RESEARCH ARTICLE

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Propolis Supplementation Reduces NLR, MPV, and FPG in Obese Individuals with Type 2 Diabetes Mellitus

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Background: Obesity is associated with chronic inflammation and metabolic disorders, including Type 2 Diabetes Mellitus (T2DM). Biomarkers such as Interleukin-1β (IL-1β), Neutrophil-to-Lymphocyte Ratio (NLR), Mean Platelet Volume (MPV), and Fasting Plasma Glucose (FPG) are commonly used to assess inflammation and metabolic status. Propolis has demonstrated anti-inflammatory effects, however evidence in obese individuals with and without T2DM remains limited. This study evaluated the effects of propolis supplementation on these biomarkers.

Materials and methods: A total of 45 obese adults aged <60 years, with and without T2DM, received 400 mg/day of propolis extract for 30 days. Participants receiving anti-inflammatory or steroid therapy, experiencing severe depression or anxiety requiring treatment, or unwilling to participate were excluded. Blood samples were collected to measure IL-1β, NLR, MPV, and FPG. IL-1β was analyzed using ELISA, while NLR, MPV, and FPG were assessed using automated laboratory analyzers. Pre- and post-intervention values were compared using paired statistical tests.

Results: Obese individuals with T2DM demonstrated more pronounced changes in Inflammatory and hematological biomarkers than obese individuals without T2DM. In obese with T2DM group, significant reductions were observed in NLR (p=0.003), MPV (p=0.031), and FPG (p=0.046), while IL-1β showed no significant. In obese without T2DM group, MPV decreased significantly, IL-1β and NLR did not change significantly. FPG increased modestly, remained within the normal range.

Conclusion: Propolis supplementation improved NLR, MPV and FPG more prominently in obese with T2DM than obese without T2DM, suggesting greater benefits under metabolically dysregulated conditions.

Keywords: *propolis, obesity, type 2 diabetes mellitus, inflammation, hematological profile*

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Introduction

Propolis is a resinous substance collected by honeybees from plant-derived materials, primarily poplar-type resins. It contains a wide range of antioxidant constituents, including Caffeic Acid Phenethyl Ester (CAPE), which plays an important role in reducing oxidative stress by suppressing the production of Reactive Oxygen Species (ROS).[1,2] CAPE also inhibits the synthesis of pro-inflammatory cytokines by macrophages and attenuates inflammatory responses through the inhibition of the Nuclear Factor Kappa Beta (NFκβ)-mediated inflammatory pathway.[2,3] Through these mechanisms, CAPE thereby supports the potential of propolis as a multi-target agent in metabolic and inflammatory disorders associated with obesity and type 2 diabetes mellitus.[4]

Type 2 diabetes mellitus (T2DM) is associated with chronic low-grade inflammation, which plays a central role in the pathogenesis and progression of the disease.[5,6] Persistent inflammation in adipose tissue contributes to metabolic dysregulation and increases the risk of long-term complications.[7] Furthermore, excess adipose tissue accumulation in obesity promotes macrophage infiltration and dysregulated secretion of pro-inflammatory cytokines, including interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α).[8] Among these cytokines, IL-1β is closely linked to NLRP3 inflammasome activation and represents a key driver of metabolic inflammation, insulin resistance, and impaired glucose homeostasis.[9,10] In addition, hematological parameters such as the Neutrophil-to-Lymphocyte Ratio (NLR) and Mean Platelet Volume (MPV) have emerged as accessible markers of systemic inflammation in obesity-related metabolic disorders.[11,12]

Although propolis has been widely reported to possess anti-inflammatory, antioxidant, and antihyperglycemic properties, with several studies demonstrating its potential to modulate inflammatory responses and improve glycemic control, evidence regarding its efficacy across different metabolic conditions remains limited.[13,14] In particular, it is still unclear whether the therapeutic effects of propolis differ between obese individuals with normal glucose metabolism and those with T2DM, who exhibit more metabolic disturbances and chronic low-grade inflammation. Given that the severity of metabolic dysregulation may influence the responsiveness of inflammatory and glycemic biomarkers to nutritional interventions, further investigation is warranted to determine whether propolis exerts comparable or differential effects in these distinct metabolic states. Therefore, this study aimed to evaluate the effects of propolis supplementation on inflammatory biomarkers, including IL-1β, NLR, and MPV, as well as the metabolic biomarker fasting plasma glucose (FPG), in obese individuals with and without T2DM. By comparing the pre- and post-supplementation changes between these two groups, this study provides novel insights into the potential role of propolis in modulating inflammatory and metabolic responses according to different metabolic profiles, thereby contributing to a better understanding of its therapeutic potential in obesity-associated metabolic disorders.

Materials and methods

Participant and Data Collection

This study employed a quasi-experimental pre–post design to examine inflammatory and hematological profile following propolis extract supplementation. This study was conducted from April 15 to May 16, 2025 at Soerojo Hospital. Participants were provided with a detailed explanation of the study protocol and signed written informed consent prior to enrollment. The study population consisted of adults aged <60 years with obesity, defined as a Body Mass Index (BMI) ≥25 kg/m² according to Asian criteria. Purposive sampling with consecutive screening of eligible patients was used to reduce selection bias. Participants were allocated into two non-randomized groups based on clinical diagnosis: obesity with T2DM and obesity without T2DM. Eligible participants were required to provide informed consent and be willing to complete all study procedures. Individuals receiving anti-inflammatory drugs or corticosteroids, those with severe depression or anxiety requiring treatment, and those unwilling to participate were excluded. Participants were withdrawn from the study if they discontinued propolis supplementation for more than 24 hours, failed to complete the study procedures, developed an allergic reaction, or experienced adverse events requiring discontinuation of the intervention. To improve internal validity, only participants with complete pretest and posttest data were included in the final analysis. A total of 45 participants completed the study.

Eligible participants received HDI Propoelix™ at a dose of 400 mg/day (2×1 capsule daily; each capsule containing 200 mg propolis extract) for 30 days, according to the manufacturer's recommended dosage for maintaining immune function. This dosage was selected based on

previous studies demonstrating the safety and potential metabolic and anti-inflammatory benefits of propolis supplementation at comparable doses.[15,16] Adherence was promoted through daily reminder messages and assessed through pill counts based on returned blister packs during weekly follow-up visits, while Adverse Events (AE) and Serious Adverse Events (SAE) were also monitored. Blood samples were collected at baseline (pretest) and after 30 days of intervention (posttest), followed by analysis for IL-1β, NLR, MPV, and FPG representing inflammatory and hematological biomarkers. All measurements were performed using standardized laboratory procedures.

ELISA-Based Measurement of IL-1β

IL-1β was selected as a key pro-inflammatory cytokine reflecting chronic metabolic inflammation associated with insulin resistance and β-cell dysfunction in obesity and type 2 diabetes mellitus.[17] Serum IL-1β levels were measured using the Quantikine® HS ELISA Human IL-1β/IL-1F2 Immunoassay kit (Cat. No. HSLB00D; Lot No. P482846, R&D Systems, Inc., Minneapolis, USA). Measurements were performed according to the manufacturer's instructions using a Microplate Reader Model 680 with Microplate Manager software version 5.2.1 (Bio-Rad Laboratories Inc., California, USA). The assay had a standard calibration range of 0.125–8 pg/mL and a detection limit of 0.033 pg/mL.

Hematology Analyzer- Measurement of NLR

NLR was included as a simple and widely available marker of systemic inflammation that reflects the balance between innate and adaptive immune responses and has prognostic relevance in metabolic disorders.[18] NLR was calculated from absolute neutrophil and lymphocyte counts obtained from complete blood count examinations performed using an automated hematology analyzer, Sysmex XN-1000 (Sysmex Corporation, Japan), at the Soerojo Hospital Laboratory according to standard laboratory procedures.

Hematology Analyzer- Measurement of MPV

MPV was selected as an indicator of platelet activation and thromboinflammatory status associated with insulin resistance.[19] MPV values were obtained from complete blood count examinations performed using the Sysmex XN-1000 automated hematology analyzer (Sysmex Corporation, Japan) at the Soerojo Hospital Laboratory according to standard laboratory procedures.

Chemistry Analyzer-Measurement of FPG

FPG was included as a standard and clinically relevant marker of glycemic control widely used to assess metabolic status in individuals with diabetes mellitus.[20] Fasting plasma glucose levels were measured at the Soerojo Hospital Laboratory using a Tokyo Boeki Chemistry Analyzer (Biolis Medical Corp., Tokyo, Japan) according to standard laboratory procedures.

Statistical Analysis

Statistical analysis was performed using appropriate statistical methods. Data were presented as mean±standard deviation, with minimum and maximum values. Within-group comparisons between pretest and posttest measurements were analyzed using paired statistical tests, applying the paired t-test for normally distributed data and the wilcoxon signed-rank test for non-normally distributed data. A p-value <0.05 was considered statistically significant.

Results

Baseline Characteristics of Obese Participants With and Without T2DM

This study involved 45 individuals, representing a diverse sample of obese adults (BMI>25kg/m2). The characteristics of participants were distributed by age, gender, education, and BMI (Table 1). The majority of subjects in this study were middle aged (45-59 years) and male participants occupying the largest proportion in the gender distribution (60% of total participants). Meanwhile, based on education level, it is dominated by higher education level with 42.2% diploma followed by 37.8% bachelor's degree. Occupationally, nurses dominated the subjects in this study. This distribution reflects hospital-based sampling due to the recruitment setting within a hospital environment.

Significant Reductions in NLR, MPV, and FPG Following Propolis Supplementation in Obese Individuals with T2DM

The obese with T2DM group demonstrated differences in several inflammatory and hematological profile between pretest and posttest measurements. IL-1β levels slightly decreased from 0.175±0.091 pg/mL to 0.167±0.073 pg/mL (Table 2). However, this change was not statistically significant (p= 0.603). Otherwise, the NLR demonstrated a significant reduction from 1.832±0.702 to 1.079±0.320 (p=0.003), indicating an improvement in systemic

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Table 1. Demographic and clinical characteristics of obese participants with and without T2DM.

Characteristics	Obesity with T2DM Group n (%)	Obesity without T2DM Group n (%)	Total (N=45)
Age			
25-44 (young adult)	7 (31.8)	9 (39.1)	16 (35.6)
45-59 (middle age)	15 (68.2)	14 (60.9)	29 (64.4)
Gender			
Male	14 (63.6)	13 (56.5)	27 (60.0)
Female	8 (36.4)	10 (43.5)	18 (40.0)
Education Level			
Senior high school	5 (22.7)	1 (4.3)	6 (13.3)
Diploma degree	9 (40.9)	10 (43.5)	19 (42.2)
Bachelor's degree	7 (31.8)	10 (43.5)	17 (37.8)
Master's degree	1 (4.5)	2 (8.7)	3 (6.7)
Occupation			
Doctor/specialist	1 (4.5)	2 (8.7)	3 (6.7)
Health workers	2 (9.1)	1 (4.3)	3 (6.7)
Others	7 (31.8)	5 (21.7)	12 (26.7)
Body Mass Index (BMI)			
<18.5 kg/m ^{2}	0 (0.0)	0 (0.0)	0 (0.0)
18.5 - 22.9 kg/m ^{2}	0 (0.0)	0 (0.0)	0 (0.0)
23.0 - 24.9 kg/m ^{2}	0 (0.0)	0 (0.0)	0 (0.0)
≥25 kg/m ^{2}	22 (100)	23 (100)	45 (100)

inflammatory status. MPV also decreased from 9.97±0.82 fL to 9.77±0.69 fL, with a statistically significant difference (p= 0.031). Furthermore, FPG levels showed a significant decline from 159.48±60.06 mg/dL at pretest to 131.71±45.88 mg/dL at posttest (p= 0.046), reflecting improved glycemic control in this group (Table 2).

Significant Reduction in MPV and Increased FPG Following Propolis Supplementation in Obese Individuals without T2DM

The obesity without T2DM group showed a different pattern of changes in inflammatory and hematological profile between pretest and posttest. IL-1β levels slightly increased from 0.160±0.048 pg/mL to 0.168±0.056 pg/mL, although this change was not statistically significant (Table 3). Similarly, the NLR showed no significant difference between the pretest and posttest, indicating a relatively stable systemic inflammatory status. However, MPV decreased significantly (p=0.000) from 10.19±0.86 fL to 9.91±0.86 fL, suggesting a meaningful change in platelet activation. Additionally, FPG levels increased significantly from 81.5±10.20 mg/dL at pretest to 87.4±8.77 mg/dL at posttest (p=0.009), although values remained within the normal range, highlighting differing metabolic responses compared with the obese with DM group.

Discussion

In this study, the observed reduction in NLR, MPV, FPG in the obese T2DM group suggests that propolis supplementation may exert beneficial effects on systemic

Table 2. Pre–post changes in inflammatory and hematological biomarkers among obese individuals with T2DM.

Inflammatory and Hematological Biomarkers	Obese Individuals with T2DM Group			*p*-Value
	Mean ± SD	Min	Max	
IL-1β (pg/mL)				
Pretest	0.175 ± 0.091	0.082	0.437	0.603
Posttest	0.167 ± 0.073	0.088	0.339	
NLR (%)				
Pretest	1.832 ± 0.702	0.9	3.0	0.003*
Posttest	1.079 ± 0.320	0.7	1.8	
MPV (fL)				
Pretest	9.97 ± 0.82	8.6	11.7	0.031
Posttest	9.77 ± 0.69	8.7	10.7	
FPG (mg/dL)				
Pretest	159.48 ± 60.06	101	275	0.046*
Posttest	131.71 ± 45.88	78	251	

inflammation, platelet activation, and glycemic control. The significant decrease in NLR reflects an improvement in inflammatory balance, as elevated neutrophil activity and reduced lymphocyte counts are established markers of chronic low-grade inflammation in type 2 diabetes mellitus.[21] Furthermore, these results are supported by previous studies reporting that anti-inflammatory interventions such as propolis supplementation can reduce inflammatory markers and improve metabolic parameters in T2DM, supporting the interpretation of decreased NLR as a marker of improved inflammatory status.[22] Similarly, the reduction in MPV indicates decreased platelet activation, a finding that is clinically relevant given the role of hyperglycemia-induced platelet hyperreactivity in endothelial dysfunction and vascular complications.[23] Previous studies have demonstrated that propolis exhibits antiplatelet activity by inhibiting platelet aggregation induced by various agonists, supporting its potential role in reducing platelet activation and thromboinflammatory processes.[24]

The improvement in FPG further supports the potential metabolic effects of propolis, potentially mediated by its bioactive compounds such as flavonoids and CAPE. These compounds have been shown to improve insulin sensitivity, reduce oxidative stress, and modulate inflammatory signaling pathways, including NF-κB inhibition.[25] Consistent with previous study stated that propolis enhances glucose metabolism by improving insulin sensitivity, upregulating GLUT4, activating PI3K/AMPK pathways, and inhibiting α-glucosidase. Its compounds, such as galangin and pinocembrin, reduce insulin resistance, and its flavonoids promote glucose utilization and glycogen synthesis.[22] However, the absence of a significant change in IL-1β suggests that the anti-inflammatory effect of propolis may be more pronounced in downstream inflammatory and hematological markers rather than upstream cytokine modulation. This finding is consistent with previous studies reporting that propolis supplementation has more consistent effects on CRP, TNF-α, and hematological indices than on IL levels in metabolic disorders.[25] In fact, the current systematic review and meta-analysis showed high, but non-significant, IL-1β levels in patients with T2DM.[17]

The differential response observed between obese individuals with and without T2DM suggests that the effects of propolis are modulated by baseline metabolic and inflammatory status. In the T2DM group, significant reductions in NLR, MPV, and FPG indicate concurrent improvements in systemic inflammation, platelet activation, and glycemic control, representing key components of diabetes-related pathophysiology. This is consistent with

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Table 3. Pre–post changes in inflammatory and hematological biomarkers among obese individuals without T2DM.

Inflammatory and Hematological Biomarkers	Obese Individuals without T2DM Group			*p*-Value
	Mean ± SD	Min	Max	
IL-1β (pg/mL)				
Pretest	0.160 ± 0.048	0.081	0.294	0.429
Posttest	0.168 ± 0.056	0.070	0.368	
NLR (%)				
Pretest	1.700 ± 0.577	00.06	2.7	0.445
Posttest	1.630 ± 0.577	00.06	2.6	
MPV (fL)				
Pretest	10.19 ± 0.86	08.01	11.7	0.000*
Posttest	9.91 ± 0.86	08.02	11.5	
FPG (mg/dL)				
Pretest	81.5 ± 10.20	62	99	0.009*
Posttest	87.4 ± 8.77	74	106	

evidence that hyperglycemia-driven oxidative stress and chronic low-grade inflammation in T2DM create a more responsive biological environment for anti-inflammatory and antioxidant interventions.[22] In contrast, the absence of significant changes in IL-1β and NLR in the non-diabetic obese group may reflect a relatively lower inflammatory burden, limiting the detectable impact of short-term intervention on circulating cytokines and leukocyte-based markers.[26]

Notably, MPV decreased significantly in both groups, suggesting that platelet-related pathways may represent a more sensitive target of propolis supplementation, independent of glycemic status. This finding is biologically plausible given previous reports demonstrating that propolis and its polyphenolic constituents inhibit platelet aggregation and modulate thromboinflammatory signaling. Previous in vitro studies indicate that the minimal antiaggregatory concentration of propolis extract ranges from 5 μM to 10.4 mM, depending on extract composition and experimental conditions.[24] The modest increase in FPG observed in the non-diabetic group, while remaining within the normal range, reflects physiological variability rather than a detrimental metabolic effect and indicates that the glycemic benefits of propolis are more evident under conditions of impaired glucose regulation. This interpretation is supported by clinical evidence demonstrating that propolis supplementation significantly improves glycemic control in patients with T2DM, whereas its effects are less pronounced under normoglycemic conditions, where baseline glucose homeostasis is already maintained.[27,28] Overall, these findings indicate that the effects of propolis are context-dependent, with greater benefits observed in metabolically dysregulated states such as T2DM.

Despite these findings, several limitations should be acknowledged. The relatively small sample size and short intervention period may have limited the detection of changes in some biomarkers. Additionally, the non-randomized pre–post design without a placebo control group may limit the generalizability of the findings. Nevertheless, it provides preliminary insights into the effects of propolis extract and a basis for future controlled studies. Further studies with larger samples and longer intervention periods are warranted.

Conclusion

Propolis supplementation showed differential effects on inflammatory and hematological biomarkers in obese individuals with and without T2DM, indicating a context-dependent biological response influenced by baseline

metabolic status. Significant reductions in NLR, MPV, and FPG in the T2DM group indicate enhanced anti-inflammatory, antiplatelet, and antihyperglycemic effects. Whereas, the non-diabetic obese group showed a limited response, with only MPV reduction and a modest increase in FPG within the normal range. Overall, propolis appears to exert greater benefits in metabolically dysregulated conditions such as T2DM. Further large-scale randomized controlled trials are needed to confirm its therapeutic potential and underlying mechanisms.

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Authors' Contributions

KKAS and HAM contributed to the conception and design of the study and were involved in the critical revision of the manuscript. RCAP, RAW, NR, and AC was responsible for data acquisition. Data analysis was conducted by RCAP and HAM. Interpretation of the study findings was performed by KKAS, RCAP, RAW, and HAM. Manuscript drafting and preparation were undertaken by KKAS, RCAP, RAW, NR, and AC. The preparation of figures and tables was performed by RCAP and RAW. All authors reviewed and approved the final version of the manuscript.

Ethical Statement

The Soerojo Hospital Research Ethics Sub-Committee granted ethical approval for this study on April 11, 2025 (No. DP.04.03/D.XXXVI.12/19/2025), and it was registered in the Indonesia Clinical Research Registry (No. INA-30042025567250C).

Conflict of Interest

The authors declare that there are no conflicts of interest related to this study.

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