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## Review Article

### Review on Antidiabetic Effects of *Justicia wynaadensis* Leaves

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#### Abstract

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*Justicia wynaadensis*, a medicinal plant traditionally used to manage diabetes, has garnered attention for its potential antidiabetic properties. This review consolidates current knowledge on the phytochemical composition, pharmacological activities, and mechanisms underlying the antidiabetic effects of *Justicia wynaadensis* leaves. Various bioactive compounds, such as flavonoids, alkaloids, and phenolics, contribute to its efficacy by modulating glucose metabolism, enhancing insulin sensitivity, and exerting antioxidant effects that mitigate diabetes-associated oxidative stress. Preclinical studies have demonstrated significant reductions in blood glucose levels, improvements in lipid profiles, and protective effects on pancreatic  $\beta$ -cells. The review also highlights the safety profile and therapeutic prospects of *Justicia wynaadensis* in diabetes management, emphasizing the need for further clinical trials to validate efficacy and dosage. Overall, *Justicia wynaadensis* leaves present a promising natural alternative or adjunct to conventional antidiabetic therapies and warrant comprehensive pharmacological and toxicological evaluations.

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## Introduction

Diabetes mellitus is a chronic disorder characterized by a tendency to develop hyperglycemia caused by alterations in insulin metabolism, and the body may be unresponsive to insulin that is being secreted. Diabetes mellitus is a major public health problem because of its increasing prevalence, complications, and economic burden on the healthcare system. Regular diabetes remedies, such as insulin injections and oral drugs, are effective; however, they have a few drawbacks, including side effects, high prices, and poor patient compliance. Therefore, there is increasing interest in exploring medicinal plants with antidiabetic potential as alternative and complementary treatments(1). *Justicia wynaadensis*, a plant of the Acanthaceae family, is traditionally used in several indigenous medicinal systems to manage diabetes and its complications. The biological source of this marine fungus is the Western Ghats of India, and it is known for its numerous pharmacological properties. The foliage of *J.* The bioactive phytochemicals in *Justicia wynaadensis*, including flavonoids, alkaloids, and phenolic compounds, are believed to play a role in regulating blood glucose levels and combating oxidative stress, which are important for diabetes management. *Wynaadensis* leaves have proven pre-clinical efficacy, emphasizing the importance of evaluating other doses of this plant soil for more definitive results. The results revealed that the multi-target actions of the plant may provide benefits over those of single-target conventional drugs. In addition, its antioxidant properties reduce oxidative stress, a major contributor to diabetic complications. Although preclinical findings seem promising, studies evaluating the safety of *Justicia wynaadensis* in humans are limited(2). It is crucial to conduct systemic clinical trials and toxicological investigations to fill these gaps and establish it as a natural antidiabetic agent. This review aims to summarize the most up-to-date information on the phytochemical analysis, pharmaceutical activity, and mechanisms of action of *Justicia wynaadensis* leaves for diabetes management. The therapeutic potential of this plant and future perspectives required for the progression of this plant from traditional use to clinical application are also highlighted(3).

The incorporation of traditional medicinal plants, such as *J.* Enhancing diabetes care through the introduction of *Wynaadensis* into modern therapeutic regimens is a current need. Comprehending the molecular mechanism of its antidiabetic effects will help in the development of new phytopharmaceuticals and the rational use of herbs. Therefore, this review could turn out to be a one-stop shop for any researcher, clinician, or pharmacologist wanting to harness the benefits of *J.* management of diabetes with *wynaadensis*(4).

### Botanical Description and Traditional Uses

*Justicia wynaadensis*, a perennial shrub of the family Acanthaceae, is endemic to the Western Ghats of India, a biodiversity hotspot. In the area, this plant occurs in tropical evergreen and semi-evergreen forests at 600-1500 m above sea level. The plant displays typical morphological features that exhibit ovate to lanceolate leaves, opposite phyllotaxy, and tubular flowers with bilabiate corolla type that aid in its identification and classification of *Justicia*. The shrub grows

to a height of about 1 – 2 meters; the leaves are dark green, smooth, and glossy and are used in traditional medicine(5). Traditionally, *Justicia wynaadensis* has been useful to the aboriginals of the Western Ghats. This plant has ethnomedicinal significance in the treatment of metabolic disorders, including diabetes mellitus. Local healers and practitioners of Ayurveda and other folk medicines use different parts of the plant (mainly the leaves). The leaves are often prepared as decoctions, infusions, or pastes and administered orally to regulate blood sugar levels and relieve diabetes. In addition to its antidiabetic use, *J.* This species is also used to treat inflammatory diseases, fever and digestive disorders, indicating its wider pharmacological potential. Ethnobotanical surveys have reported the use of *Justicia wynaadensis* for the treatment of these diseases and physiological disorders in Tribals of North Wayanad. The involvement of *wynaadensis* in traditional medical practices indicates that this natural medicine can be obtained in rural areas that do not have access to modern medicine. The plant is often used with dietary control and lifestyle modification along with herbal treatment in a complete treatment schedule. This body of traditional knowledge has sparked a scientific impetus to validate the pharmacological efficacy and safety of *Justicia wynaadensis*, attempts to integrate indigenous knowledge with modern-day medicine; therapeutic application of *Justicia wynaadensis* leaves are from its phytochemical richness. Research suggests the presence of varied bioactive compounds, such as flavonoids, alkaloids, phenolic acids, tannins, and saponins(6). The antioxidants and anti-inflammatory properties of flavonoids can influence oxidative stress, which is linked to the pathology of diabetes. All alkaloids affect glucose metabolism and insulin sensitivity, whereas phenolic compounds' free radical scavenging activities protect the pancreatic  $\beta$ -cell from oxidative damage. The synergistic action of these phytochemicals has resulted in enhanced insulin secretion, improved peripheral glucose uptake, and inhibition of carbohydrate-digesting enzymes(7). The conventional cooking techniques of *J.* The cultural practices affecting *Wynaadensis* leaves vary; however, these are generally intended to optimize the extraction of these bioactive constituents. Decoctions are prepared by boiling the leaves. An infusion is prepared by soaking fresh or dried leaves in hot water. The doses of these preparations are adjusted to an individual's needs and are often monitored by a traditional healer. Practices like these illustrate the need for dosage standardization and quality control, which present challenges in the conversion of traditional remedies into standardized phytopharmaceuticals. In addition to its antidiabetic use, *Justicia wynaadensis* shows other pharmacological activities that indicate its traditional use (8). It has anti-inflammatory effects that can help treat complications of diabetes, such as neuropathy and cardiovascular diseases. The plant also shows antimicrobial properties, as it is used to treat infections. These juxtaposed activities improve the therapeutic profile of *J.* Conservation of *Justicia wynaadensis* is important because of its limited geographical range and increasing demand for medicinal use. Integrated disease management is possible with this species. Its natural populations are threatened by habitat

degradation and overharvesting. To conserve this resource, sustainable harvesting, cultivation, and in situ conservation of this species are essential(9). However, documenting traditional knowledge and community engagement are also critical for ethical utilization and benefit-sharing. The botanical and ethnopharmacological profile of *Justicia wynaadensis* highlights its potential as a natural anti-diabetic agent. Further research, comprising phytochemical standardization, mechanistic studies, and clinical validations, is required to verify traditional claims and ensure safe therapeutic use. This section provides a basic framework to provide the plant's botanical identity and traditional context, which are the basic ingredients for developing a phytomedicine for diabetes(10).

### Phytochemical Constituents of *Justicia wynaadensis* Leaves

*Justicia wynaadensis*, a medicinal plant that has been traditionally used in the management of diabetes, owes its medicinal properties to the large number of bioactive phytochemicals that it contains in its leaves. These phytochemicals act in concert with the pharmacological action of the plant by acting on several pathways that regulate glucose, reduce oxidative stress, and protect the cell. Intensive phytochemical studies have revealed the presence of various classes of compounds such as flavonoids, alkaloids, phenolic acids, tannins, saponins and other secondary metabolites that have different roles in antidiabetic action of *Justicia wynaadensis*(11).

Flavonoids are among the most abundant phytochemical groups in the leaves of *Justicia wynaadensis*. These polyphenolic compounds are reputable in terms of their strong antioxidant, anti-inflammatory and enzyme modulatory effects. Related *Justicia* species have been found to contain flavonoids like quercetin and kaempferol and their glycosides which are presumed to be present in *Justicia wynaadensis*, which are thought to play a role in its hypoglycemic effects. These substances increase insulin release in pancreatic cells, improve the sensitivity of peripheral tissues to insulin, and suppress the activity of carbohydrate-digesting enzymes, such as 8-amylase and 8-glucosidase, thus curbing postprandial hyperglycemia. Flavonoids also have antioxidant properties that protect cells against oxidative damage caused by chronic hyperglycemia, a crucial element in the pathogenesis of diabetes. Another important group of bioactive compounds detected in the leaves of *Justicia wynaadensis* is alkaloids. Alkaloids have various pharmacological effects, such as regulating glucose metabolism and increasing insulin signaling pathways(12). These nitrogenous compounds may promote the release of insulin, enhance the uptake of glucose by muscle and fat tissues, and have anti-inflammatory properties that reduce insulin resistance(13). Alkaloids found in *Justicia wynaadensis* justify its use in the traditional management of blood sugar levels and alleviation of inflammation related to diabetes. Phenolic acids and other phenolic compounds are highly abundant in the leaves and play a role in antioxidative defense systems. These substances scavenge free radicals, inhibit lipid peroxidation, and shield cellular components against damage caused by oxidative stress. Phenolics also

regulate important enzymes in glucose metabolism and affect gene expression in insulin sensitivity. Phenolic acids and flavonoids have a synergistic effect on the overall therapeutic activity of *Justicia wynaadensis* in the management of diabetes. Tannins, another category of polyphenolic compounds present in *Justicia wynaadensis*, are antidiabetic and act by inhibiting digestive enzymes and decreasing glucose absorption in the gastrointestinal tract. They are also astringent, which helps repair tissues and decrease inflammation. Tannins play a role in the regulation of lipid profiles and have protective properties towards pancreatic tissues, in addition to the functions of other phytochemicals(14). The leaves also contain saponins, which are foaming glycosides associated with hypoglycemic and hypolipidemic effects(15). Saponins are insulin secretagogues, increase glucose tolerance, and have antioxidant properties. In addition, they affect cholesterol metabolism, which is advantageous to their pharmacologic profile, as well as other secondary metabolites in the *Justicia wynaadensis* leaves, including terpenoids, steroids, and glycosides. Terpenoids have anti-inflammatory and antioxidant properties, whereas steroids are capable of regulating metabolic pathways that have been implicated in glucose homeostasis. *Justicia wynaadensis* has a multi-targeted effect on diabetes treatment owing to its intricate phytochemical composition, which can treat hyperglycemia, oxidative stress, and metabolic imbalance complications(16). Research has used extraction and characterization methods (solvents, chromatography, spectroscopic analyses, such as HPLC, GC-MS, and NMR) to isolate and identify these phytochemicals. These techniques verify the existence of bioactive constituents and allow quantification, which is necessary for standardizing extracts for use in pharmacological studies(17). The inconsistency of phytochemical composition based on geographical origin, time of harvest, and extraction technique supports the need for standard procedures to guarantee similar therapeutic effects. *Justicia wynaadensis* also has antidiabetic potential that is affected by the bioavailability of these phytochemicals and their pharmacokinetics. Flavonoids and phenolics tend to have low oral bioavailability (poorly absorbed and rapidly metabolized); therefore, methods of formulation to improve their stability and delivery are the focus of research. It is also important to understand the metabolism of alkaloids and saponins to maximize their therapeutic effects and reduce toxicity(18).

In summary, the phytochemical composition of *Justicia wynaadensis* leaves is a complex and effective mixture that supports its traditional use and recent pharmacological confirmation as an antidiabetic agent. The combination of antioxidant flavonoids, insulin-sensitizing alkaloids, and enzyme-inhibiting tannins and saponins provides a complex mechanism to fight hyperglycemia and resultant oxidative damage. Further studies on the isolation of particular active compounds, their molecular mechanisms of action, and clinical trials are essential to realize the full therapeutic potential of *Justicia wynaadensis* in the management of diabetes(19).

### Mechanisms of Antidiabetic Action

*Justicia wynaadensis* exerts antidiabetic actions through various interrelated pathways that enhance glucose homeostasis, insulin activity, and reduce oxidative stress linked to diabetes. The phytochemical compositions of the leaves, such as flavonoids, alkaloids, phenolics, tannins, and saponins, have a synergistic effect on different molecular targets and metabolic pathways involved in the pathogenesis of diabetes. One of the major mechanisms is the regulation of insulin secretion and pancreatic  $\delta$ -cell protection. The *Justicia wynaadensis* bioactive compounds promote the release of insulin in pancreatic  $\beta$ -cells, increasing endogenous insulin levels. This effect plays a vital role in diabetes, in which insulin secretion is impaired(20). In addition, the antioxidant effects of flavonoids and phenolic acids rescue  $\beta$ -cells against oxidative damage due to chronic hyperglycemia and inflammation, maintaining their functional integrity and avoiding apoptosis. This twofold activity promotes long-term insulin production and secretion. *Justicia wynaadensis* also enhances insulin sensitivity in peripheral tissues, such as muscle and adipose tissue. The alkaloids and flavonoids increase the insulin receptor signaling pathway to stimulate glucose uptake by improving the translocation of glucose transporter type 4 (GLUT4) to the cell membrane. This process lowers insulin resistance, which is a characteristic of type 2 diabetes, and helps effectively use glucose, as well as decrease the level of glucose in the blood. Another important mechanism is that flavonoids and tannins in the leaves inhibit carbohydrate-digesting enzymes, namely  $\alpha$ -amylase and  $\alpha$ -glucosidase. Inhibition of these enzymes is one way that *Justicia wynaadensis* converts complex carbohydrates into glucose, which in turn results in decreased postprandial blood glucose spikes. This enzyme inhibition helps to achieve improved glycemic regulation and reduce the insulin secretion load(21).

The antioxidant activity of *Justicia wynaadensis* is important in alleviating oxidative stress associated with diabetes, which is a contributing factor to the onset of complications, such as neuropathy, nephropathy, and cardiovascular diseases. Flavonoids, phenolics, and saponins scavenge reactive oxygen species (ROS), thereby reducing lipid peroxidation and cellular damage. This protective action not only spares pancreatic function but also enhances general metabolism. Moreover, the phytochemicals of the plant have anti-inflammatory effects that reduce chronic, low-grade inflammation, which is common among diabetic patients(22). *Justicia wynaadensis* alters insulin resistance and tissue damage by modulating proinflammatory cytokines and signaling pathways, which underlies enhanced metabolic performance. Saponins and flavonoids affect cholesterol and triglyceride levels, positively impact lipid profiles, and lower the risk of cardiovascular complications associated with diabetes. This glycemic control is achieved by other mechanisms and is complemented by this hypolipidemic effect. Together, these processes emphasize the complex antidiabetic potential of *Justicia wynaadensis* leaves. The bioactive compounds in the plant address important pathological characteristics of diabetes, such as impaired insulin release, insulin resistance, postprandial

hyperglycemia, oxidative stress, inflammation, and dyslipidemia. This multi-targeting therapy can provide therapeutic benefits to traditional single-target therapeutics as a holistic method for managing diabetes. Future studies in this area should aim to clarify the exact molecular targets and signaling pathways that are affected by single phytochemicals, their pharmacokinetics, and bioavailability. These studies will help in the design of standardized extracts or isolated compounds with the best efficacy and safety profiles for use in clinical practice(23).

### Pharmacological Evidence from Preclinical Studies

The leaves of *Justicia wynaadensis* have been the subject of many preclinical trials aimed at confirming the traditional application of the plant in diabetes treatment and explaining the pharmacological action of the plant. These experiments mainly include in vitro experiments and in vivo animal models, which determine the hypoglycemic, antihyperlipidemic, antioxidant, and protective properties of leaf extracts and single compounds. The overall results of these studies indicate that *Justicia wynaadensis* has a potent antidiabetic effect through several biological pathways, validating its possible use as a natural therapeutic agent(24).

### Hypoglycemic Activity

A few in vivo experiments with diabetic rodent models, including streptozotocin (STZ)-induced and alloxan-induced diabetic rats, have indicated that the use of *Justicia wynaadensis* leaf extracts can greatly reduce fasting blood glucose levels. Its hypoglycemic effect is dose-dependent and is similar to that of conventional antidiabetic agents, such as metformin and glibenclamide, in certain situations. The extracts have been demonstrated to elevate glucose intolerance in oral glucose tolerance tests (OGTT), suggesting that they increase peripheral glucose metabolism and insulin sensitivity. The proposed mechanisms of insulin secretion stimulation and translocation of GLUT4 increase are in agreement with these results, as described in previous sections(9).

### Antihyperlipidemic Effects

Diabetes is frequently associated with dyslipidemia, which is characterized by an increase in serum cholesterol, triglycerides, and low-density lipoprotein (LDL), leading to cardiovascular problems. Preclinical investigations have revealed that *Justicia wynaadensis* leaf extracts can enhance lipid profiles in diabetic rats by reducing total cholesterol, triglycerides, and LDL cholesterol, and raising the levels of high-density lipoprotein (HDL) cholesterol. The latter effect can be explained by the presence of saponins and flavonoids, which regulate lipid metabolism enzymes and facilitate cholesterol efflux. Lipid-lowering effects, in addition to glycemic control effects, imply a holistic metabolic advantage(12).

### Effects of Antioxidants and Protection

The role of oxidative stress in the pathogenesis and complications of diabetes is pivotal. Antioxidant in vitro tests, including DPPH radical scavenging and ferric reducing antioxidant power (FRAP), confirmed that *Justicia wynaadensis* leaf extracts have high free radical scavenging

power. Treatment of diabetic animals in vivo resulted in a decrease in the levels of malondialdehyde (MDA), which is an indicator of lipid peroxidation, and an increase in the activities of endogenous antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). These antioxidant activities help protect pancreatic  $\beta$ - cells against oxidative damage and maintain their insulin-secretory activity(22).

#### **Pancreatic $\beta$ -Cell Preservation and Renewal.**

Histopathological examination of pancreatic tissues in diabetic animals fed *Justicia wynaadensis* extracts showed less destruction of the  $\beta$ -cells and improvement in the architecture of the islets than in the untreated control. This implies that the phytochemicals in the plant not only block oxidative and inflammatory damage to the  $\beta$ -cells but also could be used to induce  $\beta$ -cell neogenesis or regeneration. Maintaining endogenous insulin production and long-term glycemic control depends on the preservation of  $\beta$ -cell mass(23).

#### **Anti-Inflammatory Activity**

In diabetes, chronic low-grade inflammation contributes to insulin resistance and  $\beta$ -cell dysfunction. Preclinical studies have revealed that *Justicia wynaadensis* leaf extracts lower pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin-6 (IL-6), and C-reactive protein (CRP), in diabetic animals. Flavonoids and alkaloids are the major contributors to anti-inflammatory effects, as they block nuclear factor kappa B (NF- $\kappa$ B) signaling pathways. *Justicia wynaadensis* increases insulin sensitivity and metabolic homeostasis by inhibiting inflammation(25).

#### **Enzyme Inhibition Studies**

In vitro enzyme inhibition assays showed that *Justicia wynaadensis* leaf extracts inhibited the activities of alpha-amylase and alpha-glucosidase, which digest carbohydrates and absorb glucose. This inhibitory effect on glucose is enzyme-mediated and slows the release of glucose into the bloodstream, thereby lowering postprandial hyperglycemia. The tannin and flavonoid concentrations in the extracts were associated with the potency of the inhibition, supporting the use of tannins and flavonoids as glycemic regulators.

#### **Safety and Toxicological Profile**

Safety and toxicological analysis of the leaves of *Justicia wynaadensis* is an important area of concern in the authorization of the use of the leaves as a therapeutic agent in the management of diabetes. The toxicity, tolerability, and adverse effects of *Justicia wynaadensis* leaf extracts have been systematically evaluated in preclinical studies to determine a safety profile to facilitate additional clinical development(26).

#### **Acute Toxicity Studies**

Acute toxicity was assessed by testing a single high dose of the plant extract on animal models, usually rodents, to determine acute toxicity or death within a set observation period, usually 14 days. Investigations into *Justicia wynaadensis* leaf extracts have shown no mortality or significant changes in behavior at very high doses used to

produce therapeutic effects. This demonstrates a safety margin and that the extract is not lethal, even when consumed at high levels. Typical parameters observed are variations in body weight, food and water consumption, locomotor activity, and evidence of distress or toxicity (tremors, convulsions, or lethargy)(27).

#### **Subchronic and Chronic Toxicity**

Subchronic toxicity tests, which entail repeat administration of the extract within a few weeks and months, offer information on possible cumulative toxicity. These studies indicate that *Justicia wynaadensis* leaf extracts, when administered orally to diabetic and normal rodents at therapeutic and higher doses, did not significantly modify vital organ function or histopathology. Markers of liver and kidney function, such as serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), and creatinine, were at normal levels, suggesting that there were no signs of hepatotoxicity or nephrotoxicity. Histological analysis of the liver, kidney, heart, and pancreas organs did not show any pathological damage or abnormalities in the cell structure that could be attributed to the extract. Prolonged administration of extracts did not affect hematological parameters, such as the levels of red and white blood cells, hemoglobin concentration, and platelet counts, indicating no hematotoxic effects. These results highlight the tolerability and safety of the extract during long-term application, which is critical in chronic diseases such as diabetes that require long-term management(28).

#### **Genotoxicity and Mutagenicity**

Few studies have investigated the genotoxic potential of *Justicia wynaadensis* extracts using assays, including the Ames test and micronucleus assay. These studies have shown that there are no mutagenic or genotoxic effects at concentrations applicable in therapeutic applications. This assures the genetic safety of the plant extract and minimizes the risk of carcinogenicity associated with long-term intake(29).

#### **Possible drug interactions and contraindications**

Given the complex phytochemical structure of *Justicia wynaadensis* leaves, their interactions with traditional antidiabetic drugs and other medications warrant attention. Although there is no specific research on drug interactions, the possibility that flavonoids and alkaloids modulate cytochrome P450 enzymes indicates a potential impact on drug metabolism. Future pharmacokinetic and clinical analyses should be carefully conducted to determine any synergistic or antagonistic interactions that may affect efficacy or safety(30).

#### **Allergic Reactions and Sensitization**

The literature on allergic reactions or hypersensitivity to *Justicia wynaadensis* is limited. Nevertheless, similar to any botanical product, there is a theoretical risk of allergic sensitization, especially in individuals with known plant allergies. During human trials, patch testing and clinical observations are significant to detect such adverse

reactions(31).

### Limitations and Future Directions

Although safety data in preclinical models are encouraging, it is important to carefully interpret the results before translating them to humans. Metabolic, dosage, and exposure-duration differences require thorough clinical toxicology testing. Chronic toxicity, reproductive toxicity, teratogenicity, and carcinogenicity studies are also required to fully define the safety profile. The reproducibility and assurance of safety depend on the standardization of extract preparation. Toxicity can be affected by variations in phytochemical content, which are caused by geographic, seasonal, and methodological variations. Quality control parameters and good manufacturing practices (GMP) of extract production will reduce the risks related to contamination, adulteration, or uneven dosing(32).

### Future Directions and Possible Clinical Applications.

*Justicia wynaadensis*, having shown a multifaceted antidiabetic effect, can be a good candidate in applying to the clinical management of diabetes. Its wide preclinical data is an indication of its possible application as a natural treatment agent or as an adjuvant to the traditional antidiabetic medications. This part will discuss potential clinical uses, translational issues and future research directions that are required to achieve the therapeutic potential of *the Justicia wynaadensis* leaves(33).

### Clinical Applications

Adjunct Therapy of Type 2 Diabetes Mellitus (T2DM). Considering its capacity to improve insulin sensitivity, increase insulin secretion, and regulate glucose metabolism, *Justicia wynaadensis* leaf extracts may be used as an adjunct to currently used oral hypoglycemic agents. Its antioxidant and anti-inflammatory properties can also reduce the complications associated with diabetes and the overall outcomes of patients. The enzyme inhibitory effect of  $\alpha$ -amylase and  $\alpha$ -glucosidase in the plant can decrease postprandial hyperglycemia, which is a key determinant in glycemic control. *Justicia wynaadensis* could be incorporated into treatment regimens, and it is possible to reduce the dose of traditional medications by means of this approach, which will reduce side effects and enhance patient adherence(34).

### Mild-to-Moderate Hyperglycemia Monotherapy

In patients with mild or early diabetes, standardized extracts of *Justicia wynaadensis* may be considered a monotherapeutic option. Multifactorial mechanisms of action address the important pathophysiology of diabetes, providing a comprehensive treatment option. This is particularly pertinent in resource-constrained environments, where available drugs are limited and the use of traditional medicine is common. Nonetheless, efficacy and safety should be determined by the well-designed clinical trials to recommend the use of monotherapy(35).

### Prevention and treatment of diabetes-related complications

The antioxidant, anti-inflammatory, and lipid-modulating properties of *Justicia wynaadensis* imply that it can be used to prevent or treat complications, such as diabetic neuropathy, nephropathy, and cardiovascular diseases. The plant can prevent tissue damage and enhance metabolic homeostasis by alleviating oxidative stress and inflammation. These protective effects have the potential to expand the therapeutic utility of *Justicia wynaadensis* beyond glycemic regulation through clinical testing(36).

#### Application in Herbal Formulations and Nutraceuticals

A possible practical use of the combination of *Justicia wynaadensis* extracts in standardized herbal preparations or nutraceutical products is the management of diabetes. These products might offer affordable and readily available alternatives with fewer side effects. The development of formulations should focus on maximizing the bioavailability and stability of active phytochemicals, ensuring uniform dosing, and enhancing therapeutic effects(37).

### Translational Challenges and Considerations

#### Standardization and quality control

One of the challenges to the clinical use of phytochemicals is the fluctuation in phytochemical composition based on geographic source, harvest time of the year, and extraction method. It is crucial to establish standardized extraction procedures and quality control parameters to guarantee reproducible efficacy and safety. Phytochemical profiling and batch consistency should be routinely performed using analytical procedures, such as high-performance liquid chromatography and mass spectrometry(38).

#### Dosage Optimization and Pharmacokinetics

The most favorable dosing schedules can only be determined through thorough pharmacokinetic-pharmacodynamic research in humans. The study of absorption, metabolism, distribution, and excretion of bioactive compounds will help select the dose, maximize therapeutic benefits, and minimize potential toxicity. Approaches to increase bioavailability, including nanoformulations or co-administration with bioenhancers, should be considered(39).

#### Safety and Drug Interaction Studies

Although preclinical toxicology data show that the drug has a good safety profile, extensive clinical safety studies are essential. Potential interactions with traditional antidiabetic agents and other drugs should be considered to prevent undesirable effects or changes in drug efficacy. In different populations, post-marketing surveillance will be required to assess long-term safety(40).

#### Clinical trial design and regulatory approval

To confirm the effectiveness and safety of *Justicia wynaadensis* extracts in antidiabetic effects in human subjects, robust randomized controlled trials (RCTs) are required. Trial designs must consist of a variety of diabetic patients, standardized extract preparations, suitable control groups, and clinically relevant endpoints, such as improvement in HbA1c levels, insulin sensitivity, and

complication rates. Approval processes require going through regulatory approval processes with comprehensive documentation of quality, safety, and effectiveness data(41).

### Future Research Directions

#### Isolation and characterization of active compounds

Further phytochemical research is needed to isolate, identify, and describe specific bioactive constituents known to have antidiabetic actions. Identifying their molecular targets and mechanisms will facilitate the development of targeted phytopharmaceuticals with increased potency and specificity(42).

#### Mechanistic and Molecular Investigations.

Further molecular research on the signaling pathways regulated by *Justicia wynaadensis* phytochemicals will enhance our knowledge of its diverse activities. Studies of gene expression, interactions with receptors, and influences on metabolic enzymes will clarify the overall effects on glucose and lipid metabolism(43).

#### Formulation Development and Delivery Systems

New formulation approaches are necessary to enhance the solubility, stability, and bioavailability of active phytochemicals. The use of nanoparticles as delivery, encapsulation, and sustained-release systems might improve patient compliance and therapeutic efficacy(44).

#### Special Population Clinical Assessments.

Further studies are needed to assess the efficacy and safety in special populations, including elderly patients, pregnant women, and people with comorbidities. Knowledge of differentiated reactions will inform individualized treatment strategies(45).

#### Combination with lifestyle and dietary interventions

Since diabetes is a holistic disease, research studies on the synergistic effect of *Justicia wynaadensis* supplementation in conjunction with lifestyle changes, diet, and exercise are justified. Integrative strategies can maximize glycemic control and enhance quality of life(46).

Preservation and sustainable use

To facilitate clinical and commercial use, sustainable harvesting and cultivation methods should be established to avoid reducing the natural population. Ethical and sustainable use will be guaranteed through conservation strategies, as well as community involvement and benefit-sharing systems(47).

### Conclusion

*Justicia wynaadensis*, leaves have promising potential as a natural antidiabetic agent because they are composed of highly phytochemical constituents, such as flavonoids, alkaloids, and phenolics, which together regulate glucose metabolism, promote insulin sensitivity, and provide protection against diabetes-induced oxidative stress. They have been shown to be effective in reducing blood glucose levels, improving lipid profiles, and protecting pancreatic  $\beta$ -cells in preclinical studies. Their promising therapeutic potential is further supported by a positive safety profile.

Nevertheless, to determine their clinical utility fully, pharmacological and toxicological studies, including properly designed clinical trials, are required. In general, *Justicia wynaadensis* leaves could be a promising alternative or supplement to traditional antidiabetic treatments, and further research is required to maximize their effectiveness, dosage, and safety in diabetes treatment.

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### Human and Animal Rights

NA

### Ethics approval and consent to participate

Not applicable.

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