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Antidiabetic Effects of Moringa oleifera Leaf Extract on Blood Glucose Levels in Alloxan-Induced Diabetic Rats (Rattus norvegicus): A Systematic Literature Review

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ABSTRACT

Introduction: This systematic literature review, guided by PRISMA guidelines, evaluates the effectiveness of Moringa oleifera leaf extracts in reducing blood glucose levels in alloxan-induced diabetic rats.

Method: Literature was searched in PubMed and Google Scholar using keywords including "Moringa oleifera," "leaf extract," "alloxan-induced diabetes," and "blood glucose." From 472 identified articles, 9 studies met inclusion criteria and were analyzed.

Results: Nearly all studies reported significant reductions in blood glucose levels following administration of Moringa oleifera leaf extracts at effective doses ranging from 200–800 mg/kg body weight over 14–28 days. Key mechanisms include protection of pancreatic β-cells from oxidative stress, enhanced insulin secretion, and improved insulin sensitivity. Both aqueous and ethanolic extracts exhibited antihyperglycemic effects, with aqueous extracts demonstrating faster onset and ethanolic extracts providing more sustained outcomes.

Conclusion: These findings support the potential of Moringa oleifera leaf extracts as a natural antidiabetic agent in preclinical models. However, further research is required to standardize extraction methods, dosages, and molecular mechanisms to facilitate clinical translation in humans.

Keywords

Moringa Oleifera, Leaf Extract, Alloxan-Induced Diabetes, Blood Glucose, Antidiabetic, Systematic Review

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both [1]. The global prevalence of diabetes has risen dramatically, with the International Diabetes Federation (IDF) Diabetes Atlas 11th edition reporting that 589 million adults aged 20–79 years were living with diabetes in 2024, representing 11.1% of the adult population, with projections indicating an increase to 853 million by 2050 [2]. This escalating epidemic poses significant public health challenges, contributing to substantial morbidity, mortality, and economic burden exceeding USD 1 trillion annually in terms of healthcare costs [2].

The limitations of conventional antidiabetic therapies, including high costs, long-term side effects, and restricted access in developing countries, have spurred interest in safer and more affordable natural alternatives [3]. Moringa oleifera L. (Moringaceae), a tropical plant widely known as the drumstick tree, has emerged as a promising candidate due to its rich bioactive profile, including flavonoids (quercetin, kaempferol), isothiocyanates (moringin), chlorogenic acid, and saponins [4,5]. These compounds exert antioxidant, anti-inflammatory, and antihyperglycemic effects through mechanisms such as protection of pancreatic β-cells

from oxidative stress, enhancement of insulin sensitivity, and inhibition of carbohydrate-digesting enzymes [6,7]. Preclinical evaluation often employs animal models, with Rattus norvegicus (rats) favored because of its physiological similarities to humans, short life cycle, and ease of laboratory handling [8]. Alloxan-induced diabetes selectively destroys pancreatic β-cells via oxidative stress, inducing hyperglycemia that mimics the characteristics of type 1 diabetes [9,10].

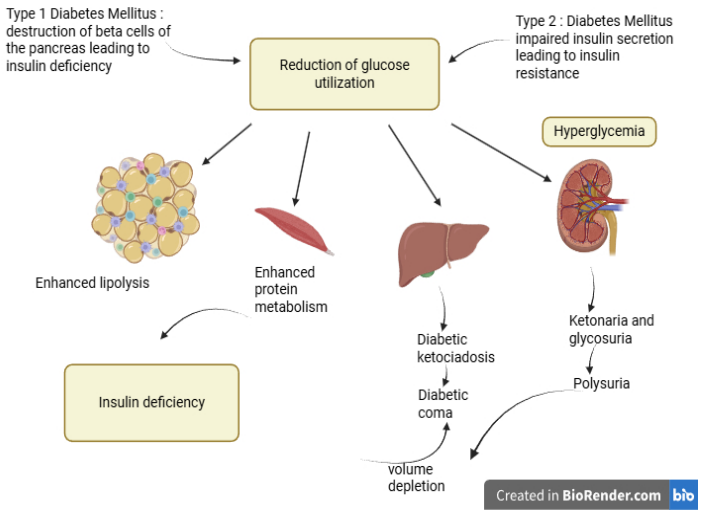

Figure 1. Pathophysiology of Diabetes Mellitus

Diabetes pathogenesis primarily involves insulin resistance, which is influenced by tissue sensitivity and utilization. Figure 1 diabetes is characterized by absolute insulin deficiency due to autoimmune β-cell destruction, often leading to rapid fat breakdown, hepatic ketone production, and diabetic ketoacidosis [11]. In contrast, Figure 2 shows that diabetes combines relative insulin deficiency with peripheral resistance, exacerbated by elevated inflammatory cytokines and free fatty acids, resulting in impaired glucose uptake, lipolysis, and hepatic gluconeogenesis [12]. Rodent models are commonly used for antidiabetic drug screening because of their small size, rapid induction, manageability, and cost-effectiveness, typically via chemical agents that elevate blood glucose levels [13].

This systematic literature review synthesizes preclinical evidence on the potential of Moringa oleifera leaf extract to lower blood glucose in alloxan-induced diabetic rats, evaluating consistency across studies, influencing factors on efficacy, and methodological/theoretical gaps to guide standardized future research with translational relevance to humans.

METHOD

This systematic literature review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to maintain a structured, transparent, and reproducible methodology. The literature search involved querying electronic databases, such as PubMed and Google Scholar, utilizing a combination of keywords related to the topic, including terms for the plant leaves, extraction methods, the animal model of diabetes induction, and blood glucose measurement, along with relevant synonyms connected through Boolean operators to refine the results. The search was confined to recent publications to emphasize contemporary evidence without imposing language barriers.

Inclusion criteria focused on primary in vivo research that examined a specified animal model of induced diabetes, administered the leaf extract as an intervention, and reported measurable changes in blood glucose levels before and after treatment, ensuring full-text availability for detailed evaluation. Conversely, the exclusion criteria encompassed outdated studies, secondary sources such as reviews or editorials, non-experimental formats such as case reports, investigations conducted in vitro or on human subjects, and any work lacking quantifiable data on the primary outcome. The selection process progressed logically through sequential stages: initial record identification from the databases, elimination of redundant entries, and

preliminary screening based on titles and abstracts to assess relevance, followed by retrieval and thorough review of full texts to confirm eligibility, culminating in the inclusion of qualifying studies for synthesis. Reference organization and duplicate handling were supported by bibliographic management software to enhance efficiency and accuracy.

The analytical framework was guided by a structured approach that defined the key elements of the review, encompassing the target population of diabetic animal models with elevated blood glucose, the intervention involving various forms and dosages of the leaf extract, comparisons often drawn against untreated control groups, and outcomes centered on blood glucose reduction alongside potential protective effects on relevant physiological structures. Data extraction systematically captured essential details from each included study, such as authorship and publication timing, experimental design, specifics of the animal model, characteristics of the extract, including preparation and administration, treatment duration, and principal results concerning glucose modulation and underlying mechanisms. A qualitative synthesis was then undertaken to appraise the overall patterns and consistency of the findings across the selected body of evidence, facilitating a coherent interpretation of the intervention's effects.

RESULTS

Qualitative synthesis of the nine included studies consistently demonstrated the significant antihyperglycemic effects of Moringa oleifera leaf extract in alloxan-induced diabetic rats. All studies reported statistically significant reductions in blood glucose levels following extract administration, with effects typically observed within 7–28 days.

Table 1. Summary of Included Studies on the Antihyperglycemic Effects of Moringa oleifera Leaf Extract

No.	Authors (Year)	Extraction Method	Doses (mg/kg BW)	Duration (days)	Key Findings
1	Egbujo et al. (2024)	Aqueous (fresh leaves, evaporated at 45°C)	200, 400, 800	28	Significant glucose reduction; most effective at 800 mg/kg with β-cell protection and increased antioxidant enzymes.
2	Nurmalasari et al. (2021)	Ethanolic 96% (dried leaves)	150, 450	28	Significant reduction; optimal at 450 mg/kg in Wistar rats.
3	Azizah et al. (2018)	Ethanolic 70% (fresh leaves)	50, 100, 150	9	Effective reduction; optimal at 100 mg/kg in male rats.
4	Aini (2019)	Ethanolic 75% (fresh leaves)	150, 450	21	Superior reduction at 450 mg/kg compared to 150 mg/kg in Wistar rats.
5	Toby et al. (2020)	Ethanolic	250, 450, 600	23–27	Consistent reduction; optimal at 450 mg/kg in Sprague-Dawley rats.
6	Yasaroh et al. (2021)	Ethanolic 96% (dried leaves)	200, 400, 600	14–21	Significant ($p<0.05$); near-normal levels at 400 mg/kg in Wistar rats.
7	Ezeigbo et al. (2016)	Aqueous & ethanolic 98% (dried leaves)	50, 100, 150	14	Aqueous more effective (45.2% reduction) than ethanolic (33.7%).
8	Mbulang'a et al. (2020)	Ethanolic 70% maceration (fresh leaves)	20, 40, 60	7–14	Significant from day 7; most effective at 20 mg/kg in Wistar rats.
9	Sari et al. (2024)	Ethanolic (dried leaves)	250, 500	21	Greater reduction at 500 mg/kg compared to 250 mg/kg in Wistar rats.

The hypoglycemic activity exhibited a dose-dependent response, with effective doses ranging from 50 to 800 mg/kg body weight, and optimal efficacy frequently noted at 400–500 mg/kg. Commonly reported mechanisms include protection of pancreatic β-cells from alloxan-induced oxidative damage, enhancement of insulin secretion, elevation of antioxidant enzyme activity, and improved glucose homeostasis. Both aqueous

and ethanolic extracts proved effective, although aqueous extracts often demonstrated a more rapid onset, while ethanolic extracts provided sustained effects.

DISCUSSION

Extensive research on the antihyperglycemic activity of Moringa oleifera L. leaves has been conducted using white rats (Rattus norvegicus), particularly Wistar and Sprague-Dawley rats. The Wistar strain is recognized for its stable metabolic response to blood glucose fluctuations and is commonly used as an experimental diabetes model [14]. In contrast, the Sprague-Dawley strain exhibits greater sensitivity to pharmacological interventions and has a larger body size, facilitating easier blood sampling [15-23]. Both strains possess glucose metabolism systems akin to humans, especially in the mechanisms of insulin secretion by pancreatic β-cells, making them suitable animal models for evaluating the antidiabetic potential of natural compounds, such as Moringa oleifera leaves [24].

The induction of hyperglycemia in experimental animals via chemical agents has been widely validated in various studies as an in vivo model. Alloxan is a commonly used inducer owing to its rapid and permanent elevation of blood glucose levels within 2–3 days, mimicking type 1 diabetes mellitus in humans [25]. Chemically, alloxan is a urea derivative with the structure 5,5-dihydroxypyrimidine-2,4,6-trione and a molecular formula of $C_3H_2N_2O_3$, possessing a relative molecular mass of 142.06 g/mol [16]. It can be synthesized through the oxidation of uric acid with nitric acid or barbituric acid by chromium trioxide, yielding a monohydrate form [26]. The mechanism of alloxan-induced diabetes involves two primary pathways: inhibition of insulin secretion by blocking glucokinase activity, and enhancement of reactive oxygen species (ROS) formation. In the first pathway, alloxan binds to thiol groups on glucokinase, thereby reducing glucose oxidation, ATP production, and insulin secretion. The second pathway elevates ROS, causing DNA damage in pancreatic β-cells, leading to cell necrosis and diminished insulin production capacity [27-31].

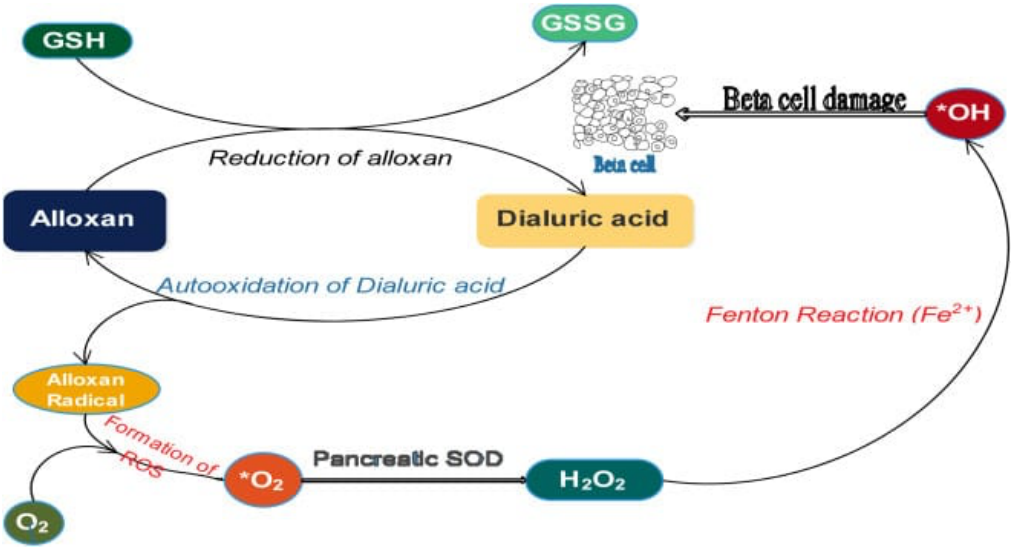

Figure 2. Formation of ROS through the Alloxan Redox Cycle

Oxidative stress arises from an imbalance between ROS production and the body's ability to neutralize these harmful molecules. In diabetes, this imbalance is often triggered by hyperglycemia and other metabolic disruptions that amplify ROS generation, impair the antioxidant defense system, and disrupt the redox balance. Consequently, this exacerbates diabetes-related pathophysiological processes, including impaired insulin synthesis and β-cell dysfunction in the pancreas [32-34]. Studies on the activity of Moringa oleifera leaves against blood glucose levels typically employ aqueous and ethanol (70–98%) solvents for extraction, which are selected based on the polarity of the active compounds. Water, as a polar solvent, extracts hydrophilic compounds such as vitamin C, phenolic acids, and certain flavonoids, whereas ethanol, being a semi-polar solvent, dissolves lipophilic flavonoids, alkaloids, tannins, saponins, and triterpenoids.

Research indicates that aqueous extracts often yield faster antihyperglycemic effects owing to their high-activity polar antioxidants against free radicals. For instance, Egbujo Ejike Amina et al. (2024) reported that 800 mg/kg body weight (BW) aqueous extract significantly reduced blood glucose levels after 28 days and protected pancreatic β-cells from oxidative damage. Conversely, ethanol extracts provide more gradual but potent long-term effects by extracting larger molecular weight compounds, such as flavonoids and saponins, which stimulate pancreatic regeneration and improve insulin sensitivity. Non-polar solvents such as n-hexane or chloroform are avoided owing to their extraction of non-antihyperglycemic essential oils and steroids, along with potential toxicity. Thus, aqueous and ethanol solvents are deemed optimal for obtaining a broad spectrum of active compounds from Moringa oleifera leaves that lower blood glucose.

Variations in the efficacy of Moringa oleifera leaf extracts on blood glucose reduction were observed across doses, treatment durations, and solvents. Amina et al. (2024) found that among 200, 400, and 800 mg/kg BW aqueous doses, 800 mg/kg BW achieved the most significant reduction after 28 days, which was attributed to higher bioactive compound delivery optimizing antioxidant and regenerative effects on the pancreas. However, Azizah et al. (2018) noted that a 100 mg/kg BW 70% ethanol extract was more effective than higher doses over 9 days, suggesting that short-term treatments may not exhibit linear dose-response due to compensatory mechanisms in rats. Yesi Nurmalasari et al. (2021) and Qurratu Aini (2019) reported optimal results with 450 mg/kg BW ethanol extracts over 21–28 days compared to lower doses, explained by the therapeutic window concept where mid-range concentrations maximize effects without receptor saturation or toxicity.

Tarsisius Ryang Toby et al. (2020) confirmed that 450 mg/kg BW was consistently effective in reducing glucose levels in Sprague Dawley rats from days 23 to 27, balancing pharmacological activity with physiological adaptation. S. Yasaroh et al. (2021) demonstrated that 400 mg/kg BW 96% ethanol extract normalized glucose levels after 14–21 days, indicating cumulative effects on pancreatic and hepatic tissues over time. Ezeigbo O. R. et al. (2016) compared extracts, showing aqueous ones reduced glucose by 45.2% in 14 days versus 33.7% for ethanol, highlighting rapid initial effects of polar compounds like vitamin C and hydrophilic flavonoids, while semi-polar ones offer sustained stability. Asti Marian Sari et al. (2024) found 500 mg/kg BW ethanol extract significantly lowered malondialdehyde (MDA) after 21 days, signifying reduced oxidative stress and enhanced β-cell function. The antihyperglycemic effects of Moringa oleifera are related to its phytochemicals, primarily flavonoids (quercetin, kaempferol, rutin), saponins, tannins, alkaloids, and polyphenols, which operate through complementary mechanisms [35].

Flavonoids act as potent antioxidants that neutralize free radicals and protect β-cells. Quercetin enhances insulin secretion by stimulating regenerative gene expression and inhibiting aldose reductase involved in sorbitol formation [35]. Saponins reduce intestinal glucose absorption, boost hepatic glucokinase activity, and accelerate glucose-to-glycogen conversion [36]. Tannins inhibit α-amylase and α-glucosidase, thereby slowing carbohydrate breakdown [37]. Alkaloids and polyphenols improve insulin sensitivity and suppress lipid peroxidation, which are common in diabetes. Dose and solvent variations in efficacy stem from differences in compound content and concentration; low doses may lack sufficient systemic impact, while high doses activate detoxification, reducing bioavailability, making mid-range doses (400–500 mg/kg BW) often optimal within efficient pharmacodynamic ranges.

CONCLUSION

This systematic review of nine preclinical studies established that Moringa oleifera leaf extract exerts potent antihyperglycemic effects in alloxan-induced diabetic rats (Rattus norvegicus). Aqueous and ethanolic extracts consistently reduced blood glucose levels at 200–800 mg/kg body weight, with optimal outcomes at 400–450 mg/kg over 14–28 days, primarily through pancreatic β-cell protection, enhanced insulin secretion/sensitivity, and glucose metabolism modulation via flavonoids, saponins, tannins, and polyphenols. Aqueous extracts showed a faster onset, whereas ethanolic extracts provided sustained efficacy. These results indicate that M. oleifera leaf extract is a promising natural antidiabetic candidate, warranting further standardized investigations into its extraction, dosing, toxicity, and molecular mechanisms for clinical advancement.

DECLARATIONS

This study is a literature review/analysis of secondary data sourced from publicly available documents, journals, books, and official reports. It does not involve human participants, human tissues, animal subjects, or any primary data collection requiring informed consent or intervention on living beings. Therefore, ethical clearance from an institutional review board or ethics committee was not required, in accordance with national guidelines on research ethics

CONSENT FOR PUBLICATION

The Authors agree to the publication in the Journal of Society Medicine.

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The authors declare that there is no conflict of interest in this report.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribution to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of this work.

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