

MOLECULAR AND BIOCHEMICAL MECHANISMS OF ANTIDIABETIC ACTIVITY OF *JATROPHA CURCAS*: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Diabetes mellitus is a chronic metabolic disorder associated with persistent hyperglycemia, oxidative stress, inflammation, and progressive organ damage. Increasing evidence suggests that *Jatropha curcas* possesses significant antidiabetic potential through multiple molecular and biochemical pathways.

Objective: This systematic review aimed to evaluate the molecular and biochemical mechanisms underlying the antidiabetic activity of *Jatropha curcas* based on available experimental evidence.

Methods: A systematic literature search was conducted in PubMed, Scopus, ScienceDirect, Web of Science, and Google Scholar following PRISMA guidelines. Original experimental studies investigating the antidiabetic activity of *Jatropha curcas* and reporting molecular or biochemical outcomes were included. Data regarding experimental models, extract types, biochemical parameters, molecular mechanisms, and principal findings were extracted and narratively synthesized.

Results: Eight experimental studies met the eligibility criteria. The findings demonstrated that *Jatropha curcas* exhibited significant antihyperglycemic activity through antioxidant, anti-inflammatory, enzymatic, and metabolic mechanisms. Administration of *Jatropha curcas* extracts increased antioxidant enzymes including superoxide dismutase, catalase, and reduced glutathione, while reducing malondialdehyde and inflammatory cytokines such as TNF- α and CRP. The extracts also improved pancreatic histology, lipid metabolism, and glucose regulation through inhibition of carbohydrate-metabolizing enzymes and preservation of pancreatic β -cell integrity.

Conclusion: *Jatropha curcas* possesses substantial antidiabetic potential mediated through integrated antioxidant, anti-inflammatory, and metabolic regulatory mechanisms, supporting its development as a multitarget phytopharmacological candidate for diabetes mellitus management.

Keywords: Diabetes Mellitus, *Jatropha curcas*, Oxidative Stress

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia caused by impaired insulin secretion, insulin resistance, or both, leading to disturbances in carbohydrate, lipid, and protein metabolism [1]. Chronic hyperglycemia induces oxidative stress, inflammation, endothelial dysfunction, and progressive organ damage [10]. Although current antidiabetic therapies are effective, their long-term use is frequently associated with adverse effects and therapeutic resistance [5]. Consequently, medicinal plants have gained increasing attention as alternative therapies because of their multitarget pharmacological effects and lower toxicity [2]. Plant-derived bioactive compounds can improve insulin sensitivity, regulate glucose metabolism, suppress oxidative stress, and preserve pancreatic β -cell integrity [1].

Jatropha curcas L. is an ethnomedicinal plant widely used for metabolic and inflammatory disorders [2]. Phytochemical studies identified flavonoids,

tannins, alkaloids, phenolics, terpenoids, and saponins as major constituents with antioxidant, antihyperglycemic, and anti-inflammatory activities [4]. Experimental studies demonstrated that extracts from leaves, roots, stem bark, and seeds significantly reduced blood glucose levels in diabetic animal models [6]. In addition, *Jatropha curcas* improved lipid profiles, reduced oxidative stress, and modulated inflammatory biomarkers associated with diabetes mellitus [8]. These findings suggest that its antidiabetic activity involves integrated molecular and biochemical mechanisms [9].

Oxidative stress is a major mechanism underlying diabetes progression and complications [10]. Hyperglycemia-induced reactive oxygen species (ROS) production damages pancreatic β -cells and impairs insulin signaling [1]. Administration of *Jatropha curcas* extracts increased antioxidant enzymes such as SOD, CAT, and GSH while decreasing malondialdehyde (MDA) levels in diabetic tissues [8]. These antioxidant effects may protect pancreatic β -cells and improve peripheral glucose

utilization [3]. Furthermore, several phytochemicals from *Jatropha curcas* may suppress inflammatory cytokines and inhibit α -amylase and α -glucosidase activity, thereby improving glycemic regulation [11].

Despite growing evidence, studies regarding the molecular mechanisms of *Jatropha curcas* remain fragmented and heterogeneous [2]. Most studies mainly reported antihyperglycemic effects without integrating the underlying biochemical pathways [6]. Therefore, this systematic review aims to comprehensively evaluate the molecular and biochemical mechanisms underlying the antidiabetic activity of *Jatropha curcas* based on available experimental evidence.

METHODS

Study Design and Reporting Guideline

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline to ensure transparent, reproducible, and comprehensive reporting of the review process. The review was designed to systematically identify, evaluate, and synthesize available evidence regarding the molecular and biochemical mechanisms underlying the antidiabetic activity of *Jatropha curcas*.

Eligibility Criteria

The eligibility criteria were determined prior to literature screening. Studies were included if they were original experimental investigations evaluating the antidiabetic activity of *Jatropha curcas* extracts, fractions, or isolated phytoconstituents. Eligible studies included in vivo, in vitro, or ex vivo experimental models investigating molecular or biochemical mechanisms associated with diabetes mellitus. Studies were required to report at least one outcome related to glycemic regulation, oxidative stress, antioxidant activity, inflammatory biomarkers, insulin signaling, carbohydrate-metabolizing enzymes, lipid metabolism, or pancreatic β -cell protection. Only full-text articles published in English were included in this review.

Studies were excluded if they were review articles, editorials, conference abstracts, commentaries, case reports, duplicate publications, or studies unrelated to the antidiabetic activity of *Jatropha curcas*. Articles lacking molecular or biochemical outcome measures associated with diabetes mellitus were also excluded (Fig.1).

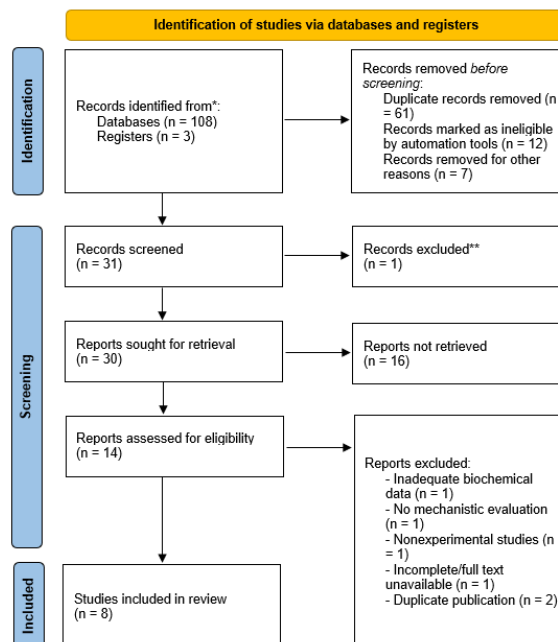


Figure 1. Prisma flowchart

Information Sources

A comprehensive literature search was performed using several electronic databases, including PubMed, Scopus, ScienceDirect, Web of Science, and Google Scholar. Additional studies were identified through manual searching of reference lists from relevant articles to ensure comprehensive retrieval of potentially eligible studies.

Search Strategy

The search strategy was developed using a combination of Medical Subject Headings (MeSH) terms and free-text keywords related to *Jatropha curcas* and diabetes mellitus. The keywords included “*Jatropha curcas*”, “antidiabetic”, “diabetes mellitus”, “hyperglycemia”, “oxidative stress”, “antioxidant”, “inflammation”, “molecular mechanism”, “biochemical mechanism”, “insulin”, “ α -amylase”, and “ α -glucosidase”. Boolean operators such as “AND” and “OR” were applied to optimize the sensitivity and specificity of the search process. The search syntax was adjusted according to the requirements of each electronic database.

Study Selection

All identified articles were exported into a reference management system, and duplicate records were removed before screening. The study selection process was conducted independently through title screening, abstract screening, and full-text assessment based on predefined eligibility criteria. Studies considered irrelevant during initial screening were excluded. Full-text articles of potentially eligible studies were further assessed to determine final

inclusion. Disagreements during the selection process were resolved through discussion and consensus.

Data Collection Process

Data extraction was independently performed using a standardized extraction form developed specifically for this review. Extracted data included author names, publication year, study design, diabetic experimental model, diabetic induction method, plant part used, extraction solvent, type of extract or isolated compound, dosage and route of administration, treatment duration, evaluated molecular and biochemical parameters, proposed mechanisms of action, and principal findings related to antidiabetic activity.

Data Items

The primary data extracted from eligible studies included biochemical and molecular parameters associated with antidiabetic mechanisms. These parameters included fasting blood glucose level, antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), oxidative stress biomarkers including malondialdehyde (MDA), inflammatory mediators such as tumor necrosis factor- α (TNF- α), C-reactive protein (CRP), interleukins, lipid profile parameters, histopathological findings, and carbohydrate-metabolizing enzymes including α -amylase and α -glucosidase.

Risk of Bias Assessment

The methodological quality and potential risk of bias of included studies were evaluated descriptively according to the clarity of experimental design, appropriateness of diabetic induction methods, adequacy of control groups, reproducibility of laboratory analyses, intervention standardization, and completeness of reported outcomes. Particular attention was given to the consistency of biochemical measurements and transparency of experimental procedures.

Synthesis Methods

Due to heterogeneity among included studies regarding experimental models, extraction methods, intervention dosages, evaluated biomarkers, and outcome reporting, quantitative meta-analysis was not feasible. Therefore, a qualitative narrative synthesis was conducted. The synthesized findings were grouped according to major mechanistic pathways involved in the antidiabetic activity of *Jatropha curcas*, including antioxidant and oxidative stress modulation, anti-inflammatory activity, glucose metabolism regulation, insulin sensitization, pancreatic β -cell protection, inhibition of carbohydrate-metabolizing enzymes, lipid metabolism regulation, and organ-protective effects involving hepatic and renal tissues.

Reporting Bias Assessment

Potential reporting bias was minimized through comprehensive database searching, manual reference screening, predefined eligibility criteria, and independent study selection and extraction processes. Studies with incomplete methodological information or unclear biochemical outcomes were carefully evaluated during full-text assessment (Fig.2).

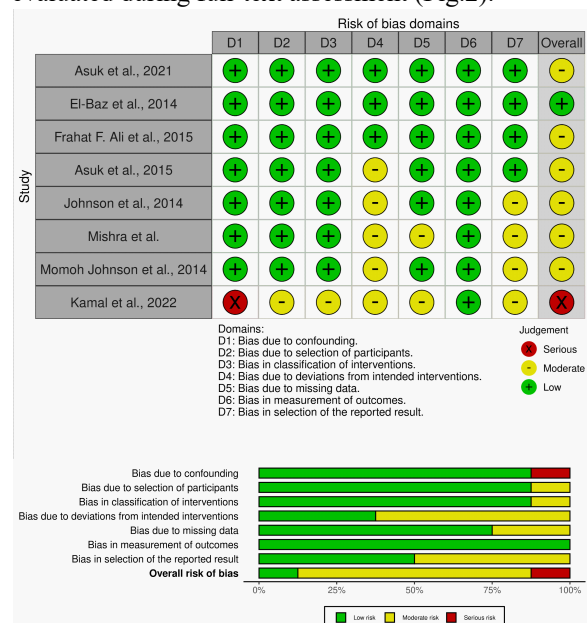


Figure 2. Risk of Bias assessment

Certainty Assessment

The certainty of evidence was assessed narratively based on consistency of findings, reproducibility of biochemical outcomes, coherence of proposed molecular mechanisms, and methodological quality of included studies. Greater emphasis was placed on studies demonstrating clear mechanistic pathways supported by biochemical, molecular, and histopathological evidence (Table 1).

The included studies demonstrated substantial evidence supporting the antidiabetic activity of *Jatropha curcas* through multiple molecular and biochemical pathways. The extracted data primarily focused on oxidative stress modulation, inflammatory regulation, antioxidant activity, pancreatic protection, and glucose metabolism improvement in experimental diabetic models.

Table 1. Study characteristic

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No	Study	Year	Study Design	Extract / Fraction	Experimental Model	Intervention / Dose	Main Molecular & Biochemical Mechanisms	Main Findings
1	Asuk et al.	2021	Experimental in vivo	Ethanol leaf extract, residue fraction, n-hexane fraction	STZ-induced diabetic Wistar rats	Oral administration of extract/fractions at 200 mg/kg BW for 14 days	Oxidative stress attenuation; antioxidant enzyme restoration; nephroprotection	Administration of <i>Jatropha curcas</i> leaf extract significantly reduced serum glucose levels through suppression of oxidative stress and restoration of endogenous antioxidant defense systems. Increased activities of SOD, CAT, and GSH reduced lipid peroxidation marked by decreased MDA levels, thereby improving cellular glucose utilization and reducing hyperglycemia-induced renal dysfunction. Improvement of electrolyte imbalance and kidney biomarkers suggested that antioxidant-mediated tissue protection contributed to stabilization of glycemic control.
2	El-Baz et al.	2014	Experimental in vivo +	Petroleum ether, ethyl	STZ-induced	Oral administration of extracts	α -amylase modulation; oxidative	<i>Jatropha curcas</i> extracts

Based on this table, the synthesized findings indicate that *Jatropha curcas* exerts antihyperglycemic effects through interconnected antioxidant, anti-inflammatory, enzymatic, and metabolic mechanisms. These findings support the therapeutic potential of *Jatropha curcas* as a multitarget phytopharmacological candidate for diabetes mellitus management.

DISCUSSION

Antioxidant-Mediated Mechanisms of *Jatropha curcas* in Diabetes Mellitus

Oxidative stress is one of the principal mechanisms underlying the development and progression of diabetes mellitus. Persistent hyperglycemia increases reactive oxygen species (ROS) production, leading to lipid peroxidation, mitochondrial dysfunction, endothelial injury, and pancreatic β -cell damage. Pancreatic β -cells are highly susceptible to oxidative injury because of their relatively weak endogenous antioxidant defense systems. Consequently, antioxidant-mediated therapies have become increasingly important in diabetes management. The findings of this review consistently demonstrated that *Jatropha curcas* possesses substantial antioxidant activity capable of reducing oxidative stress and improving glycemic regulation in diabetic experimental models [15].

Asuk et al. demonstrated that administration of *Jatropha curcas* extracts significantly increased

superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) levels while simultaneously decreasing malondialdehyde (MDA) concentrations in diabetic rats. Similar reductions in oxidative biomarkers were observed in studies evaluating medicinal plant-derived flavonoids with antihyperglycemic activity. Reduction of oxidative stress may improve insulin signaling, preserve cellular membrane integrity, and enhance peripheral glucose utilization. These findings suggest that antioxidant modulation represents one of the primary biochemical mechanisms underlying the antidiabetic effects of *Jatropha curcas* [16].

The antioxidant properties of *Jatropha curcas* are likely associated with its rich phytochemical composition, particularly flavonoids, phenolic compounds, tannins, and terpenoids. El-Baz et al. isolated quercetin, apigenin, and luteolin derivatives from *Jatropha curcas* leaves and proposed their contribution to glucose-lowering activity through antioxidant pathways. Flavonoids have been widely reported to neutralize free radicals, suppress oxidative enzymes, and preserve pancreatic β -cell viability under diabetic conditions. Phenolic compounds may additionally regulate intracellular antioxidant pathways and reduce mitochondrial oxidative stress associated with chronic hyperglycemia [17].

Collectively, these findings indicate that antioxidant-mediated activity may provide broad metabolic protection during diabetes mellitus. Suppression of oxidative stress not only contributes to improved glycemic regulation but may also reduce secondary diabetic complications involving hepatic, renal, neural, and cardiovascular tissues. Such multitarget antioxidant activity provides an important therapeutic advantage for *Jatropha curcas* as a potential phytopharmacological candidate in diabetes management. However, further molecular studies investigating pathways such as AMPK, Nrf2, and mitochondrial ROS regulation remain necessary to clarify the precise antioxidant mechanisms of *Jatropha curcas* [18].

Anti-Inflammatory and Cytoprotective Effects of *Jatropha curcas*

Chronic inflammation is strongly associated with insulin resistance and progressive metabolic dysfunction in diabetes mellitus. Hyperglycemia-induced inflammatory signaling stimulates production of pro-inflammatory cytokines including TNF- α , IL-6, and CRP, which interfere with insulin receptor signaling pathways and promote pancreatic β -cell injury. Persistent inflammatory activation further contributes to endothelial dysfunction and tissue fibrosis during diabetes progression. Therefore, suppression of inflammatory pathways may

significantly improve insulin sensitivity and glucose homeostasis [19].

Frahat F. Ali et al. reported that administration of *Jatropha curcas* extracts significantly reduced TNF- α and CRP levels while increasing anti-inflammatory IL-10 concentrations in diabetic rats. Reduction of inflammatory mediators may preserve pancreatic β -cell architecture and improve endogenous insulin secretion. In addition, anti-inflammatory activity may reduce oxidative-inflammatory interactions that contribute to chronic tissue damage in diabetes mellitus. These findings suggest that immunomodulatory effects represent another important mechanism underlying the antidiabetic activity of *Jatropha curcas* [20].

Histopathological findings further support the cytoprotective properties of *Jatropha curcas*. El-Baz et al. demonstrated regeneration of pancreatic islets and improvement of hepatic tissue architecture following treatment with *Jatropha curcas* extracts in diabetic rats. Preservation of pancreatic β -cells is particularly important because progressive β -cell loss directly worsens hyperglycemia and metabolic instability. Cytoprotective activity may therefore enhance insulin secretion capacity and improve long-term glycemic regulation in diabetic conditions [21].

The anti-inflammatory effects of *Jatropha curcas* are likely mediated by flavonoids and phenolic compounds capable of modulating inflammatory signaling pathways. Quercetin and luteolin derivatives identified in *Jatropha curcas* have been reported to inhibit NF- κ B activation and suppress cytokine overexpression in experimental inflammatory conditions. Such mechanisms may synergistically improve insulin sensitivity while simultaneously reducing oxidative tissue injury. Therefore, the combined antioxidant and anti-inflammatory activities of *Jatropha curcas* may provide integrated metabolic protection against diabetes progression and organ complications [22].

Regulation of Glucose Metabolism and Enzymatic Activity

Maintenance of glucose homeostasis involves coordinated regulation of insulin secretion, glucose uptake, hepatic glucose production, and carbohydrate digestion. Several studies included in this review demonstrated significant reductions in fasting blood glucose levels following administration of *Jatropha curcas* extracts in diabetic animal models. The antihyperglycemic effects of *Jatropha curcas* may involve modulation of carbohydrate-metabolizing enzymes, preservation of pancreatic β -cell function, and improvement of insulin sensitivity. Such multitarget mechanisms are advantageous because diabetes mellitus involves complex metabolic

dysregulation affecting multiple physiological pathways [23].

El-Baz et al. proposed that *Jatropha curcas* extracts may regulate glucose metabolism through inhibition of α -amylase activity and restoration of pancreatic integrity. Inhibition of α -amylase and α -glucosidase delays carbohydrate digestion and reduces intestinal glucose absorption, thereby lowering postprandial hyperglycemia. Flavonoids and tannins present within *Jatropha curcas* likely contribute to this enzymatic inhibitory activity. Reduced glucose absorption may subsequently stabilize glycemic fluctuations and decrease hyperglycemia-induced oxidative stress [24].

Several included studies additionally demonstrated improvements in lipid metabolism following treatment with *Jatropha curcas* extracts. Johnson et al. observed normalization of triglycerides, cholesterol, and hepatic biomarkers in diabetic rats treated with methanolic leaf extract. Dyslipidemia is closely associated with insulin resistance and impaired glucose metabolism in diabetes mellitus. Therefore, improvement of lipid homeostasis may indirectly enhance insulin responsiveness and peripheral glucose utilization. These metabolic improvements further support the potential role of *Jatropha curcas* in comprehensive diabetes management [25].

Therapeutic Potential and Future Perspectives

The present review demonstrated that *Jatropha curcas* possesses considerable therapeutic potential as a multitarget antidiabetic phytopharmacological agent. Its antihyperglycemic effects appear to involve integrated antioxidant, anti-inflammatory, enzymatic, and metabolic mechanisms acting synergistically to improve glycemic regulation. Such multitarget activity is particularly beneficial because diabetes mellitus involves interconnected pathogenic pathways affecting multiple organs and metabolic systems. Moreover, phytochemical-based therapies may provide broader therapeutic benefits with relatively lower toxicity compared with certain synthetic antidiabetic agents [15].

Despite promising findings, several limitations remain evident within the currently available literature. Considerable heterogeneity exists regarding extraction methods, plant parts utilized, dosage regimens, diabetic induction models, and evaluated biomarkers. Most studies primarily focused on biochemical observations without extensive molecular pathway analysis. Furthermore, current evidence remains largely limited to experimental animal studies, while clinical investigations evaluating efficacy and safety in humans remain unavailable. These limitations reduce the translational applicability of current findings into clinical diabetes management [16].

Standardization of *Jatropha curcas* extracts also represents an important challenge for future therapeutic development. Variability in phytochemical composition may significantly influence biological activity and reproducibility across studies. Therefore, future investigations should focus on phytochemical standardization, molecular target validation, long-term toxicity assessment, and clinical evaluation. Integration of transcriptomic, proteomic, and metabolomic approaches may further improve understanding of the molecular mechanisms underlying the antidiabetic activity of *Jatropha curcas*. Overall, the findings of this review support the therapeutic potential of *Jatropha curcas* as a promising source of multitarget antidiabetic phytochemicals requiring further translational investigation [17].

CONCLUSION

This systematic review demonstrates that *Jatropha curcas* possesses significant antidiabetic activity through multiple interconnected molecular and biochemical mechanisms, including antioxidant activity, anti-inflammatory effects, modulation of glucose metabolism, inhibition of carbohydrate-digesting enzymes, preservation of pancreatic β -cell integrity, and improvement of lipid metabolism. The phytochemical constituents of *Jatropha curcas*, particularly flavonoids, phenolics, tannins, terpenoids, and alkaloids, appear to contribute synergistically to glycemic regulation by reducing oxidative stress, suppressing inflammatory mediators, enhancing insulin sensitivity, and stabilizing metabolic homeostasis. Experimental evidence consistently supports its antihyperglycemic and cytoprotective effects in diabetic models, although current findings remain largely limited to preclinical studies with heterogeneous methodologies. Therefore, further standardized molecular investigations, toxicity assessments, pharmacokinetic evaluations, and clinical trials are necessary to validate the therapeutic potential and translational applicability of *Jatropha curcas* as a multitarget phytopharmacological agent for diabetes mellitus management.

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Conflict of Interest

The authors declare no conflict of interest related to this study.

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Author Contributions

All authors contributed substantially to the conceptualization, literature screening, data extraction, analysis, manuscript preparation, and final approval of the manuscript.

Data Availability Statement

All data analyzed in this systematic review were obtained from published articles included in the study and are available within the manuscript and referenced sources.

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