Ayurveda Sahiti Prabha's
International Journal of Ayurvedic Medicine
ISSN No: 0976-5921

Research Article

# Effect of *Piper Betel* Linn Leaf Extract on Glycemic Control in Type 2 Diabetes Mellitus

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Received: 20-07-2025 Accepted: 19-02-2026 Published: 31-03-2026

## Abstract

Despite the availability of pharmacological interventions for diabetes, long-term use of these drugs is often associated with adverse effects and financial burden, particularly in low-resource settings. Herbal remedies like *Piper Betle* (betel leaf), known for its antidiabetic properties, have shown promise in glycemic control. Hence, the current study was conducted to evaluate the impact of betel leaf extract on fasting and postprandial blood glucose levels among patients with T2DM. A quasi-experimental study was conducted at the diabetic clinic of Saveetha Medical College and Hospital. A total of 60 participants were selected using a convenience sampling technique, based on their fasting blood glucose levels and predefined inclusion criteria, and were assigned either the study group (n = 30) or the control group (n = 30). The intervention group received betel leaf extract daily on an empty stomach for two weeks, while the control group received standard routine care. Fasting blood sugar levels were measured pre- and post-intervention. The study group showed a significant reduction in fasting blood sugar levels from 131.76 ± 3.12 mg/dL to 118.23 ± 1.47 mg/dL, while the control group showed no significant change (133.47 ± 1.13 to 131.92 ± 2.24 mg/dL, p = 0.78). Between-group comparison revealed a statistically significant difference in post-test fasting and postprandial blood glucose levels (p = 0.001). Betel leaf extract significantly reduced fasting blood glucose levels among individuals with T2DM, suggesting its potential as a safe and cost-effective adjunct to conventional diabetes management. Further randomized controlled trials are needed to substantiate and expand the current findings including optimal dosing.

**Keywords:** Betel Leaf extract, Type 2 Diabetes Mellitus, Blood glucose level, Piper betle, Diabetes.

**Access this article online**

Website: https://ijam.co.in

DOI: https://doi.org/10.47552/ijam.v17i1.6380

## Introduction

Type 2 Diabetes Mellitus (T2DM) is an increasingly prevalent global health issue marked by chronic hyperglycemia. At the onset of the disease, the pancreatic β-cells are mainly impacted, resulting in disrupted blood glucose regulation caused by reduced insulin secretion and a relative deficiency of insulin. As reported by the International Diabetes Federation (IDF), more than 537 million adults worldwide had diabetes in 2021, and this figure is expected to rise to 643 million by 2030. The burden of the disease is especially high in low- and middle-income nations (1). The increasing occurrence of T2DM is mainly linked to inactive lifestyles, poor eating habits, and inherited genetic factors (2). A recent study titled *Secular Trends in Diabetes in India* examined changes in diabetes prevalence between 2016 and 2023 across urban and rural regions of Tamil Nadu. The findings revealed that in urban areas, the prevalence rose from 18.6% in 2016 to 21.9% in 2023. In semi-urban towns, it increased from 16.4% to 20.3%, while in peri-urban villages, it went up from 9.2% to 13.4% (3). Common symptoms associated with T2DM include weight loss, polyuria, polydipsia, and hyperglycemia. The World Health Organization states that diabetes can be managed and its complications delayed or prevented through a combination of diet, physical activity, medication, and regular screening (4). However, diabetes-related complications significantly reduce life expectancy, with some estimates suggesting a reduction by nearly one-third (5). These complications include neuropathy, retinopathy, atherosclerosis, nephropathy, digestive disorders, oral health issues, and increased susceptibility to infections. Microvascular complications are strongly associated with depression and cognitive impairment (6). While T2DM has no known cure, lifestyle interventions such as exercise, a balanced diet, and weight loss play a vital role in disease management. When lifestyle changes are insufficient, insulin therapy or oral antidiabetic medications may be recommended. Numerous safe and effective pharmacological treatments are available, including Metformin, Sulfonylureas, SGLT2 inhibitors, Thiazolidinediones, Dipeptidyl Peptidase IV inhibitors, Insulin, Amylinomimetics, Dopamine agonists, and incretin-based therapies. Despite these advancements, long-term use of antidiabetic drugs may lead to

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adverse effects, decreased patient compliance, and significant economic burden—especially in low-income countries. Consequently, there is growing interest in low-cost, preventive strategies, including the use of herbal medicine as a natural, non-chemical alternative for the treatment and management of diabetes (7, 8). Many herbs, such as aloe vera, curry leaves, and basil leaf, fish mint, licorice weed, etc have therapeutic benefits in treating metabolic syndrome due to their bioactive components (9). Among the various herbal remedies, **betel leaf** (*Piper betle Linn)* has garnered attention due to its longstanding use in Ayurvedic and traditional medicine across South and Southeast Asia. Betel leaf contains a variety of bioactive compounds, compounds including chavicol, hydroxychavicol, and eugenol which possess antioxidant, anti-inflammatory, and antidiabetic properties (10). Red betel leaf is especially rich in phytochemicals such as alkaloids, saponins, tannins, and flavonoids (11). Flavonoid compounds that act as antioxidants capable of neutralizing hydroxyl radicals, which damage the pancreatic islet cells. These compounds may support insulin activity and have been associated with therapeutic effects in conditions such as gout, cancer, hypertension, and diabetes (12). Betel leaf has also been reported to be highly effective in treating a wide range of conditions, including wound healing, conjunctivitis, constipation, voice disorders, gum inflammation, ringworm infections, cuts and injuries, high blood pressure, brain toxicity, diabetes, headaches, leucorrhea, and obesity (13). The chemical compound β-caryophyllene found in betel leaf, along with recent in vivo and in vitro studies, indicates that betel leaf extract may aid in reducing blood glucose levels by improving insulin sensitivity, regulating carbohydrate metabolism, and safeguarding pancreatic β-cells (14). Although traditional use supports the role of betel leaf in managing diabetes, there is limited scientific validation through controlled clinical trials. Therefore, evaluating the effectiveness of betel leaf extract in lowering blood glucose levels among individuals with T2DM could provide valuable evidence for integrating this natural supplement into modern diabetes care protocols.

## Materials and Methods

### Design & Setting

A quasi-experimental non-equivalent control group design was adopted to conduct the study. It was carried out at the diabetic clinic of Saveetha Medical College and Hospital in the Kancheepuram district of Tamil Nadu. The clinic functions twice a week, offering comprehensive care to individuals with diabetes and serving around 20–30 patients each week. Official approval was secured from the hospital administration before initiating the study.

### Sample Size

Sample size was calculated assuming a 10% improvement in the reduction of fasting blood glucose, with a standard deviation of 30%, 85% power, a 5% level of significance, and a 10% dropout rate. It was estimated using Sigma Plot 13 Systat Software Inc., USA. The final sample size was rounded off to 60, with 30 individuals assigned to the study group and 30 to the control group.

### Sample & Sampling Technique

A total of 60 participants were selected using a convenience sampling technique, following an initial assessment of their fasting blood glucose levels and based on inclusion criteria. The study group (n=30) was selected during the first month of data collection, and the control group (n=30) was selected in the following month.

### Criteria for sample selection

The inclusion criteria comprised both male and female patients with Type II diabetes mellitus, aged between 30 and 60 years, who were on regular oral anti-diabetic treatment. Eligible participants had a duration of diabetes ranging from 1 to 5 years, fasting blood glucose levels between 120 and 150 mg/dl, and were willing to provide informed consent to participate in the study. Patients were excluded if they had severe comorbidities, were seriously ill, had uncontrolled diabetes, were on anticoagulant therapy, insulin, any other dietary modifications, or were undergoing alternative therapies such as acupuncture or reflexology. Additionally, those with psychiatric disturbances, gastritis, known allergies to betel leaf extract, or who were uncooperative were also excluded from the study.

### Outcome of the Study

Demographic and clinical variables were collected to obtain baseline information. The primary outcomes measured were fasting blood sugar and postprandial blood sugar levels.

### Collection and Extract Preparation

The intervention involved administering betel leaf extract for two weeks. The extract was prepared using fresh betel leaves. Approximately 2–3 betel leaves, weighing around 3 grams in total, were gently washed with fresh water. The leaves were then hygienically crushed using a mortar and pestle. Thirty milliliters of water were taken and brought to a boil with the crushed leaves at 100°C. The mixture was boiled until the volume was reduced to 5 mL. The resulting decoction was allowed to cool to room temperature and then filtered. Participants were instructed to consume 5 mL of the extract on an empty stomach each morning for two weeks. A fresh extract was prepared daily.

### Data Collection Procedure

The study's purpose was communicated to the participants in their local language, and any questions they had were addressed, and any queries were clarified. Written informed consent was obtained, and confidentiality was maintained. Baseline data were collected using a structured questionnaire through individual interviews. Fasting blood sugar and postprandial blood glucose levels were measured before the intervention. Participants in the study group received the betel leaf extract under the direct supervision of the investigators for 15 consecutive days. Tolerance and any side effects were monitored throughout the study period. The control group continued with routine care practices. Post-intervention measurements of fasting blood sugar and postprandial blood glucose were conducted at the end of two weeks.

### Analysis

The collected data were coded and entered into Microsoft Excel, then analyzed using IBM SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Baseline information were summarized using percentages, means, and standard deviations. Paired and unpaired t-tests were used to assess the effectiveness of the intervention. A p-value less than 0.05 was regarded as statistically significant, using a 95% confidence interval.

### Ethical Approval

The study was approved by the Institutional Scientific Review Board of Saveetha College of Nursing, Saveetha Institute of Medical and Technical Sciences (Deemed to be University), under

reference number 786/2022/ISRB/SCON dated 27th September 2022. Ethical principles were strictly followed to ensure the protection of participants' rights and confidentiality throughout the study.

## Results

Table 1 shows that the mean age of participants in Group I and Group II was 49 ± 4.32 years and 48 ± 6.52 years, respectively. In terms of gender distribution, the majority of participants were males, comprising 60% in Group I and 63% in Group II. The mean Body Mass Index was similar between groups, with 38.21 ± 3.12 in Group I and 38.34 ± 2.19 in Group II. With regard to family history of diabetes mellitus, 53% of participants in Group I and 60% in Group II reported having a positive family history. The majority of participants in both groups followed a non-vegetarian diet, accounting for 80% in each group. A small proportion of participants followed a vegetarian diet (13% in Group I and 17% in Group II), while ovo-vegetarians constituted 7% and 3% in the respective groups. Regarding occupational activity, a sedentary lifestyle was reported by 60% in Group 1 and 56% in Group 2. Moderate physical activity was observed in 30% and 17% of participants in Group I and Group II, respectively. Notably, a higher proportion of participants in Group 2 (27%) engaged in heavy work compared to 10% in Group I. The average duration of diabetes was 3.14 ± 1.36 years in Group I and 3.45 ± 1.75 years in Group II. Most participants in both groups were treated with sulfonylureas (86% in Group 1 and 90% in Group 2), while biguanides were used by 14% and 10%, respectively. Regarding the duration of treatment, a majority had been on treatment for more than 5 years (60% in Group 1 and 64% in Group 2). A small proportion (3%) in both groups had been on treatment for less than a year. Treatment duration between 1–5 years was reported in 37% of Group 1 and 33% of Group 2. Finally, treatment follow-up was regular in 67% of participants in Group 1 and 72% in Group 2, while irregular follow-up was observed in 33% and 28%, respectively.

**Table 1: Baseline information on participants with Type 2 DM**

| Background Variables | Group I (SG) | Group II (CG) |
|---|---|---|
| Age (in Years) | 49 ± 4.32 | 48 ± 6.52 |
| Gender (Male/Female) | 60% / 40% | 63% / 37% |
| Body Mass Index | 38.21 ± 3.12 | 38.34 ± 2.19 |
| Family History of DM (Yes / No) | 53% / 47% | 60% / 40% |
| Dietary Pattern (Vegetarian / Non-veg / Ova-veg) | 13% / 80% / 7% | 17% / 80% / 3% |
| Type of Work (Sedentary / Moderate / Heavy) | 60% / 30% / 10% | 56% / 17% / 27% |
| Duration of DM (Years) | 3.14±1.36 | 3.45±1.75 |
| Type of Oral Hypoglycaemic agent (Sulfonylureas / Biguanides) | 86% / 14% | 90% / 10% |
| Treatment Period (< 1 year / 1-5Years / >5 years) | 3% / 37% / 60% | 3% / 33% / 64% |
| Treatment Follow up (Regular / Irregular) | 67% / 33% | 72% / 28% |
| **SG – Study Group CG – Control Group** | | |

Table 2 shows that the pre-test and post-test mean values of fasting blood sugar in the control group were 133.47 ± 1.13 mg/dL and 131.92 ± 2.24 mg/dL respectively. The difference was analyzed using a paired t-test, which was not statistically significant, as indicated by a t-value of 4.321 and a p-value of 0.78. In contrast, the study group, which received the intervention, showed a marked reduction in fasting blood sugar levels from a pre-test mean of 131.76 ± 3.12 mg/dL to a post-test mean of 118.23 ± 1.47 mg/dL This reduction within clinical range was found to be statistically significant, with a paired t-test value of t = 9.532 and a p-value of 0.05 with 5% statistical significance.

The postprandial blood glucose levels in the control group showed a minimal decrease from the 149.48 ± 1.06 to 148.35 ± 1.25, which was not statistically significant (t = 2.321, p = 0.89; ). In contrast, the study group exhibited a notable reduction in postprandial blood glucose levels from the pre-test (148.98 ± 1.23) to the post-test (134.24 ± 2.13), and this change was statistically significant (t = 10.641, p < 0.05).

These findings suggest that betel leaf extract was effective in reducing fasting and postprandial blood glucose levels in the study group, while no significant change was observed in the control group.

**Table 2: Within Group Analysis**

| Variable | Group | Mean ± SD | Paired 't' test | |
|---|---|---|---|---|
| | | | Control Pre –Post | Experimental Pre – Post |
| Fasting Blood Glucose Level | CG: Pre-test | 133.47±1.13 | t = 4.321 p = 0.78 NS | t = 9.532 p < 0.05 S* |
| | CG: Post-test | 131.92±2.24 | | |
| | SG: Pre-test | 131.76±3.12 | | |
| | SG: Post- test | 118.23±1.47 | | |
| Postprandial Blood Glucose Level | CG: Pre-test | 149.48±1.06 | t = 2.321 p = 0.89 NS | t = 10.641 p < 0.05 S* |
| | CG: Post-test | 148.35±1.25 | | |
| | SG: Pre-test | 148.98±1.23 | | |
| | SG: Post- test | 134.24±2.13 | | |
| CG – Control Group, SG – Study Group, *p<0.05, S – Significant, NS – Not Significant | | | | |

Table 3 shows that an unpaired t-test was used to compare the post-test values between the control and study groups. The post-test mean fasting blood sugar level was 131.92 ± 2.24 mg/dL in the control group and 118.23 ± 1.47 mg/dL in the study group. The t-value was 7.873 with a p-value of 0.001, indicating a highly statistically significant difference between the two groups.

The control group had a mean postprandial blood glucose level of 148.35 ± 1.25 mg/dL, while the study group showed a lower mean level of 134.24 ± 2.13 mg/dL. The t-value of 9.789 and a p-value of 0.001 indicate that this difference is highly significant.

These results suggest that the intervention administered to the study group was effective in significantly reducing postprandial blood glucose levels compared to the control group.

**Table 3: Between Group Analysis**

| Variable | Mean± S.D | Unpaired 't' test |
|---|---|---|
| **Fasting Blood Glucose Level** | | |
| Control Group - Post test | 131.92±2.24 | t = 7.873<br>p = 0.001<br>S** |
| Study group - Post test | 118.23±1.47 | |
| **Postprandial Blood Glucose Level** | | |
| Control Group - Post test | 148.35±1.25 | t = 9.789<br>p = 0.001<br>S** |
| Study group - Post test | 134.24±2.13 | |
| **p<0.001, S – Significant | | |

## Discussion

The management of diabetes mellitus typically requires lifelong drug therapy, which can impose a financial burden and may lead to poor adherence to the treatment regimen, resulting in increased physical and psychological distress. Traditional medicine systems often utilize hypoglycemic agents to help reduce the risk of developing DM (15). Various herbal medicines are available for managing diabetes, offering potential non-chemical alternatives for treatment and rehabilitation. Among these, *Piper betel* Linn is one herbal remedy that shows potential in diabetes management. Abdul Ghani et al reported that the bioactive compounds found in betel leaf may influence insulin sensitivity, blood glucose regulation, and lipid metabolism (16). Furthermore, Subramni K et al mentioned that betel leaf possesses strong antioxidant properties due to the presence of polyphenol compounds such as allyl pyrocatechol and chavicol etc that help combat oxidative stress, which is commonly associated with diabetes (17). Safithri M et al, stated that red betel leaves contain flavonoantds capable of regenerating Langerhans islet cells, thereby enhancing insulin production in diabetic experimental rats. Hence the current study analyzed the effect of betel leave extract on fasting blood sugar level in T2DM (18). The results of the current study demonstrate a statistically significant decrease in fasting blood glucose levels among participants who consumed betel leaf extract for a period of two weeks, suggesting its potential effectiveness as a complementary therapy for managing T2DM. These results are consistent with preclinical studies demonstrating the antihyperglycemic potential of Piper betle. A study by Thirunavukkarasu et al**,** using alloxan-induced diabetic rats found that betel leaf extract significantly improved glycemic control by enhancing insulin secretion and protecting pancreatic β-cells (14). The biological plausibility in betel leaf is supported by the presence of bioactive compounds like flavonoids, eugenol, hydroxychavicol, and chavicol which possess potent antioxidant and anti-inflammatory effects, as reported by Saha et al (10). The antioxidant effects of red betel leaf, as explained by Kustiawan 2021, are crucial in neutralizing reactive oxygen species such as hydroxyl radicals that can damage pancreatic cells and impair insulin secretion. By preventing oxidative stress, betel leaf extract may contribute to preserving pancreatic function and enhancing insulin sensitivity, key mechanisms in T2DM management. Moreover, the improvement in blood glucose levels observed in this study aligns with the ethnomedicinal usage of betel leaf in traditional systems of medicine like Ayurveda and Siddha, which have long recognized its role in treating metabolic disorders (11). In another study, Kumar et al demonstrated that that the aqueous extract of betel leaves significantly lowered blood glucose levels in diabetic rats following an overnight fast. Rats treated with the extract had markedly reduced levels of blood glucose and glycosylated hemoglobin compared to untreated diabetic controls. Furthermore, the extract led to a significant reduction in the activity of hepatic glucose-6-phosphatase and fructose-1,6-bisphosphatase, along with a notable increase in liver hexokinase activity (19). Hossain et al, reported that betel leaf extract exhibits strong antidiabetic effects and is effective in controlling blood sugar levels (20). Chauhan et al observed significant improvements in glucose tolerance tests, indicating that the betel leaf extract exhibited antihyperglycemic activity by effectively reducing elevated blood glucose levels following external glucose administration (21). Pane Hw et al recently found that administering red betel leaf decoction was more effective in reducing blood sugar levels in individuals with diabetes compared to aloe vera decoction (22). Mahral Effendi Sembiring et al 2023 also reported that Red betel leaf extract lowered blood glucose and improved pancreatic tissue structure in male mice (23). In the study by Kamble et al, it was demonstrated that chewing 3.5 grams of betel leaf with *Tambula* granules after meals for 60 days resulted in significant changes in fasting blood glucose, postprandial blood glucose, and glycated hemoglobin levels in individuals with prediabetes (24). While existing studies support the findings of the present study, human experimental research in this area remains limited. Such traditional claims have often lacked empirical support, this quasi-experimental study contributes to bridging the gap between anecdotal use and scientific validation It is also noteworthy that all participants well-tolerated the intervention without any adverse effects. This finding supports the safety profile of betel leaf extract when administered in moderate quantities over a short duration. However, future studies should evaluate long-term safety and the potential for interaction with standard antidiabetic drugs. Several factors strengthen the internal validity of the present study: standardized preparation of the betel leaf extract, supervised administration, and control of confounding variables by including only

participants with similar treatment backgrounds and glycemic levels at baseline. However, limitations exist. The relatively small sample size, short intervention period (2 weeks), and non-random sampling may restrict the broader applicability of the findings. The absence of HbA1c outcome data in the analysis is also a limitation, as it could provide a more stable marker of long-term glycemic control. In light of these findings, betel leaf extract holds promise as a natural, accessible, and culturally acceptable adjunct in T2DM management. However, further randomized controlled trials with larger samples, longer follow-up periods, and mechanistic studies are warranted to fully elucidate its therapeutic potential and establish clinical guidelines for its use.

## Conclusion

The present study demonstrates that the administration of betel leaf extract was effective in significantly reducing fasting blood glucose levels within the clinical range among individuals with type 2 diabetes mellitus compared to the control group. These findings suggest that betel leaf extract may serve as a potential, safe and cost-effective adjunct to conventional diabetes management. Further studies involving larger sample sizes and extended follow-up durations are recommended to substantiate and expand the current findings.

**Acknowledgment**

The authors sincerely thank all the study participants for their valuable contributions and cooperation, which were essential to the success of this research.

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