



## Harnessing the Power of *Moringa Oleifera* and *Pithecellobium Dulce*: Synergistic Approaches to Diabetes Care – A Review

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### ABSTRACT:

Diabetes mellitus, a chronic metabolic disorder characterized by high blood glucose levels, poses a significant global health challenge. The limitations and adverse effects associated with conventional antidiabetic medications have spurred interest in alternative treatments derived from natural sources. This review explores the synergistic potential of two medicinal plants, *Moringa oleifera* and *Pithecellobium dulce*, in diabetes management. *Moringa oleifera* is renowned for its rich nutrient profile and diverse bioactive compounds, including isothiocyanates, flavonoids, and phenolic acids, which exhibit anti-diabetic properties. *Pithecellobium dulce* contains saponins, tannins, and alkaloids contributing to its hypoglycemic effects. The review synthesizes existing literature on the pharmacological activities of these plants, emphasizing their mechanisms of action in glucose regulation, insulin sensitivity, and beta-cell function preservation. Furthermore, it discusses the potential synergistic effects when these plants are used in combination, potentially enhancing their therapeutic efficacy through complementary mechanisms. Preclinical and clinical studies are analyzed to provide a comprehensive understanding of their benefits and safety profiles. By consolidating current knowledge, this review aims to highlight the promise of *Moringa oleifera* and *Pithecellobium dulce* as a natural, integrative approach to diabetes management, encouraging further research and development in this area.

### INTRODUCTION

Diabetes mellitus is a major global health challenge. This metabolic disorder, involving impaired insulin function or secretion, significantly impacts individual health and healthcare systems. The World Health Organization predicts the number of people with diabetes will rise from over 220 million to over 440 million by 2030.[1] With its prevalence surging worldwide, diabetes has assumed epidemic proportions, necessitating urgent and innovative approaches to its management. Amidst this landscape of escalating health burdens, the use of medicinal plants is continuing in this

modern era, and it has been estimated that approximately one-fourth of prescription medicines worldwide are derived from plants.[2] The spotlight has increasingly turned towards natural remedies and botanical interventions, driven by a quest for effective, sustainable, and holistic therapeutic modalities. Among the diverse array of botanical agents under scrutiny, two herbals have emerged: *Moringa*, and *Pithecellobium*. Revered for their rich pharmacological effects and centuries-old traditional uses, these botanical resources have considerable attention for their potential to mitigate the complexities of diabetes mellitus.



*Moringa oleifera*, commonly known as the drumstick tree, is often referred to as the "miracle tree" for its multifaceted health benefits.[3] It is rich in bioactive compounds such as flavonoids, phenolic acids, vitamins, and minerals. Studies have demonstrated its potential to regulate blood glucose levels through multiple pathways: enhancing insulin secretion, improving insulin sensitivity and inhibiting enzymes responsible for carbohydrate breakdown. Additionally, *Moringa oleifera* exhibits antioxidant properties, which mitigate oxidative stress, it is a key factor in diabetic complications.[4-6].

*Pithecellobium* is a genus encompassing notable medicinal properties and also shows promising antidiabetic potential. Research on *Pithecellobium* preliminary studies suggests it contains unique phytochemicals that improve insulin action, stimulate glucose uptake in cells, and improve lipid metabolism. [7] Recent research endeavours have promising evidence regarding their efficacy in diabetes management, spurring an increasing interest in exploring their therapeutic potential through rigorous scientific inquiry.

Against this backdrop, this article embarks on a comprehensive exploration of the therapeutic landscape of *Moringa* and *Pithecellobium* in the context of diabetes mellitus. By synthesizing and scrutinizing existing knowledge, this review aims to unravel the intricate mechanisms through which these botanical allies exert their beneficial effects on glucose metabolism, insulin sensitivity, and related pathways. Through a meticulous examination of scientific literature and clinical studies, we endeavour to elucidate harnessing the therapeutic potential of *Moringa* and *Pithecellobium* for the management of diabetes mellitus. As we delve into this exploration, we are poised to unravel novel insights that may not only enhance our understanding of diabetes pathophysiology but also pave the way for the development of innovative and nature-inspired therapeutic medication. By bridging the realms of traditional wisdom and modern scientific inquiry, we aspire to illuminate a path towards a more sustainable, holistic, and effective approach to combating the global health challenge of diabetes mellitus.

## DESCRIPTION AND BACKGROUND OF MORINGA OLEIFERA

**Family:** Moringaceae

**Synonyms:** Guilandina Moringa. Hyperanthera Moringa, Vahl Moringa pterygosperma Gaertn. nom. illeg.

**Common name:** Horseradish tree, Radish tree, Drumstick tree, Mother's Best Friend, West Indian ben.

**Medicinal Applications of Plant Components:** Root Leave Stem Bark Gum Flower Seed.[8]



Fig.1 *Moringa oleifera* tree

## MORINGA OLEIFERA'S KEY COMPOUNDS FOR ANTI-DIABETIC EFFECT

The anti-diabetic effect of *Moringaoleifera* is attributed to the presence of several compounds, including:

- 1. Flavonoid:** Quercetin-3-glucoside, a flavonoid, has demonstrated anti-inflammatory and antioxidant characteristics, potentially enhancing insulin sensitivity and lowering blood sugar levels.[9] Isothiocyanates, which are natural flavonol-type flavonoids, are present in both the seeds and leaves of *Moringa oleifera*. Studies indicate that these compounds possess anti-hyperglycemic properties. Myricetin is present in *Moringa* which has an antioxidant effect.[10,11]
- 2. Phenolic acids:** Chlorogenic acid is located in *Moringa oleifera* leaves. It has the potential to slow the absorption of glucose from the intestines. [12]
- 3. Fibre:** *Moringa oleifera* leaves serve as an effective resource, aiding in the slowing of glucose digestion and mitigating post-meal blood sugar surges.[13]



4. **Nutrients:** In addition to these compounds, *Moringa oleifera* also includes several nutrients that could be advantageous for individuals with diabetes, such as vitamins A and C, potassium, and magnesium.[14]

#### **MORINGA OLEIFERA'S POTENTIAL MECHANISMS FOR MITIGATE DIABETES**

The specific compound in *Moringa oleifera* that is most crucial for its anti-diabetic effects remains under investigation. However, the combined presence of various compounds in *Moringa oleifera* likely contributes to its overall anti-diabetic effect. Specifically, this effect is probably due to the combination of several compounds, including quercetin-3-glucoside and isothiocyanates.[15,16]

1. **Blood Glucose Regulation:** *Moringa oleifera* contains bioactive compounds such as quercetin and chlorogenic acid, which inhibit the activity of the enzymes  $\alpha$ -glucosidase and  $\alpha$ -amylase in the digestive system. These enzymes are responsible for breaking down carbohydrates into glucose. Inhibiting their action, slows down carbohydrate digestion, reducing the rate at which glucose is released into the bloodstream after meals, thereby helping to maintain more stable blood sugar levels.[17,18] *Moringa oleifera* may boost insulin sensitivity in cells by activating AMP-activated protein kinase (AMPK), a crucial enzyme in glucose metabolism. Increased AMPK activity can improve glucose uptake and utilization, thereby lowering insulin resistance.[19]

2. **Protection of Pancreatic Beta Cells:** *Moringa oleifera* is abundant in antioxidants, such as vitamins C and E. These antioxidants can safeguard pancreatic beta cells from oxidative stress, helping to maintain their ability to secrete insulin. This protection is essential for individuals with type 2 diabetes, as dysfunction of beta cells leads to reduced insulin production.[20,21]

3. **Reduction of Chronic Inflammation:** Chronic inflammation is strongly linked to insulin resistance and type 2 diabetes. *Moringa oleifera* contains anti-inflammatory compounds such as quercetin, kaempferol, and beta-sitosterol, which may help reduce chronic inflammation. Lowering inflammation can enhance insulin sensitivity and overall glucose metabolism.[18,22]

4. **Gut Microbiota Modulation:** Emerging studies indicate that gut microbiota is involved in diabetes. The fibre content and possible prebiotic properties of *Moringa oleifera* may promote a healthier gut microbiome, positively affecting glucose metabolism and insulin sensitivity.[23]

#### **DESCRIPTION AND BACKGROUND OF PITHECELLOBIUM DULCE**

*Pithecellobium dulce* is a small to medium-sized tree that produces twisted, pod-like fruits containing a sweet and tangy pulp. The plant is widely used in traditional medicine across various cultures, including India.[24]

**Family:** Fabaceae (Leguminosae)

**Synonyms:** Mimosa dulcis

**Common Name:** Madras Thorn, Manila Tamarind, Bread-and-cheese, Huamuchil, Opiuma, Asam Keranji, Blackhead, Asam Kranji, Asam Tjina.[25]

**Medicinal Uses of Plant Parts:** Seeds, Leaves, Fruits, [1,26]



**Fig.2 Pithecellobium dulce**

#### **PITHECELLOBIUM DULCE'S KEY COMPOUNDS AND MECHANISMS FOR ANTI-DIABETIC EFFECT**

The antidiabetic properties of *Pithecellobium dulce* are attributed to several bioactive compounds found in the seeds and other parts of the plant. These compounds help to manage diabetes through the following mechanisms:



1. **Flavonoids:** These compounds possess antioxidant properties that reduce oxidative stress, a common problem in diabetic patients. Specific flavonoids in *Pithecellobium*, such as quercetin and kaempferol, stimulate insulin secretion, protect pancreatic beta cells from reactive oxygen species (ROS), and enhance the cells' antioxidant defence mechanisms. [27-29]

2. **Catechins:** These are a type of flavanol, a class of antioxidant compounds. Catechins have demonstrated the ability to enhance insulin sensitivity and facilitate glucose uptake in cells, aiding in the regulation of blood sugar levels.[27-29]

3. **Alkaloids:** These compounds exhibit diverse pharmacological effects, including antidiabetic properties. Alkaloids found in *Pithecellobium* may assist in reducing blood sugar levels by stimulating insulin secretion. They effectively combat hyperglycemia by promoting glucose consumption and glycogen synthesis. Phyto-drugs regulate metabolism by either inhibiting or inducing various molecules, including AMP-activated protein kinase (AMPK), Glucose transporter 4 (GLUT4), glycogen synthase kinase-3 (GSK3), sterol regulatory element-binding proteins 1 (SREBP1), glucokinase (GK), glucose-6-phosphatase (G6Pase), acetyl-CoA carboxylase (ACC), peroxisome proliferator-activated receptor (PPAR), and protein tyrosine phosphatase 1B (PTP1B) expression, thereby promoting insulin stimulation.[30]

4. **Tannins:** Tannins exhibit antioxidant properties and can contribute to lowering blood glucose levels. They might inhibit enzymes involved in carbohydrate digestion, thereby inducing glucose transport through activation of the insulin-mediated signalling pathway in adipocytes, ultimately resulting in reduced blood glucose levels.[31]

5. **Saponins:** They can prevent the rise in blood glucose levels by inhibiting enzymes (maltase, sucrose, lactases) responsible for breaking down disaccharides into monosaccharides. This property is significant for managing both Type I and Type II diabetes, aiding in the prevention of elevated blood sugar levels and contributing to the regulation of glucose levels in the blood.[14,32,42]

6. **Phenolic Compounds:** Renowned for their antioxidant properties, these compounds can regulate

the activity of enzymes engaged in glucose metabolism. Additionally, they enhance  $\beta$  cell function, influencing insulin synthesis and secretion, diminish hepatic glucose production, and modify the efficacy of glucose transporters and insulin receptors.[33] Phenolic acids like gallic acid, chlorogenic acid, and ellagic acid found in *Pithecellobium dulce* play a role in its anti-diabetic effects.[27-28]

7. **Terpenoids:** These compounds have been found to have antihyperglycemic effects. They may work by improving pancreatic  $\beta$  cell function and improving insulin sensitivity that helps in maintaining normal blood glucose levels.[34-35]

The effects of these bioactive compounds in *Pithecellobium dulce* contribute to its overall antidiabetic potential. Studies have shown that extracts from various parts of the plant, such as the leaves, bark, and seeds, exhibit significant antidiabetic activity by improving insulin sensitivity, reducing blood glucose levels, and enhancing antioxidant defences.

## PRELIMINARY PHYTOCHEMICAL ANALYSIS OF THE EXTRACTS

To assess the chemical composition of the various extracts qualitatively, a preliminary phytochemical analysis should be conducted according to the standard methods.

1. **Sterol Test (Salkowski Reaction):** A few milligrams of the plant extract are dissolved in 2 ml of chloroform. Then, 2 ml of concentrated  $H_2SO_4$  is carefully added down the sides of the test tube. The tube is shaken for a few minutes. The development of red colour in the chloroform layer indicates the presence of sterols. [29]

2. **Tannin Test (Ferric Chloride Reagent Test):** The extracted sample is taken separately in water, warmed, and filtered. A few drops of a 5% w/v ferric chloride solution prepared in 90% alcohol are then added to a small volume of the filtrate. The presence of tannins is indicated by the appearance of a dark green or deep blue colour. [29]

3. **Test for Proteins (Xanthoproteic Test):** A few milligrams of the extract are dissolved in 2 ml of water, and 0.5 ml of concentrated  $HNO_3$  is added. The presence of proteins is indicated by the development of a yellow colour. [29]





4. **Test for Sugars (Fehling's Test for Free Reducing Sugar):** Approximately 0.5 g of extract is dissolved in distilled water and filtered. The filtrate is heated with 5 ml of equal volumes of Fehling's solution A and B. The formation of a red precipitate of cuprous oxide indicates the presence of reducing sugars. [29]

5. **Test for Flavonoids (Ferric Chloride Test):** About 0.5 g of extract is boiled with 5 ml of distilled water and then filtered. To 2 ml of this filtrate, a few drops of 10% ferric chloride solution are added. A green-blue or violet colouration indicates the presence of a phenolic hydroxyl group. [29]

6. **Test for Saponins:** One gram of extract is boiled with 5 ml of distilled water and filtered. To the filtrate, about 3 ml of distilled water is added and shaken vigorously for about 5 minutes. Persistent frothing upon warming indicates the presence of saponins. [29]

7. **Test for Anthraquinones (Borntrager's Test):** An aliquot of 0.5 g of the extract is boiled with 10 ml of sulphuric acid and filtered while hot. The filtrate is shaken with 5 ml of chloroform. The chloroform layer is transferred to another test tube, and 1 ml of dilute ammonia is added. The resulting solution is observed for colour changes. [29]

8. **Test for Terpenoids (Salkowski Test):** To 0.5 g of extract, 2 ml of chloroform is added, followed by 3 ml of concentrated  $H_2SO_4$  to form a layer. A reddish-brown

colouration at the interface indicates the presence of terpenoids. [29]

9. **Test for Cardiac Glycosides (Keller-Killiani Test):** To 0.5 g of the extract diluted to 5 ml in water, 2 ml of glacial acetic acid containing one drop of ferric chloride solution is added. This mixture is under-layered with 1 ml of concentrated sulphuric acid. The presence of a brown ring at the interface indicates a deoxy sugar characteristic of cardenolides. A violet ring might appear below the brown ring, and a greenish ring might form just above the brown ring in the acetic acid layer and gradually spread throughout this layer. [29]

10. **Determination of Phytochemicals by Gas Chromatography-Mass Spectrum Analysis (GC-MS):** This method is used to determine the phytochemical compounds present in the extracts.

#### COMPARISON OF THE BIOACTIVE COMPOUNDS RESPONSIBLE FOR DIABETES MITIGATION IN *MORINGA OLEIFERA* AND *PITHECELLOBIUM DULCE*:

This comprehensive comparison of the bioactive compounds in *Moringa oleifera* and *Pithecellobium dulce* highlights their respective antidiabetic properties and synergistic effects as in the following table.[5,11,16]

**Table. 1. Comparison of Bioactive compounds in *Moringa* and *P dulce***

Bioactive Compound	<i>Moringa oleifera</i> (Drumstick Tree)	<i>Pithecellobium dulce</i> (Manila Tamarind)
Flavonoids	Myricetin, Quercetin, Kaempferol,	Catechins , Quercetin, Kaempferol
Alkaloids	Present	Present
Tannins	Present	Present
Saponins	Present	Present
Phenolic Compounds	Gallic acid, Chlorogenic acid, Caffeic acid	Gallic acid, Chlorogenic acid, Ellagic acid
Terpenoids	Present	Present
Vitamins	Vitamin C, Vitamin A, Vitamin E, Vitamin K	Vitamin A, Thiamine, Riboflavin, Niacin, Ascorbic acid
Minerals	Chromium, Zinc (important for insulin function)	Not significantly noted for antidiabetic activity
Proteins	Moringin (a unique protein with antidiabetic properties)	Present



## SCIENTIFIC VALIDATION OF *MORINGA* AND *PITHECELLOBIUM DULCE* IN DIABETES MANAGEMENT

Recent studies have provided some scientific basis for the traditional use of *Moringa* and *Pithecellobium dulce* in diabetes management:

- 1. Reduced fasting blood glucose:** Badriyah Aljazzaf *et al.*, 2023, research study concluded the oral administration of the combined leaf/seed extract of *Moringa oleifera* reduced fasting blood glucose to normal levels much more effectively than if only the leaf or seed extract was administered. Additional studies on the combined extracts of different plant parts (e.g., leaf, seed, root, pod, fruit, and flower) of *M. oleifera* are recommended to find the most potent hypoglycemic and antioxidant combination. The experimental findings of this study appear to indicate a promising opportunity to support the development of a potent antidiabetic drug from *M. oleifera* for the treatment and management of diabetes.[36]
- 2. Natural antihyperglycemic agent:** Gómez-Martínez *et al.*, 2022, published a research study report titled: *Moringa oleifera* leaf supplementation as a glycemic control strategy in subjects with prediabetes. In the study conclusion, *Moringa oleifera* supplementation resulted in favourable changes in glycaemia markers compared to placebo in the subjects with prediabetes studied, suggesting that *Moringa oleifera* might act as a natural antihyperglycemic agent.[37]
- 3. Benefits in glucose regulation and enterobacteria control in a diabetes mellitus rat model:** Villarruel-López *et al.*, 2018, findings suggest that consumption of *Moringa oleifera* powder leaves could be beneficial in the diabetes mellitus rat model over glucose values and enterobacteria enumeration.[38]
- 4. Decreasing LDL serum levels in hyperlipidemic patients:** Waode Fitrah Sari1 *et al.*, 2022, study conclusion was: the intervention of *Moringa* leaf extract for at least 14 days to 30 days effectively reduces total cholesterol, LDL, and triglyceride levels and increases HDL in hyperlipidemic patients, which is beneficial for to overcome the diabetes complications.[43]
- 5. Potential in managing meal-induced blood glucose spikes through enzyme inhibition:** Mahesh Kumar, *et al.*, 2017, study demonstrates that *Pithecellobium dulce* effectively mitigates meal-

induced blood glucose spikes under experimental conditions (both in vivo and in vitro). The experimental conditions and resulting data indicate that this effect is likely due to the inhibition of key enzymes ( $\alpha$ -glucosidase and  $\alpha$ -amylase) responsible for polysaccharide digestion. Overall, these findings strongly suggest that *P. dulce*, a widely available fruit, holds significant potential and could be used alone or in combination with other herbs to manage sudden blood glucose increases in diabetic patients.[39]

- 6. Antidiabetic and organ-protective effects of aqueous and ethanolic extracts of *P. Dulce* in alloxan-induced diabetic rats:** Mule *et al.*, 2016, study show that both aqueous and ethanolic extracts of *P. dulce* exhibit antidiabetic effects in alloxan-induced diabetic rats. The lipid profile results suggest that both extracts have hypolipidemic activity, which is dose-dependent. The oral glucose tolerance test indicates that the extracts enhance glucose tolerance. Additionally, the effects on blood urea, uric acid, and creatinine levels suggest a protective effect on the kidneys. The significant decrease in AST and ALT levels implies that the extracts may also protect the liver.[1]

- 7. Hypoglycemic and antioxidant properties:** Sukantha T A *et al.*, 2016, This study demonstrates that the aqueous extract of *Pithecellobium dulce* fruit peel effectively controls blood glucose levels in diabetic rats. Its hypoglycemic and free radical scavenging properties are beneficial in preventing complications associated with diabetes.[40]

- 8. Antidiabetic and hypolipidemic effects of *P. dulce*:** Mule *et al.*, 2016, study exhibits antidiabetic effects in dexamethasone-induced diabetic rats. The extracts show hypolipidemic effects, significantly increase liver and muscle glycogen levels, and reduce kidney glycogen levels.[7]

- 9. Improvement in glucose tolerance:** Pradeepa S *et al.*, 2016, Studies suggest that the plant extracts improve glucose tolerance, which is beneficial for diabetic patients. The results of the present study indicate that *Pithecellobium dulce* fruit extract possesses significant antidiabetic activity which is evidenced by improved Oral glucose tolerance tests, HbA1c, and glycogen content. Also, the effect of the fruit extract on biochemical alterations indicates the nontoxic as well as beneficial effect of fruits in maintaining normoglycemia.[26]



**10. Antidiabetic and antioxidant activity:** Ranjith Gupta *et al.*, 2012, study conclusion, *Moringa oleifera* exerts protective effects against Streptozocin-induced diabetes. The *Moringa oleifera* exhibited significant antidiabetic and antioxidant activity and active constituents may be isolated from the extract for evaluation in future clinical studies.[41]

## DISCUSSION

Both plants contain quercetin and kaempferol, which are known for their anti-diabetic properties. *Moringa* also contains myricetin, which has additional antidiabetic effects. Both plants contain alkaloids that contribute to their antidiabetic effects. Both plants have tannins, which help in lowering blood glucose levels by inhibiting carbohydrate digestion and absorption. Both plants have saponins, which enhance insulin secretion and improve insulin sensitivity. Both plants are rich in phenolic compounds. *Pithecellobium* contains gallic acid, chlorogenic acid, and ellagic acid, whereas *Moringa* contains gallic acid, chlorogenic acid, and caffeic acid. Both plants have terpenoids, which have antihyperglycemic effects. *Moringa* is richer in vitamins and significant amounts of chromium and zinc, which are important for insulin function. *Moringa* has unique proteins such as moringin, which have specific antidiabetic properties. *Pithecellobium* contains catechins which can enhance insulin sensitivity and facilitate glucose uptake in cells, aiding in the regulation of blood sugar levels. These compounds in both *Moringa* and *Pithecellobium* may work synergistically to provide antidiabetic benefits through various mechanisms, including improving insulin sensitivity, enhancing insulin secretion, and exerting antioxidant effects.

The scientific evidence supporting the traditional use of *Moringa oleifera* and *Pithecellobium dulce* as effective agents in diabetes management is substantial and compelling. Both plants exhibit a rich array of bioactive compounds that contribute to their antidiabetic properties through various mechanisms.

## SYNERGISTIC POTENTIAL

This review aims to explore the possibility of potential synergistic benefits of *Moringa oleifera* and *Pithecellobium dulce* in diabetes management, potentially paving the way for future studies. The

complementary nature of these plants suggests that their combined use could harness the strengths of both. For instance, both plants quercetin and chlorogenic acid, which inhibit the activity of the enzymes  $\alpha$ -glucosidase and  $\alpha$ -amylase in the digestive system, *Moringa's* moringin and *Pithecellobium's* catechins can enhance insulin sensitivity and facilitate glucose uptake in cells properties, providing a balanced approach to lowering blood glucose levels and improving overall metabolic health. This synergy could lead to more effective natural therapeutic strategies for diabetes management.

## CONCLUSION

The comparative analysis of *Moringa oleifera* and *Pithecellobium dulce* underscores their significant potential as natural antidiabetic agents. Each plant offers unique benefits, and their combined use may provide a comprehensive and synergistic approach to diabetes management. *Moringa oleifera's* rich vitamin and mineral content, along with its unique proteins, enhance its antidiabetic efficacy, while *Pithecellobium dulce's* ability to manage postprandial glucose spikes and protect vital organs further complements this effect. Future research should focus on elucidating the mechanisms of action, optimal dosages, and potential combinations of plant parts to maximize their therapeutic benefits. Specifically, studies exploring the synergistic effects of combined extracts from both plants could lead to the development of potent, natural antidiabetic formulations. Such formulations could offer a holistic and effective approach to managing diabetes and its associated complications, providing a promising alternative to conventional antidiabetic therapies.

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