ANTI-INFLAMMATORY EFFECTS OF ROBUSTA COFFEE ON IL-6 AND IL-18 LEVELS IN DIABETIC RATS

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Persistent low-grade inflammation accompanies diabetes mellitus and drives the disease forward, largely because pro-inflammatory mediators such as interleukin-6 (IL-6) and interleukin-18 (IL-18) are produced in excess. Because robusta coffee carries a substantial load of chlorogenic acid together with other bioactive constituents, it has been proposed as an agent capable of dampening the inflammation that accompanies diabetes. The objective of this work was to determine how robusta coffee affects circulating IL-6 and IL-18 in a diabetic rat model. Twenty-eight male Wistar rats were allocated at random into four arms in an experimental design: an untreated diabetic control, a metformin-treated arm, and two arms receiving 1 mL and 2 mL of robusta coffee, respectively. The diabetic state was established through streptozotocin and nicotinamide administration, and cytokine concentrations in serum were quantified by ELISA. Relative to untreated diabetic animals, both cytokines were markedly lower after coffee administration, with the lowest levels observed in animals given 2 mL. The two cytokines showed a very strong positive correlation. Taken together, the data point to robusta coffee as a candidate natural adjunct for reducing systemic inflammation in diabetes, although the underlying mechanisms require further confirmation.

Keywords: Diabetes Mellitus, Inflammation, Interleukin -18, Interleukin -6, Robusta Cofee

INTRODUCTION

Sustained hyperglycemia arising from defective insulin secretion, defective insulin action, or a combination of the two defines diabetes mellitus (DM) as a chronic metabolic disorder. Over the past twenty years the number of affected individuals has risen sharply, and the disease now ranks among the foremost contributors to illness and death globally. Roughly 90–95% of the total burden is attributable to type 2 diabetes mellitus (T2DM), a form closely tied to excess adiposity, physical inactivity, and metabolic syndrome (Committee, 2023). Once hyperglycemia persists, it sets off a chain of metabolic derangements oxidative stress, smouldering inflammation, endothelial impairment, and disturbed immune regulation that eventually manifests as damage to both small and large vessels (Yan *et al.*, 2020). Nephropathy, retinopathy, neuropathy, and cardiovascular disease all become considerably more likely as a result, which erodes quality of life for patients and drives up healthcare expenditure across health systems (Nguyen *et al.*, 2024).

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A growing body of work argues that inflammation in diabetes is not simply a downstream effect of the disease; it actively pushes the disease forward. When glucose remains elevated, mitochondria generate more reactive oxygen species (ROS), and nuclear factor-κB (NF-κB), mitogen-activated protein kinase (MAPK), and NLRP3 inflammasome signalling become activated, which in turn drives the overproduction of pro-inflammatory cytokines (Williamson, 2020). Two of these mediators, IL-6 and IL-18, have drawn particular interest, since each participates centrally in insulin resistance, pancreatic β-cell failure, endothelial damage, and persistent inflammatory activity (Osama *et al.*, 2021). These two cytokines were prioritised over other established markers, such as tumor necrosis factor-α (TNF-α) and IL-1β, because they represent two complementary upstream arms of diabetic inflammation. IL-6 is a principal product of NF-κB-dependent transcription, circulates at readily measurable concentrations, and impairs insulin signalling through induction of suppressor of cytokine signalling 3 (Rehman and Akash, 2016); elevated IL-6 also predicts the development of T2DM in prospective cohorts (Pradhan *et al.*, 2001). IL-18, in contrast, becomes biologically active only after cleavage by caspase-1 following NLRP3 inflammasome activation, and its circulating level likewise predicts incident T2DM (Thorand *et al.*, 2005; Swanson, Deng and Ting, 2019). IL-1β shares this inflammasome processing step but is often difficult to detect reliably in serum, whereas TNF-α acts largely in a paracrine manner within adipose and other tissues. Measuring IL-6 and IL-18 together therefore captures both the NF-κB-driven and the inflammasome-driven components of systemic inflammation within a single serum panel.

Interest in natural products as complementary therapies for diabetes continues to grow, chiefly because such products engage several molecular targets at once and tend to carry a lighter burden of side effects than many pharmaceutical agents. Among dietary sources of polyphenols, coffee ranks near the top, and robusta coffee (*Coffea canephora*) in particular supplies chlorogenic acids alongside caffeine, trigonelline, cafestol, and kahweol (Nguyen *et al.*, 2024). Antioxidant, anti-inflammatory, and metabolic-regulatory properties of these constituents help maintain glucose balance and guard against diabetes-related complications (Sofyanita *et al.*, 2024). Reports on chlorogenic acid the dominant phenolic in robusta coffee describe inhibition of glucose-6-phosphatase, improved insulin sensitivity, reduced oxidative stress, and blunted inflammatory signalling achieved by blocking NF-κB activation and by acting on AMP-activated protein kinase (AMPK) (Zamani-Garmsiri *et al.*, 2021). Trigonelline, meanwhile, aids glucose utilisation, while cafestol and kahweol help govern inflammatory and antioxidant responses. Such a range of activities raises the possibility that robusta coffee acts synergistically against the chronic inflammatory milieu of T2DM.

An inverse relationship between habitual coffee intake and T2DM incidence has emerged consistently across recent experimental and clinical work. Drinking coffee regularly has been linked with better glycemic control, greater insulin sensitivity, lower oxidative stress, and reduced circulating inflammatory mediators (Sofyanita *et al.*, 2026). Broad reviews add that chlorogenic acid shapes carbohydrate metabolism by slowing glucose absorption in the intestine, promoting peripheral glucose uptake, and acting on incretin signalling, all of which favour metabolic homeostasis (Kolb, Martin and Kempf, 2021). Encouraging as these results are, earlier investigations have mostly confined their outcome measures to fasting glucose, glycated hemoglobin, oxidative stress markers, or one inflammatory cytokine at a time (Kunutsor, Lehoczki and Laukkanen, 2025). A

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closer look at this literature reveals three specific gaps. First, human evidence linking coffee to inflammatory markers is largely observational and has focused on IL-6 and C-reactive protein, rarely addressing inflammasome-derived cytokines such as IL-18 (Osama *et al.*, 2021). Second, experimental studies demonstrating anti-inflammatory effects have mostly administered purified chlorogenic acid rather than brewed coffee, so the effect of the whole beverage, with its mixture of bioactive constituents, remains uncertain (Lee, Bae and Ahn, 2022; Bao *et al.*, 2025). Third, previous work on robusta coffee in diabetic rats has concentrated on antioxidant markers such as superoxide dismutase and Nrf2 (Sofyanita *et al.*, 2024), leaving its influence on circulating cytokines, particularly IL-18, largely unexplored. To our knowledge, no study has yet measured IL-6 and IL-18 simultaneously after administration of brewed robusta coffee in a rat model of T2DM.

Given how centrally IL-6 and IL-18 figure in the chronic inflammation of advancing diabetes, the anti-inflammatory potential of robusta coffee deserves closer scrutiny. Measuring the two cytokines in parallel should yield a fuller picture of inflammatory modulation than any single biomarker can offer. The present work was therefore designed to assess the anti-inflammatory action of robusta coffee by quantifying serum IL-6 and IL-18 in streptozotocin-induced diabetic rats given different doses. The novelty of this study lies in the simultaneous evaluation of an NF-κB-associated cytokine (IL-6) and an inflammasome-dependent cytokine (IL-18) after administration of brewed robusta coffee, benchmarked against metformin as a standard antidiabetic comparator. Two volumes were tested to represent moderate and high habitual intake, equivalent to approximately 2 and 4 cups of coffee per day in humans after human-to-rat dose conversion, and/or the doses used in our previous study (Sofyanita *et al.*, 2024). We hypothesised that coffee administration would lower both cytokines and that the higher volume would be associated with a greater reduction, however, because only two volumes were compared, the design was intended to compare doses rather than to establish a full dose–response relationship.

METHOD

Twenty-eight male Wistar rats (*Rattus norvegicus*), aged 8–10 weeks and weighing approximately 250 g, were obtained from Universitas Islam Sultan Agung Semarang. The experiment was conducted at UNISSULA in April 2026. Before experimentation, the animals underwent a seven-day acclimatisation period. Rats were housed individually in stainless-steel cages under controlled conditions of 24 ± 2 °C, 50–60% relative humidity, and a 12-h light/12-h dark cycle, resulting in seven cages per experimental group. Standard pellet feed and drinking water were provided ad libitum, except during fasting periods. Each individual rat constituted one experimental unit.

All procedures followed institutional guidelines for the care and use of laboratory animals. The study protocol was approved by the Health Research Ethics Committee of Poltekkes Kemenkes Semarang, Indonesia (approval No. 268/EA/F.XXIII.38/2026, dated 3 March 2026). The animals were monitored periodically throughout the experiment to assess their general condition and signs of distress. No animal deaths occurred during the study.

After acclimatisation, diabetes was induced by a single intraperitoneal injection of streptozotocin (STZ; 40 mg/kg body weight), dissolved in 0.1 M citrate buffer (pH 4.5). Seventy-two hours after STZ administration, fasting blood glucose

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was measured in tail-vein blood using an EasyTouch® glucometer (GCU model ET-301; Bioptik Technology, Taiwan). Rats with fasting blood glucose concentrations ≥200 mg/dL were considered diabetic and eligible for inclusion.

The diabetic rats were allocated using simple randomisation to four groups of seven animals each: untreated diabetic control (DM), diabetes plus metformin (Met), diabetes plus 1 mL robusta coffee (G1), and diabetes plus 2 mL robusta coffee (G2). Laboratory personnel performing the ELISA measurements were blinded to group allocation. The untreated DM group served as the reference group because the study aimed to compare treatment effects within the diabetic state. The absence of a non-diabetic control group limits conclusions regarding restoration of cytokine concentrations to non-diabetic levels.

Robusta peaberry coffee beans were obtained from a local supplier in Banyuwangi, Indonesia. Roasted beans from the same production batch were ground into a fine powder. An aqueous coffee preparation was freshly prepared each day by mixing coffee powder with distilled water at a ratio of 1 g:10 mL (w/v), followed by extraction with stirring at 90 °C for 15 min. The preparation was filtered through Whatman No. 1 filter paper, and the filtrate was diluted to a working concentration of 25 mg/mL. Preparation consistency was maintained by using the same coffee batch, powder-to-water ratio, extraction temperature, extraction duration, and filtration procedure throughout the intervention. Chlorogenic acid and caffeine concentrations were not quantitatively measured.

The coffee-treated groups received 100 and 200 mg/kg body weight/day, corresponding to 25 and 50 mg/day, respectively, for a 250-g rat. At a working concentration of 25 mg/mL, these doses corresponded to administration volumes of 1 and 2 mL/day, respectively. Metformin hydrochloride (99.60%; PT Phapros Tbk, Indonesia) was administered at 500 mg/kg body weight/day. All interventions were administered by oral gavage once daily at the same time of day for 14 consecutive days. The untreated DM group received distilled water by the same route and schedule.

At the end of the intervention, the rats were fasted overnight and anaesthetised with ketamine. Blood was collected by retro-orbital puncture using a glass capillary tube and allowed to clot at room temperature. Serum was separated by centrifugation at 3,000 rpm for 15 min and stored at −80 °C until analysis.

Serum IL-6 and IL-18 concentrations were measured using a Rat Interleukin-6 ELISA Kit (FineTest, Catalogue No. ER0042) and a Rat Interleukin-18 ELISA Kit (FineTest, Catalogue No. ER0036), respectively, manufactured by Wuhan Fine Biotech Co., Ltd., China. Both assays were performed according to the manufacturer's instructions, and the results were expressed in pg/mL.IBM SPSS Statistics version 27.0 served for all analyses. Distribution and variance assumptions were checked with the Shapiro–Wilk and Levene tests. Group differences were examined by one-way analysis of variance (ANOVA) with Tukey's honestly significant difference (HSD) post hoc comparison, and the IL-6/IL-18 relationship was quantified by Pearson correlation. A threshold of $p < 0.05$ defined statistical significance.

RESULTS AND DISCUSSION

A total of 28 diabetic rats were included in the analysis and divided equally into four experimental groups, with seven rats in each group. Serum IL-6 and IL-18 levels were measured after the intervention period. Following induction and

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before treatment, mean fasting blood glucose concentrations were 301.0 ± 68.0, 408.5 ± 49.3, 281.1 ± 97.4, and 418.0 ± 73.4 mg/dL in the DM, metformin, 1 mL coffee, and 2 mL coffee groups, respectively. Pretreatment fasting blood glucose differed significantly among groups (one-way ANOVA, $p = 0.009$), indicating an initial imbalance in glycaemic status. Descriptive analysis showed that the DM group had the highest concentrations of both inflammatory cytokines. The metformin-treated group had lower IL-6 and IL-18 concentrations than the DM group, while robusta coffee was also associated with lower concentrations, particularly at the 2 mL dose. The mean concentrations of IL-6 and IL-18 in each group are presented in Table 1.

Table 1. Serum IL-6 and IL-18 levels in the experimental groups (mean ± SD)

Experimental group	n	IL-6 (pg/mL)	IL-18 (pg/mL)
DM	7	244.29 ± 24.37	257.86 ± 35.32
DM + metformin	7	139.86 ± 16.36	158.43 ± 29.45
DM + robusta coffee 1 mL	7	89.57 ± 12.46	82.57 ± 14.35
DM + robusta coffee 2 mL	7	49.29 ± 9.74	48.43 ± 7.50

The Shapiro–Wilk test showed that IL-6 data were normally distributed in the DM, metformin, robusta coffee 1 mL, and robusta coffee 2 mL groups, with p-values of 0.862, 0.997, 0.861, and 0.146, respectively. Similarly, IL-18 data were normally distributed in all groups, with p-values ranging from 0.248 to 0.967. The Levene test also demonstrated homogeneity of variance for IL-6 ($p = 0.058$) and IL-18 ($p = 0.061$). Therefore, one-way ANOVA was applied to evaluate differences among the four experimental groups.

One-way ANOVA revealed a significant difference in serum IL-6 concentrations among the experimental groups ($F = 178.838$; $p < 0.001$). The highest IL-6 concentration was observed in the DM group, whereas the lowest concentration was found in the group treated with 2 mL of robusta coffee. Compared with the untreated DM group, serum IL-6 levels were approximately 42.7% lower in the metformin group, 63.3% lower in the 1 mL robusta coffee group, and 79.8% lower in the 2 mL robusta coffee group.

Serum IL-18 levels also differed significantly among the experimental groups ($F = 103.153$; $p < 0.001$). The DM group showed the highest IL-18 concentration, followed by the metformin group, the 1 mL robusta coffee group, and the 2 mL robusta coffee group. Compared with the untreated DM group, serum IL-18 concentrations were approximately 38.6% lower following metformin treatment, 68.0% lower following administration of 1 mL of robusta coffee, and 81.2% lower following administration of 2 mL of robusta coffee. The greater reduction observed in the 2 mL robusta coffee group indicates that the higher coffee dose was associated with stronger suppression of circulating IL-18 levels.

Table 2. One-way ANOVA results for serum IL-6 and IL-18 levels

Parameter	F-value	*p*-value
IL-6	178.838	<0.001
IL-18	103.153	<0.001

Every pairwise contrast reached significance for both cytokines on Tukey HSD analysis ($p < 0.001$). Cytokine concentrations in the DM group exceeded those

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in the metformin and both coffee groups. Animals receiving 1 mL of coffee registered lower IL-6 and IL-18 than those on metformin, and the 2 mL group fell below the metformin and 1 mL groups alike.

Table 3. Summary of Tukey post hoc comparisons

Group comparison	IL-6	IL-18
DM vs. metformin	$p < 0.001$	$p < 0.001$
DM vs. robusta coffee 1 mL	$p < 0.001$	$p < 0.001$
DM vs. robusta coffee 2 mL	$p < 0.001$	$p < 0.001$
Metformin vs. robusta coffee 1 mL	$p < 0.001$	$p < 0.001$
Metformin vs. robusta coffee 2 mL	$p < 0.001$	$p < 0.001$
Robusta coffee 1 mL vs. robusta coffee 2 mL	$p < 0.001$	$p < 0.001$

Pearson correlation analysis demonstrated a very strong positive correlation between serum IL-6 and IL-18 concentrations ($r = 0.987$; $p < 0.001$). This result indicates that rats with higher IL-6 levels also tended to have higher IL-18 levels. Conversely, reductions in IL-6 following metformin or robusta coffee treatment were accompanied by corresponding reductions in IL-18.

Table 4. Correlation between serum IL-6 and IL-18 levels

Variables	Correlation coefficient (r)	*p*-value	Interpretation
IL-6 and IL-18	0.987	<0.001	Very strong positive correlation

DISCUSSION

Robusta coffee administration went together with substantially reduced serum IL-6 and IL-18 in the diabetic animals studied here. Untreated diabetic rats carried the heaviest cytokine burden, whereas coffee-treated animals showed distinctly lower inflammatory markers, the minimum occurring at 2 mL. Read together, these observations are consistent with an attenuating effect of robusta coffee on the systemic inflammatory response accompanying diabetes mellitus. Because oxidative stress markers and intracellular signalling pathways were not measured in the present study, the mechanisms discussed below are offered as plausible explanations derived from previous studies rather than as direct evidence from these data. Prolonged hyperglycemia amplifies mitochondrial ROS output, accelerates advanced glycation end-product formation, and switches on inflammatory transcription factors; jointly these events push pro-inflammatory cytokine secretion upward and inflict progressive tissue damage (Yan *et al.*, 2020; Nguyen *et al.*, 2024). Falling IL-6 and IL-18 after coffee administration may therefore partly reflect the antioxidant and anti-inflammatory actions of its bioactive constituents working in concert. Chlorogenic acids, caffeine, trigonelline, and additional phenolics occur at appreciable concentrations in robusta coffee and may operate through complementary routes to curb oxidative stress and inflammatory signalling (Nguyen *et al.*, 2024).

That IL-6 stood highest in untreated diabetic animals is consistent with a role for sustained hyperglycemia in triggering systemic inflammation. Oxidative stress generated under high glucose can switch on nuclear factor kappa B, which then drives transcription of IL-6, tumor necrosis factor-α, IL-1β, and further mediators that entrench insulin resistance and tissue injury (Rehman and Akash, 2016). Beyond this, IL-6 disrupts insulin receptor signalling by inducing suppressor

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of cytokine signalling proteins, so insulin sensitivity declines and glucose handling deteriorates further (Rehman and Akash, 2016). Elevated IL-6 therefore functions simultaneously as an indicator and a driver of metabolic inflammation in T2DM. Although the responsible constituents were not identified here, the lower IL-6 values in coffee-treated rats may be partly attributable to chlorogenic acid, coffee's principal polyphenol. In lipopolysaccharide-stimulated microglial cells, chlorogenic acid dampened Toll-like receptor 4-mediated inflammatory signalling and diminished downstream nuclear factor kappa B activation, with a consequent fall in pro-inflammatory mediator production (Xu *et al.*, 2022). It may additionally turn on nuclear factor erythroid 2-related factor 2 and raise antioxidant enzyme expression, thereby curtailing the ROS that set inflammatory signalling in motion (Bao *et al.*, 2025). Because none of these pathways was measured in the present study, their involvement should be regarded as a hypothesis that requires direct testing.

The IL-18 findings are compatible with the possibility that robusta coffee restrains inflammasome-linked inflammation under diabetic conditions. IL-18 first appears as an inactive precursor and only acquires biological activity once caspase-1 acts on it, an event that follows activation of the nucleotide-binding oligomerization domain-like receptor protein 3 inflammasome (Swanson, Deng and Ting, 2019). Assembly of that inflammasome is encouraged by hyperglycemia, surplus ROS, mitochondrial dysfunction, and signals of cell damage; caspase-1 is then activated and more mature IL-18 is released. Where IL-18 production continues unchecked, inflammatory responses intensify, interferon-γ secretion is stimulated, and vascular and tissue injury accumulates as diabetes advances (Yan *et al.*, 2022). The markedly higher IL-18 in untreated diabetic rats here may thus signal heightened inflammasome activity under prolonged metabolic stress, while the pronounced fall after coffee administration may reflect suppression of that same pathway, although inflammasome components were not measured here. Bao and colleagues showed that chlorogenic acid lowered expression of nucleotide-binding oligomerization domain-like receptor protein 3, cleaved caspase-1, IL-1β, and IL-18 in experimental diabetic nephropathy by engaging the nuclear factor erythroid 2-related factor 2 pathway (Bao *et al.*, 2025). Comparable modulation of nuclear factor kappa B and inflammasome signalling by chlorogenic acid has been documented in other inflammatory models as well (Zeng *et al.*, 2020).

Cytokine levels were lower at 2 mL than at 1 mL. Measured against untreated diabetic rats, IL-6 fell by roughly 63.3% at the lower volume and 79.8% at the higher one, while the corresponding reductions for IL-18 were approximately 68.0% and 81.2%. Under the conditions applied here, the larger volume was therefore associated with a greater reduction in both cytokines. Greater delivery of chlorogenic acids and other coffee-derived bioactives at 2 mL offers a plausible explanation for the gap between the two coffee groups. Chlorogenic acid can blunt inflammation by neutralising reactive oxygen and nitrogen species and by downregulating inflammatory mediator expression in streptozotocin-induced diabetic rats (Lee, Bae and Ahn, 2022). Caffeine, trigonelline, caffeic acid, ferulic acid, and various minor phenolics are likewise present in robusta coffee and may act together in shaping oxidative stress, glucose metabolism, and inflammatory signalling (Nguyen *et al.*, 2024). Even so, these data do not establish a dose–response relationship, since only two volumes were tested and individual bioactive concentrations in the preparation went unmeasured. Because the coffee preparation was not chemically characterised, the actual amount of bioactive

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compounds delivered to each group cannot be specified, and the difference between the two coffee groups should be interpreted as a comparison of two volumes rather than as evidence of a dose-dependent effect. Chlorogenic acid content and biological activity can shift considerably with coffee variety, growing region, roasting profile, brewing method, and extraction yield (Tamimi *et al.*, 2024).

Beyond the coffee comparison, it is also worth situating these results against the standard pharmacological comparator used here. Metformin likewise lowered both cytokines significantly relative to untreated diabetic animals, which supports the view that improved glycemic regulation travels alongside reduced systemic inflammation. Apart from suppressing hepatic glucose output and improving insulin sensitivity, metformin exerts anti-inflammatory effects by activating AMP-activated protein kinase and by curbing nuclear factor kappa B-driven cytokine production (Du *et al.*, 2022). Reduced mitochondrial ROS generation, restrained inflammasome activation, and altered immune-cell metabolism have also been attributed to the drug, each of which limits inflammatory mediator release (Bharath and Nikolajczyk, 2021; Sakata, 2024). Tukey post hoc comparisons showed that IL-6 and IL-18 levels in both coffee groups were significantly lower than in the metformin group ($p < 0.001$; Table 3). However, this finding should not be interpreted as therapeutic superiority of robusta coffee over metformin: the study was not designed or powered as a superiority comparison, only a single metformin dose was tested, the coffee preparation was not standardised, and post-treatment glycaemic outcomes were not compared between groups. One possible explanation is that robusta coffee acts on inflammation through routes that are not limited to glucose lowering. Based on previous studies, its polyphenols could concurrently limit ROS formation, strengthen endogenous antioxidant capacity, block nuclear factor kappa B activation, and hold nucleotide-binding oligomerization domain-like receptor protein 3 inflammasome signalling in check (Zeng *et al.*, 2020; Nguyen *et al.*, 2024).

Chlorogenic acid has been reported to contribute to such a coordinated response by reducing reactive oxygen species and modulating nuclear factor erythroid 2-related factor 2, nuclear factor kappa B, and nucleotide-binding oligomerization domain-like receptor protein 3 pathways (Zeng *et al.*, 2020; Bao *et al.*, 2025). If confirmed, several interconnected molecular routes, rather than a single target, may mediate the anti-inflammatory effects observed here. Activation of AMP-activated protein kinase and nuclear factor erythroid 2-related factor 2 signalling, combined with suppression of nuclear factor kappa B, has been attributed to chlorogenic acid and results in less ROS and fewer inflammatory cytokines (Nguyen *et al.*, 2024). In parallel, the compound has been reported to block NLRP3 inflammasome activation and the caspase-1 step downstream, which limits maturation of interleukin-1β and interleukin-18 (Zeng *et al.*, 2020). Caffeine, trigonelline, and the other phenolics native to robusta coffee may further improve mitochondrial function, sharpen insulin sensitivity, and steer macrophage polarisation toward a less inflammatory phenotype, complementing what chlorogenic acid contributes (Kolb, Martin and Kempf, 2021).

Taken alongside these mechanistic considerations, several caveats still apply to the present results. To begin with, measurement was restricted to serum IL-6 and IL-18, so the molecular routes behind the observed cytokine changes were never assessed directly. Furthermore, no chemical quantification was

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performed on chlorogenic acid or the remaining bioactive constituents of the coffee preparation, which rules out any attribution of the biological effects to particular compounds. Finally, because the work rests on an animal model, translating the findings straight to human diabetes calls for caution. Fourth, no non-diabetic control group was included, so it cannot be determined whether IL-6 and IL-18 in the treated groups returned to physiological baseline levels. Fifth, only two coffee volumes and a single metformin dose were tested, and the study was not powered to compare treatments for superiority. Sixth, post-treatment blood glucose was not compared between groups, so the extent to which cytokine reductions were mediated by improved glycaemia could not be assessed. Subsequent work would benefit from combining phytochemical profiling of the coffee with transcriptomic and proteomic interrogation of inflammatory pathways, measurement of oxidative stress biomarkers, and histopathological assessment across several organs in order to pin down causal mechanisms. Clinical studies are equally needed to establish whether standardised robusta coffee preparations, consumed regularly, can lower inflammatory markers safely and improve metabolic outcomes among people with T2DM.

CONCLUSION AND SUGGESTIONS

In this study, robusta coffee administration was associated with significantly lower systemic inflammatory markers in streptozotocin-induced diabetic rats, as reflected by markedly lower serum IL-6 and IL-18 concentrations than in untreated diabetic animals. The lowest cytokine levels were observed in the 2 mL group; however, because only two volumes were tested and the coffee was not chemically characterised, a dose–response relationship cannot be concluded. The significant positive correlation between IL-6 and IL-18 further suggests that these cytokines are closely associated with the inflammatory response during diabetes progression. Collectively, these findings indicate that robusta coffee may represent a promising natural adjunctive intervention for mitigating chronic inflammation associated with diabetes mellitus, possibly through the combined actions of chlorogenic acid and other coffee-derived bioactive compounds, a hypothesis that requires mechanistic confirmation.

Future studies should investigate the molecular mechanisms underlying the anti-inflammatory effects of robusta coffee by evaluating key signaling pathways, including NF-κB, NLRP3 inflammasome, Nrf2, AMPK, and oxidative stress biomarkers. Standardization of coffee preparation and quantitative analysis of chlorogenic acid and other bioactive constituents are also necessary to identify the compounds primarily responsible for the observed biological effects. Furthermore, studies that include a non-diabetic control group and more than two coffee doses, long-term studies involving multiple diabetic complications and well-designed clinical trials are warranted to confirm the efficacy, safety, optimal dosage, and translational potential of robusta coffee as a complementary nutritional strategy for individuals with type 2 diabetes mellitus.

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