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# From Seed to Solution: Expert Insights on Sesame's Role in Diabetes and Beyond

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## Abstract

Sesame (*Sesamum indicum L*) has garnered attention for its potential in diabetes management due to its rich bioactive compounds, including sesamin, sesamolin, and unsaturated fatty acids. This commentary explores recent advances in sesame research, emphasizing its role in improving glycemic control, lipid profiles, inflammation, and oxidative stress, as evidenced by a systematic review and meta-analysis. Mechanistic insights reveal sesame's effects on PPARα activation, Nrf2 signaling, and NF-κB suppression, which underpin its metabolic benefits. Recent trials across diverse populations demonstrate the efficacy of sesame oil, seeds, paste, and sesamin supplements in reducing HbA1c, fasting glucose, and cardiovascular risk factors. However, challenges such as study heterogeneity, limited generalizability, and unclear optimal dosing hinder clinical translation. Future research should prioritize large-scale, long-term RCTs, mechanistic studies on gut microbiota and neuroprotection, and personalized nutrition approaches to fully harness sesame's therapeutic potential in combating the global diabetes epidemic.

**Keywords:** Sesame, Sesamin, Diabetes, Metabolic Syndrome, Nutritional Supplement

## Introduction

The global burden of diabetes and its associated cardiovascular complications continue to escalate, necessitating innovative dietary interventions to complement conventional therapies [1]. Sesame (*Sesamum indicum* L), a nutrient-rich seed with a long history in traditional medicine, has emerged as a promising candidate for managing metabolic disorders [2]. A recent systematic review and meta-analysis highlighted sesame's potential to improve glycemic control, inflammatory markers, and lipid profiles, offering a foundation for its role in cardiovascular risk reduction [3]. This commentary extends those findings, exploring recent advancements in sesame research, particularly its implications for diabetes management, and addresses unresolved challenges in translating these benefits into clinical practice. By delving into sesame's bioactive compounds and their mechanistic pathways, we aim to illuminate its broader therapeutic potential while identifying critical areas for future investigation.

## Sesame's Bioactive Arsenal: Mechanisms Driving Metabolic Benefits

Sesame seeds and their derivatives, including oil and lignan-rich extracts, owe their metabolic benefits to a diverse array of bioactive compounds, such as sesamin, sesamolin, and unsaturated fatty acids [2]. These components exert multifaceted effects on key physiological pathways. For instance, sesamin enhances lipid metabolism by activating peroxisome proliferator-activated receptor alpha (PPARα), which promotes fatty acid oxidation and reduces cholesterol synthesis through inhibition of HMG-CoA reductase [4,5]. This mechanism aligns with observed reductions in total cholesterol (TC) in patients with chronic diseases, particularly at doses of 10 g/day or less [3]. Additionally, sesame's high fiber content slows glucose absorption, improving insulin sensitivity via enhanced incretin secretion, which supports significant reductions in glycated hemoglobin (HbA1c) [6].

Beyond lipid and glycemic regulation, sesame's antioxidant properties, driven by lignans and γ-tocopherol, mitigate oxidative stress, a key driver of diabetic complications [7]. The meta-analysis reported a notable, though non-significant, reduction in malondialdehyde (MDA) in females over 50, suggesting a protective effect against oxidative damage [3]. These antioxidant effects are likely mediated by the upregulation of the Nrf2/ARE pathway, which enhances endogenous antioxidant enzyme activity [8]. Furthermore, sesame's anti-inflammatory potential, evidenced by significant reductions in C-reactive protein (CRP) and interleukin-6 (IL-6), stems from its ability to suppress NF-κB signaling, reducing pro-inflammatory cytokine production [3,9,10]. These findings underscore sesame's potential as a holistic intervention for diabetes management, targeting multiple facets of metabolic dysfunction.

Among sesame's diverse bioactive compounds, sesamin has recently garnered attention for its ability to modulate cellular processes beyond conventional metabolic pathways. Emerging evidence suggests that sesamin interacts with the anti-aging gene Sirtuin 1 (SIRT1), a $NAD^+$-dependent deacetylase integral to regulating aging, metabolism, and stress resistance mechanisms [11]. Activation of SIRT1 enhances insulin sensitivity and mitigates metabolic dysfunction by modulating key signaling pathways, including peroxisome proliferator-activated receptor alpha (PPARα), nuclear factor erythroid 2–related factor 2 (Nrf2), and nuclear factor kappa B (NF-κB), which collectively orchestrate lipid metabolism, antioxidant defense, and inflammatory responses [11]. Notably, SIRT1 activation promotes fatty acid oxidation through upregulation of PPARα, while concurrently suppressing oxidative stress and inflammation via positive regulation of Nrf2 and inhibition of NF-κB signaling [11]. These mechanistic insights suggest that sesamin's role as a SIRT1 activator could represent a critical avenue for improving metabolic resilience and preventing insulin resistance in individuals with diabetes [11].

Building upon these mechanistic underpinnings, dietary strategies aimed at enhancing SIRT1 activation have been proposed as promising adjuncts for diabetes management [12]. Inactivation or downregulation of SIRT1 has been implicated in the pathogenesis of metabolic syndromes and multiple organ dysfunctions, underscoring the necessity of nutritional approaches to restore its activity [12]. Moreover, nutritional interventions that modulate SIRT1 and associated anti-aging genes have demonstrated beneficial effects on appetite regulation, cellular senescence, and apoptotic pathways, all of which are relevant to metabolic homeostasis in diabetic populations [13]. These findings support the rationale for incorporating sesame-derived sesamin into dietary regimens to optimize SIRT1-mediated protective effects and counteract the progression of insulin resistance and type 2 diabetes [14]. By elucidating these emerging mechanisms, we emphasize the importance of future clinical research evaluating optimal dosages and bioavailability of sesamin to effectively harness its therapeutic potential in metabolic disease management [11].

## Recent Advances in Sesame Research for Diabetes

Recent years have witnessed a surge in research exploring the potential of sesame and its derivatives in the management of type 2 diabetes mellitus (T2DM). This section delves into a series of studies that have investigated the effects of various sesame products on diabetic patients.

Several studies have focused on sesame oil, demonstrating its efficacy in improving multiple health parameters in diabetic patients. In a crossover study conducted in India, researchers administered 35,000 mg/day of sesame oil alongside standard medications to hypertensive diabetic patients, resulting in significant reductions in systolic and diastolic blood pressure, body weight, BMI, waist and hip circumferences, fasting glucose, HbA1c, and lipid levels, as well as improvements in antioxidant enzyme activities [15]. These findings suggest that sesame oil could play a crucial role in managing both diabetes and its associated cardiovascular risks.

Building on this, a randomized trial in India with a similar dose of sesame oil combined with glibenclamide, a common antidiabetic drug, showed that the combination therapy led to better glycemic control, improved lipid profiles, and enhanced antioxidant status compared to glibenclamide alone [16]. This underscores sesame oil's potential as an adjunctive treatment.

In a larger study, researchers explored the effects of sesamin oil, a variant of sesame oil rich in the lignin sesamin, in 200 diabetic patients. The intervention group, receiving 34,500 mg/day of sesamin oil plus glibenclamide, exhibited significant reductions in fasting plasma glucose, HbA1c, total cholesterol, triglycerides, LDL-C, and non-HDL-C, along with an increase in HDL-C [17]. These results highlight the potential of sesamin-rich oil in comprehensive diabetes management.

Comparing sesame oil to other dietary oils, a study found that sesame oil outperformed coconut oil in improving lipid profiles and fasting blood sugar levels in diabetic patients, suggesting its superiority as a dietary fat source for this population [18].

Beyond oil, sesame seeds and their derivatives have also shown promise. In Brazil, a controlled trial used 30,000 mg/day of roasted and ground sesame seeds in female diabetic patients, leading to significant improvements in fasting and postprandial blood glucose, HbA1c, and body weight [19]. This indicates that whole sesame seeds can be an effective dietary addition for glycemic control.

Iranian researchers have explored the benefits of Ardeh, a traditional sesame paste. Two randomized, double-blind trials using 28,000 mg/day of Ardeh reported reductions in fasting blood sugar, triglycerides, blood pressure, and waist circumference in one study [20], while the other observed favorable changes in lipid profiles and atherogenic indices [21]. Furthermore, another study found that Ardeh improved insulin sensitivity, reduced inflammation (as measured by hs-CRP), and lowered fasting serum insulin levels [22]. These studies collectively suggest that sesame paste can be a valuable component of a diabetic diet.

Extracts and supplements derived from sesame, particularly those containing sesamin, have also been investigated. Two randomized, double-blind, placebo-controlled trials in Iran used 200 mg/day of sesamin capsules. One study demonstrated improvements in lipid profiles and reductions in malondialdehyde (MDA), a marker of oxidative stress [23], while the other showed positive effects on anthropometric measures, glycemic control, inflammatory markers (TNF-α, IL-6, hs-CRP), and adiponectin levels [24]. These results indicate that sesamin supplements could offer targeted benefits for diabetic patients, particularly in managing oxidative stress and inflammation.

Some studies have taken a more holistic approach, examining a broad spectrum of outcomes. A trial in Pakistan used white sesame seed oil (27,600 mg/day) and reported improvements not only in glycemic control and lipid profiles but also in oxidative stress markers, liver enzymes (ALP, ALT, AST), and kidney function tests, suggesting a protective effect on multiple organ systems [25].

In a high-dose intervention, researchers administered 60,000 mg/day of sesame seeds to diabetic patients, resulting in significant reductions in FBS, HbA1c, cholesterol, triglycerides, LDL-C, and liver enzymes [26]. This study underscores the potential of whole sesame seeds in managing diabetes and its complications.

Most recently, a randomized, placebo-controlled, double-blind trial in Iran used 15,000 mg/day of sesame oil, revealing improvements in waist-to-hip ratio, lipid profiles, body composition, oxidative stress markers, inflammation, insulin sensitivity, and skeletal muscle mass [27]. This study exemplifies the multifaceted benefits of sesame oil in diabetes management.

The studies reviewed here span multiple countries (**Table 1**), including India [15–18], Iran [20–24,26,27], Brazil [19], and Pakistan [25], reflecting a global interest in sesame's therapeutic potential. The consistency of positive findings across diverse populations and study designs strengthens the evidence base for sesame's role in diabetes care.

**Table 1.** Characteristics of recent studies on sesame treatment for diabetes.

| Title of the study | First author | Year of publication | Study design | Study population | Outcomes |
|---|---|---|---|---|---|
| The effect of oral consumption of sesame oil on anthropometric, metabolic and oxidative stress markers of patients with type 2 diabetes: a double-blind, randomized controlled trial | Tobeiha *et al.* [27] | 2024 | Randomized, Placebo-controlled, Double-blind | Type 2 Diabetes Mellitus | Waist-to-Hip Ratio, Triglycerides, Cholesterol, Low-Density Lipoprotein, High-Density Lipoprotein, Weight, Body Mass Index, Percent Body Fat, Reduced Glutathione, Malondialdehyde, C-Reactive Protein, Insulin, Homeostasis Model Assessment of Insulin Resistance, Quantitative Insulin Sensitivity Check Index, Total Antioxidant Capacity, Fasting Blood Sugar, Skeletal Muscle Mass |
| The effect of sesame seeds on fast blood sugar, hemoglobin A 1C, liver enzymes and lipid profile in patients with type 2 diabetes: a randomized clinical trial | GhoreiShi *et al.* [26] | 2022 | Randomized, Clinical trial | Type 2 Diabetes Mellitus | Fasting Blood Sugar, Hemoglobin A1c, Cholesterol, Triglycerides, Low-Density Lipoprotein Cholesterol, Alanine Aminotransferase, Aspartate Aminotransferase, Alkaline Phosphatase |

| | | | | | |
|---|---|---|---|---|---|
| White sesame seed oil mitigates blood glucose level, reduces oxidative stress, and improves biomarkers of hepatic and renal function in participants with type 2 diabetes mellitus | Aslam *et al.* [25] | 2019 | Randomized, Placebo-controlled | Type 2 Diabetes Mellitus | Blood Glucose, Insulin, Hemoglobin A1c, Thiobarbituric Acid Reactive Substances [Malondialdehyde], Superoxide Dismutase, Catalase, Alkaline Phosphatase, Alanine Aminotransferase, Aspartate Aminotransferase, Creatinine, Total Protein, Albumin |
| Effect of sesamin supplementation on glycemic status, inflammatory markers, and adiponectin levels in patients with type 2 diabetes mellitus | Shahi *et al.* [24] | 2017 | Randomized, Placebo-controlled, Double-blind | Type 2 Diabetes Mellitus | Weight, Body Mass Index, Waist Circumference, Hip Circumference, Waist-to-Hip Ratio, Body Adiposity Index, Body Fat, Fasting Blood Sugar, Hemoglobin A1c, Insulin, Homeostasis Model Assessment of Insulin Resistance, Tumor Necrosis Factor-alpha, Interleukin-6, High-Sensitivity C-Reactive Protein, Adiponectin |
| Effects of sesamin on the glycemic index, lipid profile, and serum Malondialdehyde level of patients with type II diabetes | Mohammadshahi et al. [23] | 2016 | Randomized, Double-blind, Placebo-controlled | Type 2 Diabetes Mellitus | Triglycerides, Total Cholesterol, Low-Density Lipoprotein Cholesterol, High-Density Lipoprotein Cholesterol, Malondialdehyde |
| A blend of sesame and rice bran oils lowers hyperglycemia and improves the lipids. | Devarajan *et al.* [17] | 2016 | Randomized, Open label | Type 2 Diabetes Mellitus | Fasting Plasma Glucose, Hemoglobin A1c, Total Cholesterol, Triglycerides, High-Density Lipoprotein Cholesterol, Low-Density Lipoprotein Cholesterol, Non-High-Density Lipoprotein Cholesterol |
| A sesame seeds-based breakfast could attenuate sub-clinical inflammation in type 2 diabetic patients: a randomized controlled trial. | Bahadoran *et al.* [22] | 2015 | Randomized, Controlled, Double-blind | Type 2 Diabetes Mellitus | Fasting glucose, Insulin Sensitivity Index, Homeostasis Model Assessment of Insulin Resistance, High-Sensitivity C-Reactive Protein, Fasting Serum Insulin |
| Ardeh (*Sesamum indicum*) could improve serum triglycerides and atherogenic lipid parameters in type 2 diabetic patients: a randomized clinical trial | Mirmiran *et al.* [21] | 2013 | Randomized, Double-blind, Controlled study | Type 2 Diabetes Mellitus | Total Cholesterol, Triglycerides, High-Density Lipoprotein Cholesterol, Low-Density Lipoprotein Cholesterol, Total Cholesterol to High-Density Lipoprotein Cholesterol ratio, Low-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol ratio, Atherogenic Index of Plasma |
| Effect of Ardeh on components of metabolic syndrome in type 2 diabetic patients: a randomized clinical trial | Golzarand *et al.* [20] | 2013 | Randomized, Double-blind, Clinical trial | Type 2 Diabetes Mellitus | Fasting Blood Sugar, Triglycerides, High-Density Lipoprotein Cholesterol, Systolic Blood Pressure, Diastolic Blood Pressure, Waist Circumference |

| | | | | | |
|---|---|---|---|---|---|
| Sesame oil exhibits synergistic effect with anti-diabetic medication in patients with type 2 diabetes mellitus | Sankar *et al.* [16] | 2011 | Randomized | Type 2 Diabetes Mellitus | Glucose, Hemoglobin A1c, Total Cholesterol, High-Density Lipoprotein Cholesterol, Low-Density Lipoprotein Cholesterol, Triglycerides, Superoxide Dismutase, Glutathione Peroxidase, Catalase, Reduced Glutathione |
| Efeito do uso da farinha desengordurada do Sesamum indicum L nos níveis glicêmicos em diabéticas tipo 2 | Figueiredo *et al.* [19] | 2008 | Controlled and open clinical trial | Type 2 Diabetes Mellitus | Fasting Blood Glucose, Postprandial Blood Glucose, Hemoglobin A1c, Weight |
| Study on the benefits of sesame oil over coconut oil in patients of insulin resistance syndrome, notably type 2 diabetes and dyslipidemia | Mitra *et al.* [18] | 2007 | Randomized, Controlled trial | Type 2 Diabetes Mellitus | Total Cholesterol, High-Density Lipoprotein Cholesterol, Low-Density Lipoprotein Cholesterol, Very Low-Density Lipoprotein Cholesterol, Triglycerides, Fasting Blood Sugar |
| A pilot study of open label sesame oil in hypertensive diabetics. | Sankar *et al.* [15] | 2006 | Cross over | Hypertensive diabetic | Systolic Blood Pressure, Diastolic Blood Pressure, Weight, Body Mass Index, Waist Circumference, Hip Circumference, Waist-to-Hip Ratio, Fasting glucose, Hemoglobin A1c, Total Cholesterol, High-Density Lipoprotein Cholesterol, Low-Density Lipoprotein Cholesterol, Triglycerides, Thiobarbituric Acid Reactive Substances, Catalase, Superoxide Dismutase, Glutathione Peroxidase, Reduced Glutathione |

Moreover, the variety of sesame products investigated—oil, seeds, paste, and supplements—offers flexibility in incorporating sesame into diabetic diets and treatment regimens. Whether used as a cooking oil, a dietary supplement, or a functional food, sesame appears to confer benefits that extend beyond glycemic control, addressing key aspects of diabetes management such as lipid metabolism, oxidative stress, inflammation, and body composition.

## Challenges and Gaps in Translating Sesame's Benefits

Despite its promise, several challenges hinder the integration of sesame supplementation into diabetes care. The meta-analysis noted significant heterogeneity in study designs, with variations in intervention duration (4–12 weeks), dosage (60 mg to 50 g/day), and sesame form (seeds, oil, or capsules), complicating direct comparisons [3]. This heterogeneity likely contributed to the inconsistent effects on anthropometric measures and blood pressure, where no significant changes were observed [3]. For example, while some studies reported reductions in body mass index (BMI) and waist-to-hip ratio (WHR) with sesame oil, others found no effect, possibly due to differences in participant health status or study duration [3].

The predominance of studies conducted in Iran raises concerns about generalizability, as dietary habits, genetic profiles, and environmental factors may influence sesame's efficacy [28]. Additionally, the short-term nature of the included trials limits insights into sesame's long-term effects on diabetes progression and cardiovascular outcomes [29]. The meta-analysis's GRADE assessment classified evidence for several outcomes as low or very low, underscoring the need for high-quality, long-term RCTs [3]. Furthermore, the optimal dosage and form of sesame supplementation remain unclear. While doses of 10 g/day or less improved CRP, HDL, and TC, higher doses showed no significant effects, suggesting a potential threshold effect that warrants further exploration [3].

Another critical gap is the lack of comprehensive mechanistic studies in humans. While animal models have demonstrated sesame's effects on PPARα activation and Nrf2 signaling, human trials often focus on clinical outcomes without dissecting underlying pathways [30]. This limits our understanding of how sesame's bioactive compounds interact with human physiology, particularly in diverse populations with varying metabolic profiles. Addressing these gaps requires standardized protocols, diverse study populations, and detailed assessments of dietary and lifestyle confounders.

## Future Directions: Expanding Sesame's Role in Diabetes Care

To fully harness, sesame's potential, future research must prioritize several key areas. First, large-scale, multi-center RCTs with diverse populations are essential to enhance generalizability and statistical power. These trials should adopt standardized measurement protocols for biomarkers like HbA1c, CRP, and MDA to ensure comparability. Extended follow-up periods will clarify sesame's long-term effects on diabetes complications, such as neuropathy and retinopathy.

Second, mechanistic studies should explore sesame's effects on emerging pathways, such as gut microbiota modulation and mitochondrial biogenesis. For instance, trials could assess changes in gut microbial composition alongside metabolic outcomes to elucidate sesame's prebiotic effects. Additionally, investigating sesame's neuroprotective potential, mediated by Nrf2/HO-1 pathway activation, could expand its applications to diabetic neuropathy. Such studies should also quantify the bioavailability of sesame's bioactive compounds in humans, as differences in metabolism may influence efficacy.

Third, personalized nutrition approaches could optimize sesame's benefits. Genetic and metabolomics profiling may identify responders to sesame supplementation, particularly for glycemic and lipid outcomes. For example, polymorphisms in PPARα or Nrf2 genes could modulate sesame's effects, warranting pharmacogenomics investigations. Finally, integrating sesame into dietary guidelines for diabetes management requires practical strategies, such as developing sesame-based functional foods or supplements with standardized lignin content.

## Conclusion

Sesame (*Sesamum indicum L*) holds significant promise as an adjunct therapy for diabetes management, with robust evidence supporting its effects on glycemic control, inflammation, and lipid profiles [3]. Recent studies reinforce these findings, highlighting sesame's role in improving insulin sensitivity and gut health, while mechanistic insights underscore its pleiotropic effects on PPARα, Nrf2, and NF-κB pathways. However, challenges such as study heterogeneity, limited generalizability, and unclear optimal dosing necessitate further research. By addressing these gaps through rigorous, long-term RCTs and mechanistic studies, sesame could emerge as a cornerstone of integrative diabetes care, offering a natural, accessible intervention to mitigate the global diabetes epidemic.

## Declaration of Competing Interest

The author listed in this article certify that they have no affiliations or involvement with any organization or entity that has a financial interest (such as honoraria, educational grants, participation in speakers' bureaus, membership, employment, consultancies, stock ownership, or other equity interest, as well as expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

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## Availability of Data and Materials

All relevant data are provided within the manuscript and supplementary file. Additionally, data analyzed for this study are available upon request from the corresponding author.

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## Human Ethics and Consent to Participate

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## Author Contributions

Ali Jafari: Conceptualization, Data curation, Investigation, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing.

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