Systematic Reviews

PROTOCOL

Open Access

Can ginger improve cardiovascular health indices? A protocol for a GRADE-assessed systematic review and planned dose–response meta-analysis of randomized controlled trials

Ali Jafari[1,2*] and Amirhossein Sahebkar[3,4,5]

Abstract

Background Cardiovascular diseases (CVDs), which encompass a range of disorders impacting the heart and blood vessels, continue to pose a significant global public health challenge. Ginger (*Zingiber officinale*) has attracted attention among various treatment options for its potential advantages in promoting cardiovascular well-being. Renowned for its anti-inflammatory, antioxidant, and anti-hypertensive properties, ginger is a widely used culinary and medicinal plant. The objective of this research is to provide a comprehensive summary and systematic analysis of the existing scientific literature pertaining to the effects of ginger supplementation on glycemic profile, lipid profile, anthropometric measures, blood pressure, inflammatory markers, liver function tests, oxidative stress parameters, and adipokines. This analysis aims to establish a foundation for clinical interventions.

Methods A methodical electronic exploration will be carried out to discover articles in various databases such as Scopus, PubMed, EMBASE, CENTRAL, and Web of Science. The search will specifically target randomized controlled trials (RCTs) that include both healthy and diseased individuals. Two evaluators will independently review articles, extract information, and evaluate the quality of the studies using the Cochrane risk of bias assessment tool (RoB 2). Any discrepancies will be addressed by involving a third reviewer. The quality of cumulative evidence will be evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) criteria. Should a sufficient quantity of suitable studies be found, a meta-analysis will be conducted on the chosen outcomes.

Discussion This protocol outlines a comprehensive approach for systematically reviewing and conducting a dose–response meta-analysis on the effects of ginger supplementation on CVD risk factors. The proposed methodological rigor, including independent evaluation and GRADE assessment, will ensure high-quality evidence synthesis from available RCTs. The findings from this planned review will help inform future research directions and potentially guide clinical recommendations regarding ginger supplementation for cardiovascular health.

Systematic review registration PROSPERO: CRD42024571362.

Keywords Ginger, Nutrition, Metabolic disease, Cardiovascular diseases, Nutritional supplements

*Correspondence:
Ali Jafari
Ajafari.nut@gmail.com
Full list of author information is available at the end of the article

Introduction

Cardiovascular diseases (CVDs) persist as a major worldwide health challenge, inflicting numerous annual fatalities and imposing a considerable societal burden. The year 2021 witnessed CVDs causing 20.5 million deaths globally, underscoring their extensive impact on public health [1]. The global burden of CVDs exhibits significant disparities across regions and income levels, with age-standardized CVD mortality rates ranging from 157 per 100,000 in high-income countries to 460 per 100,000 in low-income countries [2]. In 2019, ischemic heart disease alone affected approximately 197 million individuals worldwide, with annual incidence rates of 1655 per 100,000 in middle-income countries compared to 696 per 100,000 in high-income regions [3]. These disparities are further evidenced by the disproportionate impact of premature CVD deaths, with over 80% occurring in low- and middle-income countries, where healthcare resources for prevention and treatment are often limited [4]. Despite advancements in treatment approaches, CVDs remain primary causes of death on a global scale and within the USA [5]. CVDs encompass a wide range of ailments including hypertension, heart failure, and coronary artery disease, and entail intricate pathophysiological processes such as inflammation, oxidative stress, and dyslipidemia, collectively presenting substantial risks to human well-being [6, 7].

The World Health Organization (WHO) has increasingly recognized the role of traditional and complementary medicine in healthcare systems worldwide, establishing the WHO Traditional Medicine Strategy 2014–2023 to promote safe and effective integration of these approaches into national health policies [8]. This aligns with the United Nations Sustainable Development Goal 3 (SDG 3), which aims to ensure healthy lives and promote well-being for all ages through accessible and affordable healthcare interventions [9]. Within this framework, natural products represent potential tools to help manage several cardiovascular and metabolic risk factors [10–14]. The WHO has emphasized evidence-based evaluation of herbal medicines to determine their safety, efficacy, and quality in managing chronic diseases [15]. Ginger, with its long history in traditional medicine systems across diverse cultures, exemplifies a natural remedy that warrants rigorous scientific investigation for its potential to contribute to cardiovascular health improvement goals outlined in global health agendas [16]. As countries work toward meeting SDG 3 targets, investigating cost-effective interventions such as ginger supplementation could provide valuable strategies for addressing cardiovascular disease burden, particularly in resource-limited settings [17, 18].

In recent years, there has been a growing focus on nutritional and pharmacological approaches designed to lower the risk factors associated with CVDs and enhance cardiovascular outcomes [19, 20]. Notably, the use of functional foods and herbal medicines have gained a wide popularity in both public and scientific communities. Among medicinal plants, ginger (*Zingiber officinale*) has garnered attention due to its potential cardioprotective properties, which are attributed to its bioactive compounds like gingerols and shogaols [21]. As a widely used spice and medicinal plant, ginger is known for its antihypertensive, antioxidant, and anti-inflammatory properties [22, 23]. These characteristics suggest that ginger supplementation could play a crucial role in mitigating risk factors associated with CVD [24, 25].

The numerous pharmacological and physiological effects associated with ginger have prompted a significant rise in research efforts investigating its potential health benefits. There is an increasing amount of research that highlights the effectiveness of ginger in enhancing human health from a clinical perspective. A substantial number of randomized controlled trials (RCTs) have been carried out to explore the therapeutic advantages of ginger in alleviating symptoms. For instance, various RCTs have focused on assessing the impact of ginger supplementation on reducing CVD risk factors in adults [26, 27]. Furthermore, a number of systematic reviews, meta-analyses, and umbrella reviews have been conducted to evaluate the clinical effectiveness of ginger. Notably, Li et al. and Anh et al. conducted systematic reviews (not meta-analyses) on the correlation between ginger supplementation and human health outcomes [28, 29]. In addition, an umbrella review demonstrated the significant positive influence of ginger on inflammatory indices, blood pressure, blood lipid profile, glycemic control, oxidative stress biomarkers, and weight [30]. Additionally, recent meta-analyses have highlighted ginger supplementation as a promising intervention for enhancing cardiovascular health outcomes, with initial evidence suggesting favorable effects on lipid profiles, glycemic control, blood pressure regulation, and biomarkers of inflammation and oxidative stress [31, 32].

Despite the existing body of literature, there is a noticeable lack of a comprehensive systematic review and meta-analysis that specifically focuses on the impact of ginger supplementation on cardiovascular health indices and risk factors. Our research aims to fill this gap by conducting an updated systematic review and dose–response meta-analysis, exclusively utilizing high-quality evidence from RCTs and employing the GRADE approach. This approach ensures a meticulous assessment of ginger's effectiveness across diverse population groups, including individuals with different health conditions, ages, and genders. By combining all reported cardiovascular risk factors in a single review and applying meta-regression and dose–response analyses, we aim to provide detailed insights into the relationship between ginger supplementation dosage, duration, and cardiovascular outcomes. Consequently, this protocol establishes a robust methodological framework for synthesizing evidence in accordance with globally recognized standards. Through a comprehensive evaluation of existing data, our meta-analysis seeks to enhance our understanding of ginger supplementation as a potential complementary treatment in the prevention and management of CVDs, thereby influencing clinical practices and shaping future research initiatives.

Our comprehensive meta-analysis aims to assess the effectiveness of ginger supplementation in modifying cardiovascular risk factors in a wide range of populations, including both individuals with poor health and those who are healthy. Our main objective is to investigate the impact of ginger on factors including adipokines, anthropometric indices, lipid levels, blood pressure, markers of inflammation, glycemic factors, oxidative stress parameters, and liver function tests. Furthermore, we will examine differences in outcomes across various primary studies and sources.

Methods

The methodology utilized in this systematic review follows the prescribed criteria outlined in the 2015 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [33]. Moreover, the review protocol strictly adheres to the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Protocols 2015 (PRISMA-P 2015) (Supplementary Table 1) [18], and the PROSPERO registration number is CRD42024571362.

Eligibility criteria

Study design/characteristics

The systematic review includes RCTs with either parallel or crossover designs. These studies must include control groups and be written in English. Excluded from the review are non-RCT research designs involving human participants, such as literature reviews, individual case reports, case series, and various types of observational studies. Also excluded are experimental studies carried out on animals or in vitro, as well as conference papers, opinion articles, commentaries, and documents lacking adequate baseline or follow-up data on cardiometabolic variables. These variables include lipid profile, glycemic control, anthropometric measurements, markers of inflammation, hormones related to adipose tissue, blood pressure, oxidative stress, and liver function within each study group. Moreover, studies that discuss the combined use of ginger with other substances are not considered in this review.

Subject types

The criteria for inclusion cover original research exploring interventions targeting individuals who are 18 years old and above, regardless of their gender.

Intervention(s)

This analysis focuses on RCTs that investigate the daily use of ginger supplements, administered in the form of powder, tablets, capsules, or other variations. The dosage may differ in terms of frequency and amount, and the duration of the interventions will vary among different research studies.

Comparator(s)/control

To be considered for inclusion, studies must compare the impact of ginger supplementation with a placebo, no intervention, or standard care in a control group.

Outcome(s)

The selected studies should present the average changes and standard deviations (SDs) of adipokines, inflammatory biomarkers, glycemic regulation parameters, anthropometric measurements, liver function markers, blood pressure, and the lipid profile components over the course of the trial for both the intervention and control groups, or provide sufficient information to compute these effect sizes.

Data sources

The systematic review will methodically explore electronic bibliographic databases. Specific keywords related to ginger will be utilized in various databases such as EMBASE (Embase.com), Cochrane Central Register of Controlled Trials, Web of Science, SCOPUS, and Medline (Supplementary Table 2). Moreover, manual searches of pertinent scholarly journals and references of relevant review publications, meta-analyses, and articles will be carried out. Gray literature, which includes theses and conference abstracts, will also be carefully examined. Communication with study authors via email will be utilized to acquire unpublished data, ensuring a comprehensive approach.

Search strategy

The objective of our strategy for reviewing literature is to pinpoint every pertinent randomized controlled trial (RCT) carried out on human participants. We will utilize a meticulously chosen collection of important search terms to clarify the concepts of “ginger” and “RCTs.”

These terms are strategically combined to guarantee a thorough search that encompasses all relevant research works, in line with the concept of search inclusiveness. Each research work will be subjected to a detailed individual evaluation in the initial screening stage, with only those that meet the specified criteria advancing to the analysis stage. A customized search method will be developed for each database, with comprehensive explanations of the search methodology and syntax used being provided in Supplementary Table 2.

Study records

Data management

Two researchers will carry out preliminary searches on electronic databases using the methodology specified in the PRISMA-P statement. Furthermore, two scholars will thoroughly examine the sources referenced in all selected studies. Data organization will be facilitated through the application of EndNote X7 software. The primary reviewer will transfer search outcomes to an EndNote library.

Selection process

The process of selecting studies for this systematic review will follow the guidelines outlined in the PRISMA framework. A three-step approach will be used to identify relevant studies. Initially, two reviewers will independently assess abstracts and titles of all records found in database searches, using specific criteria to determine suitable articles. Any discrepancies in the inclusion process at different stage will be resolved by consulting with a research supervisor specializing in nutritional and pharmacoepidemiology. Following this, the full texts of articles that meet the criteria will be obtained for further examination. Two evaluators will individually review the full texts of the selected abstracts. Detailed documentation of the reasons for excluding specific studies will be maintained during the selection process and compiled into a table for inclusion in the primary publication. A PRISMA flow chart (Fig. 1) will visually illustrate the number of studies that have been excluded or included in the review process.

Data extraction

A data extraction form will be developed by the main reviewer and the statistician to extract data from all selected research studies. Before fully implementing the form, the research team plans to conduct a preliminary trial run on a sample of five studies. The goal is to identify any potential issues and make necessary adjustments to ensure consistency and accuracy in the data extraction process. Two reviewers will independently gather information from the selected studies. Data extraction will include details from published reports or direct

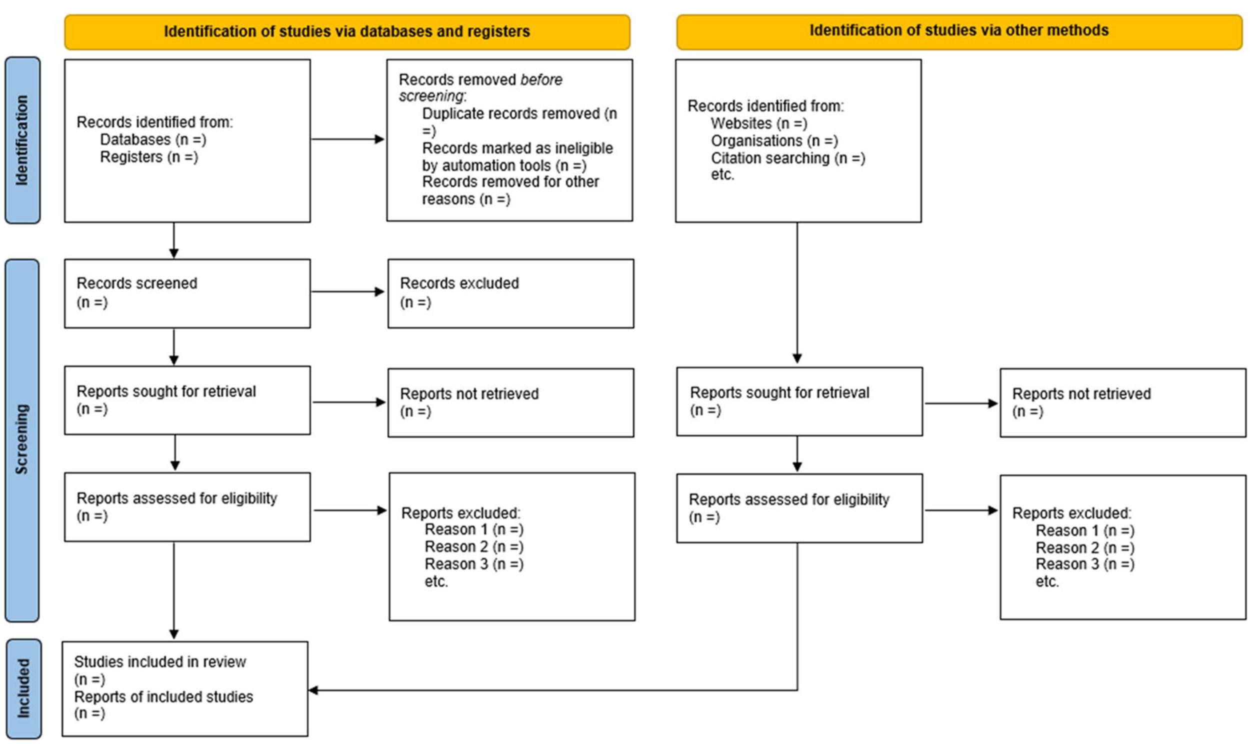

Fig. 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of study selection

communication with study authors if the information in published articles is insufficient. If discrepancies arise during the data extraction phase and cannot be resolved through team discussion, these issues will be escalated to the project supervisor for further examination and resolution. This systematic approach to data extraction aims to improve the reliability and validity of the research findings by ensuring a consistent and rigorous data collection process.

Data items

Data retrieval will be systematically structured and conducted by adhering to the PICOS criteria, which serves as a comprehensive framework for organizing and categorizing the relevant information necessary for the research process:

a) The summarization of study characteristics will involve identifying the primary author, explaining the research design employed, and specifying the study location, duration, country of origin, and publication year, as well as classifying the sample size into various distinct groups. This comprehensive analysis aims to provide a detailed overview of the essential components that contribute to the overall structure and context of the research being conducted. By delving into these specific details, researchers can gain a deeper understanding of the study's background and framework, which is crucial for interpreting and evaluating its findings accurately.
b) The sociodemographic details of the participants will include a wide range of information such as age, gender, total number of individuals involved, specific type of disease being investigated, and their initial health condition at the start of the study. These details are important for establishing the baseline characteristics of the study population and for assessing the potential impact of these factors on the outcomes of interest. Understanding the sociodemographic profile of the participants can also assist researchers in identifying any potential confounding variables that may influence the results and conclusions drawn from the study.
c) The implemented interventions and their distinct characteristics will offer a comprehensive overview of the treatment protocols being evaluated, including specific details about the sample size of the treatment group, method of administration, dosage administered, and duration of intervention. These details are essential for replicating the study and for assessing the feasibility and effectiveness of the interventions in different settings or populations. By documenting these intervention-related factors in detail, researchers can ensure transparency and reproducibility in their findings, thereby enhancing the credibility and validity of the study outcomes.
d) The outcomes to be examined will encompass a wide array of definitions and measurements related to cardiovascular health indicators. These may include inflammatory biomarkers such as CRP and IL-6, glycemic markers like FBG and HbA1c, components of the lipid profile such as LDL-C and TG, blood pressure readings, liver function markers, and various anthropometric measurements. By evaluating these diverse outcomes, researchers can obtain a comprehensive understanding of the impact of the interventions on different aspects of cardiovascular health and overall well-being. This multifaceted approach to outcome assessment can provide valuable insights into the mechanisms underlying the observed effects and inform future research directions in the field of cardiovascular health promotion and disease prevention.

Variability in primary studies will be assessed by examining the mean and standard deviation values of cardiovascular risk factors at various time points, including pre-intervention, post-intervention, and changes within each group. This comprehensive evaluation aims to provide a detailed understanding of the variations in the data and how the intervention may have influenced these factors over time. Additionally, the analysis will delve into other relevant aspects that could impact the interpretation of the results, ensuring a thorough examination of the study findings.

Missing data

Adhering to protocols outlined by the Cochrane Institute, our group will begin communication via email with the authors of selected studies to request further details if the data presented in their research publications are deemed insufficient. If the initial email inquiries go unanswered, a maximum of three subsequent reminders will be sent electronically. Failure to receive a response after these follow-up efforts will lead to categorizing the requested information as missing data.

Risk of bias assessment

The evaluation of bias within individual studies will be conducted by two separate reviewers using the Cochrane Collaboration tool, which is a reliable method for this purpose [34]. Before fully adopting this tool, a preliminary trial will be carried out on a selection of five primary articles to verify the consistency and reliability of the assessment process. In cases where discrepancies arise between the two reviewers, a third independent reviewer will intervene to facilitate consensus and ensure the accuracy of the evaluation. The categorization of bias within each specific domain will be based on the degree of its impact, classifying it as either low, moderate, or high. This allows for a comprehensive analysis of the potential sources of bias within the studies under review. The risk of bias will then be classified as low, moderate, or high, according to our findings and utilizing the Risk-of-bias VISualization (robvis) tool [35].

Meta-analysis plan

Meta-analysis will be performed using Stata software (version 15.0; Stata Corp, College Station, TX), allowing for a comprehensive synthesis of data from the included studies. Data on pre- and post-treatment means, standard deviations (SDs), and participant numbers will be meticulously extracted for both intervention and placebo groups across various clinical outcomes, including adipokines, oxidative stress, inflammation, anthropometric indices, glycemic control, liver function, blood pressure, and lipid profile.

The effects of ginger supplementation will be assessed through a comparative analysis of the intervention and control groups. If feasible, the analysis will utilize the weighted mean difference (WMD) model for unit conversion between variables. In cases where unit conversion is not possible, the standardized mean difference (SMD) model will be implemented to account for differences in measurement units with a random-effects model applied to account for variability in populations and study settings. The DerSimonian-Laird weighting method will be utilized to estimate the overall effect from the SMDs. To ensure accuracy, the SDs of the change difference will be calculated using the formula: (SD = square root [(SD pre-treatment)^2 + (SD post-treatment)^2 − (2R × SD pre-treatment × SD post-treatment)], where R is the correlation coefficient, which will be derived from the data where available. If only standard errors (SEs) are reported, SDs will be calculated using the formula: SD = SE × sqrt (n).

Heterogeneity among studies will be assessed using the I^2 statistic and Cochran's Q test, with significant heterogeneity indicated by an I^2 value exceeding 50% or a p value < 0.05. Subgroup analyses will explore potential sources of heterogeneity, such as study population, follow-up duration, ginger dose, and the nature of the control group allocation (e.g., placebo or standard care). Meta-regression will be employed to examine the influence of ginger dosage (mg/day) and duration of supplementation on cardiovascular risk factors.

Additionally, non-linear models will be used to assess dose–response relationships across studies [36]. Sensitivity analyses, including the leave-one-out method, will evaluate the robustness of the findings by systematically excluding each study to assess its impact on the overall effect size. To explore potential publication bias, techniques such as funnel plots, Begg's, and Egger's regression tests will be applied to ensure the reliability of the results.

Assessment of possible reporting bias

To evaluate the presence of reporting bias, including publication bias and other forms of outcome reporting bias, several techniques will be employed. A funnel plot will be used to visually assess asymmetry, provided that there are at least 10 studies included in the meta-analysis. For a more formal assessment, Begg's rank correlation test and Egger's regression test will be conducted to detect statistical asymmetry in the funnel plot.

A significance level of $p \leq 0.05$ will be used to determine statistically significant bias. Additionally, the "trim and fill" method will be applied to adjust for any detected publication bias, thereby enhancing the robustness and reliability of the results. Sensitivity analyses, including the leave-one-out approach, will be conducted to assess the impact of individual studies on the overall effect size, ensuring that the findings are not unduly influenced by any single study.

Assessing the quality of the evidence

The evaluation of the quality of evidence regarding the impact of ginger on CVD risk factors will be conducted based on the established GRADE guidelines [37]. This comprehensive assessment will consider various key elements, including the study's design, susceptibility to biases, coherence of findings, relevance to the research question, precision of the results, and the potential influence of publication bias on overall conclusions. Adhering to these rigorous guidelines is crucial to ensure a thorough and reliable evaluation of the effects of ginger on CVD risk factors. This, in turn, contributes to the advancement of evidence-based practice in cardiovascular health.

Discussion

Systematic reviews and meta-analyses are essential for synthesizing high-quality evidence and translating research findings into clinical practice [38]. This systematic review and meta-analysis is poised to make a significant impact by addressing the effects of ginger supplementation on cardiovascular risk factors with several key strengths. Our approach features a comprehensive and updated search strategy that ensures the inclusion of the latest and most relevant randomized controlled trials (RCTs), providing the most current evidence available. By focusing exclusively on RCTs, we mitigate biases inherent in observational studies, thereby strengthening the validity of our findings.

Moreover, this review will integrate a wide range of cardiovascular risk factors into a single analysis, offering a holistic assessment of ginger's effects. The application of the GRADE approach will enhance the rigor of our evidence evaluation, ensuring a clear understanding of the quality and strength of the recommendations. Additionally, through advanced meta-regression and dose–response analyses, we will explore how different doses and durations of ginger supplementation influence cardiovascular outcomes, adding depth and precision to our insights. Collectively, these methodological advancements position this review to provide actionable, evidence-based recommendations for clinical practice and public health strategies.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13643-025-02867-3.

Supplementary Material 1.

Acknowledgements

We acknowledge the use of ChatGPT (GPT-4, an advanced language model developed by OpenAI) for linguistic refinement and stylistic editing of the manuscript. The AI tool was employed solely for enhancing clarity, coherence, and readability and was not involved in generating content, interpreting data, or compiling references. The authors have thoroughly reviewed, revised, and verified all AI-assisted text and assume full responsibility for the accuracy, integrity, and originality of the work.

Transparency statement

The authors unequivocally assert the integrity of this manuscript, emphasizing its fidelity in providing a truthful, precise, and openly documented narrative of the study under review. They emphasize the meticulous inclusion of all pertinent details and ensure that any deviations from the original study design, including those from pre-registration, are thoroughly elucidated.

Authors' contributions

Conceptualization: Ali Jafari, Amirhossein Sahebkar. Data curation: Ali Jafari, Amirhossein Sahebkar. Investigation: Ali Jafari, Amirhossein Sahebkar. Methodology: Ali Jafari, Amirhossein Sahebkar. Project administration: Ali Jafari, Amirhossein Sahebkar. Supervision: Ali Jafari, Amirhossein Sahebkar. Validation: Ali Jafari. Writing—original draft: Ali Jafari. Writing—review and editing: Amirhossein Sahebkar.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability

All relevant data are within the manuscript.

Declarations

Ethics approval and consent to participate

No ethical approval is required for this systematic review, as it involves the analysis and synthesis of existing literature. The findings of the forthcoming review will be disseminated through reputable peer-reviewed journals, ensuring that the knowledge generated contributes meaningfully to the advancement of scientific understanding in this field.

Competing interests

The authors listed in this publication confirm that they do not have any connections or engagements with any organization or entity that has a financial stake. This includes receiving honoraria, educational grants, being part of speakers' bureaus, having membership, employment, consultancies, stock ownership, or other equity interests. Additionally, they do not provide expert testimony or participate in patent licensing agreements. Furthermore, they do not have any non-financial interest in the topic or materials deliberated in this manuscript. This includes personal or professional relationships, affiliations, knowledge, or beliefs.

Author details

[1]Student Research Committee, Department of Community Nutrition, Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [2]Systematic Review and Meta-Analysis Expert Group (SRMEG), Universal Scientific Education and Research Network (USERN), Tehran, Iran. [3]Centre for Research Impact & Outcome, Chitkara College of Pharmacy, Chitkara University, Rajpura, Punjab 140401, India. [4]Applied Biomedical Research Center, Basic Sciences Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran. [5]Biotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran.

Received: 8 August 2024 Accepted: 22 May 2025
Published online: 02 June 2025

References

1. Mensah GA, Fuster V, Murray CJ, Roth GA, Diseases GBoC, Collaborators R. Global burden of cardiovascular diseases and risks, 1990–2022. J Am Coll Cardiol. 2023;82(25):2350–473.
2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. J Am Coll Cardiol. 2020;76(25):2982–3021.
3. Mensah GA, Roth GA, Fuster V. The global burden of cardiovascular diseases and risk factors: 2020 and beyond. American College of Cardiology Foundation Washington, DC; 2019. p. 2529–32.
4. Yusuf S, Joseph P, Rangarajan S, Islam S, Mente A, Hystad P, et al. Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. Lancet. 2020;395(10226):795–808.
5. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, et al. Heart disease and stroke statistics-2021 update: a report from the American Heart Association. Circulation. 2021;143(8):e254–743.
6. Francula-Zaninovic S, Nola IA. Management of measurable variable cardiovascular disease' risk factors. Curr Cardiol Rev. 2018;14(3):153–63.
7. Flora GD, Nayak MK. A brief review of cardiovascular diseases, associated risk factors and current treatment regimes. Curr Pharm Des. 2019;25(38):4063–84.
8. Qi Z. Who traditional medicine strategy. 2014–2023. Geneva: World Health Organization. 2013;188.
9. Bennett JE, Kontis V, Mathers CD, Guillot M, Rehm J, Chalkidou K, et al. NCD Countdown 2030: pathways to achieving Sustainable Development Goal target 3.4. The Lancet. 2020;396(10255):918–34.
10. Alidadi M, Jamialahmadi T, Cicero AFG, Bianconi V, Pirro M, Banach M, et al. The potential role of plant-derived natural products in improving arterial stiffness: a review of dietary intervention studies. Trends Food Sci Technol. 2020;99:426–40.
11. Momtazi AA, Banach M, Pirro M, Katsiki N, Sahebkar A. Regulation of PCSK9 by nutraceuticals. Pharmacol Res. 2017;120:157–69.
12. Sahebkar A, Serban MC, Gluba-Brzózka A, Mikhailidis DP, Cicero AF, Rysz J, et al. Lipid-modifying effects of nutraceuticals: an evidence-based approach. Nutrition. 2016;32(11–12):1179–92.
13. Alum EU. Role of phytochemicals in cardiovascular disease management: insights into mechanisms, efficacy, and clinical application. Phytomed Plus. 2025;5(1):100695.
14. Wang XF, Chen X, Tang Y, Wu JM, Qin DL, Yu L, et al. The therapeutic potential of plant polysaccharides in metabolic diseases. Pharmaceuticals (Basel). 2022;15(11):1329.

15. Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. Front Pharmacol. 2014;4:177.
16. Mao QQ, Xu XY, Cao SY, Gan RY, Corke H, Beta T, et al. Bioactive compounds and bioactivities of ginger (Zingiber officinale Roscoe). Foods. 2019;8(6):185.
17. Jafari A, Abbastabar M, Alaghi A, Heshmati J, Crowe FL, Sepidarkish M. Curcumin on human health: a comprehensive systematic review and meta-analysis of 103 randomized controlled trials. Phytother Res. 2024;38(12):6048–61.
18. Shaito A, Thuan DTB, Phu HT, Nguyen THD, Hasan H, Halabi S, et al. Herbal medicine for cardiovascular diseases: efficacy, mechanisms, and safety. Front Pharmacol. 2020;11:422.
19. Jafari A. Can coenzyme Q10 supplementation reduce cardiovascular disease risk factors? A protocol for a GRADE-assessed systematic review and dose-response meta-analysis of randomized controlled trials. Health Sci Rep. 2025;8(2):e70452.
20. Jafari A, Kordkatuli K, Mardani H, Mehdipoor F, Jami PB, Abbastabar M, et al. Ginseng supplementation and cardiovascular disease risk factors: a protocol for GRADE-assessed systematic review and dose-response meta-analysis. BMJ Open. 2024;14(7):e080926.
21. Tavares L, Smaoui S, Pinilla CMB, Hlima HB, Barros HL. Ginger: a systematic review of clinical trials and recent advances in encapsulation of its bioactive compounds. Food Funct. 2022;13(3):1078–91.
22. Jalali M, Mahmoodi M, Moosavian SP, Jalali R, Ferns G, Mosallanezhad A, et al. The effects of ginger supplementation on markers of inflammatory and oxidative stress: a systematic review and meta-analysis of clinical trials. Phytother Res. 2020;34(8):1723–33.
23. Ebrahimzadeh A, Ebrahimzadeh A, Mirghazanfari SM, Hazrati E, Hadi S, Milajerdi A. The effect of ginger supplementation on metabolic profiles in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. Complement Ther Med. 2022;65:102802.
24. Singletary KW. Ginger update: potential health benefits. Nutr Today. 2023;58(6):263–73.
25. Matin M, Matin FB, Ksepka N, Wysocki K, Mickael M-E, Wieczorek M, et al. The clinical research on ginger (Zingiber officinale): insights from ClinicalTrials.gov analysis. Planta medica. 2024.
26. Ghoreishi PS, Shams M, Nimrouzi M, Zarshenas MM, Lankarani KB, Fallahzadeh Abarghooei E, et al. The effects of ginger (Zingiber officinale Roscoe) on non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus: a randomized double-blinded placebo-controlled clinical trial. J Diet Suppl. 2024;21(3):294–312.
27. Foshati S, Poursadeghfard M, Heidari Z, Amani R. The effect of ginger (Zingiber officinale) supplementation on clinical, biochemical, and anthropometric parameters in patients with multiple sclerosis: a double-blind randomized controlled trial. Food Funct. 2023;14(8):3701–11.
28. Li H, Liu Y, Luo D, Ma Y, Zhang J, Li M, et al. Ginger for health care: an overview of systematic reviews. Complement Ther Med. 2019;45:114–23.
29. Anh NH, Kim SJ, Long NP, Min JE, Yoon YC, Lee EG, et al. Ginger on human health: a comprehensive systematic review of 109 randomized controlled trials. Nutrients. 2020;12(1):157.
30. Crichton M, Davidson AR, Innerarity C, Marx W, Lohning A, Isenring E, et al. Orally consumed ginger and human health: an umbrella review. Am J Clin Nutr. 2022;115(6):1511–27.
31. Zhang X, Chen X, Tang Y, Guan X, Deng J, Fan J. Effects of medical plants from Zingiberaceae family on cardiovascular risk factors of type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. J Food Biochem. 2022;46(7):e14130.
32. Salih AK, Alwan AH, Khadim M, Al-qaim ZH, Mardanov B, El-Sehrwy AA, et al. Effect of ginger (Zingiber officinale) intake on human serum lipid profile: systematic review and meta-analysis. Phytother Res. 2023;37(6):2472–83.
33. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Items PR, for Systematic Review and Meta-Analysis Protocols (PRISMA-P), et al. elaboration and explanation. BMJ. 2015;2015:349.
34. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
35. McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. Res Synth Methods. 2021;12(1):55–61. https://doi.org/10.1002/jrsm.1411.
36. Xu C, SAR. The robust error meta-regression method for dose-response meta-analysis. Int J Evid Based Healthc. 2018;16(3):138–44.
37. Guyatt G, Oxman AD, Sultan S, Brozek J, Glasziou P, Alonso-Coello P, et al. GRADE guidelines: 11. Making an overall rating of confidence in effect estimates for a single outcome and for all outcomes. J Clin Epidemiol. 2013;66(2):151–7.
38. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. Cochrane handbook for systematic reviews of interventions: John Wiley & Sons; 2019.

Publisher's Note