

Invitro and Invivo Anti-diabetic Studies on *Bougainvillea spectabilis* and *Bougainvillea glabra*: A Comprehensive Review

Mehavarshini Senthilkumar^{ID} and Sakthi Priyadarsini Sethuraman*^{ID}

Department of Pharmacognosy, SRM College of Pharmacy, Faculty of Medicine and Health Sciences, SRM Institute of Science and Technology, Kattankulathur, 603203, Chengalpattu District, Tamil Nadu, India

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Corresponding Author: Sakthi Priyadarsini Sethuraman | E-Mail: (sakthips1@srmist.edu.in)

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ABSTRACT

Diabetes mellitus (DM), is a chronic metabolic disorder that can lead to irreversible nerve and vascular damage. Type 2 DM, the most prevalent form, is a growing global health concern. Although several therapeutic options are available, maintaining optimal blood glucose levels remains challenging, and in addition the current drugs in use are associated with various side effects particularly gastrointestinal disturbances. This has driven the need for safer, more effective antihyperglycemic agents of natural origin. Literature evidences indicate that medicinal plants, through both crude extracts and isolated bioactive compounds, significantly influence blood glucose regulation. Further promising outcomes reported in previous studies underscore their potential in the development of antidiabetic drugs and supplements. Traditionally, *Bougainvillea* species have been used as anti diabetic agent. Also, recent in vitro and in vivo studies have further validated their antidiabetic properties, highlighting mechanisms such as modulation of carbohydrate metabolism and antioxidant activity. The current review holds a strong rationale for herbal research and paves the way for novel herbal formulations in diabetes management.

Keywords: Diabetes mellitus, medicinal plants, *Bougainvillea* species, bioactive compounds, metabolism.

Introduction

Herbal medicine is the oldest form of medical practice and plays a pivotal role in the health care development of modern civilization[1]. Diabetes mellitus is a rapidly spreading metabolic disorder, triggered by impaired insulin action due to abnormal insulin metabolism or an absolute deficiency of insulin, leading to an imbalance in glucose homeostasis [2]. It is one of the major health concerns affecting both humans and animals.

In traditional Indian medicine, numerous plants have been documented as potential remedies for diabetes; several of these have undergone experimental validation, and their bioactive constituents have been isolated [3]. By 2025, India is projected to have the highest diabetic cases worldwide, with an estimated 57.2 million affected individuals [4]. Chronic hyperglycemia is strongly linked to organ damage, dysfunction, and multiple organ failure, particularly in the kidneys, heart, eyes, nerves, and blood vessels[5].

Based on its pathophysiology, diabetes can be classified into gestational diabetes, insulin-dependent Type I, and non-insulin-dependent Type II DM. Type 2 diabetes, characterized by insulin resistance reduces the effectiveness of circulating insulin and in response, pancreatic β -cells increase the secretion of insulin; however, prolonged overproduction can lead to β -cell exhaustion and a decline in insulin output [6].

Inhibitors of α -glucosidase and α -amylase reduce postprandial blood glucose levels. Pancreatic α -amylase breaks down dietary starch into smaller oligosaccharides, which are further hydrolyzed by α -glucosidase into glucose.

The resulting glucose is absorbed into the bloodstream, leading to an elevation in postprandial blood glucose levels [7]. Insulin resistance, coupled with impaired insulin secretion, leads to an overproduction of reactive oxygen species (ROS) and increased oxidative stress. These ROS, in turn, induce tissue damage along with altered cellular metabolism and structural or functional modifications of proteins, lipoproteins, and DNA [8].

The most widely used and potent Indian medicinal plants with antidiabetic properties include *Acacia arabica*, *Aegle marmalade*, *Agrimonia eupatoria*, *Azadirachta indica*, *Benincasahispida*, *Beta vulgaris*, *Caesalpinia bonducella*, *Coccinia indica*, *Ficus benghalensis*, *Gymnemasylvestre*, *Hibiscus rosa-sinesis*, *Jatropha curcas*, *Tinospora cordifolia*, *Syzygiumcumini*, *Pterocarpus marsupium*, *Mucuna pruriens*, *Ocimum sanctum*, and *Trigonella foenum-graecum*[9].

Bougainvillea spectabilis, a member of the Nyctaginaceae family, is a well-known ornamental plant. Studies reported the leaves of *Bougainvillea* possessing various therapeutic qualities, including antimicrobial, antiviral, antibacterial, anticancer, antifungal, and potentially antidiabetic. Additionally, reports state that the ethanolic leaf extract of *Bougainvillea spectabilis* aids in reducing serum cholesterol levels. The plant has been historically employed in treating diabetes mellitus as it is believed to have a hypoglycemic effect, indicating potential for use in diabetes treatment [10].

Focusing on the potential hypoglycemic effect of numerous *Bougainvillea* species in both traditional and modern medicine, in the current review, we analyzed various studies on the reported antidiabetic potency on *Bougainvillea spectabilis* and

Bougainvillea glabra for the management of diabetes.

Method

The keywords antidiabetic, *Bougainvillea*, folklore medicine, α -amylase, α -glucosidase, were searched from journal and databases such as Pub Med, Google Scholar, Scopus. ScienceDirect, Web of Science. The studies were extracted and analyzed comprehensively.

Results

Pancreatic α -amylase, a member of the α -1,4-glucanohydrolase family, is a key therapeutic target in diabetes management. The α -amylase enzyme hydrolyze dietary starch into maltose and glucose.

Table 1 Anti-diabetic activity of *Bougainvillea* in vitro

S.No	Study	Bougainvillea	Part	Extract	Method	Activity
1.	In vitro	<i>Bougainvillea spectabilis</i>	Flower	Hydroethanolic extract (HE extract)	α -amylase inhibition	Percentage inhibition At 1000 μ g/ml, Hydroethanolic extract - 65.2 % inhibition [7]
					Non enzymatic glycosylation of hemoglobin method	At 1000 μ g/ml Percentage inhibition 76.8% (HE extract) 85.3 % (Metformin)
					Glucose diffusion assay method	Relative movement at 180mins: HE-extract 64.51% compared to standard metformin 85.3%
		<i>Bougainvillea alba</i>	Flower	Hydroethanolic extract (HE extract)	α -amylase inhibition	Percentage inhibition At 1000 μ g/ml, Hydroethanolic extract - 65.2 % inhibition
					Non enzymatic glycosylation of hemoglobin method	Percentage inhibition 60.7% (HE extract) 85.3 % (Metformin)

Moreover, blood lipid profiles, significantly increase the risk of coronary heart disease. Therefore, lowering these serum lipid parameters are beneficial for improving the long-term prognosis of diabetes. *B. glabra* extract may possess therapeutic potential in managing multifactorial atherosclerotic conditions, which are among the most severe complications of diabetes. By reducing atherosclerosis risk, such interventions could contribute to more effective and comprehensive management of diabetic hyperlipidemia.

A study by Zamin et al. aimed to investigate the antidiabetic effects of methanolic extract of *B. spectabilis*. In this study, alloxan-induced diabetic as well as normal rats, were given methanolic leaf extract of *B. spectabilis*. The levels of alkaline phosphatase and acid phosphatase at 7, 14, and 21 days were measured at 300mg/kg/b,w, Acid phosphatase and alkaline phosphatase levels in diabetic albino rat's various organs were significantly decreased by the methanolic extract of *Bougainvillea spectabilis* [12].

Another study by Bhat, M. et al. investigated the effects of *B. spectabilis* extracts on biochemical markers associated with diabetes in streptozotocin (STZ) induced diabetic mice. STZ promotes hyperglycemia by specifically targeting pancreatic beta cells. A single intraperitoneal STZ injection to normal mice caused hyperglycemia in 7 days, with blood glucose levels ranging from 200 to 250 mg/dL. The study revealed that 21 days of treatment with *B. spectabilis* extract reverted the glucose levels to normal, indicating that it possesses anti-hyperglycemic effects. The extracts showed promising anti-hyperglycemic potential within 10 days of treatment. The *B. spectabilis* aqueous extract treatment raised the body weight of control and treated mice, whereas continuous loss in weight was observed in diabetic

The enzyme inhibitors bind to the α -1,4-glycosidic linkages of polysaccharides, preventing their breakdown into mono- and disaccharides, thereby reducing postprandial glucose levels by suppressing amylase activity [7].

In a study by Loganathan et al., the anti-diabetic potential of *B. spectabilis* and *B. alba* flowers was evaluated using the α -amylase inhibition assay. The study demonstrated a concentration-dependent increase in α -amylase inhibitory activity for both plants. At 1000 μ g/mL, *B. spectabilis* and *B. alba* exhibited a percentage inhibition of 65% and 55%, respectively. In comparison, the reference drug metformin showed 85.3% inhibition of hemoglobin glycosylation [7].

control group [2].

In yet another study, the blood glucose levels in rats treated with *B. spectabilis* aqueous extract were assessed at the end of 7, 14, and 28 days. Blood glucose levels increased significantly upon streptozotocin induction compared to control. Diabetic rats showed a significant hyperglycemic control in fasting blood sugar level on treatment with aqueous extract of *B. spectabilis*. Further, the decrease in fasting blood glucose caused by *B. spectabilis* extract was comparable to that of glibenclamide. Additionally, diabetic rats treated with *B. spectabilis* extract also showed reduced glycosylated hemoglobin levels [13].

A study by Devi et al. showed oral ingestion of methanol extract of *B. spectabilis* leaves at effectively reduced the blood glucose level in diabetic rats ($P < 0.05$). The leaf extract was found to be significant at 400 mg/kg. and was comparable to standard glibenclamide [14].

A report by Jawal et al., the oral intake of *B. spectabilis* root bark powder significantly reduced the blood glucose levels ($P < 0.05$). ($n = 6$) in alloxan-induced diabetic rats. The highest effective dose of root bark extract tested was found to be 100 mg/kg. However, the blood glucose levels were significantly lowered by glibenclamide from 313.9 ± 4.10 to 201.9 ± 4.12 mg/dl at a dose of 0.2 mg/kg [15].

Studies reported by Adebayo et al., showed the aqueous extract of *B. glabra* significantly decreased blood sugar levels in alloxan-induced diabetes. This is consistent with the reports of local traditional medicine practitioners in their folklore usage to treat diabetes. The study also reported that the *Bougainvillea glabra* extract increased the HDL-C levels in diabetic groups [16].

Methanolic extracts of *Bougainvillea glabra* are effective anti-diabetic medications.

B. glabra alcohol extract demonstrated considerable antidiabetic potential in alloxan-induced hyperglycemic rats with no obvious difference in body weight [17].

In another study by Tata Yohanna, F. et al., the ethanolic flower extract of *B. glabra* showed a notable and substantial drop in blood glucose after 24 hours. Compared to the diabetic control, the extract-treated rats showed decreased blood glucose levels dose-dependently after 24 hours of administration. The ethanol crude extract at a modest dosage continued to lower blood glucose levels for 48 hours. However, in the diabetic control group, a steady rise in blood glucose levels was noted. Further the results of the study also showed that when compared to the crude extract-treated groups, the insulin treatment showed a highly significant hypoglycemic impact at 1, 3, and 6 hours of administration [11].

Table.2 In-vivo Anti-diabetic Studies on Bougainvillea species

S. No	Plant	Part	Extract	Dosage (mg/kg)	Experimental Model	Induction of diabetes
1.	<i>Bougainvillea spectabilis</i>	Flower	Ethanolic extract	100, 200 and 400 mg/kg,	Wistar strain albino rat model	Alloxan [11]
2.	<i>Bougainvillea spectabilis</i>	Leaves	Methanol extract	200mg/kg, 400mg/kg	Albino Wistar rats rat model	Streptozotocin [14]
3.	<i>Bougainvillea spectabilis</i> and <i>Catharanthus roseus</i> (Coadministration)	Leaves	Methanol extract	300 mg/kg	albino rats model	Alloxan [12]
4.	<i>Bougainvillea glabra</i>	Leaves	Methanol extract	100 mg–2000 mg/kg	Wistar albino rats	Alloxan [17]
5.	<i>Bougainvillea spectabilis</i>	Leaves	Aqueous extract	100 mg/kg	Wistar rat model	Streptozotocin [13]
6.	<i>Bougainvillea spectabilis</i> And <i>Azadiracta indica</i> .	Leaves	Chloroform extract (<i>A. indica</i>) aqueous and methanolic extracts (<i>B. spectabilis</i>)	3mg/25kg, 2mg/4ml	Wistar rat model	Streptozotocin [2]
7.	<i>Bougainvillea spectabilis</i>	Root	Ethanol extract	100mg/kg	Albino Wistar rats rat model	Alloxan [15]
8.	<i>Bougainvillea glabra</i>	Leaves	Aqueous extract	400mg/kg	Wistar rat model	Alloxan [16]

Anti-diabetic activity of D-pinitol isolated from Bougainvillea Species

In a study by Fatma Abo-Elghie et al., the D-pinitol concentration in methanol extracts from five *B. spectabilis* cultivars was quantified with LC-ESI-MS/MS. The value of D-pinitol concentrations varied between 5.08 to 6.95 mg/gram extract. The results showed that the LOE cultivar, which is known for its orange bracts, had the maximum amount of D-pinitol and the highest efficacy, outperforming the antidiabetic drug glibenclamide groups treated with crude extract ($p < 0.05$) [18]. In another study by Sanchez-Hidalgo et al., 2021, D-pinitol has been demonstrated to have an insulin-like action in a hypo-insulinemic diabetes model caused by STZ. In STZ-diabetic mice, D-pinitol administered orally or intraperitoneally lowered glycemic levels. The results of the study suggested that D-pinitol could potentially influence the insulin post-receptor signaling pathway, which is facilitated via protein kinase B/phosphatidylinositol 3-kinase (PI3K/Akt). This, in turn, could enhance the uptake of glucose in L6 muscle cells [19].

B. spectabilis stem bark was allowed to air dry in the shade before being ground into a fine powder using an electric grinder and extracted with methanol at 45°C. The yield of the crude extract was around 10%, and its weight was 122.5 g. Using conventional quantitative and qualitative techniques, the phytochemical analysis of stem bark extract revealed the presence of glycosides, alkaloids, tannins, flavonoids, anthraquinones, triterpenes, reducing sugars, saponins, and steroids. *B. spectabilis* stem bark showed the presence of pinitol, quercetin, β -sitosterol, and quercetin 3-O- α -L-rhamnopyranoside [20].

Discussion

Insulin is essential for the conversion of sugars and starches into energy, and its deficiency or dysfunction can lead to multiple complications. Globally, diabetes is a major cause of premature mortality, with one death occurring approximately every 10 seconds, primarily due to cardiovascular complications.

A survey of ethnobotanical literature revealed that 108 plant species from 56 families are commonly used in diabetes management. The growing interest in herbal medicine for diabetes care both in developing and developed nations is largely

attributed to its natural origin and lower risk of adverse effects.

Both *Bougainvillea spectabilis* and *Bougainvillea glabra* have been explored for their antidiabetic potential using *in vitro* and *in vivo* approaches. *In vitro* studies often target α -amylase, a pancreatic key enzyme in carbohydrate digestion belonging to the α -1,4-glucanohydrolase family, which catalyzes starch hydrolysis into glucose and maltose. Inhibition of α -amylase reduces postprandial hyperglycemia.

In vivo studies have evaluated the effects of *B. spectabilis* extracts on biochemical markers of diabetes, particularly in streptozotocin (STZ)-induced diabetic mice. Similarly, aqueous leaf extracts of *B. glabra* have been shown to significantly reduce hyperglycemia in alloxan-induced diabetic models ($p < 0.05$), supporting its traditional use by local practitioners for diabetes treatment.

Alcohol-based extracts of *B. glabra* also exhibited significant antidiabetic activity in alloxan-induced diabetic rats without causing significant changes in body weight. Additionally, these extracts improved several metabolic parameters, including lipid profile, serum urea, serum creatinine, and serum alkaline phosphatase, suggesting their potential in managing both hyperglycemia and diabetes-associated complications.

Conclusion

In conclusion, the antidiabetic effect of *B. spectabilis* and *B. glabra* was reviewed comprehensively for the management of hyperglycemia. The outcomes of experiments conducted verified the effectiveness of *Bougainvillea spp.* in treating type 2 diabetes. The *in vitro* experiments concentrated on the inhibitory activity of the enzyme α -amylase, α -glucosidase, non-enzymatic glycosylation, and glucose diffusion. *In vivo* studies of *Bougainvillea spectabilis* and *B. glabra* suggest that both the plants deserve further clinical research in order to develop into an herbal supplement against diabetes mellitus.

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