# Exploring the Therapeutic Potential of Herbal Plants in Managing Blood Sugar Levels: A Comprehensive Evaluation

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## ABSTRACT

Hyperglycemia, characterized by persistently high blood glucose levels due to insufficient insulin release or insulin resistance, is a major global health concern. The World Health Organization (WHO) reports a substantial increase in the number of diabetic patients, from 108 million in 1980 to 422 million in 2014, and further to 463 million in 2020. As a result, there has been a growing demand for medicinal plants to address this issue. Traditional medicine has long recognized and utilized various medicinal herbs with hypoglycemic properties. This review focuses on eight specific medicinal plants: *Ficus religiosa* (Moraceae), *Syzygium cumini* (Myrtaceae), *Momordica charantia* (Cucurbitaceae), *Curcuma longa* (Zingiberaceae), *Ocimum tenuiflorum* (Lamiaceae), *Morinda citrifolia* (Rubiaceae), *Trigonella foenum-graecum* Linn. (Fabaceae), and *Peganum harmala* (Zygophyllaceae), which have been found to play a significant role in managing hyperglycemia. The article explores the phytochemical constituents of these plants responsible for their hypoglycemic effects and elucidates their mechanisms of action. By providing a comprehensive review of these medicinal plants, this article offers valuable insights into their potential use for managing hyperglycemia.

**Keywords:** Herbal plants, Hyperglycemia, Insulin resistance, Phytoconstituents, Therapeutic potential.

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# INTRODUCTION

According to WHO, diabetes or hyperglycemia can be defined as a chronic, metabolic disease that is characterized by a persistent increased level of blood glucose. The most common type of diabetes is type II diabetes, which occurs when the body becomes resistant to insulin or is incapable of making sufficient insulin.

The WHO gives figures showing the linear increase in patients who have diabetes. In 1980, there were a total of 108 million diabetic patients, which increased to 422 million in 2014, and this figure again increased to 463 million in 2020. As a result, the demand for medicinal plants has increased due to their fewer or no side effects. The hypoglycemic effect obtained from treatment with medicinal plants is often due to their ability to improve the performance of pancreatic tissue, which is done by increasing insulin secretions or reducing the intestinal absorption of glucose.



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It was reported that medicinal plants with carotenoids, flavonoids, terpenoids, alkaloids or glycosides can often have anti-diabetic effects. So, with all of the evidence in mind, the following medicinal plants have been selected, and their phytochemical constituent responsible for the anti-hyperglycemic activity is discussed.<sup>[1]</sup>

# Ficus religiosa

Synonyms: Ashwatha, Arara

Family: Moraceae

Genus: Ficus

Species: Religiosa

*Ficus religiosa*, also known as Pipal in India, has been used for centuries in Ayurveda for its therapeutic benefits as shown in Table 1. One of these benefits is its ability to treat hyperglycemia caused by aggravated kapha dosha. According to Ayurvedic Pharmacopoeia of India, one action of *Ficus religiosa* is Kaphapittavinasa.<sup>[6]</sup> In modern science, it is also evident that it decreases the blood glucose level by initiating insulin release. The plant contains various bioactive compounds, such as saponins,

tannins, flavonoids, polyphenolic compounds, and sterols, contributing to its therapeutic properties. The phytochemical constituent from the bark,  $\beta$ -sitosterol-D-glucoside, a sterol glycoside has reported significant hypoglycemic activity.<sup>[7]</sup> Recent studies showed that *F. religiosa* bark-loaded solid lipid nanoparticles' ethanolic extract decreases blood glucose levels by stimulating insulin release from  $\beta$ -cells in streptozotocin-induced diabetic rats.<sup>[8]</sup> It was also reported that up to 2000 mg/kg of  $\beta$ -sitosterol-D-glucoside can be considered a safe dose.

Other compounds, such as quercetin, myricetin, and isoleucine, also affect the plant's hypoglycemic effects. Various studies showed that quercetin enhances cellular glucose uptake and insulin resistance.<sup>[9]</sup> Furthermore, myricetin shows its hypoglycemic activity by reducing the body's serum glucose and insulin while increasing the expression of the insulin receptor, glucose transporter 4 (GLUT 4) gene, glucose-6-phosphatase (G-6-Pase) and Phosphoenolpyruvate Carboxykinase (PEPCK) gene.<sup>[10]</sup> Additionally, isoleucine has been found to lower blood glucose levels by increasing muscle glucose uptake and wholebody glucose oxidation while reducing hepatic gluconeogenesis. This means that isoleucine helps the body use glucose more efficiently and reduces the amount of glucose produced by the liver, leading to lower blood glucose levels [Figure 1].<sup>[11]</sup>

# Syzygium cumini

Synonyms: Jambolan, Indian Blackberry

Family: Myrtaceae

Genus: Syzgium

# Species: S. cumini

Syzygium cumini, commonly known as "jamun" in India, is a widely used medicinal plant with various health benefits, particularly in managing blood sugar levels as shown in Table 2. Its hypoglycemic properties are attributed to its ability to decrease insulin resistance, improve the functioning of  $\beta$ -cells in the pancreas, and reduce free radicals. The plant also promotes the activity of different enzymes, such as catalase glutathione-stransferase. Among the different parts of the jamun plant, the seeds are most commonly used for their hypoglycemic properties. They contain ellagic acid, a polyphenol known for its blood sugar-lowering effects. Studies have shown that the ethanolic extract of jamun seeds reduces blood glucose levels by up to 42.85% in diabetic mice by enhancing insulin secretion from  $\beta$ -cells.<sup>[15]</sup>

Additionally, other studies have confirmed that administering jamun seed extract at doses of 200 mg/kg and 400 mg/kg for 15 days can reduce blood glucose levels by up to 65%.<sup>[16]</sup> Other chemical constituents identified from *Syzgium cumini* responsible for hypoglycemic activity include jambosine, a water-soluble alkaloid known to reduce blood sugar levels by

inhibiting the conversion of starch into glucose.<sup>[17]</sup> Additionally, anthocyanins and flavonoids lower blood glucose levels by improving glucose uptake by skeletal muscles and adipose tissues. Tannins also show hypoglycemic activity by improving glucose homeostasis by increasing insulin secretion and reducing insulin resistance [Figure 2].

# Momordica charantia

Synonyms: Bitter gourd/ melon, Bitter apple

Family: Cucurbitaceae

Genus: Momordica

Species: M. charantia

*Momordica charantia*, known as karela in Hindi and Kāravallaka in Sanskrit, contains several plant chemicals such as polypeptide-p and charantin that work similarly to insulin, helping to lower blood glucose levels as depicted in Table 3. It was also established that they might enhance cellular glucose uptake and processing.<sup>[22]</sup> Indian Ayurveda also established that fresh juice of Kāravallaka (karela) at the dose of 10-15 mL is helpful in the treatment of "prameha," i.e., diabetes.<sup>[23]</sup> Several scientific studies also showed that karela extract at 200 mg/kg for 45 days increases insulin secretion and decreases oxidative stress in streptozotocin-induced diabetic rats.<sup>[24]</sup>

Various studies identified the chemical constituents involved in the hypoglycemic action, such as charantin, a mixture of two steroids, which lowers blood glucose levels by increasing insulin sensitivity and reducing glucose production in the liver.<sup>[25]</sup> Vicine and convincing also stimulate insulin secretion and improve glucose uptake.<sup>[26]</sup> Apart from treating hyperglycemia, the essential oil extracted from seeds of *Momordica charantia* is also known for the normalization of metabolic changes such as alteration in lipid profiles, urea, enzymes, and protein that occurs due to the persistent increased blood glucose level in streptozotocin-induced diabetic rats [Figure 3].<sup>[27]</sup>

# Curcuma longa

Synonyms: Harira, Haldi



Figure 1: Phytoconstituents of Ficus religiosa.

SI. No.	Part	Chemical constituents	Therapeutic activity
1.	Seed	Caoutchoue, Albuminiods.	Laxative.
2.	Root Bark	β-sitosteryl-D-glucoside.	Hyperglycemia.
3.	Stem Bark	β-sitosteryl-D-glucoside, Methyl oleanolate, n-octacosanol, Stigmasterol, Lupen-3-one, Lanosterol.	Anti-bacterial, Astringent, Burns.
4.	Leaves	Compesterol, Stigmasterol, Isofucosterol, Lupeol, Serine, Aspartic acid, Tryptophan, Tyrosine, Hexa- cosanol, n-octacosan.	Gonorrhoea, Asthma, Gastric problems, Vomiting, Cough.
5.	Fruits	Isoleucine, Phenylalanine, Phytosterolin, β- sitosterol, Kaempeferol, Quercetin, Myricetin.	Paralysis Tuberculosis, Fever, Hyperglycemia.

#### Table 1: Phytochemical constituents of *Ficus religiosa* with therapeutic activity.<sup>[2-5]</sup>

Table 2: Phytochemical constituents of Syzygium cumini with therapeutic activity.<sup>[12-14]</sup>

SI. No.	Part	Chemical constituents	Therapeutic activity
1.	Seed	Jambosine, Ellagic acid, Gallic acid, Uorolagin, 3-galloylglucose, β-sitosterol, 3,6, m- hexahydroxydiphenoylglucose, Ellagitannins.	Hyperglycemia, Anti-oxidant, Anti-Inflammatory.
2.	Stem Bark	Betulinic acid, $\beta$ -sitosterol, Ellagic acid, Eugenin, Gallic acid, Myricetin, Quercetin, Kaempferol.	Digestive, Bronchitis, Ulcers, Astringent, Anti-helmintic, Dysentry, Hyperglycemia.
3.	Leaves	Acylated flavonol glycosides, Quercetin, Myricetin, Myricitin, Esterase, Galloyl carboxylase, Triterpenoids.	Opium poisoning, Diabetes, Renal Problems, Stomachache, Indigestion, Jaundice.
4.	Fruits	Cyanidin diglycoside, Raffinose, Petunidin-3- gentiobioside, Malvidin-3-laminaribioside, Anthocyanins, Delphinidin-3-gentiobioside.	Hyperglycemia, Chronic diarrhea, Gastric problems, Enteric disorders, Headache.

### Family: Zingiberaceae

# Genus: Curcuma

### Species: longa

Curcuma longa L. belongs to the family Zingiberaceae and is cultivated in south-east Asian countries. A phytochemical constituent known as curcumin (diferuloylmethane), extracted from Curcuma longa rhizomes, is used as an active pharmaceutical ingredient for the treatment of many chronic diseases as it possesses multiple therapeutic properties. Still, it is primarily known for its anti-diabetic effect as shown in Table 4. Several mechanisms have been proposed for the action of curcumin, such as curcumin enhances insulin sensitivity and signaling, leading to improved glucose uptake and utilization by cells.<sup>[31]</sup> Another proposed mechanism is that curcumin inhibits the activity of certain enzymes involved in glucose metabolisms, such as alpha-glucosidase and aldose reductase. By inhibiting these enzymes, curcumin may slow down the breakdown and absorption of carbohydrates, leading to a more gradual and sustained release of glucose into the bloodstream [Figure 4].<sup>[32]</sup>





Recent studies showed that extract of *Curcuma longa* rhizomes with fruit extract of *Emblica officinalis* at 1000 mg/kg is more effective than metformin, a first-class anti-diabetic drug, in lowering the blood glucose level in streptozotocin-induced diabetic rats. Additionally, curcumin postpones diabetes advancement, improves  $\beta$ -cell capacities, forestalls  $\beta$ -cell passing, and decreases insulin obstruction in creature models.<sup>[33]</sup> Turmerone, on the other hand, is an essential oil and a sesquiterpene compound found in turmeric. It is one of the significant components of the essential

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SI. No.	Part	Chemical constituents	Therapeutic activity
1.	Seed	Amino acids (leucine, valine, phenylalanine, glutamic acid, threonine, methionine, isoleucine), Vicine, Convicine.	Hyperglycemia, Ulcers, Intestinal Parasites.
2.	Plant Body	Cryptoxanthin, Cucurbitacins, Cucurbitanes, Diosgenin, Momordicine, Momordin, Charantin, Polypeptide- p insulin, Ascorbigen, Glycosides, Proteins, Cucurbitins, Saponins, Fixed oils, Alkaloids, Cucurbitane-type triterpenes, Cycloartenols, and Steroids.	Hyperglycemia, Hodgkin's Lymphoma, Demulscent, Digestion, Constipation.
3.	Leaves	Calcium, Potassium, Magnesium, Phosphorous, Iron, and Vitamins.	Menstrual troubles, burning sensation, Colic infections, Hepatitis, Wound infections, Piles, Alcoholism, Cholera.
4.	Fruits	Fatty acids (palmitoleic, linolenic, stearic, Lauric, myristic, palmitic, oleic, linoleic). Amino acids (serine, glutamic acid alanine, threonine, g-amino butyric acid, aspartic acid, pipecolic acid).	Asthma, Hyperglycemia, Cough, Constipation, Leprosy, Gout.

#### Table 3: Phytochemical constituents of *Momordica Charantia* with therapeutic activity.<sup>[18-21]</sup>





oil of turmeric and is responsible for its characteristic aroma. Turmerone has been found to have various biological activities, including anti-inflammatory, antioxidant, and hypoglycemic effects. In particular, ar-turmerone, a specific type of turmerone, has been shown to improve glucose uptake and insulin sensitivity in animal studies.<sup>[34]</sup>

## **Ocimum tenuiflorum**

Synonym: Holy basil, Tulsi

Family: Lamiaceae

Genus: Ocimum

#### Species: tenuiflorum

Ayurveda *Surasā rasa* (tulsi juice) is established for its numerous therapeutic effects as shown in Table 5. In modern science, leaves of *Ocimum sanctum* are utilized in treating diabetes mellitus as they contain eugenol.<sup>[37]</sup> Various studies reported that blood glucose levels could be lowered after administering tulsi leaves for up to 30 days in a portion of 2 g/kg. It will result in a massive rise in degrees of superoxide dismutase, reduced glutathione, and

stamped decline in peroxidized lipid levels.<sup>[38]</sup> It was additionally reported that ethanolic concentrate of tulsi essentially diminishes the blood glucose levels, glycosylated hemoglobin, and urea with an increment in glycogen, hemoglobin, and protein.<sup>[39]</sup> These concentrates likewise brought about an increment in insulin and peptide levels and glucose resistance. With so many benefits coming with tulsi extract, one limitation also comes along, which is the poor aqueous solubility of eugenol. Still, this limitation can be overcome by formulating the nanoformulations of eugenol, such as liposomes, micelles, nanocapsules, and so on, to enhance the bioavailability.<sup>[40]</sup>

There are also some other chemical constituents reported from *Ocimum tenuiflorum* which are responsible for lowering blood glucose, such as ursolic acid, which increases glucose uptake by peripheral tissues and inhibit gluconeogenesis in the liver, possibly through the activation of the AMP-activated protein Kinase (AMPK) signaling pathway.<sup>[41]</sup> Then there is rosmarinic acid which stimulates glucose uptake by peripheral tissues, possibly through the activation of the insulin signaling pathway.<sup>[42]</sup> Additionally, methyl eugenol is reported to increase insulin sensitivity and glucose uptake by peripheral tissues, possibly through the activation of protein kinase B or Akt signaling pathway [Figure S5].<sup>[43]</sup>

### Morinda citrifolia

Synonyms: Indian Mulberry

Family: Rubiaceae

Genus: Morinda

Species: M. citrifolia

*Morinda citrifolia*, commonly known as noni, has gained the spotlight in the past few decades for its various therapeutic properties as shown in Table 6. These properties include

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SI. No.	Part	Chemical constituents	Therapeutic activity
1.	Rhizomes	Curcumin, Turmerone.	Hypoglycemic.
2.	Leaves	Eucalyptol, $\alpha$ -pinene, $\beta$ -phellandrene, $\beta$ -pinene, Limonene.	Anti-microbial properties, including antifungal and anti-bacterial activity.
3.	Stem	Fibers containing cellulose content of about 50%, Lignin content (12%).	Anti-microbial activity against both gram-positive and gram-negative bacteria.
4.	Flower	p-cymen-8-ol and Terpinolene.	Sedative, Insect repellent, Mosquitocidal activity.





Figure 4: Phytoconstituents of Curcuma longa.

immunostimulatory, anti-diabetic, anti-obesity, anti-bacterial, antiseptic, anti-oxidant, and neuroprotective activities. Noni has become popular as a hypoglycemic agent due to its ability to stimulate  $\beta$ -cells of the pancreas to secrete more insulin, thereby maintaining normal blood glucose levels. Research has shown that noni fruit extract containing phenols and flavonoids significantly improves insulin resistance, oxidative stress, glycolipid metabolism, and blood glucose levels through the AMPK pathway in diabetes mellitus type 2 mice.<sup>[46]</sup> Additionally, noni juice has improved glucose metabolism via phosphorylation of the transcription factor FOXO1.

Also, Morinda citrifolia has various other reported chemical compounds responsible for hypoglycemic activity such as damnacanthal, which has been shown to inhibit alpha-glucosidase, an enzyme responsible for the breakdown of carbohydrates in the intestine, thereby reducing the absorption of glucose.<sup>[47]</sup> Furthermore, scopoletin has been reported to increase glucose uptake in skeletal muscle cells and adipocytes by stimulating the translocation of glucose transporter type 4 to the plasma membrane.<sup>[48]</sup> Quercetin, a flavonoid, has also been reported to lower blood glucose levels by inhibiting alpha-glucosidase activity and reducing glucose absorption in the intestine.<sup>[49]</sup> Additionally, ursolic acid, a triterpenoid, has been shown to improve insulin sensitivity and reduce blood glucose levels in diabetic mice and lastly, kaempferol, which is another flavonoid that has been shown to improve glucose uptake in muscle cells by stimulating the AMP-activated protein Kinase (AMPK) pathway [Figure S6].

# Trigonella foenum-graecum Linn

Synonyms: Fenugreek

Family: Fabaceae

Genus: Trigonella

Species: T. foenum-graecum

Fenugreek is a plant that has been used for medicinal purposes for centuries. It is commonly used as a spice in Indian and Middle Eastern cuisine and has been shown to have hypoglycemic effects. In addition to its hypoglycemic effects, fenugreek has also been shown to have other health benefits as shown in Table 7. Fenugreek seed has a long history of use as a substance that can aid digestion, act as an expectorant, promote bowel movements, and soothe the digestive tract. The mature fenugreek seed comprises various active components, including fibers, flavonoids, polysaccharides, fixed oils, and alkaloids, such as trigonelline and choline. Flavonoids such as quercetin, vitexin, and isovitexin have been identified in fenugreek seeds. These compounds have been shown to have antioxidant and hypoglycemic effects and may also stimulate insulin secretion from pancreatic beta cells.<sup>[52]</sup> Trigonelline also improves glucose uptake by peripheral tissues and hence shows hypoglycemic action. The high content of soluble dietary fiber, particularly galactomannan, is also known to slow down glucose absorption from the intestine, resulting in a lower postprandial blood glucose level.

In addition to these constituents, the seed also contains amino acids, fatty acids, vitamins, and saponins, such as diosgenin, gitogenin, neogitogenin, homorientin, saponaretin, and trigogenin which are also responsible for hypoglycemic effect.<sup>[53]</sup> The hypoglycemic effects of fenugreek are believed to be due to its ability to improve insulin sensitivity and secretion [Figure S7]. Several studies have investigated the potential of fenugreek to help manage hyperglycemia and found that fenugreek seed powder supplementation for 12 weeks improved fasting blood glucose levels and insulin resistance in type 2 diabetic patients.<sup>[54]</sup>

While examining the bioactive compounds in *T. foenum*graecum seeds, it was noted that 4-Hydroxyisoleucine (4-HIL), a non-proteinogenic amino acid, was the predominant marker. This compound has been documented to exhibit significant

SI. No.	Part	Chemical constituents	Therapeutic activity
1	Leaves	Eugenol (70%), Carvacrol (3%), and Eugenol-methylether (20%).	Anti-cancer, Anti-diabetic, Anti-bacterial.
2	Flower, aerial parts	Basilol, Ocimol, α-phellandrene, 1,8-cineole, α-pinene, Limonene, Citronellol, p-cymene.	Anti-bacterial.
3	Stem	Saponins, Flavonoids, Triterpenoids, and Tannins.	Antioxidant and Anti-inflammatory.
4	Whole plant	Rosmarinic acid, Coumarin, Quercetin, oleanolic acid, Carvacrol, Rosmarinic acid, Eugenol, Ursolic acid, Linalool.	Anti-bactericidal, Anti-inflammatory, Antioxidative, Anti-ulcer, Anti-diarrheal Chemopreventive, and Hypoglycemic.

 Table 5: Phytochemical constituents of Ocimum tenuiflorum with therapeutic activity.

Table 6: Phytochemical constituents of Morinda citrifolia with therapeutic activity.<sup>[44,45]</sup>

SI. No.	Part	Chemical constituents	Therapeutic activity
1.	Fruits	Anthraquinones (damnacanthal), Iridoid glycosides, Triterpenoids (ursolic acid), Flavonol glycosides, Quercetin, Ketones, Saccharides, Rutin, Vanillin.	Tooth decay, Urinary tract ailments, Gonorrhea, Hyperglycemia.
2.	Roots	Anthraquinones (damnacanthal, rubiadin), Naphthoquinone derivatives, and Sterols.	Anti-septic, Menstruation, beri-beri, Anti-hyperglycemic, Malnutrition.
3.	Leaves	Roseoside, Phytol, Barbinervic acid, Clethric acid, Hederagenin, Oleanolic acid, Asperuloside, Chlorophyll derivatives.	Purgative, Cough, Enlarged spleen, Inflammation, Rheumatism, Ulcers.

anti-diabetic effects and various other pharmacological activities.<sup>[55]</sup> Studies investigating the potential anti-diabetic properties of 4-HIL have determined that its ability to lower blood glucose levels is attributed to its ability to stimulate insulin secretion. This insulinotropic effect was first demonstrated using isolated perfused rat pancreas, human pancreatic islet cells, and isolated rats. Furthermore, it was found that 4-HIL enhances insulin secretion in response to glucose within the concentration range of 100  $\mu$ mol/L to 1 mmol/L.<sup>[56]</sup>

# Peganum harmala

Synonyms: Syrian rue, African rue

Family: Zygophyllaceae

Genus: Peganum

### Species: Peganum harmala

*Peganum harmala*, commonly known as Syrian Rue, is a perennial herbaceous plant native to Central Asia and the eastern Mediterranean region. It has been used for centuries in traditional medicine for its various therapeutic properties, including hypoglycemic activity as shown in Table 8. The hypoglycemic activity of *Peganum harmala* is believed to be due to the presence of several bioactive compounds, including harmine, harmaline, harmalol, and 4-hydroxypipecolic acid (4-HPA), which has been shown to enhance glucose uptake and utilization in cells, increase insulin secretion, and improve insulin sensitivity [Figure S8].<sup>[58]</sup>

The mechanism of harmine, harmaline, and harmalol in reducing blood glucose levels is thought to involve the inhibition of the alpha-glucosidase enzyme, which is responsible for breaking down complex carbohydrates into simple sugars in the intestine. By inhibiting this enzyme, glucose absorption is slowed, lowering blood glucose levels.<sup>[59]</sup>

# **RESULTS AND DISCUSSION**

The selected medicinal plants have been studied for their therapeutic properties for many years, dating back to ancient Ayurvedic practices. Modern science has also confirmed their effectiveness in treating hyperglycemia through various mechanisms. For example, phytochemical constituents in plants can increase insulin secretion from  $\beta$ -cells of the pancreas or reduce insulin resistance through different mechanisms.

Despite the established efficacy of herbal formulations, humans still tend to rely more on synthetic drugs. However, herbal formulations offer several advantages over synthetic drugs, such as fewer or no side effects, and are an attractive alternative. In the past, limitations such as solubility and bioavailability of phytochemical constituents have hindered the development of effective herbal formulations. However, modern techniques have the potential to overcome these limitations, and herbal formulations are increasingly being studied as potential treatments for various ailments, including hyperglycemia.

In conclusion, the cited plants have the potential to be used in many formulations that may prove to be more effective than synthetic

SI. No.	Part	Chemical constituents	Therapeutic activity
1	Seeds	Trigonelline, Diosgenin, 4- hydroxyisoleucine (4- HIL).	Anti-diabetic, Antioxidant, Neuroprotective, Anit-inflammatory.
2	Leaves	Polyphenols, Flavonoids (orientin, vitexin, isovitexin), Carotenoids, Vitamin A, C, and K.	Antioxidant, Anti-cancer, Anti-hypertensive, Anti-diabetic.
3	Roots	Polysaccharides, Saponins (yamogenin, gitogenin, tigonin), Flavonoids, Alkaloids.	Immunomodulatory, Anti-tumor, Cholesterol-lowering effect.

## Table 7: Phytochemical constituents of Trigonella foenum-graecum Linn. with therapeutic activity.<sup>[50,51]</sup>

 Table 8: Phytochemical constituents of Peganum harmala with therapeutic activity.

SI. No.	Part	Chemical constituents	Therapeutic activity
1	Seeds	Harmine, Harmaline, Harmalol.	Anti-inflammatory, Anti-cancer, Anti-microbial, Anti-diabetic, Anti-viral.
2	Leaves	Kaempferol, quercetin.	Anti-diabetic, Anti-inflammatory, Anti-microbial.
3	Roots	Scopoletin, Isofraxidin.	Anti-inflammatory, Anti-tumor, Anti-microbial.

Table 9: Patent formulations of phytochemical constituents extracted from the above-cited plants.

SI. No.	Patent Name/ Patent Number	Inventors	Invention Description	Therapeutic Action	References
1	US Patent (8859020)	Benny Antony (Arjuna Naturals Extract Ltd.).	BCM9 95 (Curcugreen); a formulation of curcumin combined with turmeric essential oil.	Improves the bioavailability of curcumin.	[60]
2	US Patent (9192644) EP Patent 1993365	Verdure Sciences Inc.	Longvida <sup>®</sup> , a formulation comprising natural high-curcumin turmeric extract and ethylene dichloride.	Improves the bioavailability of curcumin.	[61]
3	European Patent Office EP1832659A1	San Ei Gen FFI Inc Suntory Holdings Ltd.	The composition contains a mixture of quercetin glycosides.	Improves <i>vivo</i> -absorbability and <i>in vivo</i> antioxidant activity.	[62]
4	EP1124561A1	Merck Patent GmbH.	The composition contains isoquercetin, quercetin-4'-glycoside, rutin and quercetin.	Antioxidant.	[63]
5	EP1721532 B1	Alkayali Ahmad (Collagen Nutraceuticals Inc).	The formulation contains pomegranate polyphenol extract in the form of fine powder.	Food supplement.	[64]

drugs. By harnessing the benefits of herbal formulations, we may develop more effective treatments with fewer side effects. While modern science has made great strides in this area as shown in Table 9, there is still much to be discovered and researched to realize herbal medicine's potential fully.

# **AUTHOR'S CONTRIBUTION**

All authors contributed equally in the preparation of manuscript. The manuscript was drafted by Archita Katrolia. The chemical structure was drawn and corrected by Dr. Rohit Singh. The manuscript was reviewed and corrected by Dr. Vedpal and Dr. VK Shukla. Finally, all authors have approved the final submission of manuscript.

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# **CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest.

# REFERENCES

- Kooti W, Farokhipour M, Asadzadeh Z, Ashtary-Larky D, Asadi-Samani M. The role of medicinal plants in the treatment of diabetes: a systematic review. Electron Physician. 2016;8(1):1832-42. doi: 10.19082/1832, PMID 26955456.
- Chandrasekar SB, Bhanumathy M, Pawar AT, Somasundaram T. Phytopharmacology of *Ficus religiosa*. Pharmacogn Rev. 2010;4(8):195-9. doi: 10.4103/0973-7847.70918 , PMID 22228961.
- Sharma D, Dangi C, Kaur M. A review on pharmacological activities and therapeutic potentials of *Ficus religiosa* (Pipal). Life science. Indian J Appl Res. 2016;6(1):623-6.
- Gautam S, Meshram A, Bhagyawant S, Srivastava N. Ficus religiosa-potential role in pharmaceuticals. Int J Pharm Sci. 2014;5:1616.
- Deepa P, Sowndhararajan K, Kim S, Park SJ. A role of Ficus species in the management of diabetes mellitus: a review. J Ethnopharmacol. 2018;215:210-32. doi: 10.1016/j.jep .2017.12.045, PMID 29305899.
- Government of India, Ministry of Health and Family Welfare, Department of Ayush. The ayurvedic pharmacopoeia of India. Part. 2016;I:I, 34.
- 7. Ahmed A, Essa ME. Alternative therapies of significance in the treatment of diabetes mellitus: review article. Int J Innov Res Med Sci. 2019;3(6):20-5.
- Priyanka K, Sahu PL, Singh S. Optimization of processing parameters for the development of *Ficus religiosa* L. extract loaded solid lipid nanoparticles using central composite design and evaluation of antidiabetic efficacy. J Drug Deliv Sci Technol. 2018;43:94-102. doi: 10.1016/j.jddst.2017.08.006.
- Qian J, Zhang J, Chen Y, Dai C, Fan J, Guo H. Hypoglycemic activity and mechanisms of myricetin. Nat Prod Res. 2022;36(23):6177-80. doi: 10.1080/14786419.2022.20589 41, PMID 35369824.
- Dhanya R. Quercetin for managing type 2 diabetes and its complications, an insight into multitarget therapy. Biomed Pharmacother. 2022;146:112560. doi: 10.1016/j.bio pha.2021.112560, PMID 34953390.
- Doi M, Yamaoka I, Nakayama M, Sugahara K, Yoshizawa F. Hypoglycemic effect of isoleucine involves increased muscle glucose uptake and whole-body glucose oxidation and decreased hepatic gluconeogenesis. Am J Physiol Endocrinol Metab. 2007;292(6):E1683-93. doi: 10.1152/ajpendo.00609.2006, PMID 17299083.
- Ayyanar M, Subash-Babu P. Syzygium cumini (L.) Skeels: a review of its phytochemical constituents and traditional uses. Asian Pac J Troical Biomed. 2012;2(3):240-6. doi: 10 .1016/S2221-1691(12)60050-1.
- 13. Swami S, Thakor N, Patil M, Haldankar P. Jamun (*Syzygium cumini* (L.)): a review of its food and medicinal uses. Adv Food Nutr Sci. 2012;3:1100-17.

- Jagetia GC. A review on the role of jamun, *Syzygium cumini* skeels in the treatment of diabetes. Int J Altern Complement Med. 2018;11(2):91-5. doi: 10.15406/ijcam.201 8.11.00374.
- Raza A, Butt MS. lahtisham UI H, Suleria HAR. Jamun (*Syzygium cumini*) seed and fruit extract attenuate hyperglycemia in diabetic rats. Asian Pac J Troical Biomed. 2017;7(8):750-4.
- Shekar B, Parikh J, Geetha M, Mehta RS, Saluja AK. Anti Diabetic Activity of Novel androstane Derivatives from Syzygium cuminii Linn. J Nat Rem. 2007;7:214-9.
- Sharma SB, Tanwar RS, Nasir A, Prabhu KM. Antihyperlipidemic effect of active principle isolated from seed of *Eugenia jambolana* on alloxan-induced diabetic rabbits. J Med Food. 2011;14(4):353-9. doi: 10.1089/jmf.2010.1227, PMID 21370965.
- Daniel P, US, Roymon MG. A review on Phytochemical analysis of *Momordica* charantia. Int J Adv Pharm Biol Chem. 2014;3(1):214-20.
- Anilakumar KR, Kumar GP, Ilaiyaraja N. Nutritional, pharmacological and medicinal properties of *Momordica charantia*. Nutr Food Sci. 2015;4(1):75-83.
- Jia S, Shen M, Zhang F, Xie J. Recent advances in *Momordica charantia*: functional components and biological activities. Int J Mol Sci. 2017;18(12):2555. doi: 10.3390/ij ms18122555, PMID 29182587.
- Gupta M, Sharma S, Gautam A, Bhadauria R. Momordica charantia linn. (Karela): Nature's silent healer. Int J Pharm Sci Rev Res. 2011;11(1):32-7.
- Miura T, Itoh C, Iwamoto N, Kato M, Kawai M, Park SR, et al. Hypoglycemic activity of the fruit of the *Momordica charantia* in type 2 diabetic mice. J Nutr Sci Vitaminol. 2006;52(4):292-7.
- 23. Government of India, Ministry of Health and Family Welfare, Department of Ayush. e Ayurvedic Pharmacopoeia of India. Part li;101.
- Ghorbani A. Clinical and experimental studies on polyherbal formulations for diabetes: current status and future prospective. J Integr Med. 2014;12(4):336-45. doi: 10.1016/S2095-4964(14)60031-5, PMID 25074883.
- Dans AM, Villarruz MV, Jimeno CA, Javelosa MA, Chua J, Bautista R, *et al.* The effect of *Momordica charantia* capsule preparation on glycemic control in type 2 diabetes mellitus needs further studies. J Clin Epidemiol. 2007;60(6):554-9. doi: 10.1016/j.jclin epi.2006.07.009, PMID 17493509.
- Sridhar MG, Vinayagamoorthi R, Arul Suyambunathan V, Bobby Z, Selvaraj N. Bitter gourd (*Momordica charantia*) improves insulin sensitivity by increasing skeletal muscle insulin-stimulated IRS-1 tyrosine phosphorylation in high-fat-fed rats. Br J Nutr. 2005;93(06):861-70.
- Mariammal BGV, Devarajan DW, Jerrin R, Viswanathan S, Siddikuzzaman GR, Gopal R. *In vivo* treatment efficacy of essential oil isolated from seeds of *Momordica charantia* in streptozotocin-induced diabetes mellitus. Recent Pat Biotechnol. 2021;15(4):316-31. doi: 10.2174/1872208315666210910092105, PMID 34515016.
- Parveen Z, Nawaz S, Siddique S, Shahzad K. Composition and antimicrobial activity of the essential oil from leaves of *Curcuma longa* L. Kasur Variety. Indian J Pharm Sci. 2013;75(1):117-22. doi: 10.4103/0250-474X.113544, PMID 23901173.
- Ilangovan M, Guna V, Hu C, Nagananda GS, Reddy N. Curcuma longa L. plant residue as a source for natural cellulose fibers with antimicrobial activity. Ind Crops Prod. 2018;112:556-60. doi: 10.1016/j.indcrop.2017.12.042.
- Dosoky NS, Setzer WN. Chemical composition and biological activities of essential oils of Curcuma species. Nutrients. 2018;10(9). doi: 10.3390/nu10091196, PMID 30200410.
- Karlowicz-Bodalska K, Han S, Freier J, Smolenski M, Bodalska A. Curcuma longa as Medicinal Herb in the Treatment of Diabetic Complications. Acta Pol Pharm. 2017;74(2):605-10. PMID 29624265.
- 32. Pivari F, Mingione A, Brasacchio C, Soldati L. Curcumin and type 2 diabetes mellitus: prevention and treatment. Nutrients. 2019;11(8). doi: 10.3390/nu11081837.
- Panda V, Deshmukh A, Singh S, Shah T, Hingorani L. An Ayurvedic formulation of *Emblica officinalis* and *Curcuma longa* alleviates insulin resistance in diabetic rats: involvement of curcuminoids and Polyphenolics. J Ayurveda Integr Med. 2021;12(3):506-13. doi: 10.1016/j.jaim.2021.05.005, PMID 34376352.
- Kim JH, Park YS, Park E, Kim SJ. Turmerones as a potential therapeutic agent for diabetes mellitus: a review of the literature. Int J Mol Sci. 2013;14(11):21751-65.
- 35. Verma S. Chemical constituents and pharmacological action of *Ocimum sanctum* (Indian holy basil-Tulsi). J Phytopharmacol. 2016;5(5):205-7. doi: 10.31254/phyto.20 16.5507.
- Marwat S, Rehman F, Khan M, Ghulam S, Anwar N, Mustafa G, et al. Phytochemical constituents and pharmacological activities of sweet basil-Ocimum basilicum L. (Lamiaceae). Asian J Chem. 2011;23:3773-82.
- Kaushik G, Satya S, Khandelwal RK, Naik SN. Commonly consumed Indian plant food materials in the management of diabetes mellitus. Diabetes Metab Syndr Clin Res Rev. 2010;4(1):21-40. doi: 10.1016/j.dsx.2008.02.006.
- Sethi J, Sood S, Seth S, Talwar A. Evaluation of hypoglycemic and antioxidant effect of *Ocimum sanctum*. Indian J Clin Biochem. 2004;19(2):152-5. doi: 10.1007/BF02894 276, PMID 23105475.
- Pattanayak P, Behera P, Das D, Panda SK. Ocimum sanctum Linn. A reservoir plant for therapeutic applications: an overview. Pharmacogn Rev. 2010;4(7):95-105. doi: 10.41 03/0973-7847.65323, PMID 22228948.
- Taleuzzaman M, Imam SS, Gilani SJ. Clove oil/eugenol as the nanotechnological perspective for healthcare applications. Nanomed Bioactives. 2020:413-30.

- 41. Gupta S, Kataria H, Gupta PK. Antidiabetic and antioxidant potential of ursolic acid in streptozotocin-induced diabetic rats. J Diabetes. 2011;3(1):29-37.
- Kwon YI, Vattem DA, Shetty K. Evaluation of clonal herbs of Lamiaceae species for management of diabetes and hypertension. Asia Pac J Clin Nutr. 2006;15(1):107-18. PMID 16500886.
- Chaudhary S, Sahu AK, Singh SK. Antidiabetic potential of methyl eugenol in streptozotocin-induced diabetic rats. J Basic Clin Physiol Pharmacol. 2016;27(6):661-9.
- Pawlus AD, Kinghorn DA. Review of the ethnobotany, chemistry, biological activity and safety of the botanical dietary supplement *Morinda citrifolia* (noni). J Pharm Pharmacol. 2007;59(12):1587-609. doi: 10.1211/jpp.59.12.0001, PMID 18053321.
- Torres MAO, de Fátima Braga Magalhães I, Mondêgo-Oliveira R, de Sá JC, Rocha AL, Abreu-Silva AL. One Plant, Many Uses: A Review of the Pharmacological Applications of *Morinda citrifolia*. Phytother Res. 2017 Jul;31(7):971-979.
- 46. Ahmad AN, Mat Daud ZA, Ismail A. Review on potential therapeutic effect of *Morinda citrifolia* L. Curr Opin Food Sci. 2016;8:62-7. doi: 10.1016/j.cofs.2016.03.002.
- Murali A, Bhosale UA, Goyal RK, Bodhankar SL. Effect of damnacanthal, a noni (*Morinda citrifolia*) anthraquinone, on glycolysis in Ehrlich ascites tumor cells. J Ethnopharmacol. 2005;97(1):27-31.
- Narasimhan KKS, Jayakumar D, Velusamy P, Srinivasan A, Mohan T, Ravi DB, *et al.* Morinda citrifolia and Its Active Principle scopoletin Mitigate Protein Aggregation and Neuronal Apoptosis through Augmenting the DJ-1/Nrf2/ARE Signaling Pathway. Oxid Med Cell Longev. 2019; 2019:2761041. doi: 10.1155/2019/2761041, PMID 31191797.
- Xue F, Nie X, Shi J, Liu Q, Wang Z, Li X, et al. Quercetin inhibits LPS-induced inflammation and ox-LDL-induced lipid deposition. Front Pharmacol. 2017;8:40. doi: 10.3389/fphar.2017.00040, PMID 28217098.
- Singh AK, Kumar R, Pandey AK. Fenugreek (*Trigonella foenum-graecum* L.) and its bioactive constituents for the prevention of various diseases: an overview. J Funct Foods. 2017;28:215-29.
- Gupta A, Singh R, Sharma R, Kumari R. Phytochemical and pharmacological potential of *Trigonella foenum-graecum* Linn. (Fenugreek): A review. Phytother Res. 2020;34(2):270-81.
- Srinivasan K. Fenugreek (*Trigonella foenum-graecum*): a review of health beneficial physiological effects. Food Rev Int. 2006;22(2):203-24. doi: 10.1080/875591206005 86315.

- Yadav UCS, Baquer NZ. Pharmacological effects of *Trigonella foenum-graecum* L. in health and disease. Pharm Biol. 2014;52(2):243-54. doi: 10.3109/13880209.2013.82 6247, PMID 24102093.
- Neelakantan N, Narayanan M, de Souza RJ, van Dam RMV. Effect of fenugreek (*Trigonella foenum-graecum* L.) intake on glycemia: a meta-analysis of clinical trials [*Trigonella foenum-graecum* L]. Nutr J. 2014;13(7):7. doi: 10.1186/1475-2891-13-7, PMID 24438170.
- Fowden L, Pratt HM, Smith A. 4-Hydroxyisoleucine from seed of Trigonella foenumgraecum. Phytochemistry. 1973;12(7):1707-11. doi: 10.1016/0031-9422(73)80391-7.
- Sauvaire Y, Petit P, Broca C, Manteghetti M, Baissac Y, Fernandez-Alvarez J, *et al.* 4-Hydroxyisoleucine: a novel amino acid potentiator of insulin secretion. Diabetes. 1998;47(2):206-10. doi: 10.2337/diab.47.2.206, PMID 9519714.
- 57. Kaur R, Arora S. Phytochemicals: a review on bioactivities, isolation and characterization of harmine from *Peganum harmala*. Nat Prod Res. 2019;33(9):1306-14.
- Zhang L, Zhang L, Huang L. 4-hydroxypipecolic acid, a constituent from *Peganum harmala*, increases glucose uptake in muscle cells via activation of AMP-activated protein kinase. J Pharm Pharmacol. 2016;68(7):901-11.
- Khalilzadeh MA, Mahdavi M, Najafi H. Hypoglycemic effects of harmine and harmaline in normal and streptozotocin-induced diabetic rats. Iran J Pharm Res. 2016;15(3):677-82.
- Ltd., A.N. BCM-95 bioavailable curcumin (turmeric extract). US Patent 8859020; 2019.
- 61. Sciences®, V. LONGVIDA® OPTIMIZED CURCUMIN. EP Patent 1993365. 2015.
- 62. Yoshiko Suntroy limited research center OnoNamino Suntory limited research center TomimoriNorifumi Suntory limited Research Center TateishiMasamitsu San-El GEN F.F.I. Inc. MoriwakiKazuhiro SAN-El GEN F.F.I. Inc. EmuraShuji SAN-El GEN F.F.I. Inc. Okuyama. Quercetin glycoside composition and method of preparing the same. European Patent Office. EP1832659A1; 2006.
- Sharma S, Sahni J, Ali J, Baboota S. Patent perspective for potential antioxidant compounds-Rutin and quercetin. Recent Pat Nanomed. 2013;3(1):62-8. doi: 10.217 4/18779123112029990002.
- Kayali A. Ellagic acid food supplement prepared from pomegranate seed. EP. 2006;B1:1721532.

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	Trigonelline Improve glucose uptake by peripheral tissues.
Trigonella	<b>Galactomannan</b>
foenum-	Now down the absorption of glucose from intestine $y_{t} = (y_{t} + y_{t}) + (y_{t} +$
graecum	Flavonoids (Quercetin, Vitexin, Isovitexin)
Linn	Stimulates insulin secretion from pancreatic β-cells

Figure S5: Phytochemical constituents of Ocimum tenuiflorum.



Figure S6: Phytochemical constituents of Morinda citrifolia.





Figure S8: Phytochemical constituents of Peganum harmala.