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The Efficacy of Oral Antioxidant on Glycemic Index and Lipid Profile in Patients With Type II Diabetes Mellitus: A Systematic Review

Ni Made Wini Jayesthiwi Wanami Putri[1]*, Sagung Intan Saraswati[2], Komang Vika Nariswari Ratna Kinasih[3], Ida Ayu Santhi Pertiwi Manuaba[4]
Universitas Udayana, Indonesia
Email: thiwiwanami@gmail.com*

ABSTRACT

Background: Type 2 diabetes is caused by insulin resistance or insufficient insulin for glucose metabolism, with its pathogenesis linked to free radical exposure. High free radical concentrations and low antioxidant levels increase the risk of complications in diabetes mellitus. Despite this, antioxidant supplementation in diabetic patients remains uncommon. This systematic review explores the efficacy of antioxidant supplementation on therapeutic outcomes in type II diabetes mellitus patients. Methods: A literature search was conducted from January to February 2024 across three databases: PubMed, Science Direct, and Google Scholar. Inclusion criteria focused on adult patients aged >18 years diagnosed with type II diabetes mellitus, randomized controlled trials (RCTs), studies on antioxidant supplementation (excluding non-supplement forms), and studies covering glycemic indices (FPG, PPG, 2hPG, HbA1c) and lipid profiles (LDL, HDL, cholesterol, TG) published from 2014 to 2024 in English or Indonesian. Pediatrics and in vitro/in vivo studies were excluded. Results: The bias risk was assessed using the 2020 PRISMA guidelines. Six journals met the inclusion criteria. The review found that supplementation with turmeric, ellagic acid, Nigella sativa, zinc, vitamins C, and E significantly affected glucose and lipid levels in type II diabetes mellitus patients. However, selenium supplementation showed inconsistent results regarding blood glucose levels and lipid profiles, indicating the need for further investigation. Conclusion: Supplementation with turmeric, ellagic acid, Nigella sativa, zinc, vitamins C, and E is effective in controlling blood glucose levels and improving lipid profiles in type II diabetes mellitus patients.

KEYWORDS Antioxidant; Type II Diabetes Mellitus; Glycemic; Lipid

INTRODUCTION

Diabetes mellitus is a chronic metabolic disease characterized by elevated blood glucose levels. It is classified into type 1, type 2, and gestational diabetes, with type 2 diabetes having the highest prevalence. Type 2 diabetes typically occurs in adults as a result of insulin resistance or insufficient insulin availability for effective glucose metabolism (World Health Organization, 2023). Insulin resistance is defined as a reduced cellular response to insulin, prompting the body to produce more insulin to meet metabolic demands. Over time, this chronic condition leads to damage of pancreatic beta cells, which are responsible for insulin production. Insulin resistance and absolute insulin deficiency can cause severe damage to organs such as the heart, blood vessels, eyes, kidneys, and nerves (Centers for Disease Control and Prevention, 2022).

According to the World Health Organization (WHO) in 2019, approximately 422 million people worldwide were living with diabetes mellitus, with 1.5 million deaths directly attributed to diabetes-related complications annually. In 2017, the global prevalence reached

6,059 cases per 100,000 population. In Asia—including China, India, Japan, South Korea, Taiwan, Saudi Arabia, Iran, and Australia—the prevalence was reported at 1,961 cases per 100,000 people, while in the Americas it reached 7,060 cases per 100,000 people.[3] A study conducted by Yan et al. in 2022 in China reported that the average age of diabetes onset was over 65 years, with a prevalence of 18.80% (Yan et al., 2022).

Complications of diabetes mellitus occur in both type 1 and type 2 diabetes and contribute significantly to morbidity and mortality. These complications are classified as acute or chronic. Chronic complications involve both microvascular and macrovascular structures and are frequently associated with metabolic syndrome. Metabolic syndrome includes obesity (waist circumference >40 inches in men and >35 inches in women), elevated lipid profiles (triglycerides, LDL, and total cholesterol), decreased HDL levels, hypertension, and increased glycemic levels.[5] This syndrome increases the risk of cardiovascular diseases, such as atherosclerosis, and contributes to multi-organ damage. Glycemic and lipid control can be achieved through lifestyle modifications, including regular physical activity, weight management, reduced intake of high-carbohydrate foods, consumption of antioxidant-rich foods, and adherence to low-fat diets (Herningtyas & Ng, 2019).

Antioxidants are substances that protect cells from damage caused by free radicals. They are molecules capable of preventing or inhibiting oxidative reactions within body cells. Oxidative processes generate free radicals, known as Reactive Oxygen Species (ROS), which initiate cellular damage. Antioxidants neutralize these free radicals and promote overall health. They may be produced internally (endogenous) or obtained externally (exogenous) through food and supplements. Exogenous antioxidants are commonly found in vegetables, fruits, eggs, nuts, and other dietary sources (Avcil, 2022a; Avcil, 2022b; Khadim & Al-Fartusie, 2021).

The pathogenesis of diabetes mellitus and other chronic diseases is closely associated with free radical exposure. Reduced antioxidant levels and increased concentrations of free radicals elevate the risk of diabetes-related complications (Ghasemi-Dehnoo et al., 2020; Suresh et al., 2021). Endogenous antioxidants such as catalase and superoxide dismutase (SOD) play essential roles in reducing oxidative stress in pancreatic beta cells, thereby protecting them from pro-inflammatory cytokines, hydrogen peroxide, and streptozotocin. Antioxidants such as alpha-lipoic acid and vitamins C and E can increase glutathione (GSH) levels by enhancing cysteine uptake, contributing to positive therapeutic effects in diabetes mellitus. Additionally, antioxidants have been reported to support weight reduction and lipid profile improvement (Balbi et al., 2018). Flavonoids, including quercetin and curcumin, inhibit ROS formation and provide therapeutic benefits for patients with diabetes (Yi et al., 2023). Alpha-linolenic acid and omega-3 fatty acids, derived from fruits and vegetables, are also associated with reduced risk of diabetes and its complications (Delpino et al., 2022). Research on antioxidants in diabetes mellitus underscores their therapeutic potential in improving glycemic indices and preventing complications, particularly through lipid profile optimization. This review therefore explores the efficacy of antioxidants in glycemic control and lipid profile management among patients with type II diabetes mellitus.

The urgency of this systematic review arises from several converging factors. First, the rising global prevalence of type 2 diabetes and its complications necessitates comprehensive,

evidence-based management strategies that extend beyond conventional pharmacotherapy. Second, the well-established role of oxidative stress in diabetes pathogenesis suggests that antioxidant interventions may offer valuable adjunctive benefits, yet these remain underutilized in clinical practice. Third, the widespread availability of over-the-counter antioxidant supplements creates a pressing need for evidence-based guidance to assist patients and clinicians in making informed decisions. Fourth, inconsistent findings across individual studies require systematic synthesis to clarify the overall evidence base and to identify areas requiring further investigation.

The novelty of this systematic review lies in its comprehensive evaluation of multiple antioxidant interventions within a unified analytical framework, its rigorous application of the PRISMA guidelines and Cochrane risk-of-bias assessment, and its focus on both glycemic and lipid outcomes in patients with type 2 diabetes. Unlike previous reviews that focused on single antioxidants or limited outcome measures, this review synthesizes evidence across six antioxidant interventions (turmeric, ellagic acid, Nigella sativa, zinc, selenium, and vitamins C and E) and evaluates both glycemic indices (fasting plasma glucose, postprandial glucose, and HbA1c) and lipid profiles (LDL, HDL, total cholesterol, and triglycerides). This comprehensive approach enables comparative evaluation of different antioxidants and identification of those with the strongest evidence base.

This systematic review aims to evaluate the efficacy of oral antioxidant supplementation on glycemic control and lipid profiles in patients with type II diabetes mellitus. Specifically, the review seeks to: (1) identify randomized controlled trials examining antioxidant supplementation in patients with type 2 diabetes; (2) assess the quality and risk of bias of included studies using standardized tools; (3) synthesize evidence regarding the effects of different antioxidants on glycemic indices; (4) synthesize evidence regarding the effects of different antioxidants on lipid profiles; and (5) identify antioxidants with consistent evidence of benefit versus those requiring further investigation. Through these objectives, this review contributes to clinical practice by providing evidence-based guidance on antioxidant supplementation in diabetes management and identifying priorities for future research to address existing knowledge gaps.

METHOD

The literature search was conducted from January to February 2024. The data used in this study consisted of both national and international journal articles. The study selection in this followed the guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The systematic review utilized three databases: PubMed, Science Direct, and Google Scholar. The Boolean operators and keywords applied in the search were: Antioxidant AND Type 2 Diabetes AND Lipid Profile AND Glycemic Index. To assess the risk of bias in randomized controlled trials, the Cochrane Risk of Bias 2 (RoB 2) tool was applied. This tool is divided into five domains, each containing several questions focusing on various aspects of trial design, implementation, and reporting. The overall risk of bias assessment categories was low risk, some concerns, and high risk.

RESULT AND DISCUSSION

Based on the literature search across the three databases using keywords adjusted to Medical Subject Heading (MeSH) terms, 798 articles were identified as relevant. Titles related theme screening excluded 709 articles, leaving 89 articles. Further selection based on study abstracts and eligibility criteria resulted in six articles suitable for use in the systematic review. After a comprehensive text review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), a total of six studies were identified and used as references for writing this systematic review (Figure 1).

The characteristics of the articles used in this systematic review consist of six Randomized Controlled Trial (RCT) studies published between 2014 and 2024 (Table 1). The study populations in these articles came from three countries. Four studies were conducted in Iran at universities, research institutes, and hospitals. One study was conducted in Egypt at hospitals, and another study was carried out in Palestine. All participants were patients with type 2 diabetes mellitus, with ages ranging from 18 to 80 years.

One study was assessed as having a low risk of selection bias in the randomization process with appropriate random sequence generation and allocation concealment methods. Moustafa et al. were considered to have a high risk of selection bias because they reported the method of random sequence generation but did not use allocation concealment. One study was judged to have concerns about bias due to deviations from the intended intervention, as they did not report blinding implementation. All six studies were assessed as having a low risk of attrition bias in data collection and outcome measurement methods. Three studies (Adab et al, Faghihi et al, and Moustafa et al) were considered to have concerns about reporting bias (based on domain 5 of the bias assessment), based on glycemic index outcomes that did not align with the hypothesis (worsening of the glycemic index). Overall, there were three studies with a low risk of bias, two studies with concerns about bias, and one study with a high risk of bias (Figure 2).

Table 1. Characteristics of Included Studies

No.	Author, year	Country	Study design	Patient (n=) and characteristic	Dose and duration	Main finding
1	Adab, Z, et al., 2018.[15]	Iran	Randomized, double blind clinical trial	80 patients with type 2 diabetes mellitus, aged 30-70 years, without insulin therapy.	2,100 mg turmeric powder (3 capsules of 700 mg turmeric after meals) daily for 8 weeks.	• There was no statistically significant reduction in fasting blood glucose, HbA1c, insulin, and HOMA-IR (p value > 0.05). • There was a significant reduction in TG levels (p value < 0.001). Total cholesterol remained unchanged (p value < 0.001). HDL-c decreased in both groups after intervention, but this decrease was only

						significant in the placebo group (p value = 0.02). LDL-c decreased significantly in the intervention group (p value = 0.009).
2	Faghihi, T, et al., 2014.[16]	Iran	Double-blind randomized placebo-controlled trial	65 patients with type 2 diabetes mellitus, aged 18-70 years.	200 µg/day selenium supplement once a day for 3 months.	• There was an increase in FBS levels and improvement in HbA1c levels. • An increase in HDL and TG levels was found, but there was an improvement in TC and LDL levels in patients who received selenium supplements.
3	Ghadimi, M, et al., 2020.[17]	Iran	Double-blind randomized placebo-controlled trial	44 patients aged 24 – 55 years with type 2 diabetes mellitus (n=44) without insulin therapy.	180 mg of *ellagic acid* capsule once a day for 8 weeks	• Significant reduction in FBS, 2hpp, HbA1c (%), insulin, HOMA-IR, TC, TG, and LDL ($p < 0.05$). • The average change in HDL at the end of the study was not significant in the intervention group ($p > 0.05$).
4	Moustafa, HAM, et al., 2019.[18]	Egypt	Prospective, open-label randomized clinical trial	62 patients with type 2 diabetes mellitus, aged 18-60 years, without previous antidiabetic treatment, and without organ dysfunction.	450 mg of *nigella sativa* capsule three times a day for 3 months	• FBS levels were significantly lower (P = 0.042). The 2hpp levels were significantly lower in the Nigella sativa group (p = 0.006). • A significant decrease in triglycerides and LDL was observed. No significant effect on HDL-C was noted.
5	Nazem, MR, et al., 2019.[19]	Iran	Randomized double-blind placebo-controlled trial	70 patients with type 2 diabetes mellitus and obesity (BMI = 25-40 kg/m²) aged 40-65 years.	25 mg of zinc capsule two times a day after meal, for 8 weeks	• The group receiving zinc supplements showed higher levels of FBS (p value <0.001), HbA1c (p value <0.001), triglycerides (p value =0.01), and insulin (p value =0.02). • Lower total cholesterol (p value =0.04) and LDL-C

						(p value =0.01), while HDL-C levels were higher (p value <0.001).
6	El-Aal, AA., et al., 2018.[20]	Palestina	Single-blinded randomized controlled clinical trial	40 male patients with type 2 diabetes mellitus on metformin treatment, aged 40-60 years.	The patients were divided into 4 groups: placebo supplement, vitamin C, vitamin E, and vitamin C and vitamin E, which were taken twice a day along with metformin for 90 days.	• The results showed a significant decrease in FBS, HbA1c, insulin, and HOMA-IR. • The lipid profile, cholesterol, and triglycerides showed significant improvement, with a drastic decrease in the group receiving vitamin supplementation.

Figure 1. Study selection results.

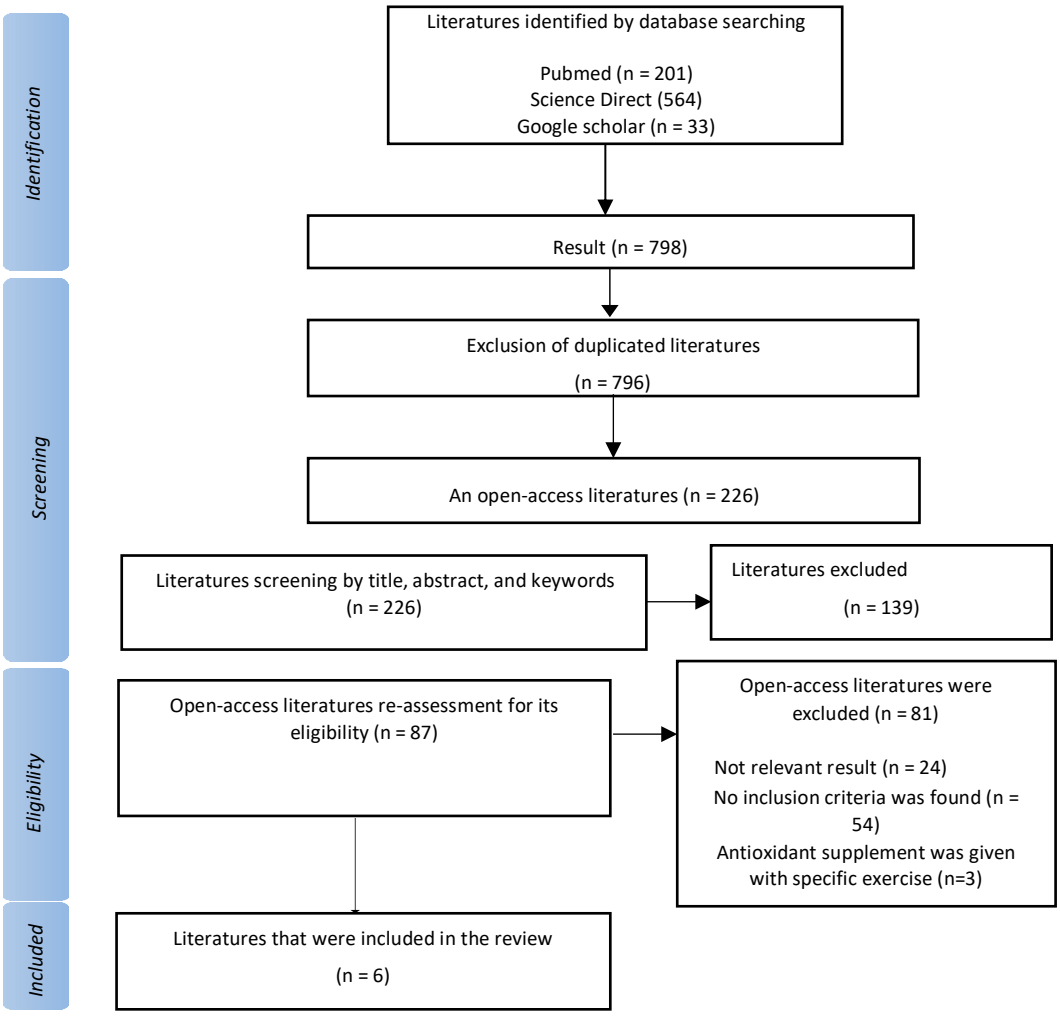
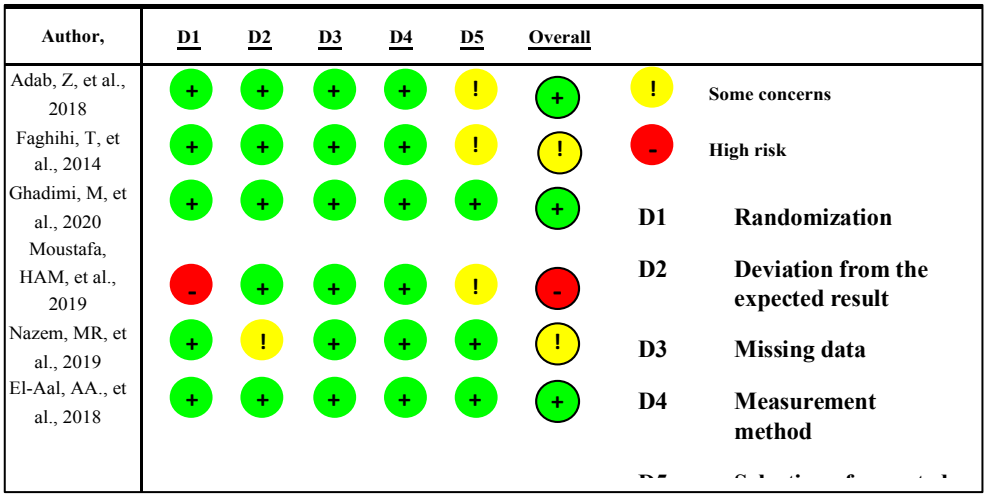


Figure 2. Risk of bias



Diabetes is a disease that often remains undetected in many patients, leading to increased long-term cardiovascular mortality and/or causing serious microvascular complications, such as kidney failure, diabetic retinopathy, and severe foot infections that may result in amputations. Poor glycemic control is more common among patients in developing countries than in those in developed countries (Aschner et al., 2021). Research has demonstrated that inadequate glycemic control is associated with both microvascular and macrovascular complications (Fasil et al., 2018). In type 2 diabetes mellitus (T2DM), lipid abnormalities are frequently observed. Typical findings include elevated total cholesterol, very low-density lipoprotein (VLDL) cholesterol, triglyceride (TG) concentrations, excessive postprandial lipemia, reduced high-density lipoprotein (HDL) cholesterol, and predominance of low-density lipoprotein cholesterol (LDL-C) (Rusdiana et al., 2020). Patients with T2DM often exhibit an atherogenic lipid profile, significantly increasing the risk of cardiovascular disease (CVD). The mechanism by which lipid variability increases mortality risk in patients with diabetes is believed to involve oxidative stress. It has been hypothesized that large fluctuations in LDL-C and HDL-C levels may cause plaque instability, releasing atherogenic substances and thereby elevating mortality risk (AL-Bahrani & Yassin, 2022; Lee et al., 2021).

Antioxidants are molecules capable of combating oxidative stress in the body by preventing the initiation and propagation of free radical oxidation. They are found in food sources such as vitamins and minerals and are also present endogenously in the form of enzymatic systems. Both exogenous and endogenous antioxidants help prevent diseases and cellular damage caused by free radicals (Franco et al., 2021a; Franco et al., 2021b).

Free radicals are unstable, highly reactive molecules, also known as reactive oxygen species (ROS). Oxidative stress occurs when there is an imbalance between ROS production and antioxidant-mediated detoxification. This imbalance increases ROS levels and disrupts normal cellular physiology. Oxidative stress–induced cellular damage contributes to diseases such as atherosclerosis, diabetes mellitus, heart disease, cancer, and other organ complications. (Hunyadi, 2019; Ji et al., 2020). Antioxidants mitigate oxidative stress through several mechanisms, including preventing free radical formation, scavenging oxidants, inhibiting toxic secondary metabolite production and inflammatory mediators, repairing damaged molecules, and enhancing endogenous antioxidant activity (Elsayed Azab et al., 2019).

Turmeric (Curcuma longa) belongs to the ginger family (Zingiberaceae), with its main active components being curcuminoid pigments, which constitute approximately 3%–5% of turmeric and include curcumin, desmethoxycurcumin, and bisdemethoxycurcumin. Curcumin inhibits the formation of oxygen free radicals and exhibits strong antioxidant properties, making it potentially effective in reducing the progression and complications of diabetes. Research has demonstrated that curcumin acts by scavenging reactive free radicals and inhibiting lipoxygenase and cyclooxygenase activity (Hodaei et al., 2019). Several studies indicate that curcumin modulates cell regeneration and insulin secretion, reduces beta-cell apoptosis, and enhances beta-cell function. Administration of turmeric extract has also been reported to inhibit LDL oxidation (Maithili Karpaga Selvi et al., 2015). A study by Adab et al. found that fasting plasma glucose, HbA1c, insulin, and HOMA-IR levels significantly decreased in the turmeric group compared to the placebo group. Similarly, Hodaei et al.

reported a significant reduction in fasting serum glucose concentration in the intervention group compared to the placebo group at the end of the study. Furthermore, Meng et al. (2013) demonstrated that curcumin supplementation reduced fasting blood glucose, HbA1c, and HOMA-IR levels in participants with type 2 diabetes (Adab et al., 2019).

Selenium is incorporated into selenoproteins, which play important roles in glucose and lipid metabolism (Huang et al., 2022). Evidence suggests that selenium regulates insulin sensitivity, and in the form of selenate, it acts as an insulin mimetic, helping to maintain blood glucose homeostasis. Selenium supplementation has been shown to increase HDL-C levels; however, its effects on FPG, TC, TG, LDL-C, and VLDL-C remain unclear (Ouyang et al., 2022). Excessive selenium intake may lead to overexpression of glutathione peroxidase 1 (GPx1), an antioxidant selenoprotein. Elevated GPx1 activity may interfere with insulin signaling, which is critical for glucose regulation and diabetes prevention (Wei et al., 2015). A study by Faghihi et al. showed significant differences in FPG, HbA1c, and HDL levels, with higher FPG, HbA1c, and HDL observed in the selenium group (Faghihi et al., 2014). Additionally, a cross-sectional study by Wei et al. revealed a significant positive association between selenium intake and diabetes prevalence (Wei et al., 2015). These findings suggest that while selenium supplementation may lower insulin levels and HOMA-IR, its effect on FPG remains ambiguous. In contrast, Abdulmalek et al. demonstrated in diabetic rats that selenium supplementation significantly decreased fasting blood glucose and insulin levels, indicating its potential role in maintaining glucose homeostasis (Abdulmalek & Balbaa, 2019).

Ellagic acid ($C_{14}H_6O_8$) is a polyphenolic compound found in fruits such as raspberries, pomegranates, grapes, blueberries, gallnuts, and walnuts. Its molecular structure, characterized by multiple phenolic hydroxyl groups, confers strong antioxidant properties. Ellagic acid has been reported to exhibit antibacterial, anti-inflammatory, hepatoprotective, and anti-obesity effects, as well as reducing fatty acid synthesis. Fatima et al. (2017) reported that ellagic acid reduced fasting blood glucose and insulin resistance while increasing total antioxidant capacity and glutathione S-transferase levels (Fatima et al., 2017). Yang et al. (2020) reported increased insulin secretion and reductions in triglycerides and free fatty acids following ellagic acid administration (Yang et al., 2020). Guo et al. (2020) demonstrated reductions in blood glucose, body weight, and body fat percentage, along with increased insulin secretion (Guo et al., 2020). Chao et al. (2009) reported increased plasma insulin and decreased plasma glucose and triglyceride levels. Xu et al. (2021) observed reduced cholesterol and LDL levels and increased HDL levels (Xu et al., 2021). Ghadimi et al. (2020) reported significant reductions in blood glucose, insulin, HbA1c, triglycerides, total cholesterol, insulin resistance (IR), LDL, and malondialdehyde (MDA), alongside increased activity of superoxide dismutase (SOD) and glutathione peroxidase (GPx) (Ghadimi et al., 2021; Hidalgo-Lozada et al., 2022).

Nigella sativa belongs to the Ranunculaceae family and includes 14 species within the Nigella genus, such as N. arvensis, N. ciliaris, and N. hispanica. Nigella sativa is known for its antidiabetic, diuretic, antihypertensive, antimicrobial, anti-inflammatory, spasmolytic, gastro-hepatoprotective, antifungal, and immunomodulatory properties. It has also been reported to improve glycemic and clinical control in patients with diabetes mellitus. A study by Seflek et al. (2019) demonstrated reductions in glucose levels and increased serum

antioxidant levels following Nigella sativa supplementation. Fararh et al. (2004) reported reductions in glucose and HbA1c levels. Clinical trials have further evaluated the effects of Nigella sativa in patients with diabetes mellitus. Moustafa et al. (2019), a key reference in this systematic review, demonstrated improvements in glycemic control and lipid profiles in patients with type 2 diabetes mellitus following Nigella sativa administration (Moustafa et al., 2019). Hadi et al. (2021) administered 450 mg of Nigella sativa oil three times daily for three months to patients with T2DM, resulting in weight reduction, increased HDL levels, and decreased LDL, total cholesterol, and triglyceride levels (Hadi et al., 2021; Moustafa et al., 2019).

Zinc is an essential micronutrient involved in carbohydrate, lipid, and insulin metabolism (Jarosz et al., 2017). It functions as a cofactor for superoxide dismutase (SOD), which plays a crucial role in antioxidant defense in patients with T2DM (Prasad & Bao, 2019). In chronic hyperglycemia, SOD enzymes may undergo glycation, impairing their activity and allowing highly reactive radicals—such as hydroxyl radicals, reactive ketoaldehydes, and superoxide anions—to accumulate, leading to irreversible cellular damage. Additionally, zinc enhances insulin sensitivity and reduces serum glucose and lipid levels, a phenomenon referred to as the "insulinomimetic effect"(Mukherjee et al., 2017). The recommended daily zinc intake for adults is 11 mg/day (Olechnowicz et al., 2018). Several studies indicate that high-dose zinc supplementation positively affects patients with T2DM. Nazem et al., (2019) reported that zinc gluconate supplementation significantly reduced fasting blood glucose (FBG), HbA1c, and HOMA-IR levels while increasing serum insulin concentration compared to placebo (Nazem et al., 2019). However, other studies did not demonstrate significant improvements in glycemic control (Ranasinghe et al., 2015). These discrepancies may be attributed to differences in participant characteristics, supplementation duration, zinc formulation (e.g., zinc sulfate versus zinc gluconate), and dosage (Fernández-Cao et al., 2019).

Zinc supplementation has also been shown to reduce total cholesterol and LDL-C levels and increase HDL-C levels.[19] A meta-analysis by Ranasinghe et al. concluded that most clinical trials reported favorable effects of zinc on lipid profiles (Ranasinghe et al., 2015).

Vitamin C (L-ascorbic acid) is one of the most abundant and potent water-soluble antioxidants in the human body. It scavenges reactive oxygen species (ROS) and reactive nitrogen species (RNS), preventing oxidative damage to lipids and lipoproteins in various cellular compartments. Vitamin E is a fat-soluble antioxidant. In the form of chylomicrons, it is transported to the liver and subsequently appears in plasma through the action of α-tocopherol transfer protein. Once delivered to tissues, vitamin E functions as a chain-breaking antioxidant in cell membranes, preventing lipid peroxidation (Retno Sari, 2023). In a study by El-Aal et al., supplementation with vitamin C (500 mg) and/or vitamin E (400 mg) twice daily for 90 days significantly reduced FBS, HbA1c, insulin, and HOMA-IR levels and significantly improved lipid profiles compared to placebo (El-Aal et al., 2018).. These findings are consistent with those of Rafighi et al., who reported improvements in FBS, HbA1c, LDL-C, total cholesterol, and triglyceride levels following supplementation with vitamin C (266.7 mg) and/or vitamin E (300 IU) for three months. They further noted that supplementation with vitamins C and E contributed to cardiovascular risk reduction in

patients with T2DM, as evidenced by significant improvements in systolic and diastolic blood pressure (Gęgotek & Skrzydlewska, 2022).

CONCLUSION

This systematic review concludes that supplementation with several oral antioxidants demonstrates efficacy in improving glycemic control and lipid profiles in patients with type II diabetes mellitus. The strongest and most consistent evidence supports the use of ellagic acid, Nigella sativa, and vitamins C and E, which showed significant improvements across multiple glycemic parameters including fasting blood glucose, postprandial glucose, HbA1c, insulin levels, and insulin resistance indices, along with beneficial effects on lipid profiles including reductions in total cholesterol, triglycerides, and LDL cholesterol. Turmeric supplementation demonstrated significant improvements in triglyceride and LDL cholesterol levels but did not produce statistically significant changes in glycemic parameters, suggesting potential utility primarily for lipid management. Zinc supplementation produced complex effects with improvements in cholesterol fractions but worsening of glycemic control and triglycerides, indicating that this antioxidant should be used cautiously with careful metabolic monitoring. Selenium supplementation showed inconsistent and sometimes paradoxical effects on both glycemic and lipid parameters, and cannot be recommended for routine clinical use based on current evidence. These findings support the potential role of specific antioxidants as adjunctive therapy in comprehensive diabetes management, complementing rather than replacing standard pharmacological treatments and lifestyle interventions.

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