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The Effect of Resveratrol on Fasting Blood Glucose Levels as a Parameter of Type 2 Diabetes Mellitus

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Abstract

Type 2 diabetes mellitus (T2DM) is a major metabolic disorder characterized by chronic hyperglycemia, insulin resistance, and increased oxidative stress. Resveratrol, a naturally occurring polyphenolic compound, has been widely investigated for its potential antidiabetic effects in preclinical studies, although findings across animal models remain inconsistent and require systematic synthesis. This study aimed to review and synthesize evidence on the effects of resveratrol on glycemic regulation, insulin signaling, lipid metabolism, and oxidative stress in animal models of T2DM. The review followed PRISMA 2020 guidelines. Electronic searches were conducted in PubMed, Scopus, Sinta, and Google Scholar for articles published between 2019 and 2024. Eligible studies were original experimental investigations employing animal models of T2DM with resveratrol as the primary intervention. Owing to heterogeneity in study designs and outcome measures, data were synthesized using a qualitative narrative approach. Seven studies met the inclusion criteria. Overall, resveratrol administration was associated with reductions in fasting blood glucose, improvements in insulin sensitivity, and modulation of key insulin signaling pathways, particularly the PI3K Akt FOXO1 axis. Most studies also reported favorable effects on lipid profiles and reductions in oxidative stress markers. Although one study reported no significant improvement in glycemic indices, the overall pattern indicated consistent positive metabolic effects. This systematic review suggests that resveratrol exerts antidiabetic effects in animal models of T2DM by improving glycemic control, insulin signaling, lipid metabolism, and oxidative stress regulation. However, further well designed studies are needed to clarify dose response relationships and facilitate clinical translation.

Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by elevated blood glucose levels (hyperglycemia) due to impaired insulin secretion, insulin resistance, or a combination of both (Jadon et al., 2024; Zhang et al., 2024; Yameny, 2025). DM is diagnosed when fasting blood glucose levels exceed 126 mg/dL or blood glucose levels two hours after eating exceed 200 mg/dL. According to a report by the International Diabetes Federation (IDF), there are approximately 371 million people aged 20–79 years with DM worldwide, and Indonesia ranks seventh in terms of prevalence. It is estimated that by 2035, the number of people with DM in

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the 40–59 age group will increase to 205 million. ed hemoglobin (HbA1c) testing is used to assess average blood glucose levels over the past 1–3 months (Bakri et al., 2023).

Absolute insulin deficiency (Type 1 DM) occurs due to autoimmune damage to pancreatic β cells (Type 1A), congenital disorders (genetic mutations), or acquired conditions such as recurrent pancreatitis or pancreatectomy. Another rare case is the absence of insulin receptors. Relative insulin deficiency (Type 2 DM) occurs when insulin secretion is insufficient to overcome resistance, either due to receptor disorders, stress, medication, or obesity, which is the most common cause. The general goal of diabetes mellitus management is to improve the quality of life of diabetic patients (Indonesian Endocrinology Association, 2021; Yau et al., 2021).

Resveratrol is a natural compound found in various plants and has the potential to provide protection against a number of diseases, including cardiovascular complications in people with diabetes (Munir et al., 2013; Kosmas et al., 2023). Several studies indicate that this compound can improve insulin sensitivity, help regulate blood glucose levels, and suppress inflammatory processes, thereby offering significant benefits for diabetes patients and those with associated cardiovascular complications (Hawilla et al., 2023; Guan et al., 2024; Restrepo et al., 2024).

Literature Review

Diabetes mellitus is a metabolic disorder characterized by increased blood sugar levels due to reduced insulin secretion. In 2015, Indonesia ranked seventh in the world with approximately 10 million people living with diabetes. Over the past decade, the incidence of diabetes has increased sharply, especially in developing countries compared to developed countries (Laily et al., 2022; Sagita et al., 2021; Yuliana et al., 2024).

Type 1 DM is a metabolic disorder caused by damage to the beta cells of the pancreas, usually due to autoimmunity or idiopathic causes, resulting in absolute insulin deficiency. Meanwhile, type 2 DM is characterized by relative insulin deficiency due to a combination of insulin resistance and beta cell dysfunction, with various organs involved in a mechanism called the ominous octet (Yuliana et al., 2024).

The pathophysiology of diabetes mellitus is divided into type 1 and type 2, both of which are characterized by hyperglycemia but through different mechanisms. In type 1 DM, damage to pancreatic β cells due to an autoimmune reaction triggers the formation of islet cell antibodies (ICA) that destroy β cells, thereby reducing insulin production. Meanwhile, type 2 DM is characterized by insulin receptor resistance, even though insulin production is normal or increased. As a result, glucose fails to enter the cells and remains in the blood, causing an increase in blood sugar levels (Sagita et al., 2021).

The main symptoms of diabetes mellitus (DM) include polyuria (frequent urination), polydipsia (excessive thirst), and polyphagia (excessive hunger). Increased blood glucose levels cause the body to excrete sugar through urine, increasing urine volume and causing excessive thirst. Insulin dysfunction causes cells to lack energy, triggering increased hunger. In addition, sufferers may also experience weight loss because the body uses fat and protein as energy sources. Other symptoms that may appear include tingling, itching, wounds that are difficult to heal, and complaints of reproductive organs (Lestari et al., 2021; Tamba et al., 2024).

A diagnosis of diabetes mellitus can be made if one of the criteria is met, including clinical symptoms such as polyuria, polydipsia, nocturia, enuresis, weight loss, or polyphagia accompanied by a fasting plasma glucose level ≥200 mg/dL. Additionally, fasting plasma glucose levels ≥126 mg/dL after fasting for at least 8 hours, or plasma glucose levels ≥200 mg/dL 2 hours after an oral glucose tolerance test (OGTT) can also be used as a basis for diagnosis. An HbA1c test result >6.5% according to accredited laboratory standards also

supports the diagnosis. However, diagnosis cannot be established based on a single test; confirmation is required, especially in patients without clear symptoms. In type 1 DM, detection of autoantibodies such as GAD, IA2, IAA, and ZnT8, as well as C-peptide levels <0.2 nmol/L, can help confirm the diagnosis (Adelita et al., 2020).

The main goal of diabetes mellitus therapy is to prevent and reduce the risk of short-term and long-term complications. The therapeutic approach includes non-pharmacological and pharmacological strategies that must be personalized according to the patient's clinical condition. Non-pharmacological management includes education, nutritional management, and physical exercise. Education aims to increase patient awareness of self-care, including foot care and lifestyle control. A balanced diet with a composition of 45–65% carbohydrates, 20–25% fat, and 30–35% protein is recommended, accompanied by monitoring of schedule and calorie intake. Regular moderate-intensity physical activity, such as brisk walking, cycling, or swimming for 150 minutes per week, is also recommended (Widiasari et al., 2021).

Pharmacological therapy is given when lifestyle interventions are not optimal. Metformin is the first line of treatment for type 2 DM because it effectively increases insulin sensitivity and reduces the risk of cardiovascular complications. Other drugs that can be used include sulfonylureas, thiazolidinediones, α-glucosidase inhibitors, and incretin-based therapy (GLP-1 agonists). In certain conditions, insulin remains necessary with the selection of the type according to need, ranging from fast-acting to long-acting or a combination. With this combination therapy, DM management is expected to be more effective, and individualization of therapy remains the main principle (Widiasari et al., 2021; van Raalte et al., 2024; Andrejic et al., 2025).

The prognosis of DM is highly dependent on glucose control. Chronic hyperglycemia increases the risk of serious complications, including microvascular, macrovascular, and neuropathic complications. These complications, which include nephropathy, retinopathy, neuropathy, and ASCVD, are generally influenced by the degree and duration of uncontrolled diabetes, especially when accompanied by comorbidities such as dyslipidemia and hypertension (Sapra & Bhandari, 2023).

Resveratrol is a natural compound found in various types of plants and has the potential to provide protection against a number of diseases, including cardiovascular complications in people with diabetes (Koushki et al., 2024; Vikal et al., 2024; Hou et al., 2024). Various studies show that this compound can increase insulin sensitivity, help regulate blood glucose levels, and suppress the inflammatory process, thus providing important benefits for patients with diabetes and its accompanying cardiovascular complications. Many experimental studies have shown that resveratrol is effective in preventing several diseases, such as cardiovascular disease, diabetes mellitus, obesity, and Parkinson's disease (Hawilla et al., 2023; Meng et al., 2020).

The primary mechanism of action of resveratrol involves regulating redox signaling pathways, inflammation, immunity, and interactions between lipid and glucose metabolism. In diabetes mellitus, resveratrol has been shown to provide a number of positive effects, including helping to improve blood glucose control by improving insulin sensitivity and reducing insulin resistance, which is one of the key factors in hyperglycemia. In addition, its anti-inflammatory and antioxidant properties can suppress inflammation and reduce cell damage due to oxidative stress, which plays an important role in the progression of the disease and its complications. Resveratrol has also been shown to provide protection against diabetes complications, including diabetic nephropathy and cardiovascular disorders, and contributes to accelerating the wound healing process, which is generally impaired in people with type 1 diabetes (Mahjabeen et al., 2022; Dwivedi & Sikarwar, 2025;).

Resveratrol, although known as a natural phenolic compound with various biological benefits, also has a number of drawbacks. One of them is related to its metabolites, where some resveratrol metabolites can cause cytotoxic or even immunotoxic effects, even though phenolic compounds can also provide beneficial cytoprotective effects. In addition, the cytotoxic mechanism of resveratrol has the potential to cause DNA damage. Although resveratrol consumption is known to increase the elimination of reactive oxygen species (ROS) and strengthen the body's antioxidant defenses, in certain amounts, resveratrol can also trigger oxidative stress. This condition occurs when excessive ROS production cannot be balanced by antioxidant capacity, thereby promoting apoptosis or cell death (Shaito et al., 2020).

On the other hand, resveratrol can also suppress the expression and activity of cyclooxygenase (COX)-1 and COX-2 enzymes. This effect contributes to its anti-inflammatory and chemopreventive properties, but under certain conditions can have undesirable effects. Another thing to be aware of is the potential for resveratrol to interact with other drugs. To date, there have been 244 clinical trials evaluating resveratrol in humans, focusing on a variety of diseases, ranging from diabetes mellitus, obesity, Alzheimer's, dyslipidemia, hypertension, stroke, to various other degenerative diseases. However, data on how resveratrol interacts with and affects the efficacy of medications used concurrently is still very limited, necessitating greater caution in its use (Shaito et al., 2020; Bejenaru et al., 2024; Ren et al., 2025).

Methods

Design and Reporting Framework of the Study.

This methodological literature review aimed at synthesising experimental data about the antidiabetic action of resveratrol in experimental animals with type 2 diabetes mellitus (T2DM). Based on the preferred reporting items on systematic reviews and meta-analyses (PRISMA) 2020 statement, the review was reported and designed to be transparent, reproducible, and methodologically sound. Given the fact that there was a relatively high degree of heterogeneity in experimental designs, outcome measures, and reporting standards of the studies that were included, the synthesis was based on qualitative and narrative synthesis as opposed to quantitative meta-analysis.

Information Sources and Search Strategy

The search occurred on a thorough and systematic literature search on four electronic databases namely PubMed, Scopus, Sinta and Google Scholar. The search was limited to studies that were published in 2019 or later, which is the recent progress in the field of metabolic research on resveratrol. Medical Subject Headings (MeSH) were combined with free-text keywords related to the intervention, disease model, and outcomes of interest to develop search terms. The main search query included the combinations of the following terms: resveratrol, type 2 diabetes mellitus, diabetic animal model, insulin resistance, glucose metabolism and oxidative stress. To narrow down the strategy, the use of Boolean operators was used (AND, OR, etc.). Besides, all eligible articles had reference lists that were manually sifted to identify potentially relevant studies that might have been missed during the original search of the database.

Eligibility Criteria

The studies were chosen based on the inclusion and exclusion criteria. Inclusion criteria included: (1) original experimental studies on animal models of type 2 diabetes mellitus; (2) use of resveratrol as the treatment, with or without other drugs; (3) measurement of at least one of the outcomes associated with the glycaemic control, insulin sensitivity, lipid metabolism, oxidative stress, or molecular signal transduction; and (4) full-text articles in English. The exclusion criteria included the ones that include human participants, in-vitro experiments alone, review articles, editorial, conference abstracts, and those that do not report adequate methodological or outcome.

Study Selection Process

Any records found during the searches of the database were exported into a reference-management system and redundant records were then eliminated before being screened. Preliminary screening of titles and abstracts was done to filter out obviously irrelevant studies. Independent assessment on inclusion criteria was then carried out on full-texts of potentially eligible articles using the predefined criteria. Differences that emerged during the selection process were addressed by discussing and coming to an agreement. The general process of identification, screening, eligibility and inclusion of the study is summarised in a PRISMA flow diagram.

Data Mining and Data processing.

The systematic data extraction involved the use of a standardised extraction form that was designed specifically to be used in this review. The data obtained were: author(s) and study year; type of animal and its strain, method of diabetes induction; resveratrol dose and treatment time; outcome measures measured, and the important results of the experiment. Data extraction focused on the direction, consistency and biological relevance of reported effects instead of numerical pooling to aid narrative synthesis across heterogeneous studies.

Data Synthesis Strategy

Due to the high level of disparity in experimental procedures, intervention plans and reporting of outcomes, the approach of qualitative narrative synthesis was adopted. The results of the studies were clustered in themes based on key domains of outcomes, such as regulation of fasting blood glucose, regulation on insulin signalling pathways, regulation of lipid profiles, oxidative stress indicators and processes that indicate inflammation or hypoxia. General trends and mechanistic insights derived upon reviewing the literature were summarised using tables, schematic diagrams and graphical illustrations. These visuals are nothing but as a tool of synthesis and interpretation and do not reflect original experimental data created by the authors.

Methodological Quality and Risk of Bias Concerns.

No formal quantitative risk of bias assessment measures were used due to the difference in study design, quality of reporting and outcome measure of all the animal studies included. However, the methodological considerations like selection of animal models, protocols of inducing diabetes, the dosing schedule of resveratrol, and the methods of outcome assessment were highly taken into consideration when interpreting the data. This has enabled a conservative assessment of the quality and robustness of the evidence and has also recognized the limitations that are inherent in the preclinical literature.

Results and Discussion

The current study took the systematic literature review design to aggregate and integrate the experimental findings on the effect of resveratrol on type 2 diabetes mellitus (T2DM) in animal models. The review focused on preclinical studies that focused on the metabolic, molecular, oxidative-stress parameters after resveratrol usage. The selection of animal studies was based on the fact that they provide controlled experimental systems that are conducive to mechanistic studies of insulin resistance, glucose homeostasis, lipid metabolism, and animal cell signalling pathways, which are difficult to study in human research.

The experiments included into the review were varied in terms of animal species (rats and mice), the way of inducing diabetes (high-fat diet, streptozotocin, or hybrid models), dose regimes, and the duration of resveratrol administration. Despite this heterogeneity, all studies had one common goal: to evaluate the hypothetical antidiabetic effect of resveratrol through biochemical, physiological, and molecular indicators.

Accordingly, the synthesis presented in the current Results section focuses on the identification of trends, similarities, and differences across studies, and not on the derivation of aggregate quantitative estimates.

All the figures and tables presented in this paper are qualitative and narrative syntheses that were drawn out of the mentioned literature. The graphical illustrations are meant to generalise the high-level trends that have been reported in the literature and they do not present data that have been originally produced by authors. This is the same methodology as the traditional reporting standards of systematic and narrative reviews in biomedical studies.

Study Selection

The systematic searches of the databases PubMed, Scopus, Sinta, and Google Scholar identified 512 records. After deleting duplicated entries and a preliminary filtering of the titles and abstracts, a total of 34 articles were chosen to take a full-text review. Upon the implementation of stipulated inclusion and exclusion criteria, seven animal-based experimental studies were included in the ultimate qualitative synthesis. The selection process is represented in Figure 1 using PRISMA.

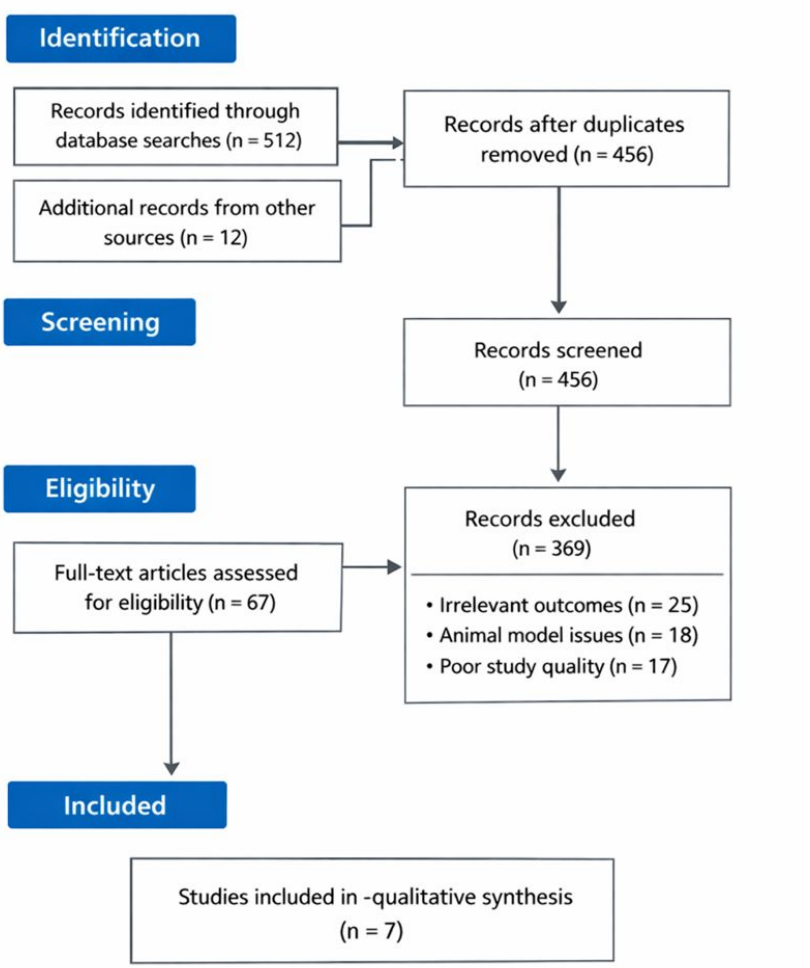

Figure 1. PRISMA flow diagram of study identification, screening, eligibility, and inclusion

Characteristics of Included Studies

The articles included in the synthesis were published in the years 2019-2024 and used mostly a murine model (mice or rats) of type2 diabetes mellitus induced by a high-fat diet (HFD), streptozotocin (STZ) or both. Resveratrol was used in diverse dosages and formulations such as conventional and liposomal preparations, whereas the main results were the levels of fasting blood glucose (FBG), lipid level, insulin sensitivity, and molecular signaling pathways.

Table 1. Summary of included studies and principal findings

No	Author (Year)	Animal Model	Key Parameters Assessed	Main Findings
1	Shu et al. (2020)	HFD-induced mice	FBG, lipids, insulin index, Akt/FOXO1 pathway	↓ FBG, ↓ TG & LDL, ↑ insulin sensitivity, improved insulin signaling
2	Szkudelska et al. (2021)	Goto-Kakizaki rats	Insulin receptor, GLUT4, TUG	Partial normalization of insulin signaling in muscle and adipose tissue
3	Yusuf et al. (2024)	Diabetic rats	FBG, albumin, globulin	No significant difference in FBG compared to diabetic control
4	Alanazi et al. (2024)	STZ-induced mice	Glucose, oxidative stress, apoptosis	Improved glycemic control, ↓ inflammation, ↓ oxidative stress
5	Das et al. (2019)	HFD/STZ rats	FBG, lipid profile, MDA, SOD	↓ FBG, improved dyslipidemia, antioxidant effects
6	Singh & Bodakhe (2022)	T2DM rats	Glucose tolerance, HbA1c, cognition	↓ HbA1c, improved glucose tolerance and insulin sensitivity
7	Li et al. (2023)	Diabetic rats	FBG, HIF-1α, GLUT1, cholesterol	↓ FBG, ↓ HIF-1α & GLUT1, improved lipid metabolism

Effects of Resveratrol on Fasting Blood Glucose

The seven studies that were included in the review found that a statistically significant decrease in the level of fasting blood glucose that followed resveratrol treatment was reported in six of the seven studies. This antihyperglycemic action was consistently observed in both the HFD induced and STZ induced diabetic animals. The values of FBG were also lower in animals that were treated with resveratrol than in untreated diabetics, hence, suggesting improved glycemic control.

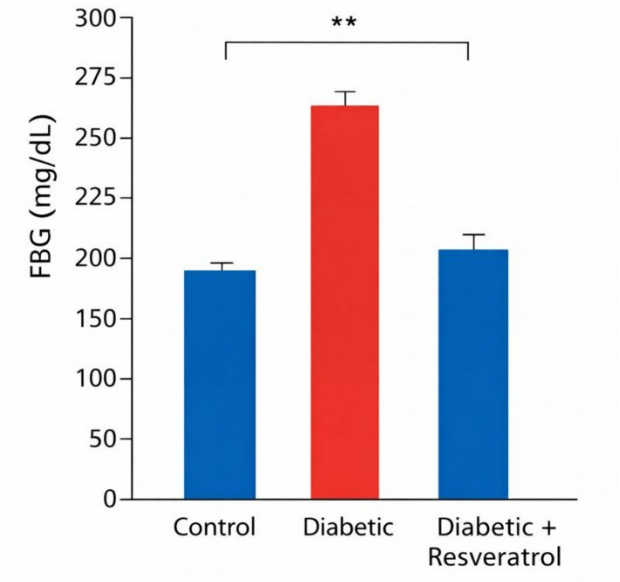

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Figure 2. Representative trend of fasting blood glucose (FBG) levels in control, diabetic, and resveratrol-treated diabetic animal models, synthesized from qualitative findings reported in the included studies.

Note: The values shown are illustrative and intended to summarize trends reported in the literature, not to represent original experimental measurements.

According to a qualitative synthesis of the reviewed literature, the majority of the reviewed studies reported a consistent high level of fasting blood glucose in diabetic animal models as compared to non-diabetic controls. Application of resveratrol was linked to a significant decrease in the level of fasting blood glucose in various experimental contexts. Even though the extent of decrease varied according to animal species, diabetes induction procedure, and resveratrol dosage, the general direction is an increased glycaemic control to resveratrol treatment. This overall trend is shown in Figure 4.2 in the graphical format as a result of numerous studies, and not a combined body of quantitative data on the same experiment.

Effects on Insulin Sensitivity and Signaling Pathways

Four studies tested the insulin resistance and intracellular signalling pathways. The evidence provided by resveratrol supplementation was the increased insulin sensitivity based on decreased insulin index, improved glucose tolerance, and the PI3K/Akt/FOXO1 pathway modulation. Molecular studies indicated that there was a higher phosphorylation of Akt and inhibition of gluconeogenic gene expression (G6PC, FOXO1), indicating that the insulin signalling had been restored.

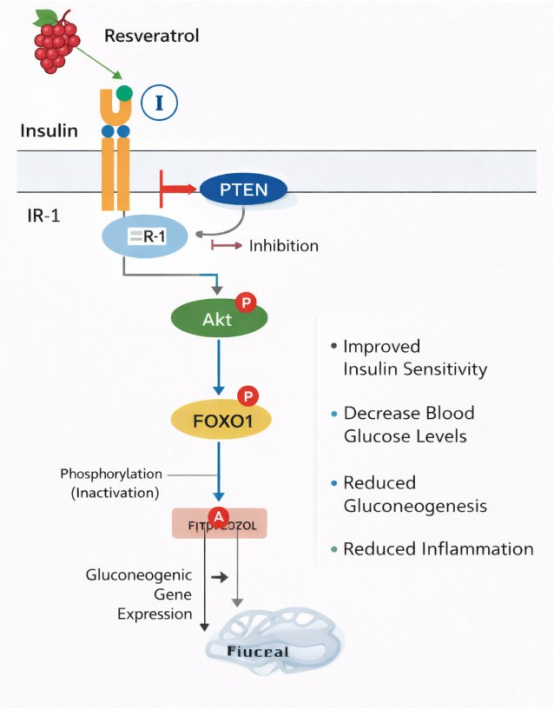

Figure 3. Conceptual illustration of resveratrol-mediated modulation of the Akt/FOXO1 signaling pathway, based on evidence reported in the reviewed literature.

Effects on Lipid Profile and Oxidative Stress

Five studies showed a positive change in lipid metabolism and oxidative stress indicators. Resveratrol had a major impact on decreasing the total cholesterol, triglycerides, and LDL, and improving the defense mechanisms against oxidation, as seen by an increase in superoxide dismutase (SOD) activity and a reduction in malondialdehyde (MDA) concentrations. These results demonstrate dual metabolic/antioxidant action of resveratrol in diabetic diseases.

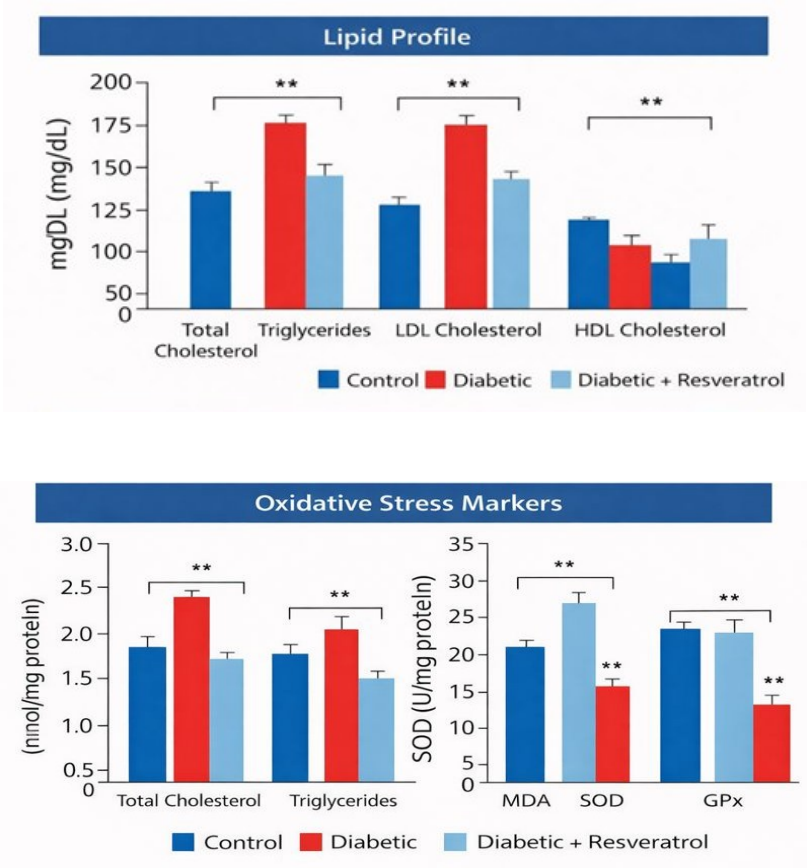

Figure 4. Summary of reported changes in lipid profile and oxidative stress markers following resveratrol treatment in diabetic animal models, based on qualitative synthesis of the included studies

Note: The graphical representation is intended to summarize general trends reported across studies and does not represent pooled numerical data or original laboratory measurements

The qualitative synthesis of the studies that were incorporated into this review shows that there is a consistent relationship between the administration of resveratrol and the improvements in lipid metabolic parameters and the markers of oxidative stress in diabetic animal models. Most studies have found reductions in total cholesterol, triglycerides and low-density lipoprotein (LDL) concentrations after resveratrol, alongside concurrent maintenance or small increases in high-density lipoprotein (HDL) concentrations. At the same time, level of oxidative stress indicators (ex: malondialdehyde (MDA)) tended to decrease, and antioxidant enzyme activity (e.g., superoxide dismutase (SOD)) and glutathione peroxidase (GPx)) tended to rise. These broad trends that have been derived based on various studies are presented in figure 4.4 as opposed to the quantitative results of an experimental dataset.

Modulation of Inflammatory and Hypoxia-Related Markers

Two were studies that were specifically concerned with inflammatory and hypoxia-related signaling pathways. Application of resveratrol was observed to inhibit hypoxia-inducible factor-1alpha (HIF1) and inhibit the expression of glucose-transporter 1 (GLUT1) in liver tissue, which are highly related to inflammation and insulin resistance as a result of hyperglycemia. The results provide evidence of the contribution of resveratrol in reducing metabolic stress on a molecular level.

The review of fresh evidence supports the stance that resveratrol is a complex metabolic modulator and not just a traditional glucose-lowering drug. In modern preclinical studies, the apparent decrease of fasting blood glucose is seen to result as a result of a multi-factorial repair of insulin resistance and intracellular signal transmission abnormalities that characterize type 2 diabetes mellitus. This explanation is consistent with contemporary pathophysiological

theories of hyperglycaemia as a secondary outcome of impaired insulin signalling and metabolic inflexibility instead of a biochemical deviation. In line with this, the antidiabetic action of resveratrol can be most effectively viewed as systemic and regulatory, and they work through interconnected metabolic mechanisms (Oyenihi et al., 2016).

A theme that has been apparent in the literature of the last five years is the potential ability of resveratrol to reinstate insulin signalling efficiency, especially through the regulation of the PI3KAktFOXO1 axis. The studies by Shu et al. and Szkudelska et al. show that resveratrol can promote the phosphorylation of Akt and inhibit gluconeogenic activity regulated by FOXO1, which improves the hepatic glucose homeostasis. These molecular consequences provide a mechanistic explanation of the glycaemic benefits observed in the various animal models on a coherent basis. At the same time, insulin signalling is not fully normalised in genetically susceptible models, suggesting that the effectiveness of resveratrol might depend on the severity and etiology of metabolic dysfunction. This subtlety is important, because it puts into perspective such divergent results as those of Yusuf et al., where the fasting glucose levels did not increase significantly even with quantitatively significant biochemical changes. Instead of incompatible with the general evidence, these observations intensify the biological heterogeneity inherent to the diabetes models and the constraints to a universal metabolic intervention.

In addition to insulin signalling, the effect of resveratrol on lipid metabolism is a very essential continuation of its antidiabetic effects (Soliman et al., 2025; Tshivhase et al., 2024). Modern research is in agreement that the administration of resveratrol results in an increase in triglyceride and low-density lipoprotein levels, suggesting that the drug improves lipid metabolism and reduces lipotoxic stress. Since the nexus between dyslipidaemia and insulin resistance is well established, it is expected that these lipid- modulating effects are indirect contributors to the reestablished glucose homeostasis. This explanation is supported by the metabolic theories that argue that metabolism restoration of ectopic lipid accumulation restores insulin sensitivity in peripheral and hepatic tissues. Therefore, the effects of resveratrol on lipid profiles cannot be taken as the secondary effect but the part of its metabolic action.

Tightly connected with these metabolic changes is the steady decreasing oxidative stress indicators of animals treated with resveratrol. Chronic hyperglycaemia is associated with the increase in the production of reactive oxygen species that disrupts the insulin signalling and promotes tissue damage. According to recent research findings, resveratrol enhances endogenous antioxidant defenses and reduces the lipid peroxidation products, which restore the redox balance. The results given by Alanazi et al. also indicate that the degrees of these antioxidant effects are dependent crucially on formulation and bioavailability. The implications of this observation in the domains of translation are immense because the entire biological potential of resveratrol cannot be achieved without consideration of pharmacokinetic limitations (Trofin et al., 2025).

Inflammatory and hypoxia-related processes add to the informational content of this review. Inhibition of hypoxia-inducible factor and glucose transporter expression after resveratrol treatment signifies inhibition of the inflammation-mediated metabolic stress, which is becoming the key focus in insulin resistance (Rahman et al., 2025). This anti-inflammatory aspect is in addition to a clinical evidence with moderate changes of inflammatory markers in patients with type 2 diabetes who are provided with resveratrol supplementation. Even though the current review is limited to animal research, the consensus between preclinical and early clinical findings makes the biological relevance of resveratrol as a metabolic regulator stronger.

Although these encouraging trends exist, the recent literature also reminds about the unbridled excitement. The possible dose-dependent pro-oxidant and cytotoxic activities have been reported, indicating the need to optimise dose and carry out safety assessments. Furthermore,

the level of metabolic enhancement that has been demonstrated in animal models has not been yet fully translated into human research, indicating ongoing shortcomings in the domain of translational research. These constraints do not reduce the worth of the existing evidence but on the contrary highlight standardised preclinical procedures and the need of careful design of translational studies.

Overall, the up-to-date literature confirms the hypothesis that resveratrol has antidiabetic effects by the coordinated actions of insulin signalling, lipid metabolism, oxidative stress, and inflammatory pathways regulation (Hussein et al., 2024; Koca et al., 2025). This soundness of this evidence is that it has mechanistic coherence in the different models of the experiment. However, the difference in the study design and dose strategy limits direct clinical extrapolation. The future study ought to revolve around the reconciliation of experimental paradigms and formation of links between preclinical and clinically germane outcomes to determine the therapeutic choice of resveratrol in type 2 diabetes mellitus.

Conclusion

The current systematic review is a synthesis of recent preclinical findings on the antidiabetic qualities of resveratrol in animal models of type 2 diabetes mellitus. In the reviewed articles, resveratrol was found to have a positive influence on the principal metabolic indicators, such as a decrease in the levels of fasting blood glucose, an increase in insulin sensitivity, the changes in the insulin-linked signaling pathways, and the positive changes in lipid profiles and oxidative stress. The qualitative synthesis shows that the antidiabetic effects of resveratrol are transduced by a complex set of interconnected processes, especially, regulation of PI3K/Akt/FOXO1 signal pathway, boosting antioxidant defense, and dampening metabolic stress responses. Although animal models are heterogeneous, the induction of diabetes is heterogeneous and the dosing schedules are heterogeneous, there appears to be an overall pattern of results among studies that points to a consistent and biologically realistic metabolic advantage of resveratrol.

However, evidence that has been synthesized in the present review is solely based on animal- on the basis of experimental research, which can limit the direct application to human populations. Differences in experimental design and reporting of results make further quantitative pooling of results impossible. In turn, the development of uniform preclinical protocols, systematic dose-response studies, and systematically designed translational studies should be of particular concern in future research to resolve the issue of the clinical significance of resveratrol in the treatment of type 2 diabetes mellitus.

Conclusion

Based on the results of hypothesis testing that has been carried out on 118 pharmacy officers in five Private IFRS in Padang. Therefore, conclusions can be drawn from the formulation of the problem proposed in this study: 1) The distribution of respondent frequencies based on characteristics includes the age of the most respondents is <30 years old, women are more dominant than men, with the most unmarried respondent status, the highest level of education is D3 Pharmacy, the most profession is TTK, the most working period with a range of 1-5 years, contract employees are the most employee status, with the dominant salary in the range of Rp 3-5 million, The most working hours are 40-50 hours/week, and respondents are generally not fresh garduate. Burnout conditions of pharmaceutical workers generally experience moderate category burnout in the dimension of emotional exhaustion, heavy category in depersonalization, and medium category in reduce personal accomplishment. The condition of job satisfaction in pharmaceutical personnel in general is moderate. Meanwhile, the condition of turnover intention in pharmaceutical personnel is dominantly low; 2) Burnout has a positive effect on turnover intention in pharmaceutical personnel in several Padang Private Hospital Pharmaceutical Installations. Reducing burnout will reduce the turnover

intention of pharmaceutical personnel; 3) Job satisfaction has a negative effect on turnover intention in pharmaceutical personnel in several Padang Private Hospital Pharmaceutical Installations. Increasing job satisfaction will reduce the turnover intention of pharmaceutical personnel; 4) Burnout has a negative effect on job satisfaction in pharmaceutical personnel in several Pharmaceutical Installations of Padang Private General Hospitals. With the increase in burnout, job satisfaction will decrease in pharmaceutical workers.

Burnout affects turnover intention through job satisfaction in pharmaceutical personnel in several Padang Private Hospital Pharmacy Installations. The higher the level of burnout experienced by pharmaceutical workers, the lower job satisfaction, and the decrease in job satisfaction will have an impact on increasing turnover intention.

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