg of *G. lucidum* per day. After 6 weeks, a slight reduction in TC levels in the *G. lucidum* group was the only parameter that changed significantly compared to the placebo group. Improvements in TG, HDL and LDL levels have been proven to be negligible.

Overall, of the seven analyzed studies, only Gao 2004b and Babamiri 2022 reported a significant decrease in TC levels after *G. lucidum* supplementation, and the first one did not compare this change with the control group.[16,19] Other, smaller but more methodologically rigorous, studies did not confirm these positive results. In addition, *G. lucidum* supplementation caused significant changes in TG, HDL and LDL levels in none of the reviewed studies, suggesting a lack of a noteworthy effect in this regard. A concise description of analyzed studies is provided in Table 1. A more quantitative synthesis could not be performed due to insufficient quality and availability of the data.

Table 1. Characteristics of the included studies

Author	Study design	Sample	Health status	Dose	Duration	Significant outcomes
Wachtel-Galor 2004a[13]	double-blind crossover study	n=10	healthy	720 mg	10 days	no significant changes in blood lipids
Wachtel-Galor 2004b[14]	double-blind crossover study	n=18	healthy	1440 mg	4 weeks	no significant changes in blood lipids
Gao 2004a[15]	RCT	n=71	type II diabetes mellitus	5400 mg	12 weeks	no significant changes in blood lipids
Gao 2004b[16]	double-blind RCT	n=170	coronary heart disease	5400 mg	12 weeks	decrease in TC (not compared to the control group)
Chu 2011[17]	double-blind crossover study	n=26	hypertension and/or dyslipidemia	1440 mg	12 weeks	partial data suggest decrease in TG and increase in HDL, which proven to be insignificant when compared to the control group; no significant between-groups changes in TC and LDL
Klupp 2016[18]	double-blind RCT	n=84	type II diabetes mellitus ant metabolic syndrome	3000 mg	16 weeks	no significant changes in blood lipids
Babamiri 2022[19]	double-blind RCT	n=72	overweight	750 mg	6 weeks	decrease in TC compared to the control group

Risk of bias

With the exception of Klupp 2016, no study reviewed provided sufficient information on randomization and allocation concealment of participants. Most studies also lacked a detailed description of blinding practices, but the objective nature of biochemical assessment of blood lipid levels allowed most studies to be designated as "low risk" with respect to blinding criteria. Deficiencies in reporting missing data and lack of available study protocol were another common flaws reflected in

"unclear risk" or "high risk" ratings. The author did not find other sources of bias in any of the reviewed studies. A complete summary of the risk of bias assessment is depicted in Figure 2 and Figure 3.

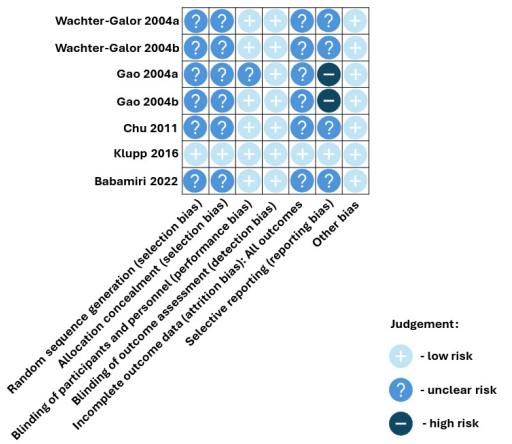

Fig. 2. Domain of risk of bias assessment

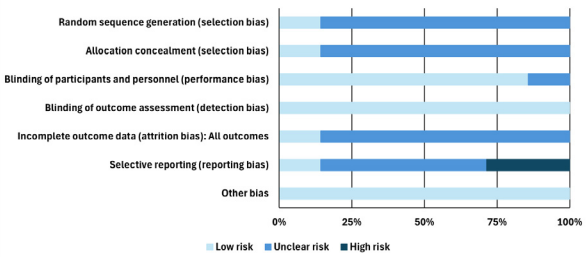

Fig. 3. The overall results of risk of bias assessment

Discussion

The literature evaluating the metabolic effects of *G. lucidum* supplementation remains relatively sparse. It consists mainly of animal studies, the vast majority of which have yielded positive results regarding blood lipid levels. A recent meta-analysis summarizing these trials concluded that *G. lucidum* effectively improves impaired lipid profile in a dose-dependent manner.[20] However, such findings cannot be directly applied to medical practice, as all animal trials are performed in strictly controlled laboratory conditions and use models which may not be representative for human physiology.

A more clinically relevant evidence comes from 2015 meta-analysis that evaluated the use of *G. lucidum* among patients at risk for cardiovascular disease.[21] Nonetheless, even this study suffered from some limitations. It excluded the two trials discussed in this review that were conducted in healthy patients (Wachtel-Galor 2004a and Wachtel-Galor 2004b studies) and did not include the newest Babamiri 2022 study.[13,14,19] As a result, it only qualified three studies to the final meta-analysis, all of which were conducted in diabetic patients. The authors confirmed the lack of statistically significant effect of *G. lucidum* on concentrations of TC, TG, HDL and LDL in this subpopulation.

Such results are in good agreement with the findings of the present study, which is, to the author's knowledge, the first one to collectively assess all good-quality human trials, regardless of participants health status. The data gathered show that the TC-lowering effect of *G. lucidum* is highly questionable. If it exists, it is probably small in size and requires long-term supplementation. The accumulated evidence also suggest that *G. lucidum* does not affect TG, HDL, and LDL levels. Still, further research is needed to definitively confirm these findings.

This study has several limitations. It included only publications in English, which may have led to the omission of potentially relevant research reported in other languages. In addition, *G. lucidum* formulation and standardization methods varied between included studies, a factor that could have affected the observed outcomes. The qualitative synthesis of gathered evidence was performed by a single author and a quantitative analysis was not conducted due to insufficient quality of the data. Finally, the risk of bias assessment was also conducted by a single author, which could have influenced the obtained results.

Conclusion

The effect of *G. lucidum* supplementation on blood lipid levels remains highly doubtful. Most studies do not confirm its positive impact on TC. No study reports any significant influence on TG, HDL, and LDL. Although a beneficial effect of *G. lucidum* supplementation on blood lipid levels seems unlikely, it cannot be definitely ruled out based on the current limited data. A bigger, longer-term, and more methodologically rigorous studies are needed to draw any stronger conclusions.

Declarations

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Author contributions

Conceptualization, J.Z.; Methodology, J.Z.; Software, J.Z.; Validation, J.Z.; Formal Analysis, J.Z.; Investigation, J.Z.; Resources, J.Z.; Data Curation, J.Z.; Writing – Original Draft Preparation, J.Z.; Writing – Review & Editing, J.Z.; Visualization, J.Z.; Supervision, J.Z.; Project Administration, J.Z.; Funding Acquisition, J.Z.

Conflicts of interest

Author states no conflict of interest.

Data availability

All data generated or analyzed during this study are included in this published article.

Ethics approval
Not applicable.

Use of AI and AI-assisted technologies in the writing process
During the preparation of this work the author used Rayyan software in order to screen the literature and detect duplicates. After using this tool, the author reviewed and edited the content as needed and takes full responsibility for the content of the published article.

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