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Clinical Efficacy of *Pistacia atlantica* in Glycemic Regulation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials in Type 2 Diabetes Mellitus

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Systematic Review

Keywords: Pistacia atlantica, blood sugar, Type 2 diabetes mellitus, Glycemic regulation, Meta analysis

Posted Date: September 2nd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10887555/v1

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Additional Declarations: The authors declare no competing interests.

Abstract

Type 2 diabetes mellitus (T2DM) is a growing global health problem associated with inadequate glycemic control and serious complications. Although pharmacological therapies are available, many patients experience side effects or fail to achieve optimal blood glucose targets. Pistacia atlantica, traditionally used for metabolic disorders, has demonstrated antihyperglycemic and anti-inflammatory effects in animal studies, but its clinical benefits in human diabetes remain uncertain. This systematic review and meta-analysis evaluated the effects of Pistacia atlantica supplementation on glycemic control in patients with T2DM. Seven randomized controlled trials from Iran and Iraq, involving intervention durations of 4–12 weeks, were included. Pooled analysis using a random-effects model showed significant reductions in fasting blood sugar (weighted mean difference [WMD] = − 18.04 mg/dL; 95% CI: −29.9 to − 6.18; p = 0.003) and glycated hemoglobin (HbA1c) (WMD = − 0.6%; 95% CI: −1.1 to − 0.10; p = 0.01). Greater improvements were observed in studies lasting at least 8 weeks, with FBS decreasing by − 28.2 mg/dL (p = 0.001) and HbA1c by − 0.7% (p = 0.02). No serious adverse events were reported. These findings suggest that Pistacia atlantica may serve as a safe and effective adjunct to conventional therapy for improving glycemic control in T2DM, particularly when administered for eight weeks or longer. Further well-designed trials with standardized formulations are needed to validate these results.

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic disease that gets worse in time. It is characterized by insulin resistance, and the relative deficiency of the pancreas to secrete insulin and the consequently increased blood sugar levels. Over 400 million people globally are afflicted by the condition. Apart from that, it is one of the most frequent causes of the incidence, progress, and death of the diseases of the heart, kidneys, and mortality, respectively [1–3]. Even with the use of specific drugs like metformin, sulfonylureas, and insulin analogs, the management of diabetes is still a big problem. In many cases, drugs can cause side effects, be of high cost, or lead to a lack of glycemic control in many patients. This explains the growing interest in developing a diabetes treatment strategy based on natural and alternative methods of medicine that will adversely affect the least number of patients and may be efficient for others. The family Anacardiaceae contains the species *Pistacia atlantica*, for example [4], It is a tree which comes originally from the Middle East and Mediterranean regions and has been widely used in traditional medicine as a treatment for many conditions, such as gastrointestinal disorders, infections, and metabolic syndromes [5]. The health-related benefits are linked to the presence in *P. atlantica* compositions of a number of biologically active substances such as phenolics, flavonoids, triterpenoids, and unsaturated fatty acids. Purely animal model research has shown that P. atlantica extracts, and the oils of the plant possess the activity of anti-oxidants, anti-inflammatory and hypoglycemic agents [6]. The findings reveal that by improving insulin sensitivity, reducing oxidative stress, and modulating lipid metabolism, *Pistacia atlantica* could affect glycemic parameters. The antidiabetic effects of *Pistacia atlantica* are supported by the plant's phytochemical profile [7]. Compounds such as β-pinene, α-pinene, and α-terpineol have been shown to improve insulin sensitivity and prevent the occurrence of fat damage in the fatty liver of diabetic animal models [8]. Moreover, the anti-inflammatory capability of the plant may also be useful in reducing the intensity of low-grade continuous inflammation, which is the main cause of insulin insensitivity in T2DM [9]. Even though there are some really great pharmacodynamic effects, clinical trials haven't yet proved the efficacy of *Pistacia atlantica* in patients with T2DM. Just a small number of randomized controlled trials (RCTs) were done in Iran and Iraq, and they were only looking at the impact on glucose variables such as fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) [10]. Nonetheless, these studies differ greatly in research design, intervention length, quantity, and subjects' features, affecting the results' constancy. A part of the researches confirms noticeable progress in blood sugar parameters, whereas the rest show only a small or non-significant effect [11]. This diversity among people makes it difficult to figure out what the results of each study are and to decide on clinical suggestions based on evidence [12]. The methodology of systematic reviews and meta-analyses has already proved to be an effective tool to summarize the results of different studies and to generate more accurate interventions effects. This kind of research is of great importance when either the separate trials are not sufficiently powered up or they give inconsistent outcomes [13]. In the instance of *Pistacia atlantica*, there hasn't been a meta-analysis so far that rigorously tested the effectiveness of the plant on the management of type 2 diabetes in patients. The absence of a review of this sort in this domain is a very important point in the literature because it creates a barrier to the licensing of medications of botanical origin in the treatment of diabetes [14]. With the rising worldwide prevalence of T2DM, the requirement for additionally aids of treatment that are risk-free and inexpensive becomes more apparent, proving the value of evaluating the safety and effectiveness of certain nutraceuticals like *Pistacia atlantica* through evidence-based methods [15]. What's more, the rising abundance of RCTs over the last decade offers a great occasion to gather together the data at hand and evaluate the clinical efficacy of this age-old cure in a systematic way [16]. We conducted this study in order to find out whether *Pistacia atlantica* improved the blood sugar values among type 2 diabetes patients. We have evaluated through clinical trials how *P. atlantica* influenced fasting blood sugar and HbA1c. A systematic review was also conducted to examine the level of the existing evidence and various factors that might affect the outcomes.

Materials and Methods

This review has got its base in the 2020 PRISMA guidelines for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [17] and the source is PROSPERO registry (registration number CRD420251035874) that licensed it. Maintaining precision and clearness rephrased from the original version. https://www.crd.york.ac.uk/PROSPERO/view/CRD420251035874

Search methodology

A literature search was conducted by a professional and was completed on October 11, 2024, to find the articles that evaluated the impact of *Pistacia* species—including *Pistacia atlantica, Pistacia terebinthus, Pistacia mutica, Pistacia khinjuk*, and their common names such as Wild Pistachio, Terebinth, and Khinjuk—on outcomes related to type 2 diabetes mellitus (T2DM). The following electronic databases and clinical trial registries were searched: PubMed/MEDLINE (n = 275), Scopus (n = 33), ISI Web of Science (n = 957), and Google Scholar (n = 200). Additional sources included the WHO International Clinical Trials Registry Platform (ICTRP; n = 1) and ClinicalTrials.gov (n = 0). The search terms combined synonyms and variants of the intervention (e.g., "Pistacia atlantica" OR "Terebinth") with outcome-related terms (e.g., "Type 2 Diabetes Mellitus" OR "T2DM") using Boolean operators. No date or language restrictions were applied during the search. The total number of records retrieved was 1466. Records were initially screened by title and abstract, followed by full-text review. No automation tools were used for screening or exclusion; all processes were conducted manually by the research team.

Criteria for eligibility

Studies were considered eligible if they met the following criteria: (i) employed a randomized controlled trial (RCT) design—either parallel or crossover—with a minimum intervention duration of two weeks; (ii) investigated the effects of Pistacia atlantica supplementation (in the form of powder, extract, or oil) on adult participants (aged ≥ 18 years) diagnosed with type 2 diabetes mellitus (T2DM); (iii) reported at least one of the primary outcomes related to glycemic control, specifically fasting blood sugar (FBS) or glycated hemoglobin (HbA1c); and (iv) included a placebo or control group for comparison. Studies were excluded if they (i) lacked randomization or a control group; (ii) had a study duration shorter than two weeks; (iii) included pregnant individuals or participants younger than 18 years of age; or (iv) failed to report relevant outcome measures. Additionally, non-clinical studies such as animal experiments, in vitro trials, case series, review articles, meta-analyses, and study protocols were excluded.

Process of selecting studies

The study selection process followed the PRISMA 2020 guidelines. An initial total of 1,467 records were identified through searches of electronic databases and clinical trial registries, including PubMed (n = 275), Scopus (n = 33), ISI Web of Science (n = 957), Google Scholar (n = 200), WHO ICTRP (n = 1), and ClinicalTrials.gov (n = 0). After removing 142 duplicates, 1,325 records remained. An additional 941 records were excluded using automation tools for being irrelevant, and 205 were removed for other reasons such as language issues or incomplete citations. This left 179 records for title and abstract screening, of which 172 were excluded for being in vitro or animal studies, reviews, case reports, or not meeting the predefined eligibility criteria. Full texts of 5 reports were retrieved and assessed for eligibility, and 1 was excluded due to insufficient data. Ultimately, 4 randomized controlled trials were deemed eligible and included in the final meta-analysis. All disagreements during the selection process were resolved through discussion and consensus between reviewers.

Data extraction

Data extraction was systematically performed using a structured template. As summarized in **Table 1**, seven randomized placebo-controlled trials conducted in Iran and Iraq were included in the meta-analysis. Extracted data included the first author's name, country of origin, study design (e.g., randomized triple-blind, double-blind, or single-blind), sample size, sex distribution, participant health status (type 2 diabetes or type 2 diabetes with hyperlipidemia), intervention dosage (ranging from 0.5 to 4 g/day), and duration of the intervention (4 to 12 weeks). Each study compared Pistacia atlantica supplementation to a placebo in both intervention and control groups. For example, Fatemeh et al. administered 4 g/day over 4 weeks to patients with type 1 or type 2 diabetes [18], while Zahra et al. conducted a 12-week single-blind trial using the same dosage [15]. All trials measured at least one glycemic control outcome, including

fasting blood sugar (FBS) or HbA1c. The extraction was conducted independently by two reviewers and discrepancies were resolved by a third party. Corresponding authors were contacted when further clarification or missing data were necessary.

Risk of Bias Assessment

The quality of the included randomized controlled trials was assessed using the Cochrane Risk of Bias Tool, covering seven standard domains. As illustrated in Fig. 1, the majority of studies showed a low risk of bias in the domains of random sequence generation and incomplete outcome data. However, high or unclear risks were observed in several key areas. Specifically, Fatemeh et al and Faezeh et al I demonstrated high risk in blinding of participants and personnel [18, 19]. Faezeh et al II and Zahra et al presented unclear risks in multiple domains, including allocation concealment, blinding of outcome assessment, and selective reporting [15, 19]. The Yosra et al trials showed a mixture of low, high, and unclear risks, particularly in blinding and reporting domains [20]. Notably, Yosra et al III was rated as unclear in almost all categories except for incomplete outcome data. Overall, the visual inspection of the risk of bias summary (Fig. 1) highlights that while randomization was generally well-reported, methodological concerns persist in blinding and reporting, which may influence the internal validity of the included studies.

Data Compilation and Examination

The data from the included studies were synthesized using a random-effects meta-analysis technique, including possible variability across trials. The main objectives were alterations in fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) levels after Pistacia atlantica supplementation vs placebo. Weighted mean differences (WMDs) and 95% confidence intervals (CIs) were computed for each outcome. When numerous endpoints were documented, the last endpoint values were used. The mean difference between the intervention and control periods was computed for crossover studies. If studies did not include standard deviations (SDs), they were inferred using standard errors (SEs) or 95% confidence intervals (CIs) utilizing existing formulae. In instances where standard deviations for change-from-baseline values were absent, they were calculated using the formula: $SD_{change} = \sqrt{(SD^2_{baseline} + SD^2_{endpoint} - 2 \times R \times SD_{baseline} \times SD_{endpoint})}$, with a presumed correlation coefficient (R) of 0.5. The chi-squared test and I^2 statistics were used to evaluate heterogeneity across studies, with I^2 values over 50% or p-values below 0.10 signifying considerable heterogeneity. Subgroup analyses were conducted depending on the length of intervention (< 8 weeks vs. ≥8 weeks). Publication bias was assessed using Egger's regression test and visual examination of funnel plots. Sensitivity analyses were performed to assess the impact of individual studies on overall findings. All statistical analyses were conducted using Stata version 15.0, with a significance level set at $p < 0.05$..

Reporting Bias Assessment

Reporting bias was evaluated by Egger's regression test and visual examination of funnel plots for the key outcomes: fasting blood sugar (FBS) and glycated hemoglobin (HbA1c). Figure 3 indicates that no substantial publication bias was identified for either FBS (Egger's test, p = 0.2) or HbA1c (p = 0.2), suggesting a little probability of small-study effects or selective outcome reporting affecting the findings. The symmetry of the funnel plots further indicated the lack of significant reporting bias. The data suggest that the aggregated estimates from the included research are improbable to be influenced by systematic publishing biases.

Results

Literature Search

A total of 1,467 records were identified through systematic searches across multiple databases and trial registries, including PubMed (n = 275), Scopus (n = 33), Web of Science (n = 957), Google Scholar (n = 200), WHO ICTRP (n = 1), and ClinicalTrials.gov (n = 0). After removing 142 duplicates, 1,325 records remained for screening. Automation tools excluded 941 irrelevant records, and an additional 205 records were excluded for other reasons such as format issues or incomplete data. Following title and abstract screening of the remaining 179 articles, 172 records were excluded for not meeting the inclusion criteria—primarily due to being animal studies, in vitro studies, case reports, or reviews. The full texts of 5 articles were retrieved and assessed for eligibility, with 1 study excluded due to insufficient outcome data. Ultimately, 4 randomized controlled trials met the inclusion criteria and were included in the final meta-analysis. The complete study selection process is outlined in Fig. 1, following the PRISMA 2020 flow diagram.

Study Characteristics

A total of seven randomized placebo-controlled trials were included in the meta-analysis, all conducted in Iran and Iraq between 2018 and 2024. As summarized in **Table 1**, the studies investigated the effects of *Pistacia atlantica* supplementation in patients with type 2 diabetes mellitus (T2DM), with one study also including participants with type 1 diabetes. Study durations ranged from 4 to 12 weeks, and sample sizes varied from 21 to 47 participants per group. The majority of participants were female, and intervention doses ranged from 0.5 to 4 g/day. All studies included a placebo control group and measured at least one glycemic outcome—fasting blood sugar (FBS) and/or glycated hemoglobin (HbA1c). Study designs varied in blinding protocols, including triple-blind, double-blind, and single-blind randomized controlled trials. Some studies also focused on patients with comorbid conditions such as hyperlipidemia. The intervention was consistently reported as *Pistacia atlantica* powder or extract, administered orally. Despite slight variations in methodology and participant profiles, all studies were comparable in terms of intervention scope and outcome assessment, allowing for meaningful synthesis and comparison.

Table 1. Characteristic of included studies in meta-analysis.

Studies	Country	Study Design	Participant	Sample size and Sex	Duration (Week)	Sample size		Intervention	
						IG	CG	Dose g/d	Control group
Fatemeh et al**[21]**	IRAN	RTBPCT	T1 or 2D	(40)F (8)M	4	24	24	4	placebo
Faezeh et al I**[10]**	IRAN	TBRCT	T2Dwith hyperlipidemia	(40)F (18)M	4	29	29	0.5	placebo
Faezeh et al II**[10]**	IRAN	TBRCT	T2Dwith hyperlipidemia	(40)F (18)M	8	29	29	0.5	Placebo
Yosra et al I**[20]**	IRAQ	RDBPCT	T2D	(45)F (47)M	4	47	45	2	placebo
Yosra et al II**[20]**	IRAQ	RDBPCT	T2D	(45)F (47)M	8	47	45	2	placebo
Yosra et al III**[20]**	IRAQ	RDBPCT	T2D	(45)F (47)M	12	47	45	2	placebo
Zahra et al **[11]**	IRAN	RSBPCT	T2D	NR	12	21	21	4	placebo

Abbreviations: T2DM, Type 2 Diabetes Mellitus; T1: type 1 diabetes mellitus ; IG, intervention group; CG, control group; TB, Triple-blinded: DB, double-blinded; SB, single-blinded; PC, placebo-controlled; CO, controlled; R, randomized; P, Parallel; F, Female; M, Male,

Results of Meta-Analysis

The pooled analysis of seven randomized controlled trials showed that Pistacia atlantica supplementation significantly reduced fasting blood sugar (FBS) levels in patients with type 2 diabetes mellitus. As shown in Table 2 and Figure 2, the overall weighted mean difference (WMD) for FBS was -18.04 mg/dL (95% CI: -29.9 to -6.18; p = 0.003), although considerable heterogeneity was observed (I^2 = 91.2%; p = 0.001). Subgroup analysis by intervention duration revealed that trials lasting less than 8 weeks showed a non-significant reduction in FBS (WMD = -7.5 mg/dL; p = 0.08; I^2 = 0.0%), whereas trials lasting 8 weeks or longer demonstrated a significant reduction (WMD = -28.2 mg/dL; p = 0.001; I^2 = 58.8%).

Similarly, the meta-analysis found a significant reduction in glycated hemoglobin (HbA1c) following Pistacia atlantica supplementation, with an overall WMD of -0.6% (95% CI: -1.1 to -0.10; p = 0.01), despite high heterogeneity (I^2 = 91.9%; p = 0.002). Stratification by duration revealed that short-term interventions (<8 weeks) did not yield statistically significant changes (WMD = -0.31%; p = 0.21; I^2 = 16.8%), while studies with interventions lasting ≥8 weeks reported a significant reduction in HbA1c (WMD = -0.7%; p = 0.02; I^2 = 81.7%).

These findings suggest that Pistacia atlantica supplementation is more effective in improving glycemic control when administered over longer durations.

Table 2. the effect of Pistacia atlantica supplementation on FBS and HBA1C

	NO	WMD (95%CI)	P-value	heterogeneity	
				P heterogeneity	I^2
Overall effect on FBS	7	-18.04(-29.9-6.18)	0.003	0.001	91.2%
Intervention Duration (Weeks)					
< 8	3	-7.5 (-16.1-1.02)	0.08	0.73	0.0%
≥ 8	4	-28.2(-39.8 -16.7)	0.001	0.06	58.8
Overall effect on HbA1C	5	-0.6(-1.1-0.10)	0.01	0.002	91.9%
Intervention Duration (Weeks)					
< 8	2	-0.31(-0.81-0.18)	0.21	0.27	16.8%
≥ 8	3	-0.7(-1.5 - -0.09)	0.02	0.002	81.7%

Sensitivity Analysis and Meta-Regression Results

To evaluate the robustness of the meta-analysis findings, sensitivity analyses were conducted by sequentially removing individual studies. Excluding the study by Fatemeh et al. had minimal impact on the pooled effect sizes. The weighted mean difference (WMD) for fasting blood sugar (FBS) remained statistically significant at -20.1 mg/dL (95% CI: -32.5 to -7.73), and the reduction in glycated hemoglobin (HbA1c) was still borderline significant at -0.62% (95% CI: -1.26 to -0.005). These results confirm the overall stability of the estimated effects and indicate that no single study disproportionately influenced the results.

Meta-regression analysis was further performed to explore the impact of intervention duration on glycemic outcomes. A significant association was found between intervention duration and changes in FBS (regression coefficient = -43.17, p = 0.03), suggesting that longer interventions led to greater reductions in blood glucose levels. However, the relationship between duration and HbA1c reduction did not reach statistical significance (regression coefficient = -2.55, p = 0.11). These findings imply that duration of supplementation is a key determinant in achieving optimal glycemic improvement, particularly for FBS

Figure 3. shows publication bias was assessed using Egger's test, with no significant bias detected for either fasting blood sugar (FBS) (P = 0.2) or HbA1c (P = 0.2), indicating a low likelihood of small-study effects influencing the results. Sensitivity analysis further confirmed the robustness of the findings. Excluding the study by Fatemeh et al. did not substantially alter the overall effect estimates; the WMD for FBS remained significant at -20.1 mg/dL (95% CI: -32.5 to -7.73), and the reduction in HbA1c was still borderline significant at -0.62% (95% CI: -1.26 to -0.005). Meta-regression analysis showed that intervention duration was significantly associated with changes in FBS (coefficient = -43.17, P = 0.03), suggesting greater reductions with longer treatment periods. However, the association between duration and HbA1c reduction was not statistically significant (coefficient = -2.55, P = 0.11).

Figure 4 offers the evaluation of bias risk for the studies included. Most investigations demonstrated a minimal risk across several areas, especially in random sequence creation. Nevertheless, several studies demonstrated elevated or ambiguous risk in aspects such as blinding and missing outcome data, underscoring possible methodological deficiencies in trial design and reporting.

Discussion

The present meta-analysis provides compelling evidence for the efficacy of Pistacia atlantica in glycemic control among patients with type 2 diabetes mellitus (T2DM). An analysis of the collected results indicated that the decreases in both fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) were statistically significant, especially when the intake of supplements lasted for more than eight weeks. This phenomenon confirms the conviction of how beneficial to health the use of *P. atlantica* in Iran and the Mediterranean region has been throughout history in the treatment of metabolic disorders. The presence of a large number of phenolic compounds, flavonoids, and essential oils including α-pinene and β-pinene, responsible for the plant's bioactivity, is anticipated. These constituents are not unknown; they are characterized by properties, such as an antioxidative and anti-inflammatory nature that are well known. The decline of FBS by −18.04 mg/dL in total is an important one that research studies have been fulfilling over time. For example, Mahjoub et al. claimed that *P. atlantica* gum was especially effective in reducing the HbA1c and the body mass index (BMI) after an 8-week treatment in diabetic patients and the postprandial symptoms and the systolic blood pressure showed the biggest change in the subjects [22]. Also, the study by Majd et al. conducting the research found that *P. atlantica* subsp. kurdica had a pronounced ameliorative effect on 2-hour postprandial glucose levels but no significant effect on fasting blood sugar (FBS) or HbA1c during the short term [19]. This

variance of results highlights the significance of drug course, quantity, and the very product—parameters investigated in the present paper by means of meta-regression.

The decrease of 0.6% in HbA1c, although small, is quite relevant when the various treatments last longer than eight weeks. A single-blind placebo-controlled trial has been the basis for the view presented here, which demonstrated that oleoresin of P. atlantica tree was the one that managed to reduce blood pressure, but this particular formulation did not have the desired effect on HbA1c or FBS. Thus, it can be deduced that not all of the existing forms of the drug are of the same effectiveness after 12 weeks only [15]. Therefore, the formulation and extraction method—whether oil, gum, or powdered extract—likely influence the bioavailability and efficacy of active constituents. Such heterogeneity partially explains the variation in outcomes across studies and highlights the need for standardized formulations in future research. The observed effects on glycemic markers may be attributed to multiple mechanisms. Pistacia atlantica has demonstrated significant α-glucosidase and α-amylase inhibitory activity, mirroring the mode of action of pharmaceutical agents like acarbose used in T2DM management [23]. In addition, polyphenolic compounds such as methyl gallate, rutin, and quercetin found in P. atlantica extracts are known to enhance glucose uptake and mitigate oxidative stress, a key driver of insulin resistance. A preclinical meta-analysis further supports this by showing that P. atlantica significantly lowers blood glucose and HOMA-IR while increasing insulin sensitivity and antioxidant defenses in animal models [24]. Another plausible pathway involves modulation of inflammatory processes. Chronic inflammation contributes to the progression of insulin resistance, and P. atlantica has been shown to reduce levels of pro-inflammatory cytokines such as TNF-α while improving antioxidant capacity and lipid peroxidation markers in diabetic models [25]. Such systemic effects suggest that P. atlantica may confer broader metabolic benefits beyond glycemic control, potentially improving cardiovascular risk profiles in T2DM patients.

The duration of intervention was a significant predictor of efficacy, with studies lasting eight weeks or longer showing greater improvements in both FBS and HbA1c. Meta-regression confirmed this relationship, especially for FBS, where longer exposure correlated with enhanced reductions. This aligns with pharmacodynamic expectations, as cumulative antioxidant and anti-inflammatory effects would logically require extended periods to manifest at clinically significant levels. This point also reinforces that future trials should consider extended durations to capture the full therapeutic potential of *P. atlantica*. The discussion of safety and tolerability is also noteworthy. None of the included studies reported serious adverse effects associated with P. atlantica supplementation, even at higher doses (up to 4 g/day). This favorable safety profile, combined with its moderate glycemic benefits, positions P. atlantica as a viable adjunctive therapy for individuals with poorly controlled T2DM or those seeking plant-based alternatives. However, the lack of large-scale, long-term safety data remains a gap in the evidence and should be addressed in future investigations. Despite the strengths of this meta-analysis—including rigorous selection criteria, sensitivity analysis, and exploration of heterogeneity—there are limitations that warrant acknowledgment. First, the number of included RCTs is relatively small, and all were conducted in Iran and Iraq, which may limit the generalizability of the findings to other populations with different dietary habits, genetic profiles, and healthcare systems. Second, several studies exhibited unclear or high risks of bias in domains such as blinding and outcome reporting. Although these issues were considered in the risk assessment, they may still introduce confounding effects and reduce confidence in pooled estimates. In addition, heterogeneity remained substantial for both FBS and HbA1c outcomes ($I^2 > 90\%$). While subgroup analyses and meta-regression partially explained this variation, unmeasured factors such as baseline glycemic control, diet, and concurrent medications may also have contributed. Moreover, some trials used different formulations and delivery methods—capsules, oil, or powder—which could influence absorption and pharmacokinetics. These methodological differences underscore the need for standardized clinical protocols and phytochemical characterization of P. atlantica interventions. A further consideration involves the complex interaction between phytochemicals and gut microbiota. Although not explored in the current studies, it is well-established that dietary polyphenols can modulate gut microbiota composition, which in turn affects glucose metabolism and insulin sensitivity. Future trials incorporating microbiome analyses could provide valuable insights into whether P. atlantica exerts part of its antidiabetic effect through gut-mediated mechanisms. In summary, this meta-analysis provides evidence that Pistacia atlantica supplementation can significantly reduce fasting blood sugar and moderately lower HbA1c levels in individuals with type 2 diabetes, especially when used over extended durations. The antidiabetic effects appear to be mediated through multiple pathways, including inhibition of carbohydrate-digesting enzymes, antioxidant and anti-inflammatory activity, and improved insulin sensitivity. While the findings are promising, larger, multicenter, and more methodologically robust clinical trials are needed to confirm these results and establish optimal dosages, treatment durations, and patient populations who are most likely to benefit from this traditional remedy.

Conclusion

This meta-analysis demonstrates that *Pistacia atlantica* supplementation significantly improves glycemic control in patients with type 2 diabetes, particularly when administered for durations of eight weeks or longer. The intervention was associated with meaningful

reductions in fasting blood sugar and moderate improvements in HbA1c. These effects are likely mediated through anti-inflammatory, antioxidant, and insulin-sensitizing mechanisms. Despite some heterogeneity and methodological limitations in the included studies, the overall findings support the potential role of *Pistacia atlantica* as a safe and effective adjunct to conventional diabetes therapies. Further large-scale, standardized trials are recommended to confirm these benefits and guide clinical use.

Declarations

Acknowledgements: The authors are highly thankful to Mr. Farhang Hameed Awlqadr for critically reviewing the text of this paper. Furthermore, all authors of the manuscript thank and acknowledge their respective Universities and Institutes.

Author Contributions: D.H.A: Writing—original draft, Conceptualization, Methodology, Software. H.L.F: Writing—original draft, Conceptualization, Software. F.H.A. and H.H.R.: Corresponding author, supervision, Validation, Writing—review & editing. S.A.Q: Conceptualization, methodology. All authors reviewed the manuscript

Informed Consent Statement: This study did not involve human participants, and therefore, informed consent was not required.

Conflict of interests: No potential conflict of interest relevant to this article was reported.

Clinical trial number: not applicable.

Ethical Approval: This research did not involve human participants, animal subjects, or any material that requires ethical approval.

Funding: "The authors received no financial support for the research, authorship, and/or publication of this article".

Data Availability Statement: This statement does not apply to this article.

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Figures

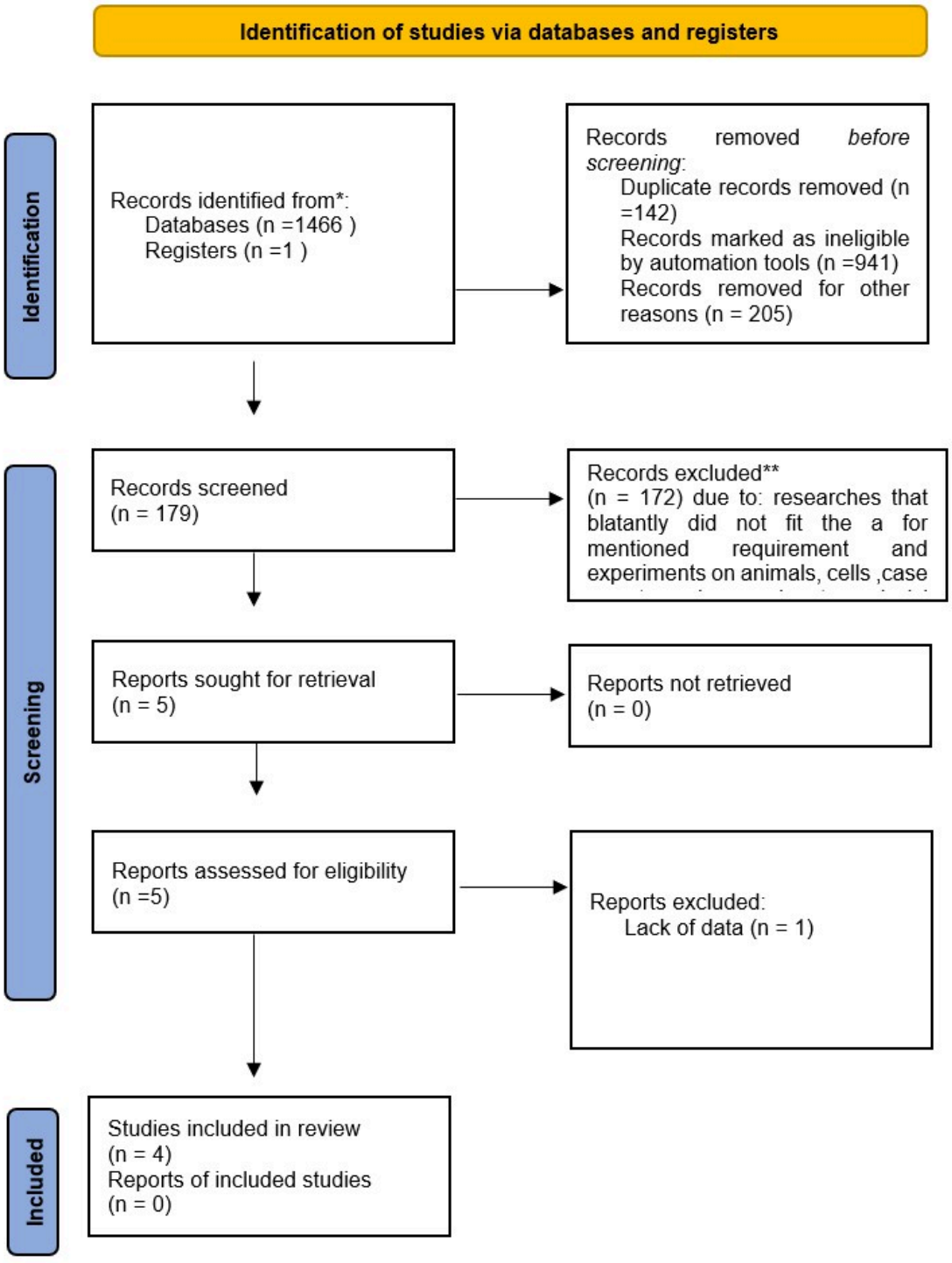


Figure 1

Flow chart of the process of the study selection

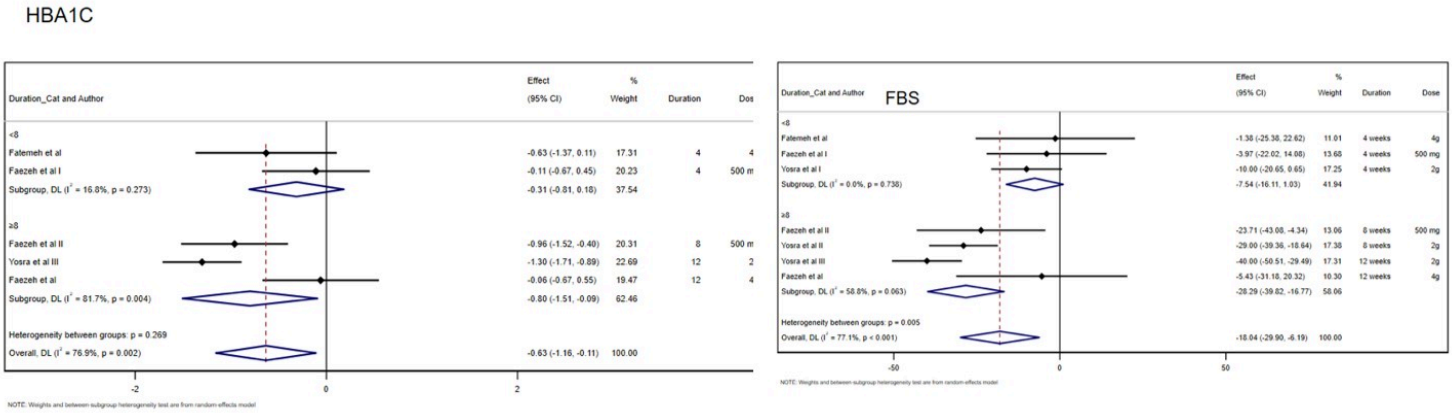


Figure 2

The effect of Pistacia atlantica supplementation FBS and HbA1c according to Intervention doses.

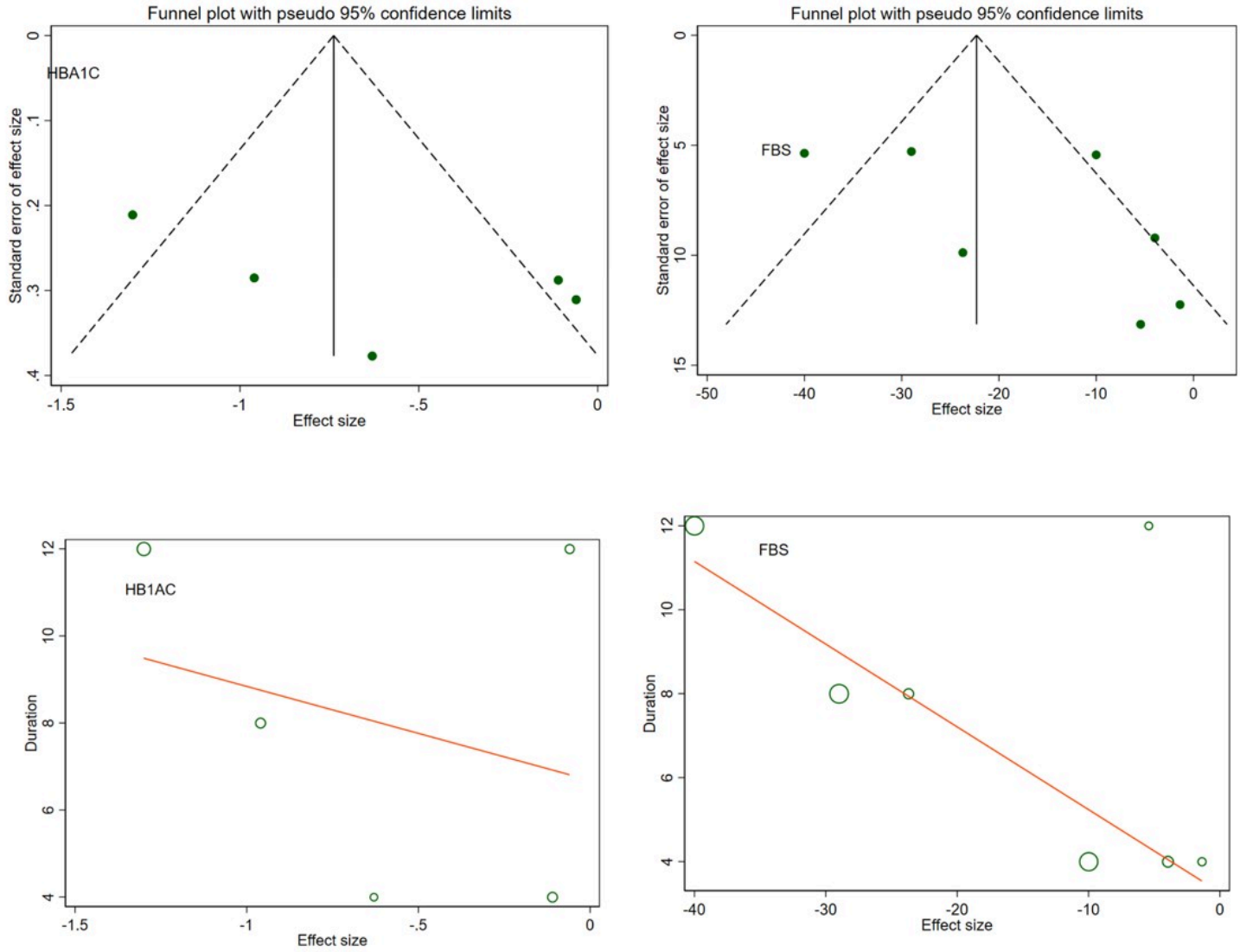


Figure 3

Meta regression and funnel plot for FBS and HbA1c.

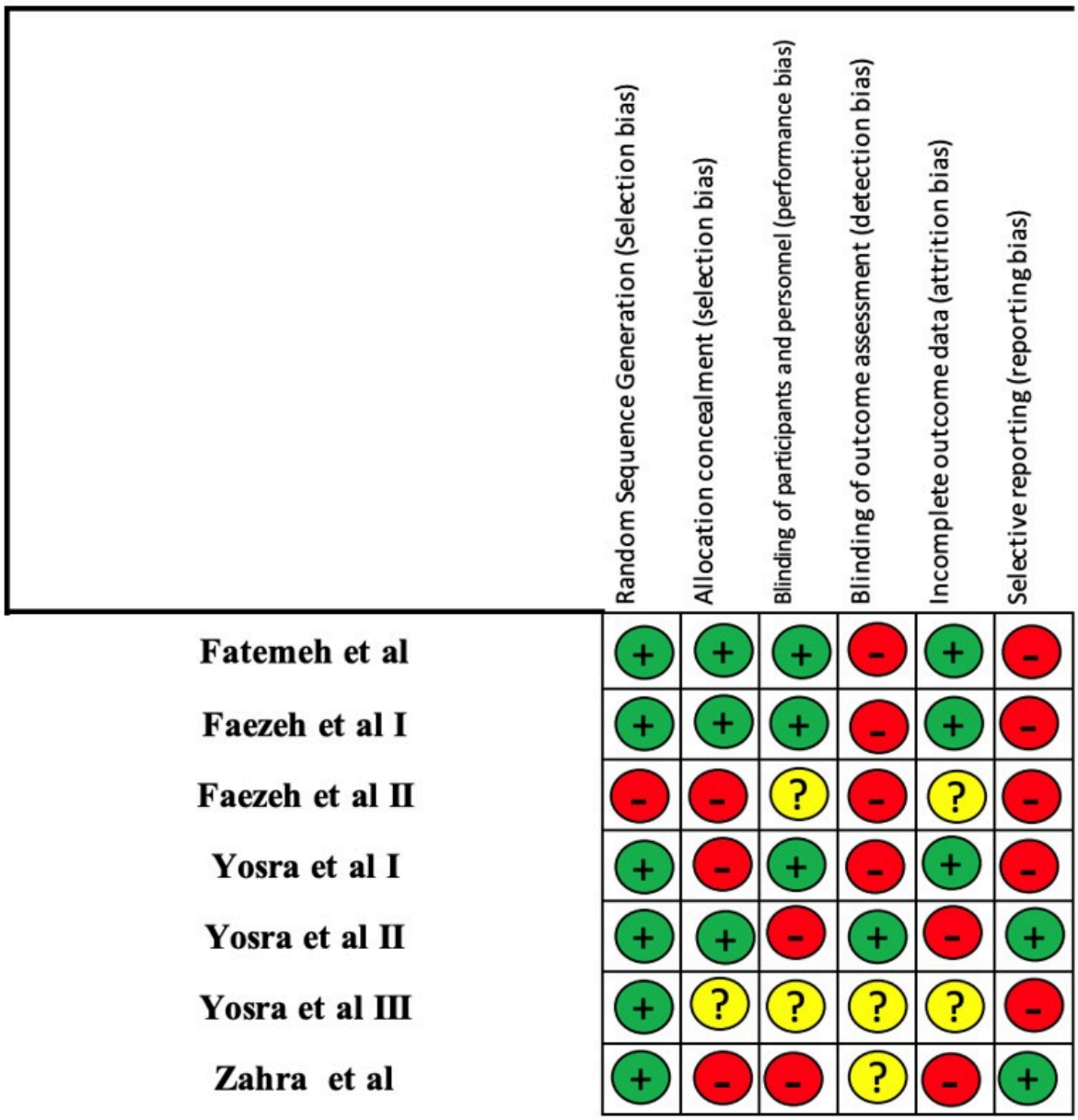


Figure 4

Risk of bias summary for included studies. Green (+) = low risk, yellow (?) = unclear risk, red (−) = high risk across key domains: selection, performance, detection, attrition, and reporting bias.

Supplementary Files

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