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The Effect of a Single Session of Resistance Exercise and Royal Jelly Supplementation on Plasma ICAM-1 and VCAM-1 Levels in Men with Coronary Artery Disease

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Original Research

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Abstract

Purpose: Coronary artery disease (CAD) is closely associated with endothelial dysfunction and vascular inflammation, often characterized by elevated plasma adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1). Royal jelly, a natural bee product with antioxidant and anti-inflammatory properties, has recently gained attention as a potential supplement to improve endothelial health. This study aimed to investigate the acute effects of a single session of resistance exercise and royal jelly supplementation on plasma ICAM-1 and VCAM-1 levels in men with CAD.

Method: Forty male patients with stable CAD (aged 45–65 years) were randomly assigned to four groups: resistance exercise with royal jelly (RE+RJ), resistance exercise only (RE), royal jelly only (RJ), and control (CON). Participants in the exercise groups performed eight resistance exercises at 60–70% of one-repetition maximum (1RM) for 45 minutes. Those in the RJ and RE+RJ groups consumed 1,000 mg of royal jelly one hour before the session. Blood samples were collected before and 24 hours after the intervention, and ICAM-1 and VCAM-1 were analyzed using ELISA.

Results: Significant reductions in ICAM-1 ($p = 0.001$) and VCAM-1 ($p = 0.001$) were observed in the RE+RJ group, with moderate decreases in the RE and RJ groups ($p < 0.05$), while no change occurred in the control group ($p > 0.05$). Between-group comparisons showed that the RE+RJ group achieved the greatest reductions ($p < 0.01$).

Conclusion: A single session of moderate-intensity resistance exercise combined with royal jelly supplementation synergistically reduced endothelial adhesion molecules, suggesting enhanced vascular protection in patients with coronary artery disease.

Keywords: Royal jelly; Resistance exercise; ICAM-1; VCAM-1; Coronary artery disease.

Introduction

Cardiovascular diseases (CVDs) are among the leading causes of mortality worldwide, primarily due to atherosclerosis and chronic endothelial dysfunction, which are strongly associated with obesity, inflammation, and oxidative stress. These disorders are characterized by increased expression of inflammatory mediators and adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1), which contribute to endothelial activation and monocyte adhesion during the early stages of atherosclerotic plaque formation. Pharmacological strategies for CVD management are often accompanied by adverse effects; thus, non-pharmacological interventions such as exercise and natural antioxidant supplements have gained increasing attention. Royal jelly, a natural secretion produced by honeybees, contains proteins, amino acids, flavonoids, and vitamins with strong antioxidant and anti-inflammatory properties, which have shown cardioprotective effects through improved vascular endothelial function and nitric oxide (NO) regulation.

Exercise training has been consistently associated with reduced systemic inflammation and improved vascular health. Regular physical activity downregulates adhesion molecule expression and enhances endothelial nitric oxide synthase (eNOS) activity, which together improve vascular reactivity and reduce atherosclerotic risk. ICAM-1, a membrane-bound glycoprotein, mediates leukocyte adhesion and transmigration through the endothelium and serves as a reliable biomarker of endothelial activation and vascular inflammation. Previous studies have demonstrated that both aerobic and resistance exercise can significantly reduce ICAM-1 levels in overweight and diabetic populations, suggesting an exercise-induced anti-inflammatory mechanism. For instance, six weeks of high-intensity interval training (HIIT) decreased ICAM-1 concentrations in young men, accompanied by improvements in body composition and aerobic capacity. Moreover, animal studies indicate that combining exercise with antioxidant supplementation, such as royal jelly, may amplify these beneficial effects on endothelial inflammation and adhesion molecule expression.

Similarly, VCAM-1, another member of the immunoglobulin superfamily, plays a pivotal role in vascular inflammation and atherosclerosis progression by promoting monocyte adhesion to vascular endothelium. Elevated VCAM-1 levels are strongly correlated with endothelial dysfunction and coronary artery disease severity. Exercise interventions, especially endurance and combined training programs, have been shown to lower VCAM-1 expression, reflecting improved endothelial integrity and vascular compliance. The synergistic impact of royal jelly supplementation with exercise may enhance antioxidant defense, suppress proinflammatory cytokine release, and further attenuate VCAM-1 expression, thereby protecting against vascular injury and atherogenesis.

Given the central role of adhesion molecules in endothelial dysfunction and the limited evidence regarding the combined effects of resistance exercise and royal jelly supplementation in coronary artery disease (CAD), further research is warranted. The importance of this investigation lies in identifying safe, effective, and non-pharmacological interventions to reduce cardiovascular inflammation and improve vascular function. Therefore, the present study aims to examine the acute effects of a single session of resistance exercise and royal jelly supplementation on plasma ICAM-1 and VCAM-1 levels in men with coronary artery disease, providing novel insight into the integrative mechanisms of exercise and antioxidant therapy in vascular health.

Methods

Study Design and Participants

This quasi-experimental study aimed to examine the acute effects of a single session of resistance exercise and royal jelly supplementation on plasma levels of intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) in men with coronary artery disease (CAD). Forty men aged 45 to 65 years with clinically stable CAD were voluntarily recruited from a cardiac rehabilitation center. Participants were screened by a cardiologist to ensure safety for moderate-intensity exercise and were randomly assigned into four equal groups (n = 10 each): (1) Resistance Exercise + Royal Jelly (RE+RJ), (2) Resistance Exercise only (RE), (3) Royal Jelly only (RJ), and (4) Control (CON). Inclusion criteria included a confirmed diagnosis of CAD, a body mass index (BMI) between 25 and 32 kg/m², and no participation in structured exercise during the previous six months. Exclusion criteria were smoking, insulin-dependent diabetes, recent myocardial infarction, the use of anti-inflammatory or antioxidant supplements, and any contraindications to resistance exercise. All participants were informed about the purpose and procedures of the study and provided written consent. The study was approved by the institutional ethics committee.

Exercise Protocol

Participants in the exercise groups completed one session of resistance training consisting of eight movements: leg press, chest press, seated row, shoulder press, leg extension, leg curl, biceps curl, and triceps pushdown. Exercise intensity was set at 60–70% of one-repetition maximum (1RM), with three sets of 10–12 repetitions per exercise and 60 seconds of rest between sets. The total duration of each session was approximately 45 minutes, including a 10-minute warm-up and a 5-minute cool-down with stretching.

Supplementation Protocol

Subjects in the RJ and RE+RJ groups consumed 1,000 mg of royal jelly orally, dissolved in 100 mL of water, one hour before exercise. The supplement was produced by an approved manufacturer and stored at 4°C until consumption. This dosage and timing were chosen to optimize antioxidant and anti-inflammatory effects.

Blood Sampling and Biochemical Analysis

Venous blood samples (5 mL) were collected 24 hours before and 24 hours after the intervention. Plasma was separated by centrifugation at 3,000 rpm for 10 minutes and stored at −80°C until analysis. Plasma ICAM-1 and VCAM-1 concentrations were measured using enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, USA). The intra- and inter-assay coefficients of variation were 4.5% and 6.2%, respectively.

Statistical Analysis

Normality of data distribution was verified using the Shapiro–Wilk test. Within-group comparisons were performed using paired t-tests, and between-group differences were analyzed with one-way ANOVA followed by Tukey's post hoc test. Cohen's d was calculated to estimate effect sizes. Statistical significance was accepted at $p < 0.05$. All analyses were conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Baseline Characteristics

All forty participants completed the study without any adverse effects. There were no significant differences between groups at baseline in age, body mass index (BMI), or resting heart rate ($p > 0.05$). The mean age of participants was 56.3 ± 5.8 years, and the average BMI was 28.6 ±

2.3 kg/m², confirming that groups were homogenous before the intervention. No significant between-group differences were found for baseline ICAM-1 or VCAM-1 values ($p > 0.05$), indicating comparability before intervention.

Table 1. Baseline characteristics of participants (Mean ± SD)

Variable	RE+RJ (Mean±SD)	RE (Mean±SD)	RJ (Mean±SD)	CON (Mean±SD)
Age (years)	56.7 ± 5.9	55.8 ± 6.2	57.1 ± 5.5	55.5 ± 6.0
BMI (kg/m²)	28.4 ± 2.4	28.9 ± 2.1	28.5 ± 2.3	28.8 ± 2.2
Resting HR (bpm)	74.2 ± 5.6	75.0 ± 4.8	73.8 ± 6.1	74.9 ± 5.3

Changes in Plasma ICAM-1

A significant reduction in plasma ICAM-1 concentration was observed in both the RE+RJ (from 311.8 ± 24.5 to 268.2 ± 21.7 ng/mL; $p = 0.001$) and RE (from 308.7 ± 22.9 to 284.1 ± 20.8 ng/mL; $p = 0.013$) groups after the intervention. The RJ group also demonstrated a moderate but significant decrease (from 312.5 ± 25.6 to 296.8 ± 23.9 ng/mL; $p = 0.037$), while no significant change was detected in the Control group (from 309.1 ± 23.3 to 307.8 ± 22.7 ng/mL; $p = 0.682$). Between-group analysis revealed a significant difference among the four groups ($F(3,36) = 6.28$, $p = 0.002$), with the RE+RJ group showing a greater reduction compared to all others (Tukey's post hoc $p < 0.01$.(

Table 2. Plasma ICAM-1 levels before and after intervention

Group	Pre-test (Mean±SD)	Post-test (Mean±SD)	Within-group p-value	% Change
RE+RJ(ng/mL)	311.8 ± 24.5	268.2 ± 21.7	0.001	−13.9%
RE(ng/mL)	308.7 ± 22.9	284.1 ± 20.8	0.013	−8.0%
RJ(ng/mL)	312.5 ± 25.6	296.8 ± 23.9	0.037	−5.0%
CON(ng/mL)	309.1 ± 23.3	307.8 ± 22.7	0.682	−0.4%

Changes in Plasma VCAM-1

VCAM-1 levels showed a similar pattern of change. The RE+RJ group exhibited a marked reduction from 742.6 ± 58.3 to 663.7 ± 55.2 ng/mL ($p = 0.001$), followed by a significant decrease in the RE group (from 738.9 ± 61.4 to 698.3 ± 57.1 ng/mL; $p = 0.009$). The RJ group experienced a smaller but significant decline (from 746.2 ± 59.5 to 721.6 ± 54.8 ng/mL; $p = 0.041$), while no significant changes occurred in the Control group (from 740.8 ± 60.2 to 736.5 ± 58.9 ng/mL; $p = 0.563$). Between-group comparison demonstrated a significant difference ($F(3,36) = 5.92$, $p = 0.003$), with the combined RE+RJ group achieving the greatest improvement relative to all others (post hoc $p < 0.01$).

Table 3. Plasma VCAM-1 levels before and after intervention

Group	Pre-test (Mean±SD)	Post-test (Mean±SD)	Within-group p-value	% Change
RE+RJ(ng/mL)	742.6 ± 58.3	663.7 ± 55.2	0.001	−10.6%
RE(ng/mL)	738.9 ± 61.4	698.3 ± 57.1	0.009	−5.5%
RJ(ng/mL)	746.2 ± 59.5	721.6 ± 54.8	0.041	−3.3%
CON(ng/mL)	740.8 ± 60.2	736.5 ± 58.9	0.563	−0.6%

Summary of Findings

The main findings indicate that both resistance exercise and royal jelly supplementation independently reduced ICAM-1 and VCAM-1 levels, but their combination elicited the most pronounced anti-inflammatory response. The post-intervention reductions were greater in the RE+RJ group compared with all other groups ($p < 0.01$), suggesting a synergistic effect between resistance exercise and royal jelly in improving endothelial function and reducing vascular inflammation in men with coronary artery disease.

Discussion

The present study aimed to examine the acute effects of a single session of resistance exercise and royal jelly supplementation on plasma ICAM-1 and VCAM-1 levels in men with coronary artery disease (CAD). The results demonstrated that both interventions independently reduced plasma adhesion molecule concentrations, while their combination produced the greatest reduction, suggesting a synergistic anti-inflammatory effect (Kadoglou et al., 2025; Jorge et al., 2011).

The observed decline in ICAM-1 following resistance exercise is consistent with previous evidence showing that physical activity mitigates endothelial activation by improving nitric oxide bioavailability and suppressing oxidative stress (Teixeira-Lemos & Nunes, 2012; Pedersen, 2006). Exercise-induced shear stress increases endothelial nitric oxide synthase (eNOS) activity, which downregulates the expression of adhesion molecules such as ICAM-1 and VCAM-1 (Abdelhamid Fathy et al., 2017). Furthermore, mechanical loading during resistance exercise reduces circulating levels of proinflammatory cytokines like TNF-α and IL-6, which are known to promote endothelial adhesion (Hotamisligil et al., 1995; Hejazi et al., 2014). These mechanisms likely contributed to the significant ICAM-1 reduction observed in the exercise and combined groups.

Royal jelly supplementation also exerted independent anti-inflammatory and vascular benefits, consistent with its high content of antioxidants, flavonoids, peptides, and 10-hydroxy-2-decenoic acid (10-HDA) (Ali, 2020; Anugrah et al., 2023). These bioactive compounds inhibit NF-κB activation and reduce oxidative stress, thereby attenuating cytokine-induced adhesion molecule expression (Bahar Zangiband et al., 2024; Etemad & Zohali, 2021). Studies have shown that royal jelly supplementation improves endothelial function, decreases vascular inflammation, and enhances nitric oxide production in both animal and human models (Pasdar et al., 2025; Ovchinnikov et al., 2022). This mechanism may explain the moderate but significant reduction in ICAM-1 and VCAM-1 levels seen in the royal jelly group of this study.

In addition, the combination of royal jelly and resistance exercise (RE+RJ) produced the most pronounced improvement, indicating a possible additive effect. Previous findings support the concept that combining structured exercise with antioxidant supplementation amplifies vascular protection by simultaneously reducing oxidative stress and increasing nitric oxide-mediated vasodilation (Castro et al., 2019; Khaki et al., 2022). Similar synergistic outcomes were reported when royal jelly supplementation was paired with aerobic training, resulting in greater modulation of endothelial biomarkers compared to either intervention alone (Bahar Zangiband et al., 2024; Gaini et al., 2024(.

The reduction in VCAM-1 levels observed after both exercise and supplementation confirms that vascular inflammation is responsive to short-term interventions that target endothelial stress and leukocyte adhesion (Kharghani et al., 2022; Mardani et al., 2022). Resistance training improves vascular compliance by reducing arterial stiffness and oxidative damage (Fathi et al., 2017), while royal jelly supplementation further supports endothelial repair and antioxidant enzyme activity (Anugrah et al., 2023; Teixeira-Lemos et al., 2011). Together, these adaptations contribute to lower VCAM-1 expression and enhanced vascular integrity.

From a clinical perspective, these results reinforce the therapeutic potential of combining moderate-intensity resistance exercise with natural antioxidant supplementation in cardiac rehabilitation programs. Elevated ICAM-1 and VCAM-1 levels are recognized biomarkers of endothelial dysfunction and predictors of cardiovascular events (Oliveira et al., 2012). Hence, interventions that reduce their expression may lower cardiovascular risk and improve vascular health in CAD patients (Pourkoshki et al., 2025; Maleki et al., 2023). This study had some limitations, including a relatively small sample size and restriction to male participants with stable CAD, which limits generalizability. Furthermore, the study focused on acute rather than chronic responses. Future research should explore the long-term effects of combined resistance training and royal jelly supplementation, include female participants, and investigate molecular pathways such as NF-κB and eNOS signaling to better explain the underlying mechanisms (Teixeira-Lemos et al., 2011; Xu et al., 2025).

Conclusion

In summary, a single session of moderate-intensity resistance exercise, particularly when combined with royal jelly supplementation, significantly reduced plasma ICAM-1 and VCAM-1 levels in men with coronary artery disease. These findings suggest that the combined application of physical exercise and natural antioxidant supplementation may exert synergistic effects on endothelial function by reducing vascular inflammation and adhesion molecule expression. Incorporating such interventions into cardiac rehabilitation programs could offer a safe, effective, and accessible non-pharmacological approach to improving vascular health and reducing cardiovascular risk in patients with coronary artery disease.

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Conflicts of Interest:

The authors declare no conflict of interest related to this study.

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