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# Antidiabetic and Antioxidant Activities of *Peperomia pellucida*: A Literature Review

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**Abstract:** Diabetes mellitus is a chronic metabolic disorder marked by persistent hyperglycemia, oxidative stress, and inflammation, driving interest in natural alternatives to synthetic antidiabetic drugs such as Peperomia pellucida. This literature review synthesizes evidence from PubMed and Google Scholar (last five years) using the terms "*Peperomia pellucida*", "ethanol extract", and "diabetes mellitus"; included studies were original in vitro, in vivo, or review articles reporting phytochemical profiles, enzyme inhibition assays, glycemic outcomes, pancreatic histopathology, inflammatory markers, or antioxidant activity, while studies lacking primary data or methodological detail were excluded. Descriptive and thematic synthesis of selected papers indicates that *P. pellucida* consistently contains flavonoids, phenolics, alkaloids, tannins, saponins, and terpenoids, and demonstrates antidiabetic effects via α-amylase and α-glucosidase inhibition, reduction of blood glucose in animal models, pancreatic tissue protection, and modulation of proinflammatory cytokines, together with robust free-radical scavenging antioxidant activity. These findings support the plant's potential as a phytopharmaceutical candidate; however, to enable clinical translation we recommend standardized extract characterization with marker compounds, dose-response and pharmacokinetic studies, comprehensive acute and chronic toxicity testing, mechanistic investigations in clinically relevant models, and randomized controlled trials with predefined endpoints, alongside development of quality-control protocols and formulation studies to determine optimal delivery and dosing.

**Keywords:** α-glucosidase inhibition; α-amylase inhibition; Blood glucose; Diabetes mellitus; *Peperomia pellucida*.

## Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia resulting from impaired insulin secretion, impaired insulin action, or both (Banday et al., 2020). Prolonged hyperglycemia can lead to various microvascular and macrovascular complications, such as nephropathy, neuropathy, retinopathy, and cardiovascular disease (Aboelmaaty et al., 2025; Hussain, 2025). According to the International Diabetes Federation (IDF), approximately 589 million adults were living with diabetes globally in 2024, and this number is projected to rise considerably in the coming decades, highlighting diabetes as one of the most pressing global public health challenges (World Health Organization, 2024; International Diabetes Federation, 2025).

The pathogenesis of diabetes mellitus is closely associated with oxidative stress, a condition characterized by an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defense system. Chronic hyperglycemia promotes excessive ROS generation through several metabolic pathways, leading to

pancreatic β-cell dysfunction, insulin resistance, inflammation, and cellular damage (Tuan & Men, 2024). Consequently, oxidative stress not only contributes to the onset of diabetes but also accelerates the progression of diabetic complications. The investigation of natural substances with both antioxidant and antidiabetic properties has garnered growing scientific attention due to the crucial role that oxidative stress plays in the pathogenesis of diabetes.

Conventional antidiabetic medications, such as insulin, biguanides, sulfonylureas, and α-glucosidase inhibitors, are frequently used to control blood glucose levels, but long-term use of these medications may result in side effects like hypoglycemia, gastrointestinal problems, weight gain, and decreased patient compliance. (Banday et al., 2020; Blahova et al., 2021). These limitations have encouraged the search for alternative therapeutic agents derived from medicinal plants that may offer efficacy with fewer side effects.

One plant that has received growing attention is Peperomia pellucida (L.) Kunth, a tropical herb traditionally utilized for various medicinal purposes, including anti-inflammatory, antimicrobial, analgesic, and antidiabetic treatments (Silalahi, 2022). Numerous bioactive secondary metabolites, including flavonoids, alkaloids, tannins, saponins, terpenoids, phenolic compounds, and steroids, are found in P. pellucida and are linked to a variety of pharmacological actions, according to phytochemical studies. (Teodhora et al., 2026). Flavonoids and phenolic compounds exhibit strong antioxidant properties that may help attenuate oxidative stress and improve glucose metabolism. Experimental studies have further demonstrated that P. pellucida extracts can reduce blood glucose levels, enhance antioxidant enzyme activities, and inhibit carbohydrate-digesting enzymes such as α-glucosidase and α-amylase, suggesting its potential as a complementary strategy for diabetes management (Tuan & Men, 2024).

Despite the growing body of evidence regarding the biological activities of P. pellucida, existing studies are largely scattered across different experimental models and primarily focus on individual pharmacological effects. To date, a comprehensive synthesis integrating its phytochemical composition with both antidiabetic and antioxidant mechanisms remains limited. This gap hinders a clear understanding of the potential role of P. pellucida as a multifunctional therapeutic agent for diabetes management. Given the increasing global burden of diabetes and the importance of identifying safe, plant-based interventions targeting oxidative stress, a comprehensive evaluation of the available evidence is warranted. Therefore, this review aims to critically summarize current findings regarding the phytochemical constituents of P. pellucida and evaluate its antidiabetic and antioxidant potential based on published experimental studies.

## Materials and Methods

### Research design

This study was conducted using a Systematic Literature Review (SLR) approach in accordance with the PRISMA 2020 guidelines. The review aimed to systematically evaluate the scientific evidence regarding the antidiabetic potential of Peperomia pellucida, with particular emphasis on its phytochemical constituents, antioxidant activity, and antidiabetic effects. Articles were identified through a structured literature search, screened based on predefined eligibility criteria, and synthesized descriptively to provide a comprehensive overview of the available evidence.

### Literature search strategy

The PRISMA 2020 standards were followed in this study's Systematic Literature Review (SLR) methodology. Relevant articles were systematically identified through searches in the Google Scholar, ScienceDirect, and PubMed databases. The literature search was conducted for articles published between 2020 and 2025 using the keywords “Peperomia pellucida,” “ethanol extract,” “antidiabetic activity,” “antioxidant activity,” and “diabetes mellitus.”

All retrieved articles were screened based on predefined inclusion and exclusion criteria. The inclusion criteria comprised original research articles published in English or Indonesian, available in full text, and specifically investigating the phytochemical composition,

antioxidant activity, and/or antidiabetic potential of Peperomia pellucida. Articles unrelated to Peperomia pellucida, review papers, conference abstracts, duplicate records, and studies lacking relevant experimental data were excluded from the review.

The article selection process consisted of identification, screening, eligibility assessment, and inclusion stages according to the PRISMA 2020 framework (Figure1). Data extracted from the selected studies included publication year, study design, plant part used, extraction method, phytochemical constituents, antioxidant activity, antidiabetic activity, and key findings. The extracted data were subsequently synthesized descriptively to provide a comprehensive overview of the antidiabetic potential of Peperomia pellucida.

Additionally, the articles used were from journals available in full text, whether from subscribed journals or free full-text sources, and contained complete associated data. Data analysis was conducted descriptively. The exclusion criteria in this study included review articles, articles discussing diseases other than diabetes mellitus, as well as publications in the form of short reports and case reports (Figure 1).

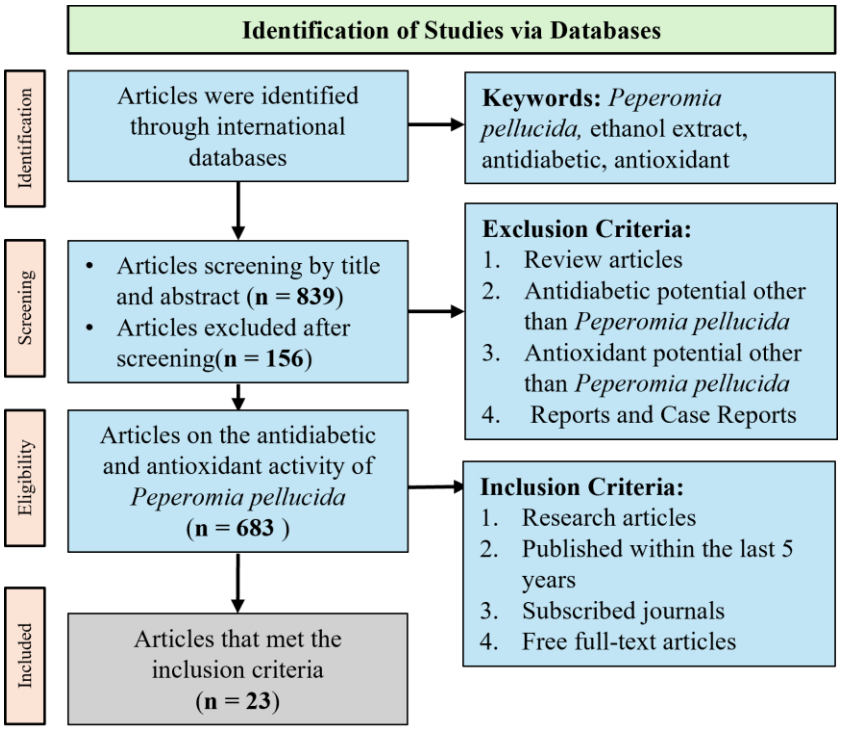


**Figure 1.** PRISMA Flow Diagram

## Results and Discussion

### Results

*Characteristics of Included Studies*

Based on the systematic literature review, a total of 839 articles were identified through searches of the Google Scholar, ScienceDirect, and PubMed databases. Following title and abstract screening, 156 articles were excluded because they did not meet the predefined inclusion criteria. The remaining 683 articles were assessed for eligibility based on their relevance to the antidiabetic and antioxidant activities of Peperomia pellucida. After full-text assessment, 660 articles were excluded due to reasons such as irrelevance to the study objectives, lack of specific data on Peperomia pellucida, duplicate publications, or insufficient experimental evidence. Ultimately, 23 articles met all inclusion criteria and were included in the systematic literature review. The detailed article selection process is presented in the PRISMA Flow Diagram.

The analysis of the selected studies (Table 1) indicates that Peperomia pellucida possesses considerable pharmacological potential, particularly regarding its antidiabetic and

antioxidant activities. The included studies employed various research approaches, including in vitro, in vivo, and in silico methods, providing comprehensive evidence of the plant's bioactive properties and its potential application in diabetes management.

*Phytochemical Constituents of Peperomia pellucida*

The phytochemical composition of Peperomia pellucida has been extensively investigated in several studies. The plant consistently contains flavonoids, phenolic compounds, alkaloids, tannins, saponins, terpenoids, and steroids (Table 1) (Almira et al., 2023; Ibe-Diala & Igwe, 2022; Norisham et al., 2023; Sari, 2025). Additional analyses using GC-MS have identified several compounds, including dill apiol and other phenolic derivatives that may contribute to its biological activities (Babu et al., 2023; Phong et al., 2025). Among these constituents, flavonoids and phenolic compounds were the most frequently reported metabolites across studies and are considered the primary contributors to both antioxidant and antidiabetic activities (Tuan & Men, 2024; Pagasian et al., 2025; Teodhora et al., 2026).

*Antidiabetic Activity of Peperomia pellucida*

The available evidence suggests that P. pellucida exerts antidiabetic activity through several complementary mechanisms (Table 1). In vitro studies demonstrated inhibition of carbohydrate-hydrolyzing enzymes, particularly α-amylase and α-glucosidase, thereby delaying glucose absorption and reducing postprandial hyperglycemia (Hidayati et al., 2022; Hidayati et al., 2023; Men et al., 2022). However, the magnitude of enzyme inhibition varied considerably among studies. Strong α-glucosidase inhibitory activity was reported by Saepudin and Susilawati (2022), whereas Teruna et al. (2022) observed relatively weak inhibition. These differences may be related to variations in extraction methods, solvent polarity, phytochemical concentration, and experimental conditions.

In-vivo studies further supported the antidiabetic potential of P. pellucida. Ethanol extracts significantly reduced blood glucose levels in diabetic animal models and improved pancreatic histopathological conditions (Hakim et al., 2024; Oktavia et al., 2025). Furthermore, reductions in inflammatory markers such as IL-1β suggest additional anti-inflammatory effects that may contribute to improved insulin sensitivity and pancreatic β-cell protection (Oktavia et al., 2025; Fadipe et al., 2024).

*Antioxidant Activity of Peperomia pellucida*

Strong antioxidant activity was consistently reported across studies employing DPPH, ABTS, FRAP, TAC, and reducing power assays (Men et al., 2022; Adejori et al., 2025; Tuan & Men, 2024). Several studies classified the antioxidant activity of P. pellucida as strong, with $IC_{50}$ values below 100 µg/mL (Almira et al., 2023; Sadik et al., 2025; Arsianti et al., 2025). Nevertheless, differences in antioxidant potency were observed among studies. For example, Arsianti et al. (2025) reported $IC_{50}$ values ranging from 14.45–22.12 µg/mL, whereas Sadik et al. (2025) obtained an IC50 value of 65.813 µg/mL. These variations are likely attributable to differences in extraction solvents, plant parts used, environmental conditions, and phytochemical composition (Phong et al., 2025; Saini et al., 2025).

**Table 1.** Antidiabetic and antioxidant activities of *Peperomia pellucida*

| No | Authors (Year) | Types of Extracts | Method | Antidiabetic Activity | Antioxidant Activity |
|---|---|---|---|---|---|
| 1. | Hakim *et al*., (2023) | Ethanol extract | In vivo (STZ-induced mice) | Significantly lowered blood sugar levels at the ideal dosage of 40 mg/kg body weight. | Contains flavonoids as antioxidants that improve insulin sensitivity. |
| 2. | Maryana *et al*., (2024) | *Peperomia pellucida* extract (non-specific, generally | In-vitro | Demonstrated antidiabetic action by inhibiting α-glucosidase and α-amylase, two enzymes involved in glucose metabolism. | Demonstrated significant antioxidant activity based on In-vitro assays. |

| No | Authors (Year) | Types of Extracts | Method | Antidiabetic Activity | Antioxidant Activity |
|---|---|---|---|---|---|
| | | ethanol or aqueous extract) | | | |
| 3. | Oktavia *et al*., (2025) | Ethanolic leaf extract | In-vivo study using STZ-induced Wistar rats | Improved pancreatic histology, lower blood glucose, and lower IL-1β levels. | Contains flavonoids and phenolic compounds that act as antioxidants |
| 4. | Almira *et al*., (2023) | Ethanolic extract, ethyl acetate fraction, and n-hexane fraction | In-vitro (DPPH assay, UV-Vis spectrophoto metry) | - | Included flavonoids, alkaloids, saponins, and tannins and showed high antioxidant activity with an $IC_{50}$ value of roughly 7.51–8.04 ppm |
| 5. | Men *et al*., (2022) | Peperomia pellucida extract | In-vitro and in-vivo | Inhibited the α-amylase enzyme ($EC_{50}$ approximately 115.3 µg/mL), thereby showing potential to reduce blood glucose levels | Demonstrated antioxidant activity through DPPH, ABTS, RP, and TAC assays and enhanced resistance to oxidative stress. |
| 6. | Hidayati *et al*., (2022) | Ethanolic extract and ethyl acetate fraction | In-vitro (α-amylase inhibition assay, UV-Vis) | Inhibited α-amylase enzyme with $IC_{50}$ of 1066.20 µg/mL (extract) and 907.19 µg/mL (fraction), indicating potential to reduce postprandial blood glucose | Contains flavonoids contributing to antioxidant activity |
| 7. | Sari, (2024) | Ethanol extract | In-vitro (Thin Layer Chromatogra phy) | - | Contains flavonoids contributing to antioxidant activity |
| 8. | Phong *et al*., (2025) | Seed extracts (ethanol, ethyl acetate, others | In-vitro (antioxidant assays) | - | Exhibited moderate antioxidant activity, with ethyl acetate extract showing higher activity; major compound identified as dill apiol |
| 9. | Teruna *et al*., (2022) | Methanol extract and fractions | In-vitro (α-glucosidase inhibition) | Showed low inhibitory activity (up to 28.19%), indicating weak antidiabetic potential | - |
| 10. | Sadik *et al*., (2025) | Ethanolic leaf extract | In-vitro (DPPH assay) | Potential antidiabetic effects via reduction of oxidative stress | Strong antioxidant activity ($IC_{50}$ 65.813 ppm) |
| 11. | Saini *et al*., (2025) | Leaf extracts (various solvents) | In-vitro (DPPH, BSLA) | – | High antioxidant activity; NADES showed strongest activity and non-toxic |
| 12. | Ibe-Diala & Igwe, (2022) | Chloroform leaf extract | In-vitro | – | Significant antioxidant activity; contains phenols, flavonoids, alkaloids |
| 13. | Saepudin *et al*., (2022) | Ethanolic leaf extract | In-vitro (α-glucosidase inhibition) | Strong enzyme inhibition ($IC_{50}$ up to 2.90 µg/mL in genus) indicating antidiabetic potential | Contains phenolics and flavonoids |

| No | Authors (Year) | Types of Extracts | Method | Antidiabetic Activity | Antioxidant Activity |
|---|---|---|---|---|---|
| 14. | Fadipe *et al*. (2024) | Plant extracts (including *P. pellucida*) | In-vivo (gene expression analysis) | Modulated genes related to insulin and glucose metabolism | – |
| 15. | Babu *et al*., (2023) | Various solvent extracts | GC-MS, in vitro | – | Contains antioxidant-related compounds (phenolics, flavonoids) |
| 16. | Tuan & Men, (2024) | Whole plant extract | In-vitro & in vivo (Drosophila, mice) | – | Strong antioxidant activity; increased oxidative stress resistance |
| 17. | Susilawati *et al*., (2024) | Compound (DEA) | In-silico (docking & dynamics) | Strong binding to diabetes-related receptors (e.g., aldose reductase) | – |
| 18. | Teodhora *et al*., (2026) | Ethanolic extract | In-vivo (OGTT in rats) | Reduced blood glucose (14.7–35.8%) though not significant | Contains phenolics and flavonoids |
| 19. | Pagasian *et al*., (2025) | Leaf extract | In-vitro | – | Moderate antioxidant activity; high flavonoid content |
| 20. | Hidayati *et al*., (2023) | Ethanolic extract & fraction | In-vitro & in-silico | Inhibited α-glucosidase ($IC_{50}$ ~9.73–13.43 mg/mL) | – |
| 21. | Norisham *et al*., (2023) | Leaf extracts (water & ethyl acetate) | FTIR & phytochemical screening | – | Contains flavonoids and phenolics indicating antioxidant potential |
| 22. | Adejori *et al*., (2025) | Whole plant extract | In-vitro & in-vivo | – | Strong antioxidant activity (DPPH, ABTS, FRAP) |
| 23. | Arsianti, (2025) | Ethanol, ethyl acetate, n-hexane extracts | In-vitro (DPPH) | – | Strong antioxidant activity ($IC_{50}$ 14.45–22.12 µg/mL) |

## Discussion

*Relationship Between Phytochemical Constituents and Biological Activities*

The pharmacological activities of P. pellucida appear to be closely linked to its phytochemical composition. Flavonoids and phenolic compounds were consistently identified across studies and are known to possess both antioxidant and antidiabetic properties (Ibe-Diala & Igwe, 2022; Tuan & Men, 2024; Pagasian et al., 2025). These compounds can neutralize reactive oxygen species (ROS), inhibit oxidative damage, and modulate carbohydrate metabolism through enzyme inhibition pathways. In addition to flavonoids and phenolics, alkaloids, tannins, terpenoids, and saponins may contribute synergistically to the biological effects of P. pellucida (Almira et al., 2023; Norisham et al., 2023; Teodhora et al., 2026). Such phytochemical complexity may explain the multiple pharmacological mechanisms reported across different studies.

*Antidiabetic Activity in Relation to Oxidative Stress and Diabetes Pathophysiology*

Oxidative stress is a major contributor to the pathogenesis of diabetes mellitus. Chronic hyperglycemia promotes excessive ROS production through mitochondrial dysfunction, advanced glycation end-product formation, activation of the polyol pathway, and protein kinase C signaling (Figure 2) (Banday et al., 2020; Caturano et al., 2023; Hussain, 2025). Elevated oxidative stress subsequently impairs pancreatic β-cell function, reduces insulin sensitivity, and accelerates diabetic complications. The antidiabetic activity of P. pellucida appears to target several aspects of this pathological process. Enzyme inhibition studies demonstrated the ability of the plant extract to reduce carbohydrate digestion and glucose absorption (Hidayati et al., 2022; Hidayati et al.,

2023; Men et al., 2022). Meanwhile, in vivo studies demonstrated reductions in blood glucose levels and improvements in pancreatic histopathology, suggesting protective effects on pancreatic tissue (Hakim et al., 2024; Oktavia et al., 2025).

Furthermore, the observed reduction in inflammatory markers such as IL-1β indicates that P. pellucida may alleviate inflammatory responses associated with insulin resistance and β-cell dysfunction (Oktavia et al., 2025; Fadipe et al., 2024). Together, these findings suggest that the antidiabetic activity of P. pellucida extends beyond simple glucose-lowering effects and involves modulation of oxidative stress and inflammation.

*Antioxidant Activity as a Supporting Mechanism for Antidiabetic Effects*

The antioxidant activity of P. pellucida likely represents one of the major mechanisms underlying its antidiabetic effects (Figure 2). Pancreatic β-cells possess relatively weak endogenous antioxidant defenses and are highly susceptible to oxidative damage induced by chronic hyperglycemia (Caturano et al., 2023). The strong antioxidant activity observed in several studies (Almira et al., 2023; Arsianti et al., 2025; Adejori et al., 2025) suggests that flavonoids and phenolic compounds from P. pellucida can reduce oxidative stress by scavenging free radicals and preventing lipid peroxidation. Consequently, antioxidant protection may preserve β-cell integrity, improve insulin secretion, and contribute to improved glucose homeostasis (Tuan & Men, 2024; Teodhora et al., 2026). This hypothesis is supported by studies reporting concurrent antioxidant and antidiabetic activities in the same extracts (Men et al., 2022; Maryana et al., 2024), indicating that both biological effects are mechanistically interconnected.

*Comparison Between Studies Reporting Strong and Weak Activities*

Although most studies reported positive biological activities, considerable differences in potency were observed. Strong antidiabetic activity was reported by Saepudin and Susilawati (2022), Hakim et al. (2024), and Oktavia et al. (2025), whereas Teruna et al. (2022) and Teodhora et al. (2026) reported weaker responses. Similarly, antioxidant activity ranged from very strong (Almira et al., 2023; Arsianti et al., 2025) to moderate (Phong et al., 2025; Pagasian et al., 2025). These discrepancies likely reflect differences in solvent polarity, extraction methods, phytochemical concentrations, plant origin, environmental conditions, and assay protocols. Ethyl acetate and ethanol extracts generally exhibited stronger activities than less selective extraction approaches, suggesting that extraction efficiency plays an important role in determining biological potency.

Strengths and Limitations of Current Evidence

The current evidence base includes complementary data from in vitro, in vivo, and in silico studies. In vitro studies provide mechanistic insights into enzyme inhibition and antioxidant activity, whereas in vivo studies demonstrate physiological effects under diabetic conditions (Hidayati et al., 2022; Hakim et al., 2024; Oktavia et al., 2025). In silico studies contribute additional molecular evidence supporting interactions between bioactive compounds and diabetes-related targets (Susilawati et al., 2024). However, important limitations remain. Most studies employed different extraction methods and experimental protocols, limiting direct comparison among results. Furthermore, nearly all available evidence is preclinical, with no robust clinical trials evaluating efficacy and safety in humans. Consequently, the translational value of current findings remains uncertain.

*Implications for the Development of Peperomia pellucida as a Phytopharmaceutical Candidate*

The combined antioxidant, antidiabetic, and anti-inflammatory properties of P. pellucida indicate promising potential for development as a phytopharmaceutical candidate for diabetes management. Nevertheless, future development requires standardization of extracts, identification of marker compounds, toxicity assessments, pharmacokinetic studies, and randomized clinical trials to establish efficacy and safety.

*Novelty and Scientific Contribution of This Review*

Previous publications have generally focused on either phytochemical characterization or individual pharmacological activities of P. pellucida (Silalahi, 2022; Tuan & Men, 2024). The present review provides a more integrated perspective by synthesizing evidence from phytochemical, antioxidant, antidiabetic, and molecular studies within the framework of oxidative stress-related diabetes pathophysiology. This approach highlights the interconnected mechanisms through which P.

pellucida may exert therapeutic effects and identifies important research gaps for future investigation.

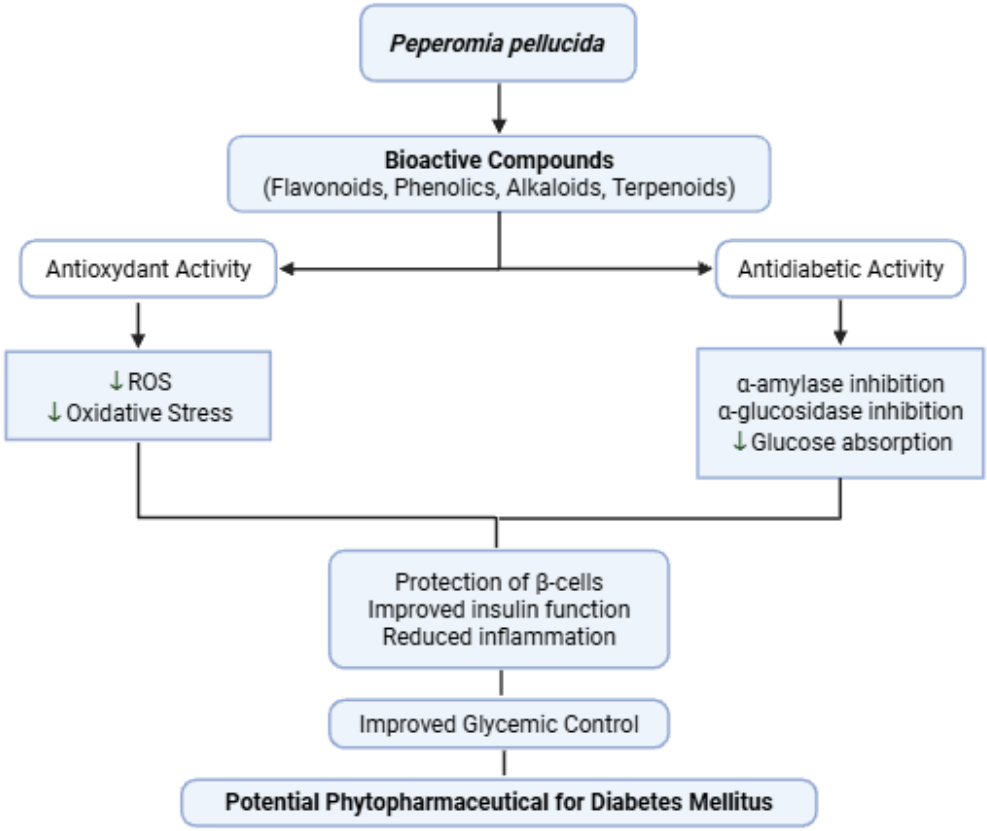


**Figure 2.** Proposed mechanisms of antidiabetic and antioxidant activities of Peperomia pellucida through oxidative stress modulation

*Scientific Synthesis of Available Evidence*

Overall, the available evidence indicates that Peperomia pellucida possesses considerable potential as a natural antidiabetic agent. Its biological activities are mediated through multiple complementary mechanisms, including α-amylase and α-glucosidase inhibition, antioxidant protection, anti-inflammatory effects, and preservation of pancreatic function (Hidayati et al., 2022; Men et al., 2022; Oktavia et al., 2025; Susilawati et al., 2024). Although the findings from in vitro, in vivo, and in silico studies are generally consistent, the current level of evidence remains predominantly preclinical. Therefore, further standardization and clinical validation are necessary before P. pellucida can be fully developed as a phytopharmaceutical for diabetes mellitus.

## Conclusion

Through a variety of methods, including enzyme inhibition, oxidative stress reduction, and improved pancreatic function, Peperomia pellucida demonstrates substantial antidiabetic and antioxidant effects. Its potential development as a natural treatment agent for diabetes mellitus is supported by these findings

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