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Metabolic and Antidiabetic Effects of *Rosa damascena* Mill. Extract in Animal Models of Diabetes Mellitus: A Systematic Review

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder affecting more than 537 million adults worldwide, with its prevalence in Indonesia projected to reach 16.09% by 2045. Rosa damascena Mill. contains bioactive compounds with antioxidant, anti-inflammatory, and antihyperglycemic properties; however, its antidiabetic potential has not been systematically reviewed. This systematic review aims to evaluate the metabolic and antidiabetic effects of Rosa damascena Mill. extract in animal models of diabetes mellitus. This review followed the PRISMA 2020 guidelines. A comprehensive literature search was conducted in PubMed, ScienceDirect, Web of Science, and ProQuest, identifying 504 records. Six in vivo animal studies met the inclusion criteria. Diabetes was induced using streptozotocin or a high-fructose diet in male Wistar rats. The risk of bias was assessed using the SYRCLE risk-of-bias tool, and reporting quality was evaluated using the ARRIVE Essential 10 guidelines. Findings were synthesised descriptively. Rosa damascena Mill. extract improved glycaemic and metabolic parameters, with a significant reduction in fasting blood glucose at a dose of 1000 mg/kg ($p < 0.0001$) and a consistent reduction in triglyceride levels (75 ± 9 vs. 217 ± 18 mg/dL). Methanolic extract demonstrated 98% α-glucosidase inhibition compared with 51% for acarbose. Improvements in insulin sensitivity, increased adiponectin levels, and reduced NF-κB expression were also observed, although changes in HbA1c were not statistically significant. Although Rosa damascena demonstrates promising antidiabetic effects, the available evidence remains limited due to the small number of studies (n = 6), methodological heterogeneity, and unclear risk of bias, highlighting the need for further standardised research.

INTRODUCTION

Diabetes mellitus is a chronic disorder characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action, or both (Goyal, Jialal and Singhal, 2023). Among its various forms, *type 2 diabetes mellitus* (T2DM) is the most prevalent and is primarily associated with insulin resistance and progressive pancreatic β-cell dysfunction. The global burden of diabetes continues to increase at an alarming rate, making it one of the leading public health challenges worldwide. Diabetes is associated with serious microvascular and macrovascular complications, including nephropathy, neuropathy, retinopathy, cardiovascular disease, and premature mortality (Goyal, Jialal and Singhal, 2023). According to the World Health Organization (WHO), diabetes caused approximately 1.5 million deaths in 2019 (World

Health Organization, 2021). Furthermore, the International Diabetes Federation (IDF) estimated that approximately 537 million adults were living with diabetes in 2021, with this number projected to increase substantially over the coming decades (International Diabetes Federation, 2021)

The burden of diabetes is particularly substantial in Indonesia, where prevalence continues to increase alongside rapid urbanization, population ageing, unhealthy dietary patterns, physical inactivity, and obesity. The *Indonesia Health Survey* (*Survei Kesehatan Indonesia*; SKI) 2023 indicated a continuing increase in diabetes prevalence in the country (Ministry of Health Republic of Indonesia, 2023). The survey further highlighted that diabetes remains highly prevalent and emphasized the need to strengthen diabetes prevention and management strategies. Furthermore, Wahidin et al. (2024) projected that, if current trends continue without adequate prevention and control strategies, diabetes prevalence in Indonesia could increase from 9.19% (18.69 million cases) in 2020 to 16.09% (40.7 million cases) by 2045, underscoring the urgency of identifying effective preventive and therapeutic interventions. Despite advances in pharmacological therapy, diabetes requires lifelong management, and the development of chronic complications substantially increases healthcare utilization and treatment costs (Marthias et al., 2020). Consequently, there is growing interest in identifying complementary therapeutic approaches that are effective, safe, and affordable.

Medicinal plants have received increasing attention as potential complementary therapies for diabetes because they contain diverse bioactive compounds capable of targeting multiple pathogenic pathways involved in disease progression (Leiwakabessy, Gondokesumo and Wahjudi, 2021). Oxidative stress and chronic inflammation are recognized as major contributors to pancreatic β-cell dysfunction, impaired insulin signaling, and the progression of insulin resistance (Cui et al., 2023). Among medicinal plants, *Rosa damascena* Mill. (*Damask rose*) has attracted considerable interest due to its rich phytochemical composition, including flavonoids, polyphenols, tannins, terpenoids, and other phenolic compounds. Mahboubi (2016) reported that these bioactive constituents exhibit antioxidant, anti-inflammatory, and antihyperglycemic activities, suggesting that *Rosa damascena* possesses considerable potential as a complementary therapeutic agent for diabetes management (Mahboubi, 2016). In particular, the petals are the most commonly utilized medicinal part of *Rosa damascena* Mill. because they contain high levels of anthocyanins, terpenoids, and phenolic acids, which demonstrate antidiabetic and hypolipidemic properties (Khezerlou et al., 2025). The petals are processed into various preparations, including methanolic, ethanolic, and aqueous extracts. Furthermore, based on Nurhidayati (2024), the price of *Rosa damascena* Mill. flowers is approximately IDR 250,000 per kg, while Gholamhoseinian, Fallah and Sharififar (2009) used 300 g of air-dried *Rosa damascena* Mill. flowers for experimental purposes. However, despite these reported pharmacological effects, the extent and consistency of the antidiabetic effects of *Rosa damascena* in preclinical diabetes models remain insufficiently investigated.

Although numerous preclinical studies have investigated the metabolic and antidiabetic effects of *Rosa damascena* Mill. in animal models, the available evidence has not been comprehensively synthesized. Moreover, substantial methodological differences exist among animal studies, including variations in animal species, diabetes induction methods, extract preparation techniques, dosage regimens, treatment durations, and outcome measurements.

These variations make it difficult to determine the consistency of reported findings and the overall therapeutic potential of *Rosa damascena*. Therefore, a systematic review is needed to critically evaluate the available preclinical evidence regarding the metabolic and antidiabetic effects of *Rosa damascena* extract in animal models of diabetes mellitus. The findings of this review are expected to provide a clearer understanding of its efficacy, identify current research gaps, and inform future preclinical and clinical investigations.

The research question formulated in this systematic review focuses on whether *Rosa damascena* Mill. extract has the potential to improve glycaemic control and metabolic outcomes in animal models of diabetes mellitus. This study aims to evaluate the antidiabetic and metabolic effects of *Rosa damascena* Mill. extract by assessing its effects on glycaemic parameters, lipid profiles, and other diabetes-related outcomes based on available preclinical evidence. Specifically, this review investigates the antidiabetic effects of *Rosa damascena* Mill. extract, evaluates its metabolic effects, particularly those related to lipid profile parameters, and describes the potential mechanisms underlying the observed therapeutic effects.

METHOD

Protocol and PICO Framework

This systematic review followed the PRISMA 2020 guidelines to ensure standardized and transparent reporting (Sohrabi et al., 2021). Study eligibility was determined using the PICO framework: (1) Population: animal models of diabetes mellitus or hyperglycaemia, including chemically induced and diet-induced models; (2) Intervention: administration of *Rosa damascena* Mill. extract, regardless of extract type, dosage, route of administration, or treatment duration; (3) Comparison: diabetic/hyperglycaemic control animals receiving no treatment, placebo, or standard antidiabetic therapy; and (4) Outcomes: diabetes-related outcomes, including glycaemic, metabolic, inflammatory, histopathological, and other relevant biomarkers.

Search Strategy

A comprehensive literature search was conducted across PubMed, ScienceDirect, Web of Science, and ProQuest using controlled vocabulary (MeSH terms), Boolean operators (AND, OR), and truncation symbols. The key search terms included combinations of "*Rosa damascena*", "diabetes mellitus OR hyperglycaemia", "antidiabetic OR hypoglycaemic agents OR blood glucose OR insulin resistance", and "animal model OR rat OR mice". Supplementary manual searches were also conducted to identify eligible studies that were not captured through electronic database searches.

Eligibility Criteria. Inclusion and exclusion criteria were established based on the PICOS framework as summarized in Table 1.

Table 1. Eligibility criteria based on the PICOS framework

No.	Criteria	Inclusion	Exclusion
1	Population	Animal models with induced diabetes/hyperglycaemia (rats, mice, rodents)	Human trials; in-vitro only studies
2	Intervention	*Rosa damascena* in extract form (aqueous, ethanolic, methanolic, hydroalcoholic, or other preparations)	Non-*Rosa damascena* interventions; non-extract forms

No.	Criteria	Inclusion	Exclusion
3	Comparison	Animals given conventional antidiabetic drugs and/or untreated controls	Absence of control/comparator group; comparisons unrelated to antidiabetic evaluation
4	Outcomes	At least one diabetic/metabolic outcome (blood glucose, insulin, lipid profile, pancreatic histology, alpha-glucosidase inhibition)	No relevant antidiabetic outcomes reported
5	Study design	In vivo preclinical animal experimental studies	Non-open access; non-English articles

Source: Developed by the researcher, 2025

Data Extraction

The following data will be extracted from each included study: first author and year; animal species, strain, sex, age, and sample size; diabetes induction model and method; *Rosa damascena* extract type and extraction method; dosage, route, and treatment duration; comparison group(s); outcome measures (glycaemic, metabolic, inflammatory, histopathological biomarkers); main findings and statistical significance; and study design characteristics.

Study Quality Assessment

Methodological quality will be evaluated using two complementary tools. The SYRCLE Risk of Bias tool (Hooijmans et al., 2014), adapted from the Cochrane RoB tool for animal research, assesses ten signaling questions across six bias domains: selection bias (sequence generation, baseline characteristics), performance bias (allocation concealment, random housing, blinding), detection bias (random outcome assessment, blinding), attrition bias, reporting bias, and other bias. Each item is judged as "Yes," "No," or "Unclear," then categorized as low, high, or unclear risk. Results will be visualized using traffic light plots and summary graphs following the robvis format (McGuinness & Higgins, 2021). Additionally, the ARRIVE Essential 10 Compliance Questionnaire (Percie du Sert et al., 2020) will assess reporting quality across 18 questions covering study design, sample size, randomization, blinding, outcome measures, statistical methods, experimental procedures, and results.

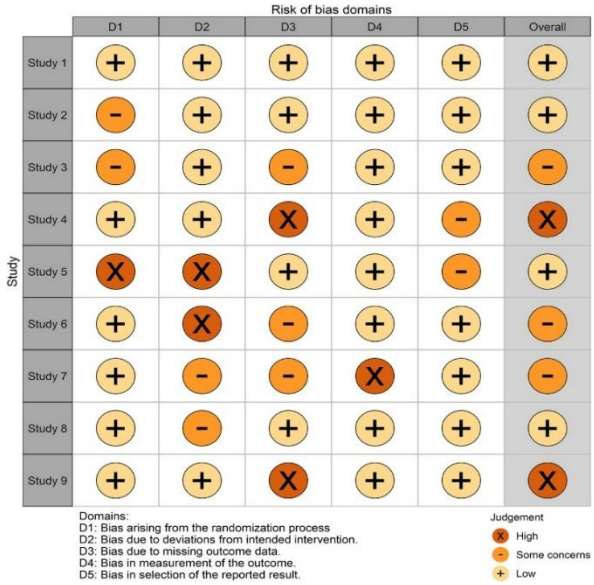

Figure 1. Risk of bias "traffic light" plot sample created using robvis
Source: SYRCLE Risk of Bias analysis using robvis (McGuinness & Higgins, 2021), 2025

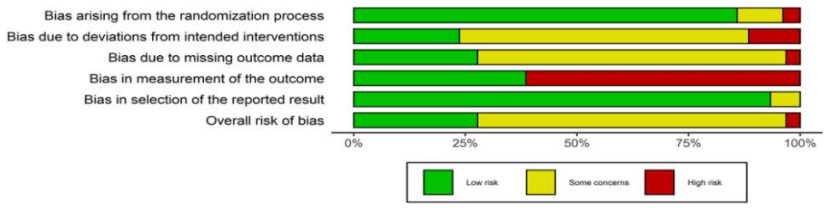

Figure 2. Risk of bias summary plot sample generated using robvis
Source: SYRCLE Risk of Bias analysis using robvis (McGuinness & Higgins, 2021), 2025

Analytical Method. A descriptive narrative approach will be employed to synthesize findings regarding the metabolic and antidiabetic effects of *Rosa damascena* extract in animal models. The review will compare findings related to glycemic control, metabolic parameters, oxidative stress markers, and pancreatic histology to identify patterns and provide a comprehensive understanding of the current preclinical evidence.

RESULTS AND DISCUSSION

Results

Study selection

The study selection process in this systematic review was conducted according to the PRISMA 2020 flow diagram guideline to ensure a systematic and transparent identification of relevant studies (Page et al., 2021). Literature searching was performed using four databases, as mentioned in previous chapter, which are PubMed, ScienceDirect, Web of Science and ProQuest. A total of 504 records were identified from the database searching, consisting of 51 records from PubMed, 202 records from ScienceDirect, 5 records from Web of Science and 246 record from ProQuest. In addition to database searching, five records were identified through Google Scholar for more eligible records to be included in the study.

Before the screening stage, duplicate records were identified and subsequently removed. There was a total of 43 duplicate records were identified, leaving 461 records for title

and abstract screening. During the initial screening process, 456 records were excluded, consisting of 352 records with wrong or irrelevant titles and 104 records with abstracts that were not relevant to the objectives, eligibility criteria and PICOS framework of this review. As a result, five reports were sought for retrieval.

Among the five reports identified through database searching and sought for retrieval, one of the reports could not be accessed because the full text was unavailable. As a result, four reports from database searching were assessed for eligibility. After full text assessment, one report was excluded because it had a different study design which was not an in vivo animal experiment paper. In addition, all five reports identified through Google Scholar were successfully retrieved and assessed for eligibility. From these reports, two were excluded, with one excluded due to unsuitable intervention and another due to an inappropriate outcome.

Following the screening and eligibility assessment, six studies were found to meet the inclusion criteria and were included in the final review. The complete study selection process is shown in the PRISMA 2020 flow diagram.

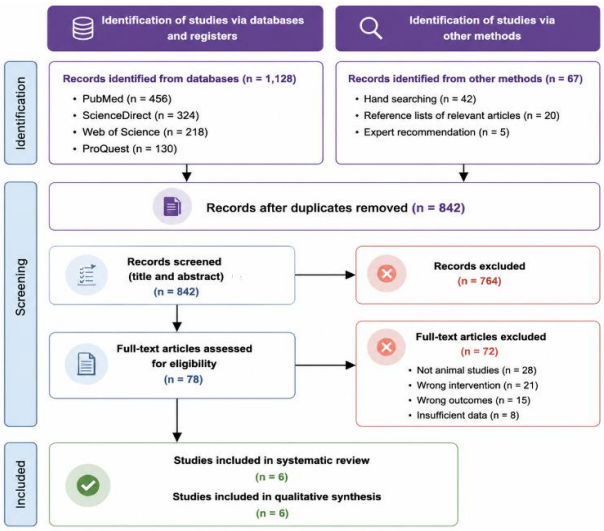

Figure 3. shows the PRISMA 2020 flow diagram illustrating the study selection process for systematic review.

Source: Study selection process following PRISMA 2020 guidelines, 2025

Six studies that met the inclusion criteria of this systematic review evaluated the metabolic and antidiabetic effects of *Rosa damascena* Mill. extract in animal models of diabetes mellitus. All studies used male Wistar rats (Rattus norvegicus) with diabetes induced by streptozotocin (STZ) or insulin resistance induced by a high-fructose diet. *Rosa damascena* extracts were primarily obtained from flower petals using maceration methods with methanol or 96% ethanol as solvents. The included studies assessed various parameters, including blood glucose levels, lipid profiles, insulin sensitivity, inflammatory biomarkers, molecular expression, pancreatic histopathology, and hematological parameters (Mohammadi et al., 2017; Choirotussanijjah et al., 2021; Inayatillah et al., 2021; Jauhar et al., 2021; Dewi, Jauhar and Wibowo, 2023).

The findings indicate that *Rosa damascena* Mill. has potential beneficial effects on metabolic and glycemic parameters. Gholamhoseinian et al. (2009) reported α-glucosidase

inhibitory activity of 98% compared with 51% for acarbose, along with a significant reduction in postprandial glucose levels ($p < 0.0001$). Mohammadi et al. (2017) observed significant reductions in fasting blood glucose, insulin levels, HOMA-IR, and triglycerides, accompanied by increased adiponectin levels and PPAR-γ expression in insulin-resistant rats. Inayatillah et al. (2021) also reported reductions in blood glucose levels and increased pancreatic islet diameter, although the differences did not reach statistical significance. Furthermore, Jauhar et al. (2021) demonstrated significant improvements in lipid profiles through reductions in triglycerides, total cholesterol, and LDL levels, while HDL levels did not show significant changes.

Beyond glycemic and metabolic parameters, several studies investigated additional mechanisms underlying the effects of *Rosa damascena* Mill. extract. Choirotussanijjah et al. (2021) reported that the extract did not significantly alter HbA1c levels but significantly reduced NF-κB expression, suggesting potential anti-inflammatory activity. Mohammadi et al. (2017) further demonstrated improved insulin sensitivity through reduced HOMA-IR and increased adiponectin levels, although GLUT4 expression remained unchanged. Meanwhile, Dewi, Jauhar and Wibowo (2023) found no significant improvements in most hematological parameters but observed a favourable trend in reducing the neutrophil-to-lymphocyte ratio (NLR). Overall, the available evidence suggests that *Rosa damascena* Mill. may exert antidiabetic effects through glucose regulation, lipid metabolism improvement, enhanced insulin sensitivity, and inflammatory modulation; however, further well-designed studies with standardized methodologies are required to confirm its therapeutic potential.

Study Quality Assessment

SYRCLE risk of bias

The results of the SYRCLE risk of bias assessment are presented in table 9 and figure 13. Table 9 displays the risk of bias judgements for each included study using a traffic-light plot, providing a visual overview of the methodological quality of the included studies. Overall, the assessment demonstrated a low risk of bias for incomplete outcome data and selective reporting across all included studies. In contrast, most studies were rated as having an unclear risk of bias for allocation concealment, random housing, blinding of caregivers and investigators, random outcome assessment and blinding of outcome assessors due to insufficient reporting of methodological procedures.

In addition, Figure 13 presents a stacked horizontal bar chart summarizing the proportion of low, unclear, and high-risk ratings across each SYRCLE domain. Incomplete outcome data and selective reporting were consistently rated as low risk of bias in all included studies (100%). Baseline characteristics were judged as low risk in 66.7% of studies and unclear in 33.3%, while sequence generation was assessed as low risk in 50% of studies and unclear in 50%. Allocation concealment, random housing, blinding of caregivers and investigators, random outcome assessment, and blinding of outcome assessors were rated as unclear risk of bias in all studies (100%). Other sources of bias were assessed as low risk in 83.3% of studies and unclear in 16.7%. No high risk of bias ratings was identified across any of the assessed SYRCLE domains.

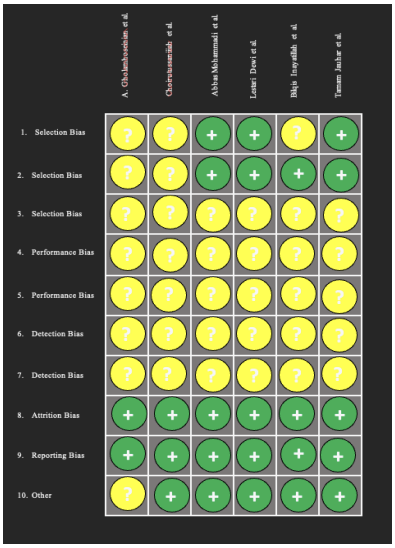

Figure 4. Quality assessment with SYRCLE's risk of bias tool for animal studies
Source: Study quality assessment using SYRCLE Risk of Bias tool, 2025

Review authors judgment:

1. Was the allocation sequence adequately generated and applied?
2. Were the groups similar at baseline or were they adjusted for confounders in the analysis?
3. Was the allocation adequately concealed?
4. Were the animals randomly housed during the experiment?
5. Were the caregivers and/or investigators blinded from knowledge which intervention each animal received during the experiment?
6. Were animals selected at random for outcome assessment?
7. Was the outcome assessor blinded?
8. Were incomplete outcome data adequately addressed?
9. Are reports of the study free of selective outcome reporting?
10. Was the study apparently free of other problems that could result in high risk of bias?

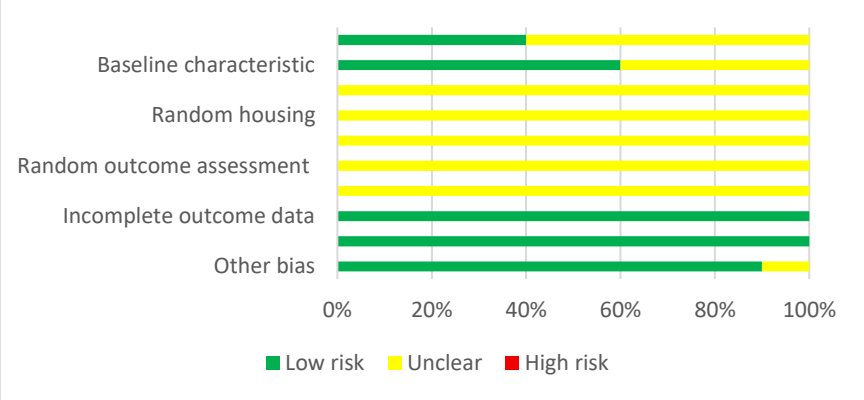

Figure 5. Overall SYRCLE Risk of Bias (RoB) of each domain for all included studies
Source: SYRCLE Risk of Bias assessment results, 2025

ARRIVE 2.0 reporting quality assessment

The completeness and transparency of reporting of the included studies were assessed using the ARRIVE Essential 10 compliance assessment, whereby each study was evaluated

with 18 reporting questions of all the ten ARRIVE items. As reported in Table 10, it is observed that the reporting compliance across the six included studies ranged from 61.1% to 72.2%. It is reported that the highest compliaceout of the six included studies was observed in Inayatilla et al. (2021) and Choirotussanijjah et al. (2021), both scoring 72.2%. In contrast, the two studies with the lowest compliance both had a compliance rate of 61.1% were observed in Gholamhoseinian et al. (2009) and Dewi et al. (2023). Meanwhile, the remaining two studies, Mohammade et al. (2017) and Jauhar et al. (2021), scored a compliance rate of 66.7%. It is worth noting that the ARRIVE guidelines do not provide any threshold to classify these studies as having a poor or good compliance score.

Overall, most studies reported basic experimental details, including the study groups, number of animals per group, outcome measures, animal characteristics, timing of procedures and descriptive statistics. However, it can be seen that there are several items that were underreported across the six included studies. None of the included studies reprted the sample size calculation, blinding or effect size with confidence intervals. Most of the included studies did not state whether any animals, experimental units or data points were excluded. In general, the included studies described the main experimental design and outcomes, but reporting was less complete for methodological details related to sample size determination, blinding, exclusion reporting and effect size estimation.

Table 2. ARRIVE Essential 10 compliance assessment of the included studies.

Author and year of publication	Study design		Sample size		Inclusion & Exclusion Criteria		Randomization	Blinding	Outcome Measures	Statistical Methods		Experimental Animals			Experimental Procedures		Results		%
	1A	1B	2A	2B	3A	3B	4	5	6	7A	7B	8A	8B	8C	9A	9B	10A	10B	
Inayatillah et al., 2021	Y	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	72.2
Mohammadi et al., 2017	Y	Y	Y	N	N	N	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	N	66.7
Jauhar et al., 2021	Y	Y	Y	N	Y	N	Y	N	Y	Y	N	Y	Y	Y	Y	N	Y	N	66.7
Choirotussanijjah, 2021	Y	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	72.2
Dewi et al., 2023	N	Y	Y	N	Y	N	Y	N	Y	Y	N	Y	Y	Y	Y	N	Y	N	61.1
Gholamhoseinian et al., 2009	Y	Y	Y	N	Y	N	N	N	Y	Y	N	Y	Y	Y	Y	Y	Y	N	61.1

Judgements:
Y: YES
N: NO

Source: Reporting quality assessment using ARRIVE Essential 10 questionnaire, 2025

Characteristics of included study

1.3.1 Fasting Blood Glucose Level Outcome

Two included studies by Mohammadi et al. and Inayatillah et al. evaluated the effect of *Rosa damascena* extract on fasting blood glucose levels in animal models of diabetes mellitus. Both studies reported a reduction in fasting blood glucose following extract administration, although the magnitude and statistical significance varied. Mohammadi et al. reported a significant reduction in fructose-induced insulin-resistant rats, with glucose levels decreasing to 129±4.7 mg/dL compared with 187±15 mg/dL in the healthy control group. Similarly, Inayatillah et al. observed reductions in STZ-induced diabetic rats treated with *Rosa damascena* extract at doses of 250 and 500 mg/kg BW, although these changes were not statistically significant. An increase in glucose levels was observed at the 1000 mg/kg BW dose. Despite these differences, both studies demonstrated a consistent trend toward improved fasting blood glucose regulation, suggesting the potential role of *Rosa damascena* in glycaemic control under diabetic conditions.

Lipid Profile Test Outcome

Two studies by Mohammadi et al. and Jauhar et al. evaluated the effects of *Rosa damascena* extract on lipid profile parameters, particularly triglycerides and cholesterol levels. Mohammadi et al. reported a significant reduction in triglyceride levels in fructose-induced insulin-resistant rats, with treated animals showing triglyceride concentrations of 75 ± 9 mg/dL compared with 217 ± 18 mg/dL in untreated controls ($p < 0.0001$). However, changes in total cholesterol were not statistically significant. Jauhar et al. also reported improvements in lipid parameters in STZ-induced diabetic rats, with the greatest triglyceride reduction observed at a dose of 500 mg/kg BW and significant reductions in cholesterol levels compared with diabetic controls. Although variations existed in animal models, extract preparation, and dosage, both studies indicated favourable effects of *Rosa damascena* on lipid metabolism, particularly through triglyceride reduction.

Other Experimental Outcomes

Several additional outcomes related to diabetes mellitus were evaluated, including postprandial glucose, α-glucosidase inhibition, HbA1c, inflammatory markers, insulin sensitivity, molecular markers, pancreatic histopathology, and hematological parameters. Gholamhoseinaian et al. reported that *Rosa damascena* methanolic extract demonstrated stronger α-glucosidase inhibitory activity (98%) compared with acarbose (51%) ($p<0.0001$) and significantly reduced postprandial glucose elevation in diabetic rats, suggesting inhibition of carbohydrate digestion as a potential mechanism. Choirotussanijjah et al. found no significant improvement in HbA1c levels but reported reduced NF-κB expression, indicating possible anti-inflammatory activity. Mohammadi et al. demonstrated improved insulin sensitivity through reductions in serum insulin and HOMA-IR values, increased adiponectin levels, and enhanced PPAR-γ expression, although GLUT4 expression remained unchanged. Inayatillah et al. reported improved pancreatic islet diameter following extract administration, although differences were not statistically significant. Meanwhile, Dewi et al. found no significant changes in most hematological parameters, but a lower neutrophil-to-lymphocyte ratio at 1000 mg/kg BW suggested a potential anti-inflammatory effect of *Rosa damascena* extract. Overall, these findings provide additional evidence regarding the potential metabolic, anti-inflammatory, and insulin-sensitizing effects of *Rosa damascena* in diabetes mellitus

models.

Antidiadiabetic and metabolic effect of *Rosa damascena* Mill

The findings of this systematic review indicate that *Rosa damascena* possesses promising metabolic and antidiabetic properties in experimental animal models. Across the included studies, administration of *Rosa damascena* Mill. Extracts were associated with favourable effects on fasting blood glucose levels, lipid profile parameters, and several markers of insulin sensitivity, although improvements in HbA1c were not consistent. Notably, Gholamhoseinian et al. (2009) reported significant reductions in postprandial blood glucose levels in both normal and diabetic rats following administration of methanolic *Rosa damascena* extract, while Mohammadi et al. demonstrated improvements in fasting blood glucose, insulin levels, and HOMA-IR in a fructose-induced insulin resistance model. Similarly, Inayatillah et al. observed reductions in fasting blood glucose following treatment with ethanolic *Rosa damascena* extract, although these changes did not reach statistical significance. Furthermore, Jauhar et al. reported reductions in triglyceride, total cholesterol and LDL concentrations following administration of *Rosa damascena* extract in STZ induced diabetic rats. The observed effects are consistent with evidence indicating that plant-derived phytochemicals, particularly polyphenols and flavonoids, can modulate glucose homeostasis through multiple biological pathways, including improved insulin sensitivity and reduced glucose absorption. as reported by Aryaeian, Khorshidi Sedehi and Arablou (2017). Similar observations have also been described by Ansari et al. (2024), where they highlighted the role of phytochemical rich plant extracts in the regulation of glucose metabolism and insulin responsiveness (Ansari et al., 2024)

The improvement in insulin resistance reported by Mohammadi et al. provides further support for the antidiabetic potential of *Rosa damascena*. In addition to reducing fasting glucose concentrations, treatment with *Rosa damascena* resulted in marked reductions in insulin levels and HOMA-IR, accompanied by a substantial increase in circulating adiponectin. This pattern of findings is noteworthy because adiponectin has consistently been identified as an important regulator of metabolic homeostasis and insulin sensitivity. Previous evidence has demonstrated that adiponectin exhibits a significant inverse relationship with HOMA-IR, fasting glucose, and triglyceride concentrations, indicating that lower adiponectin levels are associated with greater insulin resistance and metabolic dysfunction (Shaheer, Akhtar and Jallo, 2025). Similarly, Khoramipour et al. (2023) reported that adiponectin enhances insulin sensitivity and contributes to the regulation of both glucose and lipid metabolism through adiponectin receptor-mediated signaling pathways. Therefore, the simultaneous increase in adiponectin and reduction in HOMA-IR observed by Mohammadi et al. suggests that the glucose-lowering effects of *Rosa damascena* may extend beyond direct glycaemic control and may also involve improvements in insulin responsiveness and overall metabolic regulation. Furthermore, the reduction in triglyceride concentrations reported by both Mohammadi et al. and Jauhar et al., together with the improvements in total cholesterol and LDL levels observed by Jauhar et al., strengthen this interpretation, as adiponectin has also been associated with favourable lipid metabolism and improved cardiometabolic health (Shaheer, Akhtar and Jallo, 2025).

A similar pattern was observed across the included studies, although the magnitude and nature of the antidiabetic effects varied according to the experimental model, outcome

measured, dosage, and treatment duration. Gholamhoseinian et al. (2009) demonstrated the extract reduced postprandial hyperglycemia through the inhibition of α-glucosidase activity, thereby inhibiting intestinal carbohydrate absorption. Mohammadi et al. (2017) reported improvements in metabolic parameters associated with insulin resistance, accompanied by increased adiponectin concentration and PPAR-γ expression. In addition, Jauhar et al. demonstrated significant improvements in lipid profile parameters, including reductions in triglyceride, total cholesterol, and LDL concentrations, suggesting a potential role of *Rosa damascena* in improving diabetes-associated dyslipidaemia. Other studies reported beneficial effects on specific pathological processes associated with diabetes, including suppression of NF-κB-mediated inflammation, while outcomes such as Hb1Ac levels, pancreatic islet morphology, and most haematological parameters did not demonstrate statistically significant improvement (Choirotussanijjah et al., 2021; Inayatillah et al., 2021; Dewi et al., 2023).

An important consideration that is noteworthy is the variation in the amount of plant material and the type of extract used across the included studies. It is observed that none of the included studies reported the exact number of petals used. Instead, most studies reported the weight of dried flowers or dried plant material used for extraction. The reported amount of *Rosa damascena* used to prepare across all studies ranged from 100g to 800g, while one study did not clearly state the weight of plant material used. Furthermore, there were noticeable differences in the type of extract used, with some studies using methanolic flower extract and others using ethanolic extract prepared with 96% ethanol. Notably, from the six included studies, the methanolic extract reported more consistent favourable effects on glycemic and metabolic outcomes. However, proving that methanol as the superior solvent in providing a better pharmacological effect of *Rosa damascena* is not applicable, as the difference in solvent and extraction duration may influence the composition of bioactive compounds in the extract.

The dose associated with the most favourable outcome was different across the included studies. Gholamhoseinian et al. (2009) reported that the effectiveness is dose dependent, with the strongest effect observed at 1000 mg/kg of methanolic *Rosa damascena* extract. Mohammadi et al. (2017) reported that there is a significant improvement in the glycemic and metabolic outcomes, although only one dose was tested, which is 100 mg/kg BW. The duration of the extract administration also varied across the studies. Most studies administered the extract for 14 days, while Choirotussanijjah et al. (2021) used a longer treatment period of 28 days. However, Choirotussanijjah et al. (2021) reported that despite the improvement of NF-κB expression, the lack of significance in the improvement of HbA1c may been partly related to the relatively short duration.

Collectively, these findings suggest that the metabolic and antidiabetic activity of *Rosa damascena* may be mediated through multiple complementary mechanisms rather than a single biological pathway. Nevertheless, differences in animal species, diabetic induction methods, extract preparation, dosage regimens, and duration of treatment may have contributed to the variability observed among studies (Hrițcu et al., 2025). Therefore, while the available preclinical evidence supports the potential antidiabetic effects of *Rosa damascena*, the findings should be interpreted with caution, and further preclinical and clinical studies are required to establish the consistency and translational relevance of these effects to clinical settings (Furman, 2021).

Potential mechanisms of the antidiabetic effect and metabolic of *Rosa damascena* Mill

The metabolic and antidiabetic effects of *Rosa damascena* may be associated with its diverse phytochemical compounds, including flavonoids, anthocyanins, phenolic compounds, glycosides, terpenes, and essential oils, which exhibit antioxidant and anti-inflammatory activities (Labban and Thallaj, 2020; Chandana et al., 2024). Oxidative stress plays an important role in diabetes progression by promoting pancreatic β-cell dysfunction, impaired insulin signalling, and insulin resistance (Caturano et al., 2023). Therefore, the antioxidant properties of *Rosa damascena* may contribute to improved glucose regulation by reducing oxidative damage. Although several compounds, such as kaempferol, cyanidin-3,5-diglucoside, quercetin, and gallic acid, have been identified as potential contributors, the included studies did not isolate individual compounds to determine their specific effects (Dewi, Jauhar and Wibowo, 2023). Choirotussanijjah et al. (2021) also reported anthocyanin content in *Rosa damascena* extract, suggesting its possible contribution to the observed pharmacological effects. One proposed mechanism is α-glucosidase inhibition, as demonstrated by Gholamhoseinian et al. (2009), where methanolic extract of *Rosa damascena* reduced postprandial glucose levels through inhibition of carbohydrate digestion. This mechanism is supported by previous findings that α-glucosidase inhibition delays glucose absorption and reduces postprandial hyperglycaemia (Akmal, Patel and Wadhwa, 2024; Dirir et al., 2022). Furthermore, flavonoids, polyphenols, tannins, and terpenoids may contribute to this activity through interaction with α-glucosidase enzymes (Leiwakabessy, Gondokesumo and Wahjudi, 2025; Cahyana and Adityanti, 2021).

Another potential mechanism involves improvement of insulin sensitivity through adiponectin and PPAR-γ pathways. Mohammadi et al. (2017) reported that *Rosa damascena* extract increased adiponectin levels and PPAR-γ expression, while reducing fasting glucose, insulin concentration, triglycerides, and HOMA-IR values. These findings are consistent with the role of adiponectin in enhancing insulin sensitivity, glucose uptake, and lipid metabolism through pathways such as AMPK activation (Khoramipour et al., 2021). Improvements in lipid parameters reported by Jauhar et al. further support the potential metabolic benefits of *Rosa damascena*. In addition, anthocyanins and polyphenolic compounds may enhance insulin responsiveness and regulate glucose metabolism through antioxidant and metabolic signalling pathways (Escobar et al., 2025). Beyond metabolic regulation, *Rosa damascena* may also exert antidiabetic effects through anti-inflammatory mechanisms. Choirotussanijjah et al. (2021) demonstrated reduced NF-κB expression following extract administration, suggesting suppression of inflammatory pathways associated with insulin resistance. Since NF-κB plays a key role in regulating inflammatory responses and diabetic complications (Mobeen et al., 2025), its inhibition may contribute to improved metabolic homeostasis. These findings are further supported by evidence that anthocyanins and phenolic compounds can reduce inflammation and oxidative stress, while enhancing glucose regulation (Kozłowska and Nitsch-Osuch, 2024; Escobar et al., 2025; Khezerlou et al., 2025). Overall, the effects of *Rosa damascena* appear to involve multiple interconnected mechanisms, including antioxidant activity, inhibition of carbohydrate digestion, improvement of insulin sensitivity, and modulation of inflammatory pathways.

These findings suggest that the metabolic and antidiabetic effects of *Rosa damascena* may be mediated through multiple interconnected mechanisms, including antioxidant activity,

inhibition of carbohydrate digestion, enhancement of insulin sensitivity, and suppression of inflammatory pathways.

Strengths, Limitations, and Future Research Directions

Despite the limitations associated with preclinical research, several strengths of the current evidence base should be acknowledged. Across the six included studies, *Rosa damascena* consistentely demonstrated beneficial effects on diabetes related outcomes, including improving the glycemic control, lipid profile parameters, insulin resistance and inflammatory markers. These findings support the biological plausibility of *Rosa damascena* as a potential antidiabetic agent and provide a foundation for future research.

While the available evidence indicated promising antidiabetic effects of *Rosa damascena*, several limitations should be considered when interpreting the findings. Substantial heterogeneity was observed across studies with respect to animal species, diabetic induction methods, extract preparation, dosage regiments and treatment duration, which may complicate comparisons and contribute to variability in outcomes (Puerto Nino et al., 2021). In addition, only fasting blood glucose and lipid profile parameters were evaluated in more than one study, limiting the ability to compare findings across other diabetes-related outcomes. The relatively small number of included studies further restricts the strength of the available evidence. Moreover, although the SYRCLE Risk of Bias assessment indicated generally low risk in domains related to incomplete outcome data and selective reporting, several studies demonstrated an unclear risk of bias due to insufficient reporting of allocation concealment, randomization procedures, and blinding methods, a common issue in animal research (Hooijimans et al., 2014). These limitations may reduce the certainty of the evidence and increase uncertainty in the interpretation of findings (Brignardello-Petersen and Guyatt, 2025). Therefore, further well-designed preclinical and clinical studies with improved methodological reporting are required to strengthen the evidence base and confirm the therapeutic potential of *Rosa damascena* in diabetes management.

CONCLUSION

Based on the findings of this systematic review, *Rosa damascena* Mill. extract demonstrates potential antidiabetic and metabolic effects in animal models of diabetes mellitus. Among the six included studies, most reported improvements in glycemic parameters, particularly fasting blood glucose levels, although the magnitude of effects and statistical significance varied across studies. In addition, *Rosa damascena* extract showed potential benefits in improving lipid profiles, with triglyceride reduction being the most consistently reported outcome, while changes in total cholesterol and LDL levels require further confirmation. However, these findings should be interpreted cautiously due to variations in animal models, diabetes induction methods, extract types, dosages, treatment durations, and measured outcomes across studies. This review has several limitations, including the limited number of available studies, the small number of outcomes that could be directly compared between studies, and substantial methodological heterogeneity among the included research. Furthermore, since all available evidence was derived from animal models, the applicability of these findings to humans requires further validation. Future studies should utilize standardized *Rosa damascena* Mill. extracts, consistent dosage regimens, and comparable treatment durations, while also investigating safety profiles, mechanisms of action, and optimal dosages.

Further preclinical studies (in vitro and in vivo) as well as clinical trials in humans are necessary to determine whether the therapeutic potential of *Rosa damascena* can be effectively translated into diabetes mellitus management.

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