



**EFFECT OF GARCINIA MANGOSTANA LINN. PERICARP EXTRACT SUPPLEMENTATION ON LIPID PROFILE AND GLYCEMIC PARAMETERS IN ELDERLY PATIENTS WITH TYPE 2 DIABETES MELLITUS: A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL**

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**ABSTRACT**

Type 2 Diabetes Mellitus (T2DM) in the elderly is frequently accompanied by dyslipidemia, increasing cardiovascular risk. Mangosteen pericarp, derived from *Garcinia mangostana* Linn., contains xanthenes with antioxidant and anti-inflammatory properties that may improve metabolic parameters. The aim of this study is evaluate the effect of mangosteen pericarp extract supplementation on lipid profile, glycemic parameters, and insulin resistance in elderly patients with T2DM. This double-blind randomized controlled trial included 72 elderly T2DM patients allocated into a supplementation group (n=36) and a placebo-controlled group (n=36). Consecutive sampling was used for this study. Baseline and post-intervention assessments included fasting blood glucose, HbA1c, serum insulin, HOMA-IR, total cholesterol, LDL, HDL, and triglycerides. Within-group and between-group analyses were performed using parametric or non-parametric tests as appropriate, with  $p < 0.05$  considered statistically significant. Significant differences in baseline HbA1c and LDL levels were observed between groups ( $p < 0.05$ ). After intervention, a significant between-group difference was found only in HDL levels ( $p < 0.05$ ). Delta analysis demonstrated significant improvements in LDL and HDL in the supplementation group compared with controls ( $p < 0.05$ ). No significant differences were observed in fasting glucose, HbA1c, insulin levels, or HOMA-IR. Mangosteen pericarp extract supplementation significantly improved LDL and HDL levels but did not significantly affect glycemic control or insulin resistance.

Keywords: elderly; HDL; LDL; lipid profile; mangosteen pericarp extract; randomized controlled trial; type 2 diabetes mellitus

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**INTRODUCTION**

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from impaired insulin secretion and/or insulin resistance. In the elderly population, the prevalence of T2DM increases with aging, which is accompanied by declining pancreatic  $\beta$ -cell function, changes in body composition, and increased insulin resistance (Sanz-Canovas et al., 2022). Chronic hyperglycemia in T2DM is closely associated with increased oxidative stress due to excessive production of reactive oxygen species and reactive nitrogen species (He et al., 2025). Oxidative stress contributes to pancreatic  $\beta$ -cell damage, decreased insulin sensitivity, and the

progression of macrovascular and microvascular complications. In older adults, this condition is exacerbated by reduced endogenous antioxidant capacity and a high prevalence of comorbidities (Xue et al., 2024).

Management of T2DM in elderly patients presents specific challenges, particularly related to treatment safety. Impaired renal function, the risk of hypoglycemia, and adverse effects of oral antidiabetic drugs often limit therapeutic options. Therefore, the development of safe and effective complementary therapies based on natural products is a critical need in the management of T2DM in this population (Sanz-Canovas et al., 2022). Indonesia has rich biodiversity with significant potential for the development of phytopharmaceuticals, one of which is mangosteen pericarp. The mangosteen rind contains xanthenes, primarily  $\alpha$ -mangostin and  $\gamma$ -mangostin, which exhibit potent antioxidant and anti-inflammatory activities. Experimental studies have demonstrated that these compounds can reduce blood glucose levels, enhance insulin sensitivity, improve pancreatic  $\beta$ -cell function, and favorably modulate lipid profiles (Bi et al., 2023; Soetikno et al., 2023).

Although several studies have reported the benefits of mangosteen rind extract in animal models and adult populations with diabetes, clinical evidence in elderly patients with T2DM remains limited. Therefore, this study aims to evaluate the effects of mangosteen rind extract supplementation on blood glucose levels, insulin resistance, and lipid profiles in elderly patients with T2DM as a basis for the development of natural-based complementary therapy.

## **METHOD**

### **Study Design and Setting**

This study was an experimental clinical trial using a double-blind randomized controlled trial design with a pre-test and post-test control group approach. The study was conducted at the Internal Medicine Outpatient Clinic of Diponegoro National Hospital, Semarang, after obtaining ethical approval from the Institutional Ethics Committee of Diponegoro University (No. 199/EC/KEPK/FK-UNDIP/V/2024).

### **Study Subjects**

The target population consisted of elderly patients with T2DM. The accessible population included elderly T2DM patients receiving outpatient care at the Internal Medicine Clinic during the study period. Subjects were recruited using a consecutive sampling method until the required sample size was achieved. The inclusion criteria were age  $>60$  years, diagnosis of T2DM according to the American Diabetes Association criteria (1), and body mass index within normal to overweight range. Exclusion criteria included acute diabetic complications requiring hospitalization, history of malignancy, end-stage renal disease, severe gastrointestinal disorders, insulin therapy use, or refusal to participate.

Sample size was calculated using the formula for comparison of two population means with a significance level of 5% and statistical power of 80%. The minimum required sample size was 26 subjects per group. Considering a potential 10% dropout rate, the total sample size was set at 60 subjects.

### **Intervention**

Subjects were randomly allocated into two groups. The treatment group received mangosteen pericarp extract supplementation, while the control group received a placebo with identical appearance and packaging. Randomization and intervention procedures were conducted in a double-blind manner. The measured parameters included fasting blood glucose, glycated hemoglobin (HbA1c), serum insulin levels, insulin resistance index calculated using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), and lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides). Laboratory examinations were performed before

and after the intervention at a standardized laboratory of the Faculty of Medicine, Universitas Diponegoro.

### Statistical Analysis

Data analysis was performed using parametric or non-parametric statistical tests according to data distribution. Within-group comparisons were conducted to evaluate differences before and after intervention, while between-group comparisons were used to assess differences between treatment and control groups. A p-value <0.05 was considered statistically significant.

### RESULT

A total of 72 subjects were analyzed, with 36 in the mangosteen pericarp extract supplementation group and 36 in the control group. Baseline characteristics showed no significant difference in age between the two groups ( $p > 0.05$ ), indicating that both groups were demographically comparable. Normality testing revealed that most metabolic variables were not normally distributed.

Table 1.

Baseline Characteristics of Study Subjects

Variable	Control Group	Treatment Group	p-value
Age (years)	65 ± 6.9	62.1 ± 8.1	0.346
Fasting Blood Glucose (mg/dL)	161.3 ± 55.1	178.1 ± 60.2	0.182
HbA1c (%)	7.54 ± 1.72	8.73 ± 2.43	0.016
Serum Insulin	27.9 ± 82.1	16.8 ± 16.3	0.632
Total Cholesterol	199.2 ± 48.5	211.2 ± 32.5	0.053
LDL Cholesterol	125.0 ± 43.8	138.9 ± 28.1	0.024
HDL Cholesterol	46.0 ± 13.6	43.3 ± 9.6	0.183
Triglycerides	164.8 ± 84.6	187.8 ± 120.3	0.362
HOMA-IR	3.09 ± 1.449	3.88 ± 2.224	0.100

At baseline (pre-intervention), significant differences between groups were observed in HbA1c and LDL cholesterol levels ( $p < 0.05$ ). In contrast, fasting blood glucose, serum insulin, HOMA-IR, total cholesterol, HDL cholesterol, and triglycerides did not differ significantly between groups ( $p > 0.05$ ). After the intervention, a significant between-group difference was observed only in HDL cholesterol levels ( $p < 0.05$ ), while other metabolic parameters showed no statistically significant differences. Analysis of changes (delta values) before and after intervention demonstrated that the changes in LDL and HDL cholesterol levels differed significantly between the supplementation and control groups ( $p < 0.05$ ). The group receiving mangosteen pericarp extract supplementation exhibited more favorable changes in LDL and HDL cholesterol compared to the control group. However, glycemic parameters and insulin resistance indices did not show significant differences in changes between groups.

### DISCUSSION

The present study demonstrated that mangosteen pericarp extract supplementation in elderly patients with T2DM produced its most pronounced effects on lipid parameters, particularly LDL and HDL cholesterol. The changes (delta values) in LDL and HDL levels differed significantly between the intervention and control groups, whereas glycemic parameters (fasting blood glucose and HbA1c) and HOMA-IR did not show statistically significant differences. These findings suggest that the primary metabolic benefit of mangosteen extract in this population may be more strongly related to lipid modulation than to direct glycemic control.

Our findings are consistent with several experimental studies in obese and dyslipidemic animal models reporting reductions in total cholesterol, LDL cholesterol, and triglycerides, along with increases in HDL cholesterol following administration of mangosteen pericarp extract or isolated mangostins (Darsono et al., n.d.; Setiawan et al., 2024). In 2023, Soetikno et al. demonstrated that

xanthone-rich mangosteen extract reduced triglyceride and total cholesterol levels by up to 38% and 36%, respectively, accompanied by improvement in hepatic fat deposition on histopathological examination (Soetikno et al., 2023).

These preclinical findings support the lipid-modifying effects observed in our clinical study. The lipid-lowering properties of mangosteen are largely attributed to its bioactive xanthenes, particularly  $\alpha$ -mangostin and  $\gamma$ -mangostin (Bi et al., 2023). These compounds have been shown to modulate key metabolic pathways involved in lipid homeostasis. Mechanistically, xanthenes can activate AMP-activated protein kinase (AMPK), leading to enhanced fatty acid oxidation and reduced lipid synthesis (Soetikno et al., 2023). They may also modulate peroxisome proliferator-activated receptor gamma (PPAR $\gamma$ ), inhibit sterol regulatory element-binding protein-1c (SREBP-1c), and suppress proinflammatory mediators such as tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-6 (IL-6) (Bi et al., 2023). Collectively, these actions reduce triglyceride and very-low-density lipoprotein (VLDL) synthesis while improving lipid clearance, thereby contributing to decreased LDL levels and increased HDL levels. The anti-inflammatory and antioxidant effects of xanthenes further attenuate oxidative modification of LDL, which may provide additional cardiovascular protection in elderly patients with T2DM (Suksamran et al., 2022).

Although early human studies have suggested potential metabolic benefits, including improvements in HOMA-IR and inflammatory markers, our study did not demonstrate significant effects on glycemic indices or insulin resistance (Habeeb et al., 2026). Several factors may explain this discrepancy. First, the elderly population often exhibits long-standing insulin resistance and  $\beta$ -cell dysfunction, which may limit the magnitude of short-term metabolic improvement (Sanz-Canovas et al., 2022). Second, baseline differences in HbA1c and LDL levels between groups could have influenced the observed treatment effects. Third, concomitant use of oral antidiabetic medications may have attenuated the measurable additional effect of supplementation on glycemic outcomes.

From a clinical perspective, the improvement in LDL and HDL levels is particularly relevant in elderly patients with T2DM, given that dyslipidemia substantially contributes to cardiovascular morbidity and mortality in this population (He et al., 2025). A complementary therapy capable of safely improving lipid profile may provide added value, especially in patients who have limited tolerance to intensified pharmacologic regimens (Xue et al., 2024).

However, several limitations should be acknowledged. First, the relatively small sample size may limit the statistical power to detect modest changes in glycemic parameters. Second, the duration of intervention may have been insufficient to observe significant changes in HbA1c, which reflects longer-term glycemic control. Third, baseline imbalances in certain metabolic variables (HbA1c and LDL) may introduce potential confounding effects. Fourth, inflammatory and oxidative stress biomarkers were not measured, limiting mechanistic interpretation in this clinical setting. Finally, dietary intake and physical activity were not strictly controlled, which may have influenced lipid outcomes.

Future studies should include larger multicenter randomized controlled trials with longer follow-up duration to better evaluate long-term metabolic and cardiovascular outcomes. Stratified analysis based on baseline dyslipidemia severity and glycemic control may clarify subgroups that benefit most from supplementation. In addition, assessment of inflammatory markers, oxidative stress parameters, and molecular biomarkers would help elucidate the translational mechanisms of xanthenes in human subjects. Dose–response studies are also warranted to determine the optimal therapeutic dosage and safety profile of mangosteen pericarp extract in elderly patients with T2DM.

## CONCLUSION

In conclusion, supplementation with mangosteen (*Garcinia mangostana* Linn.) pericarp extract in elderly patients with Type 2 Diabetes Mellitus demonstrated significant beneficial effects on lipid profile, particularly in improving LDL and HDL cholesterol levels, while no significant effects were observed on glycemic parameters or insulin resistance indices. These findings suggest that mangosteen extract may serve as a promising complementary therapy for lipid modulation in elderly individuals with T2DM, potentially contributing to cardiovascular risk reduction. However, larger-scale studies with longer follow-up periods are required to confirm its long-term efficacy, metabolic impact, and safety profile before routine clinical implementation can be recommended.

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