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REVIEW

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Effect of sesame (*Sesamum indicum L.*) consumption on glycemic control in patients with type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials

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Abstract

Conflicting evidence exists on the effect of sesame consumption on glucose metabolism in patients with type 2 diabetes (T2D). Therefore, this meta-analysis focuses on the relationship between sesame (*Sesamum indicum L.*) intervention and glycemic control in patients with T2D. Published literature was retrieved and screened from PubMed, Scopus, ISI Web of Science, and the Cochrane Library up to December 2022. Outcome measures included fasting blood sugar (FBS) concentrations, fasting insulin levels, and hemoglobin A1c (HbA1c) percentage. Pooled effect sizes were reported as weighted mean differences (WMDs) and 95% confidence intervals (CIs). Eight clinical trials (395 participants) were eligible for meta-analyses. Overall, sesame consumption significantly reduced serum FBS (WMD: −28.61 mg/dL, 95% CI: −36.07 to −21.16, $p<0.001$; $I^2 = 98.3\%$) and HbA1c percentage (WMD: −0.99%, 95% CI: −1.22 to −0.76, $p \le 0.001$; $I^2 = 65.1\%$) in patients with T2D. However, sesame consumption did not significantly influence fasting insulin levels (Hedges's: 2.29, 95% CI: −0.06 to 4.63, $p = 0.06$; $I^2 = 98.1\%$). In summary, the current meta-analysis showed a promising effect of sesame consumption on glycemic control through reducing FBS and HbA1c, yet additional prospective studies are recommended, using higher doses and longer intervention period, to confirm the impact of sesame consumption on insulin levels in T2D patients.

KEYWORDS
glycemic control, meta-analysis, sesame, type 2 diabetes

1 | INTRODUCTION

Diabetes mellitus (DM), one of the non-communicable diseases (NCDs) with high prevalence (more than 300 million people among the adult population), is a public health challenge that affects the quality of life with a high direct and indirect costs (Guariguata et al., 2014; Triposkiadis et al., 2021). It is projected this prevalence will increase by 55% by 2035 (Guariguata et al., 2014). Type 2 diabetes (T2D), diagnosed by the relative lack of insulin, insulin resistance, and high blood glucose; is known as the most common form of diabetes (Galicia-Garcia et al., 2020; Hadi et al., 2018; Molavi et al., 2020; Sivakumar & Jeganath, 2021). It has been well known that T2D is the world's leading cause of motility and morbidity (Ali et al., 2022; Danaeifar, 2022). In addition, this metabolic disease can lead to the failure of different organs, especially the heart, nerves, eyes, kidneys, and blood vessels (Ali et al., 2022; Demir et al., 2021; Mohsen et al., 2022). Obesity, a sedentary lifestyle, energy-dense diets, and aging are the most important risk factors for the occurrence or development of NCDs, especially T2D (Azadnajafabad et al., 2021; Pillon et al., 2021; Sharin et al., 2021; Storz, 2020). Due to the increasing prevalence of the mentioned disorder and the burden of this metabolic disease on health systems around the world, trying to find effective ways to control blood sugar has always been important.

Currently, there is a growing interest regarding the potential beneficial effects of alternative therapies to improve the metabolic parameters in T2D (Hadi et al., 2020; Heshmati et al., 2020; Nauck et al., 2021). In this context, herbal medicine has been introduced as an auxiliary method along with lifestyle interventions and drug therapy (Heshmati et al., 2021; Kumar et al., 2021; Moholkar Aparark et al., 2021; Sundaram et al., 2020; Tajaddini et al., 2021). In recent years, many studies have reported the beneficial effects of herbal compounds such as green tea (Xu et al., 2020), nettle (Ziaei et al., 2020), barberry (Safari et al., 2020), and saffron (Sohaei et al., 2020) on the control of glycemic markers. Considering the medicinal properties of a sesame seed, researchers have been interested in investigating its beneficial effects in the prevention or treatment of various diseases since ancient times (Andargie et al., 2021).

Sesame (*Sesamum indicum L.*), belonging to the *Pedaliaceae* family, is widely used in Middle Eastern cuisine as cooking oil and seasoning ingredients (Nagar & Agrawal, 2022). Sesame seeds are rich sources of vitamin E, polyunsaturated fatty acids (PUFAs), fiber, phytosterol, and bioactive lignans including sesamin, sesamolin, sesamol, and episesamin (Andargie et al., 2021; Nagar & Agrawal, 2022). Research has shown that sesame seeds can have beneficial effects in lowering blood pressure (Khosravi-Boroujeni et al., 2017), improving lipid profile (Khalesi et al., 2016), reducing inflammatory factors (Rafiee et al., 2021), and increasing the antioxidant capacity (Raeisi-Dehkordi et al., 2020) of the body. The results of clinical trials on the effect of sesame consumption on glycemic indices in T2D patients have been inconsistent (Aslam et al., 2019; Bahadoran et al., 2015; Figueiredo & Modesto-Filho, 2008; Ghoreishi et al., 2022; Mohammad Shahi et al., 2017; Raeisi-Dehkordi et al., 2021; Sankar et al., 2006, 2011). Therefore, a systematic review and meta-analysis of randomized controlled trials (RCTs) have been conducted to clarify the effects of sesame consumption on glycemic markers in patients with T2D.

2 | METHODS

The present meta-analysis was designed and reported based on the guidelines of the preferred reporting items for systematic reviews and meta-analyses (PRISMA) (Appendix S1) (Page et al., 2021). The protocol for this systematic review and meta-analysis was not registered.

2.1 | Search strategy

In this systematic review and meta-analysis, two investigators searched PubMed, Scopus, ISI Web of Science, and the Cochrane Library from the database inception to February 2022. To identify the relevant studies, a combination of Medical Subject Heading terms of ("Sesame") AND ("Diabetes" OR "Hyperglycemia" OR "Glucose Intolerance" OR "Insulin Resistance") (Supplementary Table 1). No language restriction was considered while searching the mentioned databases. Moreover, we reviewed the reference lists of all review articles to avoid missing any publications. Gray literature (abstracts, conference proceedings or editorials) and reviews were excluded.

2.2 | Study selection

Studies were selected for inclusion by two independent reviewers, any disagreements were discussed and resolved by consensus. First, the title and abstract of the obtained articles were checked. Unrelated articles were excluded at this stage. In cases where it was not possible to make a decision based on the title and abstract, the full text of the articles was received. Studies were included if they met all of the following inclusion criteria: (a) Study design: RCT with either a parallel or crossover design; (b) Population: patients with T2D; (c) Intervention: investigated sesame as an intervention for over 1 week; (d) Comparators: placebo or a comparison group were used; and (e) Outcomes: including fasting blood sugar (FBS) concentrations, fasting insulin levels, and hemoglobin A1c (HbA1c) percentage. The exclusion criteria included: (a) non-randomized, non-control, or experimental studies; (b) investigations that prescribed sesame in combination with other herbs or ingredients as a mixture; (c) studies that were conducted in patients with type 1 diabetes or women with gestational diabetes; (d) studies with lack of sufficient data required for meta-analysis. When multiple publications reported the same or overlapping data, we used the most recent or largest population.

2.3 | Data extraction

The eligible studies were reviewed and the following data were extracted by two independent investigators: first author's name, publication year, country of investigation, sample size, the mean age of subjects, research design, duration of intervention, dose and type of sesame supplement, and outcome measures (baseline and post-intervention concentrations). To obtain missing data in studies without a complete dataset, we contacted the corresponding author. Any discrepancies were resolved through group discussion with two additional investigators.

2.4 | Quality assessment

The risk of bias for each article was assessed by two independent authors using the Cochrane collaboration tool (Higgins & Green, 2011), which contained seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessments, incomplete outcome data, selective reporting, and other biases. Each item was recorded as low risk of bias, high risk of bias, or unclear risk of bias. If there was any inconsistency, that was settled by consensus.

2.5 | Statistical analysis

Changes in FBS, insulin, and HbA1c during the intervention, for the intervention and control groups, were used to calculate the weighted mean difference (WMD) using the random-effects model. The reported standard error (SE) was converted to SD by multiplying SE with √n. If only SD for the baseline and final values was provided, SD for the net changes was assigned based on the Follmann method (Follmann et al., 1992). The I^2 index was evaluated to assess heterogeneity. Low, moderate, and high heterogeneity were defined as I^2 index equal to 25%, 50%, and 75%, respectively. To distinguish probable sources of heterogeneity, we performed a subgroup analysis in conformity with the study duration (≤8 and >8weeks), and type of intervention (sesame oil and other types).To conduct sensitivity analysis, we removed each study one after another and recalculated the pooled assessments. To detect potential publication bias, Egger's regression test was performed. Statistical analysis was conducted using STATA, version 11 (Stata Corp, College Station, Texas, USA). p value <0.05 was considered statistically significant.

3 | RESULTS

3.1 | Systematic search results

Our initial search resulted in 986 probably related articles. After removing duplicate records ($n = 265$), 721 records remained for screening the titles or abstracts; and of them, 15 studies were selected for the full-text evaluation. At this stage, seven studies were excluded due to: trials with the same population ($n = 3$), did not have a suitable control group ($n = 3$), and studies that reported incomplete data ($n = 1$). Finally, eight articles (Aslam et al., 2019; Bahadoran et al., 2015; Figueiredo & Modesto-Filho, 2008; Ghoreishi et al., 2022; Mohammad Shahi et al., 2017; Raeisi-Dehkordi et al., 2021; Sankar et al., 2006, 2011) were entered into the present meta-analysis. The flow diagram of study selection is shown in Figure 1.

3.2 | Study characteristics

The basic characteristics of the eligible articles are summarized in Table 1. A total of 395 individuals were enrolled in the studies. Six

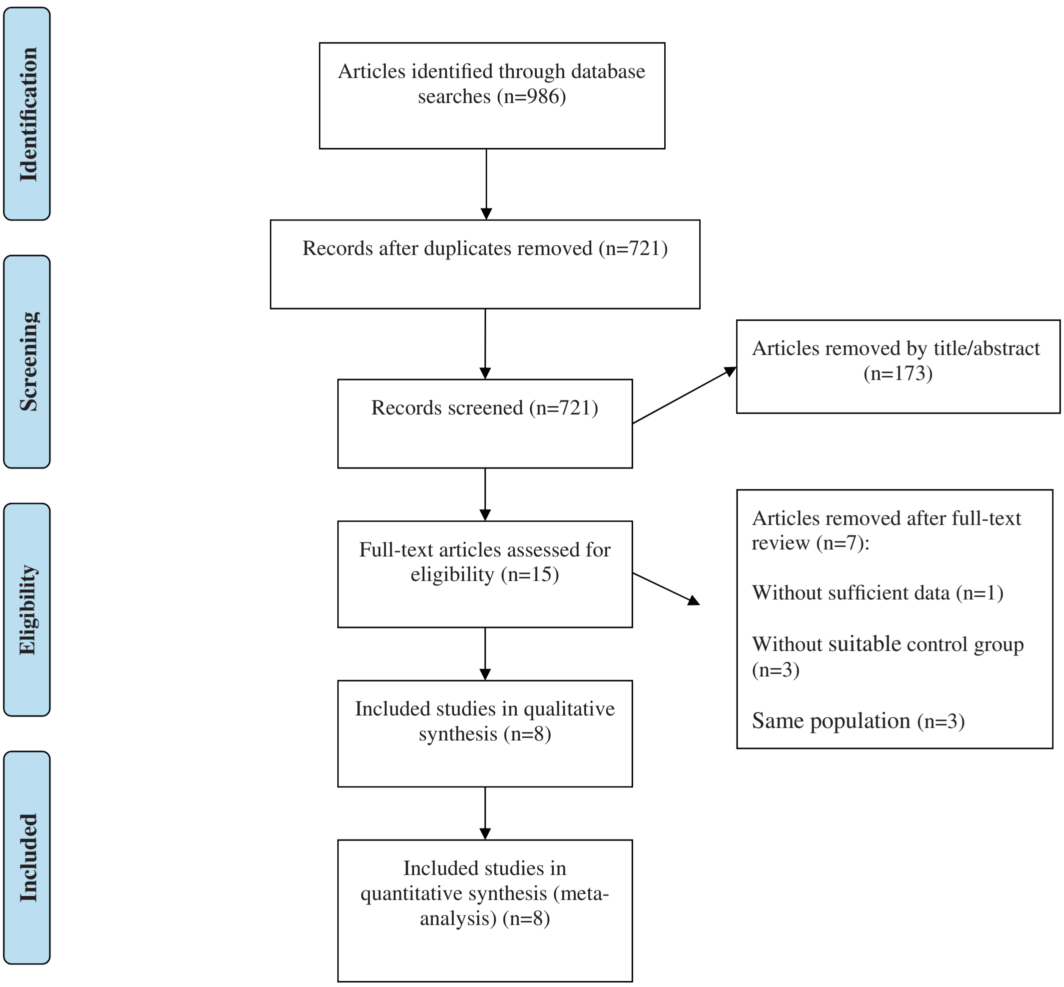

FIGURE 1 Flow diagram of included and excluded studies.

TABLE 1 Characteristic of studies evaluating the effect of sesame consumption on glycemic indices which were eligible to be included in the systematic review.

First author (publication year)	Country	RCT design	Sample size	Gender	Mean age (years)	Duration (weeks)	Intervention	Control	Reported outcomes
Ghoreishi et al. (2022)	Iran	Parallel	60	Both	54	8	Sesame seeds	Control	FBS HbA1c
Raeisi-Dehkordi et al. (2020)	Iran	Crossover	95	Both	49	9	Sesame oil + canola oil	Canola oil	FBS Insulin
Aslam et al. (2019)	Pakistan	Parallel	46	Both	39	12	Sesame oil	Placebo (soybean oil)	FBS HbA1c Insulin
Mohammad Shahi et al. (2017)	Iran	Parallel	48	Both	50	8	Sesamin capsule	Placebo (starch)	FBS HbA1c Insulin
Bahadoran et al. (2015)	Iran	Parallel	36	Both	51	6	Grounded sesame seed	Control	FBS Insulin
Sankar et al. (2011)	India	Parallel	42	Both	58	8	Sesame oil + glibenclamide	Glibenclamide (5 mg/d)	FBS HbA1c
Figueiredo and Modesto-Filho (2008)	Brazil	Parallel	28	Female	47	8	Sesame flour	Control	FBS HbA1c
Sankar et al. (2006)	India	Crossover	40	Both	56	6	Sesame oil	Placebo (palm or groundnut oils)	FBS HbA1c

Abbreviations: FBS, fasting blood sugar; HbA1C, hemoglobin A1C; RCT, randomized controlled trial.

RCTs had a parallel design (Aslam et al., 2019; Bahadoran et al., 2015; Figueiredo & Modesto-Filho, 2008; Ghoreishi et al., 2022; Mohammad Shahi et al., 2017; Sankar et al., 2011), while two studies (Raeisi-Dehkordi et al., 2021; Sankar et al., 2006) had a crossover design. These studies were published between 2006 and 2022 and were conducted in different countries including Iran (Bahadoran et al., 2015; Ghoreishi et al., 2022; Mohammad Shahi et al., 2017; Raeisi-Dehkordi et al., 2021), India (Sankar et al., 2006, 2011), Brazil (Figueiredo & Modesto-Filho, 2008), and Pakistan (Aslam et al., 2019). The mean age of the participants ranged between 39 and 58 years. The intervention period varied from 6 to 12 weeks. Four studies (Aslam et al., 2019; Raeisi-Dehkordi et al., 2021; Sankar et al., 2006, 2011) used sesame oil for the intervention, and the remaining trials used the seed or ground powdered sesame or its extracts.

3.3 | Assessment of the risk of bias

Among all included studies, four studies (Bahadoran et al., 2015; Ghoreishi et al., 2022; Mohammad Shahi et al., 2017; Raeisi-Dehkordi et al., 2021) were categorized as high quality, and the remaining articles (Aslam et al., 2019; Figueiredo & Modesto-Filho, 2008; Sankar et al., 2006, 2011) were classified as fair, based on seven domains of the Cochrane collaboration's tool. The details of quality assessment for articles included in the present systematic review are illustrated in Table 2.

3.4 | Meta-analysis results

3.4.1 | The effects of sesame consumption on fasting blood sugar concentrations

The pooled estimate from the random-effects model performed on eight trials (Aslam et al., 2019; Bahadoran et al., 2015; Figueiredo & Modesto-Filho, 2008; Ghoreishi et al., 2022; Mohammad Shahi et al., 2017; Raeisi-Dehkordi et al., 2021; Sankar et al., 2006, 2011) showed that sesame consumption significantly decreased FBS concentrations (WMD: −28.61 mg/dL, 95% CI: −36.07 to −21.16, $p < 0.001$) with a significant between-study heterogeneity ($I^2 = 98.3\%$, $p < 0.001$), (Figure 2). Subgroup analysis indicated that when the studies were stratified according to the intervention of duration, interestingly, the reduction of SBP was significant only in studies with duration ≤8 weeks (WMD: −22.18 mg/dL, 95% CI: −28.94 to −15.42, $p < 0.001$). In addition, the duration of intervention did not explain between-study heterogeneity. However, the type of intervention could explain the heterogeneity (other types subset; $I^2 = 13.3\%$, $p = 0.32$). All these findings are provided in Table 3.

3.4.2 | The effects of sesame consumption on hemoglobin A1c percentage

Combining effect sizes from six trials (Aslam et al., 2019; Figueiredo & Modesto-Filho, 2008; Ghoreishi et al., 2022; Mohammad Shahi

TABLE 2 Study quality and risk of bias assessment using the Cochrane Collaboration's tool.

First author (publication year)	Random sequence generation	Allocation concealment	Blinding of participants, personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Ghoreishi et al. (2022)	L	L	H	U	L	L	U
Raeisi-Dehkordi et al. (2020)	L	L	L	U	L	L	L
Aslam et al. (2019)	U	U	H	U	L	L	U
Mohammad Shahi et al. (2017)	U	L	L	L	L	L	L
Bahadoran et al. (2015)	L	L	H	L	L	L	L
Sankar et al. (2011)	U	U	U	U	L	L	U
Figueiredo and Modesto-Filho (2008)	U	U	H	U	L	L	U
Sankar et al. (2006)	H	H	H	U	L	L	U

Abbreviations: H, high risk of bias; L, low risk of bias; U, unclear risk of bias.

et al., 2017; Sankar et al., 2006; Sankar et al., 2011), we showed that sesame consumption significantly decreases HbA1c percentage (WMD: −0.99%, 95% CI: −1.22 to −0.76, $p \le 0.001$), with a significant between-study heterogeneity ($I^2 = 65.1\%$, $p < 0.01$) (Figure 3). In the subgroup analysis, we found that type of intervention explained this heterogeneity (sesame oil subset; $I^2 = 0.0\%$, $p = 0.97$). All these findings were provided in Table 3.

3.4.3 | The effects of sesame consumption on fasting insulin levels

Overall, four trials (Aslam et al., 2019; Bahadoran et al., 2015; Mohammad Shahi et al., 2017; Raeisi-Dehkordi et al., 2021) reported the effect of sesame consumption on fasting insulin levels. Overall, the meta-analysis could not show any beneficial effect of sesame consumption on fasting insulin levels (Hedges's: 2.29, 95% CI: −0.06 to 4.63, $p = 0.06$). Between-study heterogeneity was significant ($I^2 = 98.1\%$, $p < 0.01$), (Figure 4). After classifying the studies based on the duration of the intervention, the heterogeneity between the studies was reduced in the group of studies with an intervention duration ≤8 weeks ($I^2 = 21.8\%$, $p = 0.25$). However, the results remained non-significant in all subgroups. All these findings were provided in Table 3.

3.5 | Sensitivity analysis

The one-by-one sensitivity analysis did not show a significant effect of individual studies on the overall meta-analysis of the effect of sesame consumption on FBS, and HbA1c. However, the results about insulin changed significantly after Bahadoran et al. (Hedges's: 3.56, 95% CI: 0.17 to 6.96) and Raeisi- Dehkordi et al. (Hedges's: 4.19, 95% CI: 0.91 to 7.47) articles were excluded.

3.6 | Publication bias

No evidence of publication bias was shown for the meta-analysis of the FBS ($p = 0.11$), and HbA1c ($p = 0.93$), using Egger's regression test. However, the result of Egger's test was significant for insulin ($p = 0.03$).

4 | DISCUSSION

This is the first systematic review and meta-analysis of RCTs investigating the effects of sesame consumption on glycemic markers in T2D patients. Performing pooled analysis on 8 RCTs consisting of 395 participants revealed that sesame consumption can decrease FBS levels and HbA1c percentage. However, sesame did not decrease fasting insulin levels compared with the control group. All analyses showed high heterogeneity, although this was explained by subgroup analysis. In addition, all the results, except the fasting insulin level, did not change with the sensitivity analysis. The magnitude of regulation of glycemic indices (FBS and HbA1c) in response to sesame consumption was considerable. Hyperglycemia is associated with a greater risk of micro and macro-vascular diseases. Therefore, effective strategies to properly control glycemic markers, even at a small level, may result in reduced adverse vascular outcomes as a consequence (An et al., 2021; Taylor et al., 2021).

Given the existence of evidence about the effectiveness of sesame in glucose metabolism, some RCTs similar to our overall pooled results found that sesame may improve glycemic indices (Aslam

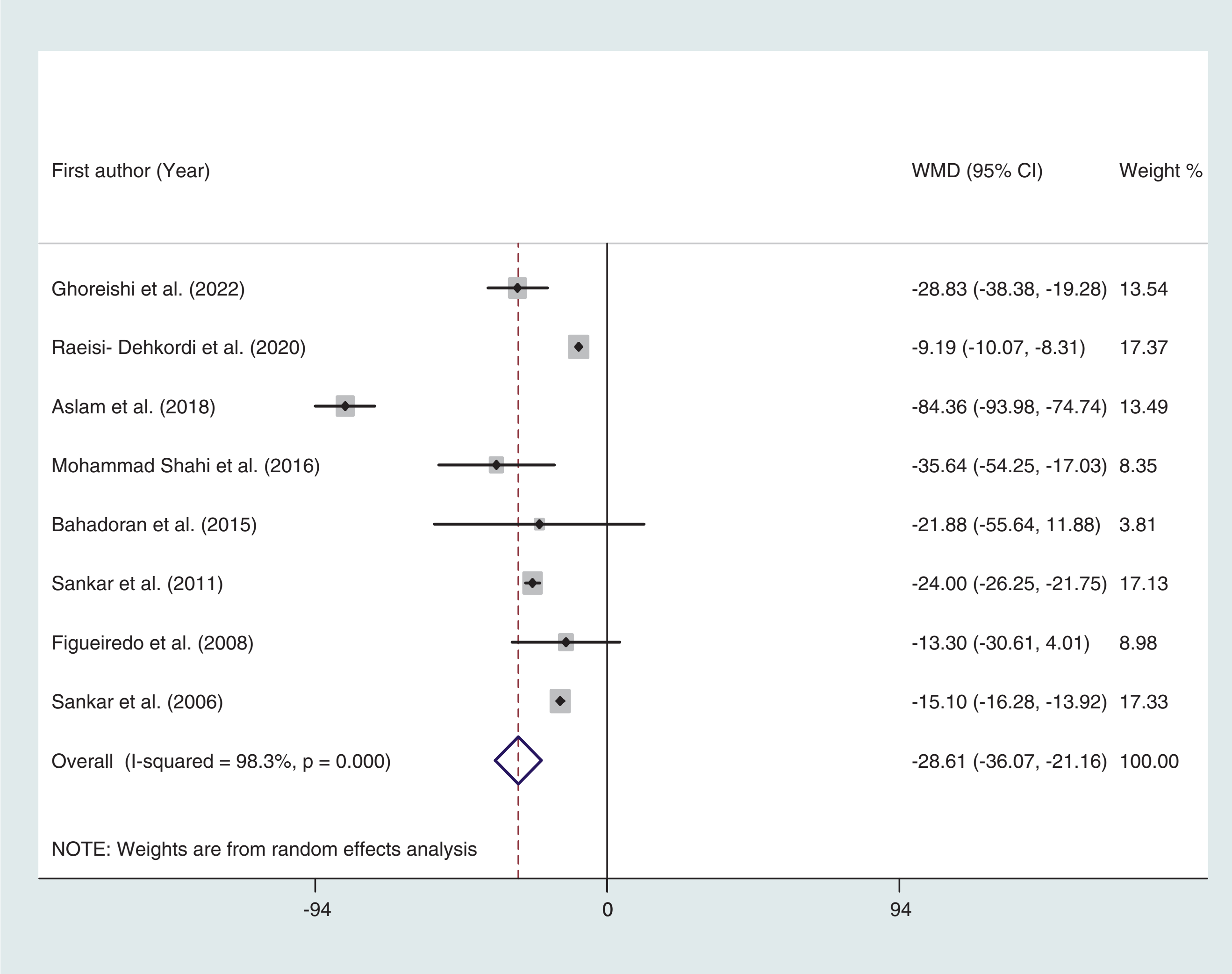

FIGURE 2 Forest plots showing the effect of sesame consumption on fasting blood sugar levels.

TABLE 3 Subgroup analyses to assess the effect of sesame consumption on glycemic markers.

Sub-grouped by	No. of trials	Effect size[a]	95% CI	I^2 (%)	*p* for effect size	P for heterogeneity
FBS						
Duration						
≤8 weeks	4	−22.18	−28.94 to −15.42	91.2	<0.001	<0.001
>8 weeks	2	−46.62	−120.18 to 27.05	99.6	0.21	<0.001
Type of intervention						
Sesame oil	4	−30.14	−39.31 to −20.97	99.2	<0.001	<0.001
Other types	4	−26.37	−34.93 to −17.82	13.3	<0.001	0.32
HbA1C						
Type of intervention						
Sesame oil	3	−1.02	−1.14 to −0.90	0.0	<0.001	0.97
Other types	3	−1.01	−1.72 to −0.30	84.6	0.005	0.002
Insulin						
Duration						
≤8 weeks	2	0.13	−0.35 to 0.61	21.8	0.58	0.25
>8 weeks	2	6.40	−10.19 to 22.98	99.1	0.45	<0.001

Abbreviations: FBS, fasting blood sugar; HbA1C, hemoglobin A1c.
[a]Calculated by Random-effects model.

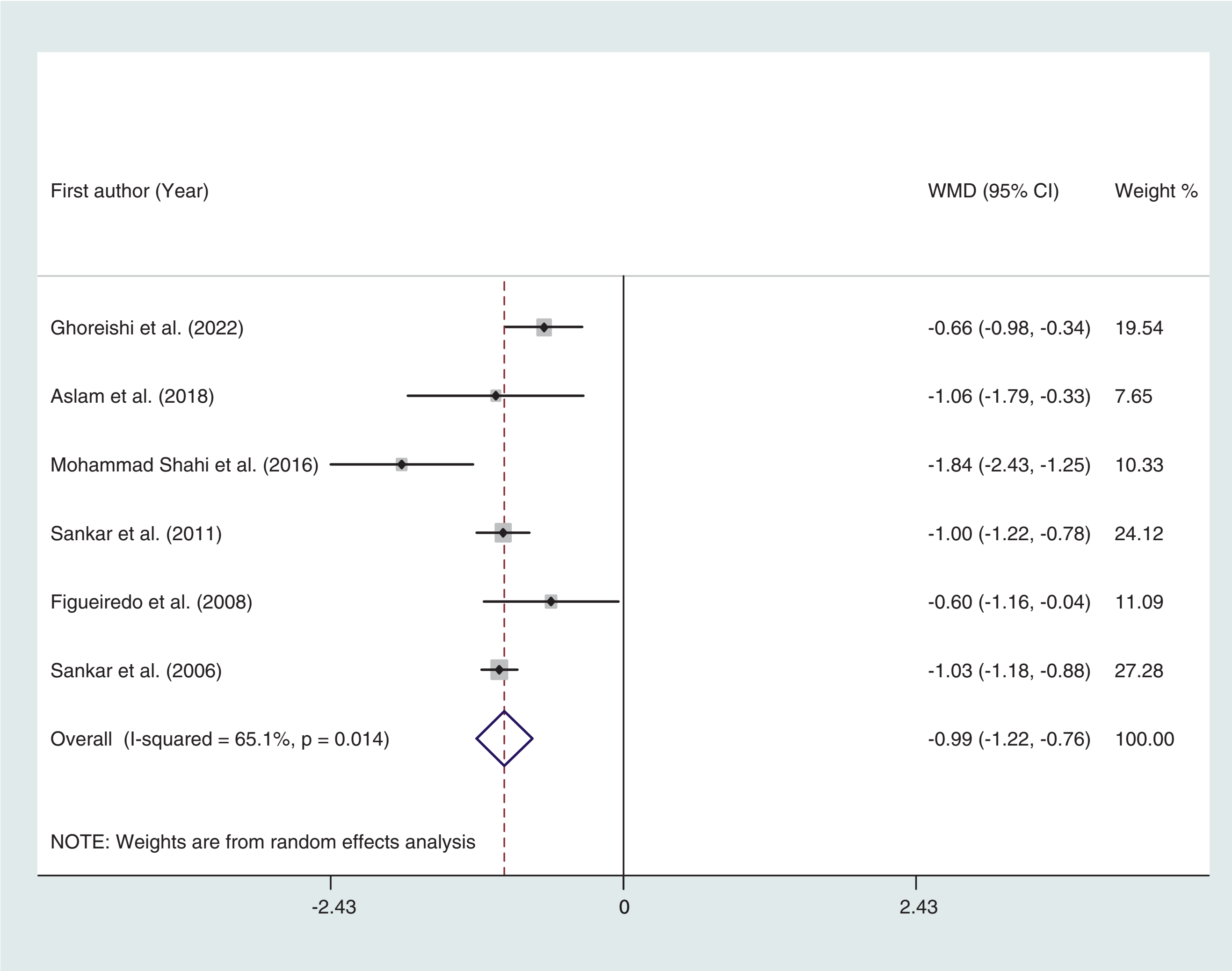

FIGURE 3 Forest plots showing the effect of sesame consumption on hemoglobin A1c percentage.

et al., 2019; Ghoreishi et al., 2022; Mohammad Shahi et al., 2017). While, others proposed that sesame could not be a useful adjuvant therapy in controlling glycemic parameters (Bahadoran et al., 2015; Moghtaderi et al., 2022). The variability of results in these studies may be attributed to the differences in study design, individual characteristics, sesame dose, and intervention duration.

Recently, herbal medicine has received the attention of researchers due to the useful compounds of these herbs, which can exert potent antioxidant effects and can lead to the regulation of glycemic metabolism. The absence of serious side effects has made medicinal plants a useful choice in the management of diabetes (Liu et al., 2002). The mechanisms of glycemic regulation induced by sesame are not well defined. However, several possible mechanisms have been proposed. Previous investigations have reported that sesame via its antioxidant compounds lowers serum levels of tumor necrosis factor-α, a pro-inflammatory cytokine that inhibits the signaling of insulin and its biological actions suggesting a possible metabolic pathway that could improve insulin sensitivity (Kanu et al., 2010; Wu et al., 2019). In addition, due to its antioxidant content, sesame can lead to an increase in antioxidant power and as a result pancreatic β-cell protection and improve insulin secretion (Nakai et al., 2003).

In addition, the reduction of body fat content decreases the production of inflammatory adipocytokines (Retnakaran et al., 2017). According to the results of the previous study (Raeisi-Dehkordi et al., 2018), which reported that the body fat percent and body adiposity index improved after supplementing with sesame seeds, it can be concluded that sesame seeds can be effective in improving glycemic status by affecting anthropometric indicators.

The consumption of sesame may reduce plasma glucose by increasing insulin secretion and insulin sensitivity, possibly through the action of PUFAs and MUFAs, as reported by previous studies (Djuricic & Calder, 2022; Hadi et al., 2022; Imamura et al., 2016; Telle-Hansen et al., 2019). MUFAs can ameliorate glycemic tolerance through an increase in the secretion of glucagon-like peptide-1 (Rocca et al., 2001). MUFAs can also act on the gene expression involved in lipid metabolism and consequently improve the fatty acid composition and reduce insulin resistance (Isharwal et al., 2009; Tierney & Roche, 2007).

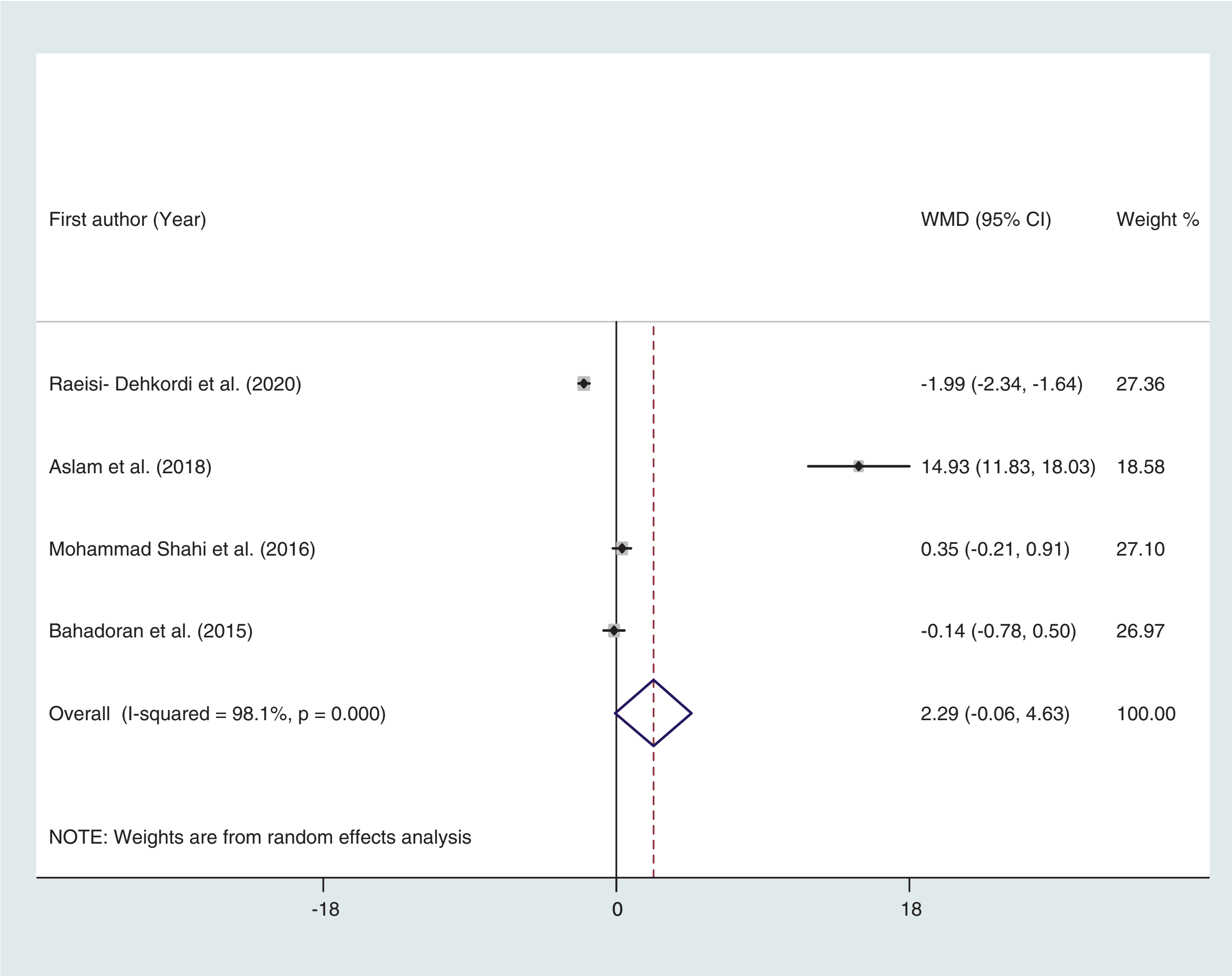

FIGURE 4 Forest plots showing the effect of sesame consumption on fasting insulin levels.

Sesame, contains several lignans such as sesamolin, sesaminol and sesamin (Tsuruoka et al., 2005). Sesamin can inhibit the augment of blood glucose by playing a role in increasing glycogen production (glycogen synthase). It has also been reported that the catechol metabolites from sesamin are involved in the following processes: glucose uptake, insulin signal transduction pathways, and carbohydrate metabolism (Hong et al., 2013; Mohammad Shahi et al., 2017).

Previous investigations indicated that increased adiponectin levels might be associated with better glycemic control (Mantzoros et al., 2005; Mohammed et al., 2021). Several studies have reported that consuming sesame can increase adiponectin levels (Janiszewska et al., 2021; Mohammad Shahi et al., 2017). Therefore, there is a hypothesis that sesame can regulate blood sugar by increasing circulating levels of adiponectin (Mohammad Shahi et al., 2017).

Although it seems that sesame is generally safe in common dosage among adults without any history of allergic reactions, like everything else, sesame seeds should also be consumed in moderation. Excessive consumption of sesame seeds causes' bowel and colon irritation. In addition, considering the previous reports about sesame seeds being allergic and the fact that it may cause anaphylaxis shocks in some people, more studies are needed to assess the long-term efficacy of sesame and its effect in various conditions before conclusive decisions about its safety and advice regarding general use in patients with T2D (Anilakumar et al., 2010; Namiki, 2007).

Due to less rigorous regulations, manufacturers in phytotherapy are often not forced to prove efficacy, safety or the quality of a marketed product. Consequently, a lot of available herbal products might be ineffective. Meta-analysis and systematic review studies can be very useful on these kinds of topics in that they help with a comprehensive conclusion that can give the ultimate idea of whether or not to use a specific nutraceutical as effective medicinal agent (Izzo et al., 2016; Williamson et al., 2020).

This meta-analysis has some limitations that must be taken into account when interpreting its findings. First, the number of articles in this meta-analysis was insufficient to reach definitive conclusions and certainly indicates the need for further clinical trials in this field. Second, the heterogeneity of the overall results in each outcome was high, which may have affected the efficacy of the results. Usually, this heterogeneity is due to the different type of study design, including intervention dose, extraction method, and intervention type. Third, the majority of trials did not account for differences in lifestyle (physical activity, diet, sleep, smoking, etc.), which may contribute to glycemic control. Fourth, Most of the included studies were conducted in Asian countries, and the results may not be generalizable. In addition, the different effects of sesame on males and females remain unknown because there was just one article on the female. The results of publication bias were also statistically significant for the effects of sesame consumption on fasting insulin levels. Therefore, additional RCTs are required to obtain the necessary pooled effect size. Finally, the protocol of this systematic review and meta-analysis was not registered in the PROSPERO due to the delay in processing the submitted protocols for studies outside the UK. This lack of registration might be a source of bias for this review.

5 | CONCLUSION

In summary, the current meta-analysis showed a promising effect of sesame consumption on glycemic control through reducing FBS and HbA1c percentage, yet additional prospective studies are recommended, using higher doses and longer intervention period, to confirm the impact of sesame consumption on insulin levels in T2D patients.

AUTHOR CONTRIBUTIONS

Andrés Alexis Ramírez-Coronel: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – original draft; writing – review and editing. **Khetam Abdalsada Ali Alhilali:** Conceptualization; investigation; methodology; project administration; resources; software; validation; visualization; writing – original draft; writing – review and editing. **Yasmin Basheer Ahmed:** Conceptualization; data curation; investigation; methodology; project administration; resources; validation; visualization; writing – original draft; writing – review and editing. **Sami G. Almalki:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; visualization; writing – original draft; writing – review and editing. **Jahangir Karimian:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

Ali, M. K., Pearson-Stuttard, J., Selvin, E., & Gregg, E. W. (2022). Interpreting global trends in type 2 diabetes complications and mortality. *Diabetologia*, *65*(1), 3–13.

An, J., Nichols, G. A., Qian, L., Munis, M. A., Harrison, T. N., Li, Z., Wei, R., Weiss, T., Rajpathak, S., & Reynolds, K. (2021). Prevalence and incidence of microvascular and macrovascular complications over 15 years among patients with incident type 2 diabetes. *BMJ Open Diabetes Research & Care*, *9*(1), e001847.

Andargie, M., Vinas, M., Rathgeb, A., Möller, E., & Karlovsky, P. (2021). Lignans of sesame (Sesamum indicum L.): A comprehensive review. *Molecules*, *26*(4), 883.

Anilakumar, K. R., Pal, A., Khanum, F., & Bawa, A. S. (2010). Nutritional, medicinal and industrial uses of sesame (Sesamum indicum L.) seeds-an overview. *Agriculturae Conspectus Scientificus*, *75*(4), 159–168.

Aslam, F., Iqbal, S., Nasir, M., & Anjum, A. A. (2019). 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. *Journal of the American College of Nutrition*, *38*(3), 235–246.

Azadnajafabad, S., Mohammadi, E., Aminorroaya, A., Fattahi, N., Rezaei, S., Haghshenas, R., Rezaei, N., Naderimagham, S., Larijani, B., & Farzadfar, F. (2021). Non-communicable diseases' risk factors in Iran; a review of the present status and action plans. *Journal of Diabetes & Metabolic Disorders*, 1–9.

Bahadoran, Z., Mirmiran, P., Hosseinpour-Niazi, S., & Azizi, F. (2015). A sesame seeds-based breakfast could attenuate sub-clinical inflammation in type 2 diabetic patients: A randomized controlled trial. *International Journal of Nutrition and Food Sciences*, *4*(1), 1.

Danaeifar, M. (2022). A non-structural protein of severe acute respiratory syndrome coronavirus 2 with a potential ability to reduce blood glucose for use in controlling type 2 diabetes mellitus. *Archives of Razi Institute*, *77*(6), 2181–2186.

Demir, S., Nawroth, P. P., Herzig, S., & Ekim Üstünel, B. (2021). Emerging targets in type 2 diabetes and diabetic complications. *Advanced Science*, *8*(18), 2100275.

Djuricic, I., & Calder, P. C. (2022). Polyunsaturated fatty acids and metabolic health: Novel insights. *Current Opinion in Clinical Nutrition and Metabolic Care*, *25*(6), 436–442.

Figueiredo, A. S., & Modesto-Filho, J. (2008). Effect of defatted sesame (Sesamum indicum L.) flour on the blood glucose level in type 2 diabetic women. *Revista Brasileira de Farmacognosia*, *18*, 77–83.

Follmann, D., Elliott, P., Suh, I., & Cutler, J. (1992). Variance imputation for overviews of clinical trials with continuous response. *Journal of Clinical Epidemiology*, *45*(7), 769–773.

Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., Ostolaza, H., & Martín, C. (2020). Pathophysiology of type 2 diabetes mellitus. *International Journal of Molecular Sciences*, *21*(17), 6275.

Ghoreishi, A. S., Chatrnour, G., & Mahmoodi, M. (2022). The effect of sesame seeds on fast blood sugar, haemoglobin A1C, liver enzymes and lipid profile in patients with type 2 diabetes: A randomised clinical trial. *Family Medicine & Primary Care Review*, *24*(3), 207–211.

Guariguata, L., Whiting, D. R., Hambleton, I., Beagley, J., Linnenkamp, U., & Shaw, J. E. (2014). Global estimates of diabetes prevalence for 2013

and projections for 2035. *Diabetes Research and Clinical Practice*, *103*(2), 137–149.
Hadi, A., Arab, A., Hajianfar, H., Talaei, B., Miraghajani, M., Babajafari, S., Marx, W., & Tavakoly, R. (2020). The effect of fenugreek seed supplementation on serum irisin levels, blood pressure, and liver and kidney function in patients with type 2 diabetes mellitus: A parallel randomized clinical trial. *Complementary Therapies in Medicine*, *49*, 102315.
Hadi, A., Asbaghi, O., Kazemi, M., Khadem, H., & Ghaedi, E. (2022). Effects of pistachios on glycemic control: A systematic review and meta-analysis of randomized controlled trials. *British Journal of Nutrition*, *129*, 1–26.
Hadi, A., Pourmasoumi, M., Mohammadi, H., Symonds, M., & Miraghajani, M. (2018). The effects of silymarin supplementation on metabolic status and oxidative stress in patients with type 2 diabetes mellitus: A systematic review and meta-analysis of clinical trials. *Complementary Therapies in Medicine*, *41*, 311–319.
Heshmati, J., Moini, A., Sepidarkish, M., Morvaridzadeh, M., Salehi, M., Palmowski, A., Mojtahedi, M. F., & Shidfar, F. (2021). Effects of curcumin supplementation on blood glucose, insulin resistance and androgens in patients with polycystic ovary syndrome: A randomized double-blind placebo-controlled clinical trial. *Phytomedicine*, *80*, 153395.
Heshmati, J., Morvaridzadeh, M., Sepidarkish, M., Fazelian, S., Rahimlou, M., Omidi, A., Palmowski, A., Asadi, A., & Shidfar, F. (2020). Effects of Melissa officinalis (lemon balm) on cardio-metabolic outcomes: A systematic review and meta-analysis. *Phytotherapy Research*, *34*(12), 3113–3123.
Higgins, J. P., & Green, S. (2011). Cochrane Handbook for Systematic Reviews of Interventions Version 5(0): 2011.
Hong, L., Yi, W., Liangliang, C., Juncheng, H., Qin, W., & Xiaoxiang, Z. (2013). Hypoglycaemic and hypolipidaemic activities of sesamin from sesame meal and its ability to ameliorate insulin resistance in KK-ay mice. *Journal of the Science of Food and Agriculture*, *93*(8), 1833–1838.
Imamura, F., Micha, R., Wu, J. H., de Oliveira Otto, M. C., Otite, F. O., Abioye, A. I., & Mozaffarian, D. (2016). Effects of saturated fat, polyunsaturated fat, monounsaturated fat, and carbohydrate on glucose-insulin homeostasis: A systematic review and meta-analysis of randomised controlled feeding trials. *PLoS Medicine*, *13*(7), e1002087.
Isharwal, S., Misra, A., Wasir, J., & Nigam, P. (2009). Diet & insulin resistance: A review & Asian Indian perspective. *Indian Journal of Medical Research*, *129*(5), 485.
Izzo, A. A., Hoon-Kim, S., Radhakrishnan, R., & Williamson, E. M. (2016). A critical approach to evaluating clinical efficacy, adverse events and drug interactions of herbal remedies. *Phytotherapy Research*, *30*(5), 691–700.
Janiszewska, J., Ostrowska, J., & Szostak-Węgierek, D. (2021). The influence of nutrition on adiponectin—A narrative review. *Nutrients*, *13*(5), 1394.
Kanu, P. J., Bahsoon, J. Z., Kanu, J. B., & Kandeh, J. (2010). Nutraceutical importance of sesame seed and oil: A review of the contribution of their lignans. *Sierra Leone Journal of Biomedical Research*, *2*(1), 4–16.
Khalesi, S., Paukste, E., Nikbakht, E., & Khosravi-Boroujeni, H. (2016). Sesame fractions and lipid profiles: A systematic review and meta-analysis of controlled trials. *British Journal of Nutrition*, *115*(5), 764–773.
Khosravi-Boroujeni, H., Nikbakht, E., Natanelov, E., & Khalesi, S. (2017). Can sesame consumption improve blood pressure? A systematic review and meta-analysis of controlled trials. *Journal of the Science of Food and Agriculture*, *97*(10), 3087–3094.
Kumar, S., Mittal, A., Babu, D., & Mittal, A. (2021). Herbal medicines for diabetes management and its secondary complications. *Current Diabetes Reviews*, *17*(4), 437–456.
Liu, J. P., Zhang, M., Wang, W., & Grimsgaard, S. (2002). Chinese herbal medicines for type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews*, *2009*(3), CD003642.
Mantzoros, C. S., Li, T., Manson, J. E., Meigs, J. B., & Hu, F. B. (2005). Circulating adiponectin levels are associated with better glycemic control, more favorable lipid profile, and reduced inflammation in women with type 2 diabetes. *The Journal of Clinical Endocrinology & Metabolism*, *90*(8), 4542–4548.
Moghtaderi, F., Amiri, M., Raeisi-Dehkordi, H., Zimorovat, A., Mohyadini, M., & Salehi-Abargouei, A. (2022). The effect of sesame, canola, and sesame-canola oils on cardiometabolic risk factors in overweight adults: A three-way randomized triple-blind crossover clinical trial. *Phytotherapy Research*, *36*(2), 1043–1057.
Mohammad Shahi, M., Zakerzadeh, M., Zakerkish, M., Zarei, M., & Saki, A. (2017). Effect of sesamin supplementation on glycemic status, inflammatory markers, and adiponectin levels in patients with type 2 diabetes mellitus. *Journal of Dietary Supplements*, *14*(1), 65–75.
Mohammed, Z., Ahmad, K. M., & Yousef, S. (2021). Adiponectin in type II diabetes mellitus. *The Medical Journal of Cairo University*, *89*(June), 1025–1028.
Moholkar Aparark, V., Jadge Dhanraj, R., & Nagoba Shivappa, N. (2021). Pharmacokinetic profile of polyherbal tablets comprising extracts of antidiabetic medicinal plants. *Journal of Complementary Medicine Research*, *12*(3), 1–20.
Mohsen, I. H., Jawad, M. A., Kadhim, A. J., & Al-Terehi, M. N. (2022). The oxidative stress state in diabetes mellitus type 2 patients with different medications types. *Journal of Chemical Health Risks*, *12*(3), 523–525.
Molavi, A., Afshar-Zanjani, H., & Hajializadeh, K. (2020). Comparison of the effectiveness of self-care group training and group-based acceptance and commitment therapy on the quality of life and psychological well-being of patients with type 2 diabetes. *International Journal of Body, Mind and Culture*, *7*(3), 163–171.
Nagar, P., & Agrawal, M. A. K. (2022). Sesame (Sesamum indicum L.) seed as a functional food: A review. *Energy (Kcal)*, *519*(516.49), 507–565.
Nakai, M., Harada, M., Nakahara, K., Akimoto, K., Shibata, H., Miki, W., & Kiso, Y. (2003). Novel antioxidative metabolites in rat liver with ingested sesamin. *Journal of Agricultural and Food Chemistry*, *51*(6), 1666–1670.
Namiki, M. (2007). Nutraceutical functions of sesame: A review. *Critical Reviews in Food Science and Nutrition*, *47*(7), 651–673.
Nauck, M. A., Wefers, J., & Meier, J. J. (2021). Treatment of type 2 diabetes: Challenges, hopes, and anticipated successes. *The Lancet Diabetes & Endocrinology*, *9*(8), 525–544.
Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., & Chou, R. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *International Journal of Surgery*, *88*, 105906.
Pillon, N. J., Loos, R. J., Marshall, S. M., & Zierath, J. R. (2021). Metabolic consequences of obesity and type 2 diabetes: Balancing genes and environment for personalized care. *Cell*, *184*(6), 1530–1544.
Raeisi-Dehkordi, H., Amiri, M., Zimorovat, A., Moghtaderi, F., Zarei, S., Forbes, S. C., & Salehi-Abargouei, A. (2020). The effects of canola oil compared with sesame and sesame-canola oil on glycemic control and liver function enzymes in patients with type 2 diabetes: A 3-way randomized triple-blind cross-over clinical trial. *Diabetes/Metabolism Research and Reviews*, e3399.
Raeisi-Dehkordi, H., Amiri, M., Zimorovat, A., Moghtaderi, F., Zarei, S., Forbes, S. C., & Salehi-Abargouei, A. (2021). Canola oil compared with sesame and sesame-canola oil on glycaemic control and liver function in patients with type 2 diabetes: A three-way randomized triple-blind cross-over trial. *Diabetes/Metabolism Research and Reviews*, *37*(5), e3399.
Raeisi-Dehkordi, H., Mohammadi, M., Moghtaderi, F., & Salehi-Abargouei, A. (2018). Do sesame seed and its products affect body weight and composition? A systematic review and meta-analysis of controlled clinical trials. *Journal of Functional Foods*, *49*, 324–332.
Rafiee, S., Faryabi, R., Yargholi, A., Zareian, M. A., Hawkins, J., Shivappa, N., & Shirbeigi, L. (2021). Effects of sesame consumption on inflammatory biomarkers in humans: A systematic review and meta-

analysis of randomized controlled trials. *Evidence-based Complementary and Alternative Medicine*, *2021*, 13.

Retnakaran, R., Ye, C., Connelly, P. W., Hanley, A. J., Sermer, M., & Zinman, B. (2017). Impact of changes over time in adipokines and inflammatory proteins on changes in insulin sensitivity, β-cell function, and glycemia in women with previous gestational Dysglycemia. *Diabetes Care*, *40*(8), e101–e102.

Rocca, A. S., LaGreca, J., Kalitsky, J., & Brubaker, P. L. (2001). Monounsaturated fatty acid diets improve glycemic tolerance through increased secretion of glucagon-like peptide-1. *Endocrinology*, *142*(3), 1148–1155.

Safari, Z., Farrokhzad, A., Ghavami, A., Fadel, A., Hadi, A., Rafiee, S., Mokari-Yamchi, A., & Askari, G. (2020). The effect of barberry (Berberis vulgaris L.) on glycemic indices: A systematic review and meta-analysis of randomized controlled trials. *Complementary Therapies in Medicine*, *51*, 102414.

Sankar, D., Ali, A., Sambandam, G., & Rao, R. (2011). Sesame oil exhibits synergistic effect with anti-diabetic medication in patients with type 2 diabetes mellitus. *Clinical Nutrition*, *30*(3), 351–358.

Sankar, D., Rao, M. R., Sambandam, G., & Pugalendi, K. (2006). A pilot study of open label sesame oil in hypertensive diabetics. *Journal of Medicinal Food*, *9*(3), 408–412.

Sharin, T., Ahammed, B., Elahi, M., Mamun, M. S. A., & Paul, D. K. (2021). Impact of physical exercise and food habit on type ii diabetes mellitus medicated patients-a cross sectional study. *Journal of Chemical Health Risks*, *11*(Special Issue: Bioactive Compounds: Their Role in the Prevention and Treatment of Diseases), 33–43.

Sivakumar, H., & Jeganath, S. J. D. S. (2021). Effect of sulfonylurea in patients with type 2 diabetes mellitus. *International Journal of Pharmacy Research & Technology*, *11*(2), 57–67.

Sohaei, S., Hadi, A., Karimi, E., & Arab, A. (2020). Saffron supplementation effects on glycemic indices: A systematic review and meta-analysis of randomized controlled clinical trials. *International Journal of Food Properties*, *23*(1), 1386–1401.

Storz, M. A. (2020). The role of vegan diets in lipotoxicity-induced beta-cell dysfunction in type-2-diabetes. *Journal of Population Therapeutics and Clinical Pharmacology*, *27*(SP2), e22–e38.

Sundaram, G., Theagarajan, R., Gopalakrishnan, K., Babu, G., & Murthy, G. (2020). Effect of fenugreek consumption with metformin treatment in improving plaque index in diabetic patients. *Journal of Natural Science, Biology and Medicine*, *11*(1), 55–60.

Tajaddini, A., Roshanravan, N., Mobasseri, M., Aeinehchi, A., Sefid-Mooye Azar, P., Hadi, A., & Ostadrahimi, A. (2021). Saffron improves life and sleep quality, glycaemic status, lipid profile and liver function in diabetic patients: A double-blind, placebo-controlled, randomised clinical trial. *International Journal of Clinical Practice*, *75*(8), e14334.

Taylor, S. I., Yazdi, Z. S., & Beitelshees, A. L. (2021). Pharmacological treatment of hyperglycemia in type 2 diabetes. *The Journal of Clinical Investigation*, *131*(2), e142243.

Telle-Hansen, V. H., Gaundal, L., & Myhrstad, M. C. (2019). Polyunsaturated fatty acids and glycemic control in type 2 diabetes. *Nutrients*, *11*(5), 1067.

Tierney, A. C., & Roche, H. M. (2007). The potential role of olive oil-derived MUFA in insulin sensitivity. *Molecular Nutrition & Food Research*, *51*(10), 1235–1248.

Triposkiadis, F., Xanthopoulos, A., Bargiota, A., Kitai, T., Katsiki, N., Farmakis, D., Skoularigis, J., Starling, R. C., & Iliodromitis, E. (2021). Diabetes mellitus and heart failure. *Journal of Clinical Medicine*, *10*(16), 3682.

Tsuruoka, N., Kidokoro, A., Matsumoto, I., Abe, K., & Kiso, Y. (2005). Modulating effect of sesamin, a functional lignan in sesame seeds, on the transcription levels of lipid-and alcohol-metabolizing enzymes in rat liver: A DNA microarray study. *Bioscience, Biotechnology, and Biochemistry*, *69*(1), 179–188.

Williamson, E. M., Liu, X., & Izzo, A. A. (2020). Trends in use, pharmacology, and clinical applications of emerging herbal nutraceuticals. *British Journal of Pharmacology*, *177*(6), 1227–1240.

Wu, M.-S., Aquino, L. B. B., Barbaza, M. Y. U., Hsieh, C.-L., de Castro-Cruz, K. A., Yang, L.-L., & Tsai, P.-W. (2019). Anti-inflammatory and anticancer properties of bioactive compounds from Sesamum indicum L.—A review. *Molecules*, *24*(24), 4426.

Xu, R., Bai, Y., Yang, K., & Chen, G. (2020). Effects of green tea consumption on glycemic control: A systematic review and meta-analysis of randomized controlled trials. *Nutrition and Metabolism*, *17*(1), 1–13.

Ziaei, R., Foshati, S., Hadi, A., Kermani, M. A. H., Ghavami, A., Clark, C. C., & Tarrahi, M. J. (2020). The effect of nettle (Urtica dioica) supplementation on the glycemic control of patients with type 2 diabetes mellitus: A systematic review and meta-analysis. *Phytotherapy Research*, *34*(2), 282–294.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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