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Effects of Lactobacillus fermentum, Lactobacillus plantarum, and Lactococcus lactis on lipid profiles in dyslipidemia: A systematic review and meta-analysis protocol

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ADMINISTRATIVE INFORMATION

Support - No specific funding was received for this work.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 September 2025 and was last updated on 23 September 2025.

INTRODUCTION

Review question / Objective This systematic review and meta-analysis aims to evaluate the effects of three probiotic strains, Lactobacillus fermentum, Lactobacillus plantarum, and Lactococcus lactis on lipid profiles and lipid metabolism in dyslipidemia. Specifically, the review will address the following question:

"Do interventions with L. fermentum, L. plantarum, and L. lactis improve lipid-related outcomes in individuals with dyslipidemia or in animal models of dyslipidemia, compared with placebo, standard therapy, or no intervention?"

The objective of this review is to systematically identify, synthesize, and quantitatively assess available evidence from randomized controlled trials and animal studies to determine whether these probiotic strains can reduce serum or plasma triglycerides, total cholesterol, and low-density lipoprotein cholesterol, while increasing high-density lipoprotein cholesterol. By providing comprehensive evidence, this review seeks to clarify the potential of these strains as functional food-derived interventions for the management of dyslipidemia.

Rationale Dyslipidemia is a critical risk factor for cardiovascular disease and metabolic syndrome, representing a global health challenge. While pharmacological treatments such as statins remain the standard of care, their long-term use raises concerns regarding side effects and adherence, creating a demand for alternative and complementary interventions.

Probiotic strains derived from Korean ginseng roots—particularly Lactobacillus fermentum, Lactobacillus plantarum, and Lactococcus lactis—have been reported to beneficially modulate lipid metabolism. Mechanistic evidence suggests that these strains may exert lipid-lowering effects through bile salt hydrolase activity, production of short-chain fatty acids, and reshaping of the gut

microbiota. Several experimental and clinical studies have investigated their impact on serum triglycerides, total cholesterol, LDL, and HDL levels.

However, the findings remain inconsistent, and no systematic review or meta-analysis has specifically synthesized evidence focusing on these three ginseng-derived strains. This review will address this gap by integrating evidence from both animal studies and randomized controlled trials, thereby providing robust and comprehensive insights into their potential role as functional food-based interventions for dyslipidemia management.

Condition being studied Dyslipidemia, a major risk factor for cardiovascular disease and metabolic syndrome.

METHODS

Search strategy We conducted a comprehensive search up to April 15, 2025, using PubMed, Cochrane Library, Embase, and Web of Science.
The search strategy combined free-text terms and controlled vocabulary (e.g., MeSH in PubMed, Emtree in Embase), applying Boolean operators such as AND and OR.
Grey literature was excluded. All search results were imported into EndNote, and duplicate records were removed.

Participant or population Patients with dyslipidemia and animal models of dyslipidemia.

Intervention Supplementation with three probiotic strains: Lactobacillus fermentum, Lactobacillus plantarum, and Lactococcus lactis.

Comparator Placebo, standard treatment, or no intervention control.

Study designs to be included Randomized controlled trials (RCTs) and animal studies investigating the effects of L. fermentum, L. plantarum, and L. lactis on dyslipidemia.

Eligibility criteria We will include randomized controlled trials (RCTs) in patients with dyslipidemia and controlled animal studies with experimentally induced dyslipidemia. Eligible interventions are supplementation with Lactobacillus fermentum, Lactobacillus plantarum, or Lactococcus lactis, compared with placebo, standard therapy, or no intervention controls. Studies must report lipid-related outcomes, including triglycerides, total cholesterol, LDL-C, or HDL-C. We will exclude multi-component interventions that combine the target strains with other agents, abstract-only publications, duplicate reports, reviews, editorials, commentaries, studies unrelated to dyslipidemia, and in vitro experiments.

Information sources We systematically search four major electronic databases: PubMed, Embase, Cochrane Library, and Web of Science.
Grey literature, including conference abstracts, dissertations, and unpublished reports, will not be included.

Main outcome(s) The primary outcomes will be lipid profile indicators, including serum or plasma triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C).

Additional outcome(s) No additional outcomes will be assessed beyond the main lipid profile indicators (TG, TC, LDL-C, and HDL-C).

Data management All search results will be imported into EndNote reference management software. Duplicate records will be identified and removed using EndNote and Excel. Two reviewers will independently screen titles, abstracts, and full texts to determine eligibility, and discrepancies will be resolved by a third reviewer. Data from included studies will be extracted into standardized Excel spreadsheets for further analysis.

Quality assessment / Risk of bias analysis Risk of bias will be assessed using the SYRCLE tool for animal studies and the Cochrane RoB 2.0 tool for randomized controlled trials. Both tools classify risk of bias as low, some concerns, or high. Two reviewers will independently perform the assessments, and any disagreements will be resolved by a third reviewer.

Strategy of data synthesis We will perform meta-analyses using R software with the meta and metafor packages. Continuous outcomes will be synthesized as standardized mean differences (SMD) with 95% confidence intervals, applying inverse variance weights. A random-effects model will be used to account for expected heterogeneity. Statistical heterogeneity will be assessed using Cochran's Q, tau-squared (τ^2), and the I-squared (I^2) statistic. Sensitivity analyses, including leave-one-out and influence diagnostics, will be conducted to evaluate the robustness of the results. Subgroup analyses will be performed by probiotic strain where data allow. A p-value < 0.05 will be considered statistically significant.

Subgroup analysis Subgroup analyses will be conducted separately for each lipid outcome (TG, TC, LDL-C, HDL-C). Within each outcome, studies will be further analyzed by study type (animal vs. clinical) and then stratified by probiotic strain (L. fermentum, L. plantarum, and L. lactis).

Sensitivity analysis Sensitivity analyses will be performed to test the robustness of the findings. Leave-one-out analyses will be conducted by sequentially omitting individual studies to assess their influence on the overall effect size. Galbraith and Baujat plots will be used to identify outlier and highly influential studies contributing to heterogeneity. In addition, prediction intervals (PI) will be calculated to account for between-study variability.

Language restriction Only studies published in English will be included.

Country(ies) involved Republic of Korea.

Other relevant information This review will follow the PRISMA 2020 guidelines. As a systematic review and meta-analysis, no ethical approval is required. The protocol is registered to ensure transparency and minimize duplication.

Keywords Systematic review; Meta-analysis; Probiotics; Dyslipidemia; Lactobacillus fermentum; Lactobacillus plantarum; Lactococcus lactis; Lipid metabolism; Triglycerides; Cholesterol; LDL-C; HDL-C.

Dissemination plans The results of this systematic review and meta-analysis will be disseminated by publication in a peer-reviewed journal (Foods, MDPI) and by presentation at national and international academic conferences.

Contributions of each author

Author 1 - CHUNG SUNGMIN - Author 1 contributed to the study design and developed the protocol, conducted the literature search, performed data extraction and analysis, and drafted the manuscript.
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