Effects of *Garcinia mangostana* Peel Extract on Glycemic Control in Type 2 Diabetes Mellitus: A Systematic Review of Human Studies

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ABSTRACT

Introduction*: Type 2 diabetes mellitus (T2DM) is a major global health concern characterized by insulin resistance, hyperglycemia, and chronic inflammation. Interest in natural adjunctive therapies has increased, particularly in mangosteen (Garcinia mangostana), which contains xanthone compounds in the peel with potential antidiabetic properties.* ***Methods:*** *This systematic review followed PRISMA 2020 guidelines. Literature searches were carried out using different platforms, including PubMed, Google Scholar, and ClinicalKey, up to December 2022, for studies assessing mangosteen peel extract (MPE) or α-mangostin in diabetic human subjects. Eligible studies included randomized controlled and quasi-experimental trials reporting glycemic or metabolic outcomes. Risk of bias was evaluated using the Cochrane RoB tool. The primary result of this study is to evaluate the effects of mangosteen peel extract supplementation on key glycemic outcomes in patients with T2DM, specifically fasting blood glucose (FBG), HOMA-IR, and HbA1c.* ***Results:*** *A total of two studies (n=2) met the inclusion criteria. A randomized controlled pilot trial reported significant improvement in insulin sensitivity (HOMA-IR −53.2% vs −15.2%; p = 0.004) after 26 weeks of standardized mangosteen extract. A small quasi-experimental study reported a significant reduction in FBG following 7 days of mangosteen peel decoction.* ***Discussion:*** *Limited clinical evidence indicates that mangosteen peel extract may improve insulin sensitivity and lower fasting glucose in T2DM. However, the conclusions are limited by the small number of available studies, the short follow-up duration in one trial, and variability in extract preparation.* ***Conclusion:*** *Mangosteen peel extract demonstrates promising glycemic benefits, including improved insulin sensitivity and reduced fasting glucose. However, the available evidence remains limited by small sample sizes, short follow-up periods, and heterogeneity in extract formulations. Larger randomized controlled trials using standardized preparations are required before clinical recommendations can be made.*

Keywords: *Garcinia mangostana, mangosteen peel extract, α-mangostin, type 2 diabetes mellitus, insulin resistance, oxidative stress.*

INTRODUCTION

Diabetes mellitus (DM) is a major global health challenge. Over the past decade, its prevalence has increased significantly, affecting hundreds of millions of people worldwide. Type 2 diabetes mellitus (T2DM), the most common form, is associated with a wide array of complications, including metabolic derangements, cardiovascular disease, and neurological impairment.[1] These complications contribute to increased morbidity and mortality, reduced quality of life, and shortened life expectancy. Moreover, DM places a substantial economic burden on healthcare systems worldwide, with an estimated 9% of adults affected in Western countries, though prevalence varies across populations, and T2DM accounts for more than 90% of these cases.[2]

Although various pharmacological agents have been developed and are widely prescribed for the management of T2DM, treatment in older adults requires special consideration. Age-related physiological changes, polypharmacy, and increased drug sensitivity in the elderly population increase the risk of adverse drug reactions and complications. Consequently, there is growing interest in exploring safer, well-tolerated, and cost-effective alternative or adjunct therapies, particularly those derived from natural products.[3]

Mangosteen (*Garcinia mangostana*), a tropical fruit widely cultivated and consumed in Indonesia and Southeast Asia, has long been used in traditional medicine. The fruit's pericarp, or peel, is rich in bioactive compounds, notably xanthones, which exhibit a broad spectrum of biological activities, including antioxidant, anti-inflammatory, antihypertensive, and antidiabetic properties.[4] Experimental evidence indicates that xanthones can improve glucose metabolism through enhanced insulin sensitivity and attenuation of oxidative stress. Mechanistically, xanthones may protect pancreatic β-cells from oxidative injury, thereby preserving insulin secretory function. Furthermore, xanthones are believed to modulate insulin signaling pathways in skeletal muscle and adipose tissue, leading to improved peripheral glucose uptake in T2DM.[5] Despite strong mechanistic evidence, there are rarely clinical trials in humans, with only a few studies evaluating its efficacy in T2DM. No previous systematic review has synthesized human-only clinical evidence on mangosteen peel extract (MPE) in T2DM. Therefore, this systematic review synthesizes human evidence on the effects of mangosteen peel extract on glycemic parameters, insulin resistance, and metabolic outcomes.

METHODS

This study was designed as a systematic review to evaluate the effects of mangosteen peel extract supplementation on glycemic control, lipid profile, oxidative stress markers, and insulin resistance in individuals with T2DM. The review adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. This study was registered in PROSPERO (registration number: CRD420251231381)

ELIGIBILITY CRITERIA

Original articles that met the following eligibility criteria were included in this study: (1) published between 1st January 2013 and 30th

Table 1. Inclusion and Exclusion

Category	Criteria
Inclusion	- Human studies (RCT or quasi-experimental) - Adults with T2DM or metabolic abnormalities - Intervention: mangosteen peel extract or α-mangostin - Outcomes: FBG, HbA1c, HOMA-IR, lipid profile, oxidative stress - Published 2013–2022; English or Indonesian
Exclusion	- Animal/in vitro studies - Reviews, case reports, narratives - Mixed interventions - No glycemic outcome data - Non-English publications

December 2022; (2) written in either English or Indonesian; (3) involved diabetic human as study subjects; (4) evaluated the effects of mangosteen peel extract or its bioactive compound α- mangostin; and (5) reported at least one relevant laboratory outcome, such as fasting blood glucose (FBG), HbA1c, HOMA-IR, malondialdehyde (MDA), total cholesterol, triglycerides, or body weight. Eligible study designs included randomized controlled trials (RCTs) and quasi-experimental studies.

In this study, articles that were review papers, editorials, case reports, or in vitro studies, as well as those that did not report sufficient outcome data related to diabetes parameters, were excluded.

Information Sources and Search Strategy

A comprehensive literature search was performed in PubMed, Google Scholar, and ClinicalKey. For PubMed, the following search strategy was applied: ("Garcinia mangostana"[Mesh] OR "mangosteen" OR "mangosteen peel" OR "mangosteen extract" OR "xanthone" OR "alpha-mangostin" OR "α-mangostin") AND ("Diabetes Mellitus, Type 2"[Mesh] OR "type 2 diabetes" OR "T2DM" OR "insulin resistance" OR "hyperglycemia") AND (humans[Filter]). Searches in Google Scholar used the following key terms in various combinations: "mangosteen peel extract" AND "type 2 diabetes"; "α-mangostin" AND insulin resistance; and "Garcinia mangostana" AND hyperglycemia. Additional manual screening of reference lists was conducted to identify relevant studies. The search was independently conducted by three reviewers to ensure a comprehensive and unbiased selection of relevant studies.

Study Selection

All identified titles and abstracts were screened for relevance by three independent reviewers. Full-text articles were then retrieved for further assessment based on the inclusion and exclusion criteria. Any disagreements between reviewers during study selection or data extraction were resolved through discussion and consensus among all reviewers.

Data Extraction

Relevant data were independently extracted by the reviewers and recorded using a standardized data extraction form. The extracted information included the author(s) and year of publication, study design, type of subject population, dosage and duration of mangosteen or α-mangostin administration, and reported outcome measures. These outcomes comprised FBG, HbA1c, HOMA-IR, MDA, total cholesterol, triglycerides, and body weight. Additionally, the main results of each study and their reported statistical significance were documented for analysis.

Risk of Bias Assessment

The methodological quality and risk of bias for RCT were evaluated using the Cochrane Risk of Bias Tool, which assesses seven domains, including random sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting. Each domain was rated as having a low, high, or unclear risk of bias.

RESULTS

Two studies met the eligibility criteria and were included in this review (Figure 1). Both studies investigated the potential glycemic or insulin-sensitizing effects of mangosteen preparations in human subjects with metabolic abnormalities (Table 2).

The first study by Watanabe et al. (2018), a randomized controlled pilot trial published in *Nutrients*, enrolled 22 obese female patients (BMI ≥ 30 kg/m², aged 18–65 years). Participants were randomly allocated to receive either mangosteen fruit pulp extract (400 mg/day, standardized to 160 mg of α- and γ-mangostins) or a placebo for 26 weeks. Although the focus was on peel extract, the study by Watanabe et al. using standardized fruit pulp extract was included due to its high xanthone content and mechanistic similarity. The intervention group demonstrated a statistically significant improvement in insulin sensitivity, as measured by a reduction in HOMA-IR (−53.22% vs. −15.23%; $p = 0.004$), with no reported adverse effects.[1]

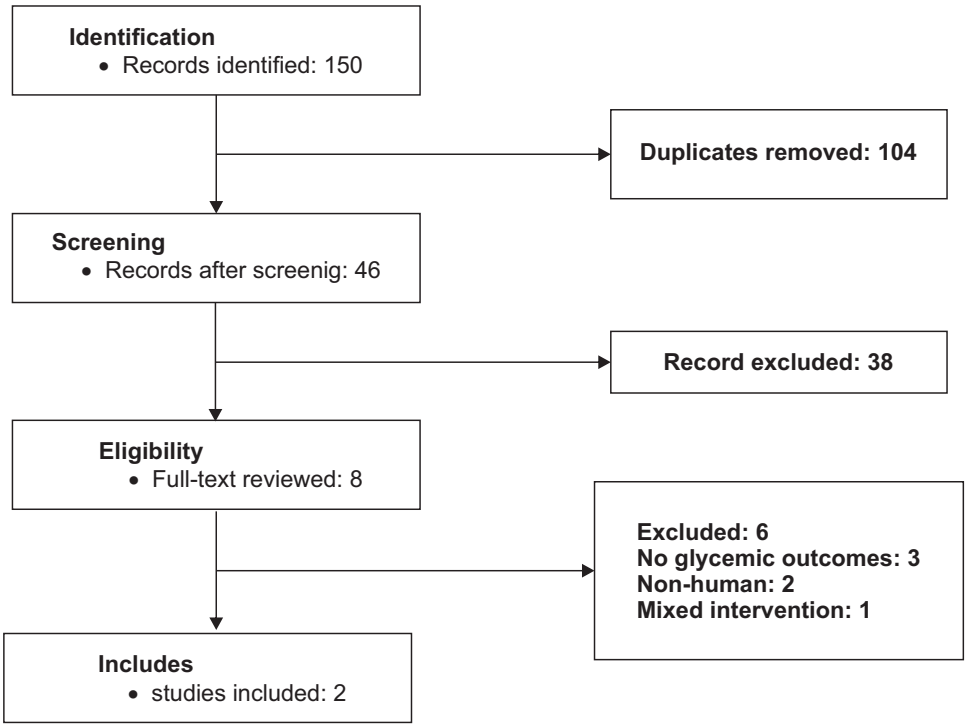

Figure 1. PRISMA 2020 Flowchart

Table 2. Included Studies

Study	Sample	Preparation	Dose	Duration	Outcomes
Watanabe 2018	22	Fruit pulp standardized to 160 mg xanthones	400 mg/day	26 weeks	↓ HOMA-IR (p=0.004), no AE
Enikmawati 2022	12	Peel decoction	200 mL × 2/day	7 days	↓ FBG 53.6 mg/dL (p=0.002)

The second study by Enikmawati et al. (2022), published in *Jurnal JRIK*, was a smaller-scale interventional study involving 12 adult diabetic participants aged 36–65 years. Subjects received a decoction of mangosteen peel (200 mL twice daily) for 7 days. The study reported a significant reduction in blood glucose levels following the intervention, although detailed statistical parameters were not provided.[2] In a quasi-experimental pre–post study of 12 adults with T2DM, daily consumption of mangosteen peel decoction for 7 days led to a significant reduction in FBG, from a mean of 278.5 ± 68.3 mg/dL to 224.9 ± 118.2 mg/dL (mean decrease 53.6 mg/dL; p = 0.002). The sample comprised predominantly older individuals (56–65 years, 33.3%) and females (58.3%).

Collectively, the included studies indicate that both mangosteen fruit and peel preparations may confer beneficial effects on glycaemic control, specifically among individuals with obesity or diabetes. However, heterogeneity in study design, sample size, preparation type, and intervention duration limits direct comparison and generalizability. Meta-analysis was not performed due to heterogeneity.

Risk of Bias

Two human studies were included in this review: one RCT and one quasi-experimental interventional study. The overall risk of bias varied between the two studies. In general, one trial was of low risk, while the quasi-experimental study had moderate concerns regarding blinding and outcome measurement.

Table 3. Risk of Bias

Study	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall Risk
Watanabe et al., (2018)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Enikmawati et al., (2022)	Some concerns	Low risk	Low risk	Some concerns	Low risk	Some concerns

DISCUSSION

This systematic review aimed to evaluate the potential antidiabetic and metabolic benefits of mangosteen and its derived compounds across both human and preclinical studies. The results suggest that mangosteen exhibits promising glycemic and metabolic effects, though the quality and consistency of evidence vary considerably.[9]

Mechanism of Action

Across two human studies, mangosteen demonstrated a positive impact on glycemic control. RCT by Watanabe et al. (2018) showed a significant reduction in insulin resistance (HOMA-IR) over a 26-week intervention with standardized mangosteen fruit pulp extract, with no reported adverse events. In contrast, Enikmawati et al. (2022) reported a decrease in blood glucose following a 7-day intervention using mangosteen peel decoction, but methodological limitations, including the lack of a control group and blinding, limit the reliability of the results. The potential antidiabetic effects of mangosteen are believed to be mediated by its high xanthone content, particularly α-mangostin and γ-mangostin. These compounds exhibit antioxidant, anti-inflammatory, and insulin-sensitizing properties.[10,11] Mechanistically, α-mangostin has been shown to modulate hepatic carbohydrate metabolism, reduce oxidative stress, and enhance insulin signaling pathways, which could collectively improve glucose uptake and reduce insulin resistance.[12-14] Mangosteen peel contains abundant bioactive compounds, primarily xanthones such as α-mangostin, γ-mangostin, and garcinone E, which contribute to its antidiabetic, antioxidant, and anti-inflammatory properties. The beneficial metabolic effects of mangosteen peel extract in T2DM appear to arise from multiple, synergistic mechanisms targeting insulin resistance, β-cell protection, oxidative stress, and chronic inflammation.[13]

Comparison with Standard Therapies

Several preclinical and clinical studies suggest that xanthones in mangosteen enhance insulin signaling pathways. α-Mangostin activates AMP-activated protein kinase (AMPK), promoting glucose uptake through GLUT4 translocation in skeletal muscle and adipose tissue. Upregulation of AMPK also increases fatty acid oxidation and decreases hepatic gluconeogenesis, thereby improving insulin sensitivity. In diabetic animal models, supplementation with mangosteen peel extract reduced fasting glucose and HOMA-IR, indicating restoration of insulin responsiveness at the cellular level.[12] Chronic hyperglycemia and oxidative stress are major contributors to β-cell dysfunction in T2DM. Antioxidant properties of mangosteen peel, largely attributed to its polyphenolic xanthones and anthocyanins, enable scavenging of reactive oxygen species (ROS) and enhancement of endogenous antioxidant enzymes, including superoxide dismutase (SOD) and catalase. This redox balance preservation helps prevent β-cell apoptosis and maintain insulin secretory capacity. Some in vitro studies demonstrate that α-mangostin reduces lipid peroxidation and modulates apoptotic signaling through inhibition of caspase-3 and upregulation of Bcl-2.[13]

α-Mangostin directly inhibits NADPH oxidase activity, suppressing superoxide production and preventing the formation of peroxynitrite—a major contributor to endothelial dysfunction. This antioxidant action not only supports β-cell integrity but also improves vascular reactivity and endothelial nitric oxide (NO) bioavailability, reducing diabetic microvascular complications. The pleiotropic

nature of mangosteen bioactive constituents suggests that its antidiabetic effects result from multi-target synergism rather than a single molecular pathway.[13-14] The combination of mangosteen peel extract with standard therapies such as metformin may potentiate glycemic control while mitigating oxidative and inflammatory damage. However, variability in extract standardization, dosage, and treatment duration across studies necessitates further controlled trials to elucidate the precise molecular targets and establish therapeutic safety profiles.[14]

For clinical translation, several key considerations must be addressed. First, dosing and treatment duration remain inconsistent across studies, ranging from short-term administration of mangosteen peel decoction (200 mL/day for 7 days) to longer courses of standardized extract (400 mg/day for 26 weeks). Second, a lack of extract standardization, particularly regarding xanthone content, limits comparability and hinders the determination of optimal therapeutic potency.[15-16] Although available data suggest good tolerability, comprehensive safety evaluation, including hepatic and renal monitoring, is still insufficient. Additionally, the pharmacokinetics and oral bioavailability of major xanthones such as α- and γ-mangostin are not well defined, and optimal delivery strategies remain unclear. Clarifying these factors is essential before mangosteen-derived products can be recommended for routine clinical use.[17-20]

Limitations and Future Studies

Mangosteen peel extract shows potential metabolic benefits. However, the evidence is limited by significant methodological weaknesses in the study by Enikmawati et al., including the absence of a control group, lack of blinding, brief intervention, and unstandardized extract, which introduce a high risk of bias. Watanabe et al. RCT offers more reliable findings but remains a small pilot trial. Despite these limitations, the favorable safety profile of mangosteen peel extract suggests it may be a useful adjunct for older adults with T2DM, who are prone to polypharmacy and oxidative stress. However, larger standardized trials are needed to establish its efficacy and safety.

CONCLUSION

In conclusion, mangosteen and its bioactive constituents demonstrate promising glycemic and metabolic benefits in both human studies. Despite promising mechanistic and preclinical data, clinical evidence remains limited. Larger, well-designed randomized controlled trials using standardized extract formulations are needed to confirm the therapeutic potential of mangosteen in diabetes management, as current evidence is insufficient for clinical recommendations. Further large-scale, long-term RCT is required. Until a larger standardized RCT is available, mangosteen peel extract should not replace standard therapy, but may be considered experimentally as an adjunctive nutraceutical.

CONFLICT OF INTEREST

Author declare that there is no conflict of interest.

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None

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