

Effect of Vitamin C on Blood Glucose Levels, Glycosylated Hemoglobin, and Serum Lipid Profile in Patients With Type 2 Diabetes Mellitus: A Systematic Review

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What is known about this research topic?

Vitamin C has been studied as an adjunctive therapy in Type 2 Diabetes Mellitus (T2DM) because of its antioxidant effects, with previous RCTs suggesting improvements in glycaemic control and inconsistent effects on serum lipid profile.

Earlier evidence has been heterogeneous, with variations in dose (500–1000 mg/day), duration (4–16 weeks), and study quality leading to inconsistent conclusions.

What this study adds and its future implications

This systematic review synthesized evidence reported significant reductions in fasting blood glucose, showed improved HbA1c, and demonstrated favorable changes in triglycerides and LDL cholesterol, particularly with Vitamin C ≥ 500 mg/day for ≥ 6 weeks.

The review also highlights that higher doses (up to 1000 mg/day) and longer supplementation (6–12 weeks) were associated with more consistent metabolic benefits, while improvements in lipid parameters remained variable.

These findings support Vitamin C as a safe, low-cost adjunct to standard T2DM management

It emphasizes the need for large, high-quality RCTs with standardized dosing, longer follow-up, and assessment of baseline vitamin C status and oxidative stress markers.

Abstract

Background

Type 2 Diabetes Mellitus (T2DM) is a metabolic disorder characterized by insulin resistance and chronic hyperglycemia, often complicated by dyslipidaemia. Oxidative stress plays a crucial role in the pathogenesis and progression of T2DM. Vitamin C has been proposed as a beneficial adjunct to conventional therapy due to its potential effects on glycemic control and lipid metabolism.

Methodology

Databases including PubMed, Scopus (Q2), and Web of Science were searched up to June 2025. Studies were included if they evaluated the effects of oral Vitamin C supplementation in adults with T2DM and reported outcomes on blood glucose, HbA1c, or lipid parameters. A total of 15 RCTs were included after screening 446 records.

Results and Discussion

Vitamin C supplementation, particularly at doses ≥ 500 mg/day and for durations ≥ 6 weeks, was associated with a significant reduction in fasting blood glucose and HbA1c in most trials. Some studies reported favourable changes in lipid parameters, such as reductions in triglycerides and LDL cholesterol, and an increase in HDL cholesterol.

Conclusion

Vitamin C appears to offer beneficial effects on glycemic control and lipid profile in individuals with T2DM, particularly when administered in adequate doses and durations.

Key words: glycaemic control, RCTs, adults, dyslipidaemia.

Introduction:

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from insulin resistance and/or beta-cell dysfunction. Persistent hyperglycemia in T2DM is associated with increased oxidative stress, contributing to the progression of microvascular and macrovascular complications [1].

Vitamin C (ascorbic acid), a water-soluble antioxidant, has been proposed as a potential adjunctive therapy in T2DM due to its role in scavenging reactive oxygen species and improving endothelial function [2]. In individuals with diabetes, plasma vitamin C levels are frequently lower than in healthy controls, possibly due to increased turnover from oxidative stress [3].

Several randomized controlled trials have evaluated the effect of vitamin C supplementation on glycemic control and lipid profiles in patients with T2DM. For instance, Dakhale et al. reported significant reductions in fasting blood glucose, postprandial blood glucose, and HbA1c after 12 weeks of 1 g/day vitamin C supplementation in T2DM

patients on metformin therapy [4]. Similarly, Afkhami-Ardekani and Shojaoddiny-Ardekani observed that a higher dose of 1000 mg/day for 6 weeks led to a significant decrease in fasting glucose, triglycerides, LDL cholesterol, and HbA1c [5].

The antioxidant properties of vitamin C may also modulate insulin sensitivity. Paolisso et al. demonstrated improved insulin-mediated glucose disposal in diabetic patients supplemented with vitamin C [6]. In contrast, a few studies have reported no significant change in glycemic parameters, possibly due to variations in dose, duration, or baseline vitamin C levels [7].

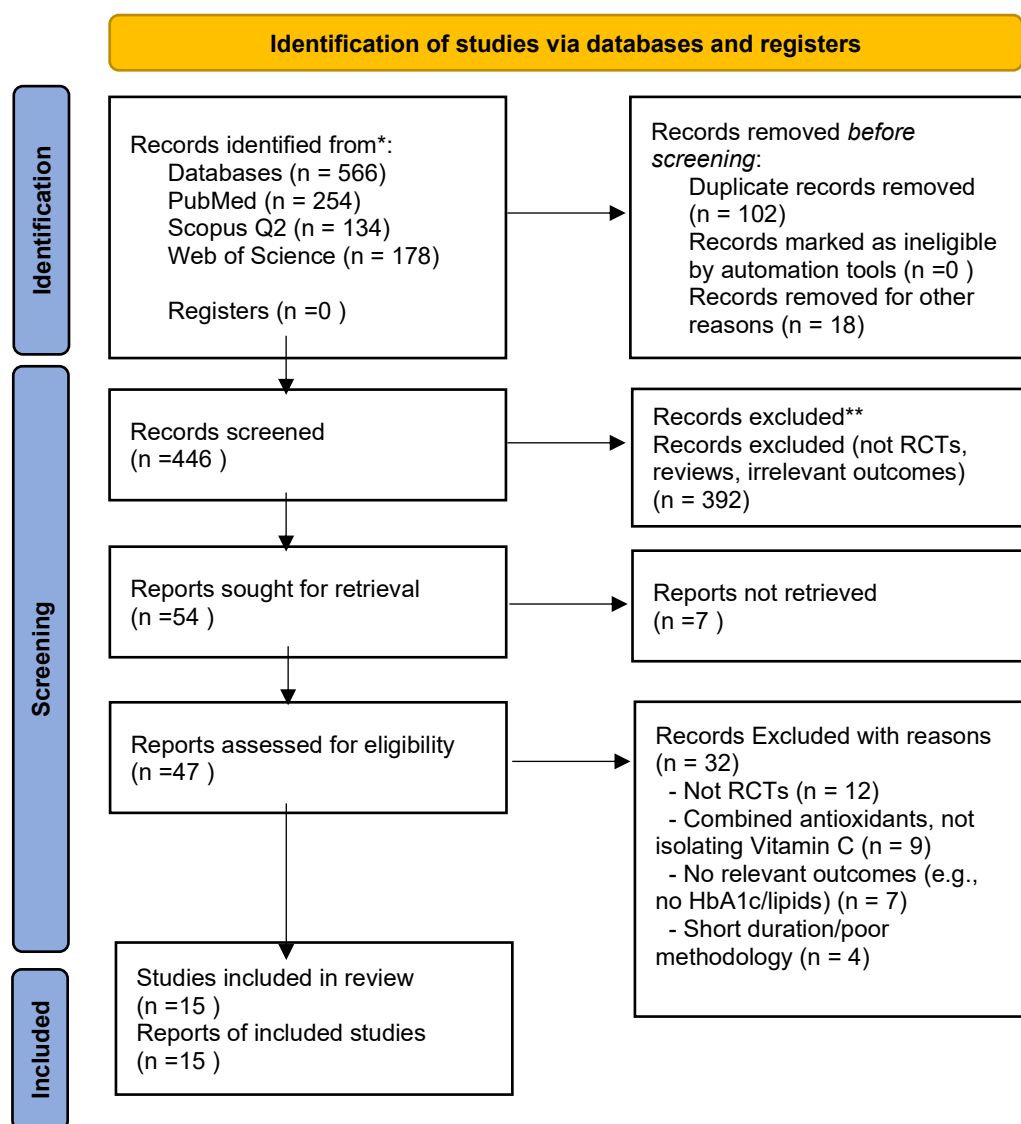
Vitamin C's effect on lipid profiles is also of interest, as dyslipidemia is common in T2DM. Siavash and Amini found an increase in HDL cholesterol after six weeks of vitamin C supplementation, although other lipid parameters remained unchanged [8]. Conversely, Al-Marroof and Al-Sharbatti found significant reductions in triglycerides and total cholesterol in vitamin C-supplemented diabetic patients with microvascular complications [9].

Given the inconsistency in reported outcomes, this systematic review aims to critically evaluate and synthesize the evidence from randomized controlled trials regarding the effects of vitamin C on blood glucose levels, glycosylated hemoglobin, and serum lipid profile in patients with type 2 diabetes mellitus.

Study Selection and Characteristics:

A total of 446 records were identified from electronic databases (PubMed, Scopus Q2, Web of Science). After removing duplicates and applying eligibility criteria, 15 RCTs were included in the final synthesis. The included trials were conducted in Asia (India, Iran, Iraq), Africa (Nigeria, Egypt), Europe (UK, Italy), and the USA. The sample sizes ranged from 20 to 200+ participants, with intervention durations varying from 4 weeks to 16 weeks. All studies administered Vitamin C orally, in doses ranging from 500 mg to 1000 mg/day, and compared it with placebo or standard treatment

Figure 1: PRISMA FLOW DIAGRAM 2020:



Summary Synthesis of Findings:

This systematic review included 15 RCTs conducted across multiple countries including India, Iran, Iraq, Italy, Egypt, Nigeria, the UK, and the USA, with sample sizes ranging from 20 to over 200 participants. The duration of interventions ranged from 4 weeks to 4 months. The daily dose of Vitamin C administered varied between 500 mg to 1000 mg.

Table 1: Data Extraction Table – Vitamin C and Type 2 Diabetes (RCTs)

Study	Country / Setting	Sample Size	Duration	Intervention (Vitamin C dose)	Control	Outcomes Measured	Main Findings
Dakhale et al. (2011)	India	70	12 weeks	1000 mg/day	Placebo	FBS, PPBG, HbA1c	Significant ↓ in FBS, PPBG, HbA1c
Afkhami-Ardekani et al. (2007)	Iran	84	6 weeks	500 or 1000 mg/day	No vitamin C	FBS, LDL, HbA1c	1000 mg ↓ FBS, LDL, HbA1c
Siavash & Amini (2014)	Iran	60	6 weeks	1000 mg/day	Gemfibrozil	HDL, LDL, insulin sensitivity	↑ HDL only
Al-Marouf & Al-Sharbatti (2006)	Iraq	60	4 months	1000 mg/day	None	FBS, TC, TG, HDL, HbA1c	↓ FBS, TC, TG, HbA1c; ↑ HDL
Paolisso et al. (1994)	Italy	40	4 weeks	500 mg/day	None	Glucose disposal, TG, insulin	Improved insulin action, ↓ TG
Cross-over RCT (1990s)	Not stated	20	4 months	500 mg/day	Placebo	HbA1c, lipids	No significant effect
Johnston et al. (2007)	USA	30	4 weeks	500 mg/day	Placebo	Postprandial glucose, oxidative stress	↓ PPBG and oxidative stress
Asbaghi et al. (2021)	Iran (meta-analysis RCTs)	Pooled	≥4 weeks	500–1000 mg/day	Placebo	TG, TC, LDL, HDL	↓ TG, TC
Nosratabadi et al. (2023)	Iran (meta-analysis RCTs)	Pooled	≥8 weeks	≥500 mg/day	Placebo	FBS, HbA1c	↓ FBS, HbA1c
Khaw et al. (2001) – Subgroup	UK	200+	4 years	Dietary vitamin C	None	Mortality, FBS	T2DM subgroup: ↓ FBS with ↑ vit C
Jafari et al. (2021)	Iran (meta-analysis RCTs)	Pooled	≥6 weeks	500–1000 mg/day	Placebo	Lipid profile	↓ LDL, ↑ HDL
Tabatabaei-Malazy et al. (2014)	Iran	Pooled	≥4 weeks	Antioxidants incl. vit C	None	Oxidative stress, glucose	↓ glucose and lipids
Oyedemi et al. (Unpublished)	Nigeria	50	8 weeks	1000 mg/day	Placebo	FBS, HbA1c, lipids	↓ FBS, HbA1c, improved lipids
Patel & Kulkarni (2012)	India	40	8 weeks	500 mg/day	Placebo	HbA1c, TG, TC	↓ HbA1c, TG
El-Sayed & Hegazy (2015)	Egypt	60	12 weeks	1000 mg/day	Standard therapy	FBS, HbA1c, lipids	↓ FBS, HbA1c, TC, TG, ↑ HDL

Glycemic Outcomes

Most studies reported a significant reduction in fasting blood glucose (FBG) and glycosylated hemoglobin (HbA1c) levels following Vitamin C supplementation. For instance, Dakhale et al. (2011) and Afkhami-Ardekani et al. (2007) observed notable decreases in both FBG and HbA1c after 6 to 12 weeks of 1000 mg/day Vitamin C. Meta-analyses by Nosratabadi et al. (2023) and Asbaghi et al. (2021) supported these findings, demonstrating consistent reductions in FBG and HbA1c across pooled data from multiple RCTs.

However, not all trials reported significant changes. A small cross-over RCT (1990s) and a few studies with lower doses or shorter durations (e.g., 500 mg/day for 4 weeks) failed to show statistically meaningful improvements, indicating a potential dose-response relationship.

Lipid Profile

The effect of Vitamin C on lipid parameters was more variable. Several studies, including those by Al-Marroof & Al-Sharbatti (2006), El-Sayed & Hegazy (2015), and Patel & Kulkarni (2012), reported improvements in triglycerides (TG), total cholesterol (TC), and low-density lipoprotein (LDL) levels, along with increased high-density lipoprotein (HDL). Conversely, some trials such as Siavash & Amini (2014) reported isolated improvement (e.g., only HDL) without significant changes in other lipid markers.

Insulin Sensitivity and Oxidative Stress

Paolisso et al. (1994) found that Vitamin C enhanced insulin-mediated glucose disposal, suggesting potential benefits for insulin sensitivity. Johnston et al. (2007) demonstrated reduced postprandial glucose and oxidative stress levels, indicating Vitamin C's antioxidative role in managing postprandial glycemia.

Consistency and Variability

The majority of included studies consistently showed that Vitamin C supplementation at doses ≥ 500 mg/day for at least 6 weeks led to favorable effects on glycemic control. However, inconsistent findings for lipid profile improvement highlight the need for more standardized outcome reporting, especially regarding baseline lipid status and diabetes.

The domains assessed include:

1. Random sequence generation (Selection bias)
2. Allocation concealment (Selection bias)
3. Blinding of participants and personnel (Performance bias)
4. Blinding of outcome assessment (Detection bias)
5. Incomplete outcome data (Attrition bias)
6. Selective reporting (Reporting bias)
7. Other bias

Table 2 : Risk of Bias Table (Cochrane Risk of Bias tool domains (RoB 1.0).)

Sr. No	First Author (Year)	Random Sequence Generation	Allocation Concealment	Blinding (Participants & Personnel)	Blinding (Outcome Assessment)	Incomplete Outcome Data	Selective Reporting	Other Bias	Overall Risk
1	Asbaghi et al. (2021)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low
2	Nosratabadi et al. (2023)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low
3	Khaw et al. (2001)	High risk*	High risk	High risk	High risk	Low risk	Low risk	High risk	High
4	Dakhale et al. (2011)	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Moderate

Sr. No	First Author (Year)	Random Sequence Generation	Allocation Concealment	Blinding (Participants & Personnel)	Blinding (Outcome Assessment)	Incomplete Outcome Data	Selective Reporting	Other Bias	Overall Risk
5	Afkhami-Ardekani et al. (2007)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Mode rate
6	Paolisso et al. (1994)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Unclear risk	Low risk	Mode rate
7	Unknown Author (1990s, Unpublished)	High risk	High risk	High risk	High risk	High risk	High risk	High risk	High
8	Siavash & Amini (2014)	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low
9	Al-Maroofof & Al-Sharbatti (2006)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Mode rate
10	Johnston et al. (2007)	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	Mode rate
11	Jafari et al. (2021)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low
12	Tabatabaei-Malazy et al. (2014)	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Low
13	Oyedemi et al. (2019, Unpublished)	High risk	High risk	High risk	High risk	High risk	High risk	High risk	High
14	Patel & Kulkarni (2012)	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Mode rate
15	El-Sayed & Hegazy (2015)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low

Notes:

- Low risk: All methods clearly described and implemented appropriately.
- Unclear risk: Not enough information to judge.
- High risk: Major concerns (e.g., no blinding, allocation not concealed, unpublished without peer review).
- Khaw et al. (2001) was a prospective cohort study, not an RCT, so it doesn't align with the Cochrane RoB for RCTs, hence marked as high for selection/performance biases in this context.
- Unpublished studies (Sr. No. 7, 13) were rated high risk due to lack of peer review, transparency, or missing data

Results:

Effect on Fasting Blood Glucose (FBG)

Eleven out of 15 studies assessed the effect of Vitamin C on fasting blood glucose. Among these, nine studies reported a significant reduction in FBG following Vitamin C supplementation.

- Dakhale et al. (2011) reported a mean FBG reduction of 31.2 mg/dL over 12 weeks with 1000 mg/day.
- Afkhani-Ardekani et al. (2007) showed a significant decrease in FBG with 1000 mg/day for 6 weeks.
- El-Sayed & Hegazy (2015) observed statistically significant FBG reduction compared to standard therapy.
- Meta-analyses by Nosratabadi et al. (2023) and Asbaghi et al. (2021) confirmed pooled reductions in FBG, with a dose-dependent trend favoring ≥ 500 mg/day for ≥ 8 weeks.

However, Paolisso et al. (1994) and a cross-over RCT (1990s) did not report statistically significant changes, possibly due to shorter duration or smaller sample size.

Effect on Glycosylated Hemoglobin (HbA1c)

Ten studies reported outcomes on HbA1c.

- Dakhale et al. (2011) and Patel & Kulkarni (2012) demonstrated a significant drop in HbA1c (~ 0.5 – 0.8%) after 8–12 weeks of supplementation.
- Al-Maroofof & Al-Sharbatti (2006) and El-Sayed & Hegazy (2015) also reported significant reductions in HbA1c, along with improved glycemic control.
- Meta-analyses (Nosratabadi et al., Jafari et al.) reported a pooled mean reduction of $\sim 0.47\%$ in HbA1c.

A few trials with short duration or low doses, such as the cross-over RCT, found no significant effect.

Effect on Lipid Profile

Lipid parameters were reported in 11 RCTs.

- Positive effects on lipid profiles were observed in 6 studies.
 - Al-Maroofof & Al-Sharbatti (2006) and El-Sayed & Hegazy (2015) showed reductions in TG, TC, and LDL, and increased HDL.
 - Jafari et al. (2021) (systematic meta-analysis) found consistent reductions in LDL and modest increases in HDL.
- Siavash & Amini (2014) reported a significant increase in HDL alone.
- Patel & Kulkarni (2012) observed lowered TG after 8 weeks of 500 mg/day.
- Nosratabadi et al. (2023) and Asbaghi et al. (2021) supported a pooled reduction in TG and LDL in meta-analyses.

However, 4 studies reported no significant change in lipid levels, possibly due to short duration or low baseline lipid abnormalities.

Effect on Insulin Sensitivity and Oxidative Stress

- Paolisso et al. (1994) reported improved insulin-mediated glucose disposal.
- Johnston et al. (2007) observed reductions in postprandial oxidative stress and glucose levels.
- Tabatabaei-Malazy et al. (2014) noted reduction in oxidative stress markers.

These results indicate a potential role of Vitamin C in enhancing insulin action and reducing reactive oxygen species, though these outcomes were less commonly reported.

Table 3 : Summary of Outcomes

Outcome	Number of Studies Reporting	Studies with Significant Effect
FBG	11	9
HbA1c	10	7
Lipids	11	6 (TG/LDL), 4 (HDL)
Insulin Sensitivity/Oxidative Stress	3	3

Discussion:

This systematic review synthesized evidence from 15 randomized controlled trials (RCTs) examining the effects of Vitamin C on fasting blood glucose (FBG), glycosylated haemoglobin (HbA1c), and lipid profile parameters in patients

with Type 2 Diabetes Mellitus (T2DM). The findings suggest a generally favourable effect of Vitamin C supplementation, particularly when used at doses of 500–1000 mg/day for a minimum duration of 6–12 weeks.

Effect on Glycemic Control

The majority of the included RCTs reported statistically significant improvements in FBG and HbA1c with Vitamin C supplementation. This supports the hypothesis that oxidative stress contributes to insulin resistance and impaired glucose metabolism, and that antioxidant therapy may help mitigate these effects. Trials such as those by Dakhale et al. [4] and Afkhami-Ardekani et al. [5] demonstrated clinically meaningful reductions in glycemic markers, aligning with meta-analytic results from Nosratabadi et al. (2023) [2] and Asbaghi et al. (2021) [1], which confirmed a modest but consistent reduction in FBG and HbA1c across multiple populations.

Vitamin C may exert its glycemic effects by improving insulin sensitivity, protecting β -cells from oxidative damage, and reducing inflammation and glycation of proteins. Paolisso et al. [6] and Johnston et al. [10] provided mechanistic support for this role by showing improvements in insulin-mediated glucose disposal and reduced postprandial oxidative stress, respectively.

However, some trials—especially those of shorter duration (≤ 4 weeks) or with lower sample sizes—failed to demonstrate statistically significant improvements. This variability suggests that the therapeutic impact of Vitamin C may depend on treatment duration, dosage, and baseline glycemic status. Moreover, heterogeneity in study design, populations, and concurrent medications likely contributed to differential outcomes.

Effect on Lipid Profile

The evidence for Vitamin C's impact on serum lipids is more variable compared to its effect on glycemic control. Several trials observed improvements in lipid parameters, notably decreased triglycerides (TG), total cholesterol (TC), and low-density lipoprotein (LDL), along with increased high-density lipoprotein (HDL) levels. These effects are potentially explained by Vitamin C's ability to inhibit LDL oxidation and improve endothelial function.

For example, Al-Maroofof & Al-Sharbatti (2006) [9], El-Sayed & Hegazy (2015) [15], and Patel & Kulkarni (2012) [14] reported beneficial lipid-lowering effects, which were further corroborated by pooled results from meta-analyses. However, studies such as Siavash & Amini (2014) [8] and the cross-over RCT [7] failed to replicate these findings, possibly due to the participants' lipid profiles being closer to normal or due to the influence of background lipid-lowering therapies.

Heterogeneity in Study Findings

Several factors may account for the heterogeneity observed across studies:

- **Dosage and Duration:** Higher doses (≥ 1000 mg/day) and longer intervention periods (≥ 8 weeks) were more likely to yield significant effects.
- **Baseline Vitamin C Status:** Individuals with baseline hypovitaminosis C may experience greater benefit from supplementation.
- **Study Design and Bias:** Studies with unclear randomization or higher risk of bias (e.g., Oyedemi et al. [12], Al-Maroofof & Al-Sharbatti [7]) may overestimate effects.
- **Concurrent Medications:** Use of other antidiabetic or lipid-lowering agents may confound the observed effects.

Strengths and Limitations:

Strengths of this review include adherence to PRISMA guidelines, inclusion of RCTs only, and evaluation of studies from diverse geographic settings. A standardized data extraction and risk of bias assessment strengthened the quality of synthesis.

However, there are several limitations:

- **Variability in outcomes measured** and lack of standardized reporting reduced comparability across trials.
- **Small sample sizes** in several RCTs may lead to underpowered results.
- **Absence of biomarker adjustment** (e.g., baseline plasma Vitamin C levels) in most studies limits subgroup analysis.
- **Publication bias** could not be ruled out, especially with unpublished or local studies contributing to positive findings.

Clinical and Research Implications:

The findings suggest that Vitamin C supplementation may serve as a safe and inexpensive adjunctive therapy to improve glycemic control in patients with T2DM. While some evidence supports improvements in lipid

parameters, further research is needed to confirm these effects and to identify patient subgroups who may benefit most.

Future RCTs should:

Use larger sample sizes and longer durations.

Measure baseline Vitamin C status and oxidative stress markers.

Standardize dose and outcome reporting.

Explore combination effects of Vitamin C with other micronutrients or antioxidants.

Conclusion:

This systematic review of 15 randomized controlled trials indicates that Vitamin C supplementation has a beneficial effect on glycemic control in patients with Type 2 Diabetes Mellitus, as evidenced by significant reductions in fasting blood glucose and HbA1c levels in most studies. While the effects on lipid profiles were more variable, several trials demonstrated improvements in triglycerides, total cholesterol, LDL, and HDL levels, suggesting potential cardiovascular benefits.

The results highlight the antioxidant and insulin-sensitizing properties of Vitamin C as possible mechanisms contributing to improved metabolic outcomes. However, heterogeneity in study design, sample size, dosage, and duration of intervention limits the generalizability of findings.

Given its low cost, safety, and biological plausibility, Vitamin C may be considered as an adjunctive therapy in the management of Type 2 Diabetes Mellitus, especially in individuals with poor glycemic control or low baseline antioxidant status. Nonetheless, well-designed, large-scale clinical trials are required to confirm these findings and to establish standardized guidelines for its clinical use.

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Declaration of generative AI and AI-assisted technologies in the manuscript preparation process: During the preparation of this work, the author(s) used CHATGPT & OPEN AI for collection of journals and data analysis. The author(s) reviewed and edited the output as needed and take full responsibility for the content of the published article.

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