Journal of Pharmacy and Pharmacology 10 (2022) 159-172
doi: 10.17265/2328-2150/2022.05.002

Recent Studies on Phytomedicine Used in Diabetic Disorder

Radheshyam, Jainul Basher, Shreyash Tripathi, Rajib Singh, Prabha Shankar Maurya, Atul Dubey, Ruchi Singh and Jitendra Singh Yadav

Department of Pharmacy, Shakti College of Pharmacy, Balrampur, U.P, India

Abstract: Diabetes mellitus is the most common endocrine disease, affecting about 300 million individuals globally. As a result, therapies based on the principles of western medicine (allopathic) are generally ineffective, carry the danger of side effects, and are prohibitively expensive, especially in developing countries. This review contains all the different method of treatment for diabetes such as Herbal medicine, home remedies, acupuncture and hydrotherapy. Due to risk of adverse effect of allopathic medicine treatment the world is searching alternative treatment therapy. So this paper helps to study the all the other methods of treatment for diabetic disorder.

Key words: Cholestrol, hydrotherapy, acupuncture.

1. Introduction

Diabetes mellitus is a collection of metabolic illnesses marked by elevated blood sugar (glucose) levels caused by insulin secretion, action, or both. Diabetes mellitus, or diabetes (as it shall be referred to in this article), was first diagnosed in the ancient world as a disease associated with “sweet urine” and severe muscle loss.

High blood sugar levels (hyperglycemia) cause glucose to leak into the urine, hence the name sweet urine. Insulin, a hormone generated by the pancreas, normally keeps blood glucose levels in check. Insulin is a hormone that reduces blood glucose levels. When blood glucose levels rise (for example, after eating), the pancreas releases insulin to bring them back to normal. Hyperglycemia is caused by the lack or insufficient synthesis of insulin in diabetic people. Diabetes is a chronic medical illness, which means that it cannot be cured and must be managed for the rest of one’s life (Table 1) [1].

Corresponding author: Radheshyam. Assistant Professor, research field: pharmacy. Email: radheshyammpharm@gmail.com.

1.1 Causes of Diabetes

Hyperglycemia and diabetes are caused by insufficient insulin synthesis (absolutely or relative to the body’s demands), faulty insulin production (which is uncommon), or the inability of cells to utilise insulin effectively and efficiently. Insulin resistance is a disorder that occurs when cells in muscle and fat tissues become resistant to the hormone insulin. This is the most serious issue with type 2 diabetes.

The major issue in type 1 diabetes is a complete lack of insulin, which is usually caused by a damaging process affecting the insulin-producing beta cells in the pancreas. There is a gradual decrease of beta cells in type 2 diabetes, which adds to the process of rising blood glucose. In essence, if someone is insulin resistant, the body can enhance insulin production to some extent and overcome the resistance. Hyperglycemia occurs over time if production declines and insulin cannot be delivered as quickly.

Glucose is a basic sugar that can be found in many foods. Glucose is a vital component that gives the body’s cells the energy they need to perform properly. Carbohydrates are broken down in the small intestine, and the glucose in digested food is absorbed into the

bloodstream by intestinal cells, where it is delivered to all of the body's cells and consumed. Glucose, on the other hand, cannot enter cells on its own and requires insulin to do so. Despite the presence of plentiful glucose in the bloodstream, cells without insulin become starved of glucose energy. The inability of certain types of diabetic cells to use glucose results in the ironic scenario of "starvation in the midst of plenty." The excess, unutilized glucose is eliminated in the urine in a wasteful manner. Insulin is a hormone generated by the pancreas' specialized cells (beta cells). (The pancreas is a deep-seated organ behind the stomach in the belly.) Insulin is vital for closely managing the quantity of glucose in the bloodstream in addition to assisting glucose entry into cells. The blood glucose level rises after a meal.

Table 1 Blood Sugar level in normal & diabetic patients.

Category of a person	Fasting Value (mg/dL)		Post Prandial (mg/dL)
	Minimum Value	Maximum Value	Value 2 hours after consuming glucose
Normal	70	100	Less than 140
Early diabetes	101	126	140 to 200
Established diabetes	More than 126	-	More than 200

Note: All values are in mg/100 ml.

The pancreas generally releases more insulin into the bloodstream in response to an increase in glucose levels to assist glucose enter the cells and drop blood glucose levels after a meal. Insulin secretion from the pancreas is reduced when blood glucose levels are reduced. It's crucial to remember that even when fasting, there's a low continuous release of insulin that swings a little and serves to keep blood sugar levels stable. In healthy people, a regulatory system like this helps to keep blood glucose levels within a narrow range. As previously stated, insulin is either absent, insufficient for the body's demands, or not utilized effectively by the body in diabetic people. All of these variables contribute to high blood glucose levels (hyperglycemia) [2].

2. Herbal Treatment of Diabetes Mellitus

2.1 Turmeric

Biological Source: It's made out of dried fresh rhizomes from the *Curcuma longa* plant, which belongs to the *Zingiberaceae* family (Figure 1).

Chemical Constituents: Turmeric has a 5% volatile oil content, as well as resin, zingiberaceous starch grains, and yellow curcuminoids. Curcumin is the primary component of curcuminoids. Alpha and beta pinene, alpha-phellandrene, camphor, camphene, zingiberene, and alpha and beta curcumenes are mono and sesquiterpens found in volatile oil [3].

Fig. 1 Turmeric.

Use: It's a type of anti-diabetic medication.

Scientific works done:

- Turmeric has been proven to have hypoglycemic, hypolipidemic, and antioxidant activities [4].
- Turmeric has also been shown to have an influence on diabetes [5].

Dosage form: Powdered form of turmeric is used.

Dose: Powdered turmeric - 500-8000 mg/day.

2.2 Onion

Biological source: It's made from the bulb of the plant *Allium cepa*, which belongs to the Liliaceae family (Figure 2).

Uses: The active substance in onions is called APDS (allyl propyl disulphide). APDS has been proven to inhibit insulin breakdown by the liver and

may promote insulin synthesis by the pancreas, boosting insulin levels and lowering blood sugar levels. It has been discovered that it lowers lipid levels, inhibits platelet aggregation, and has antihypertensive properties. As a result, diabetics should consume a lot of onion.

Fig. 2 Onion.

Scientific work done:

- *Allium cepa* (Red onion) has been shown to have a clinical hypoglycemic impact.

Dosage forms: Raw & boiled onion extracts are used. APDS can also be administered orally.

Dose: APDS - 125 mg/kg to fasting humans.

2.3 Garlic

Biological source: It is made up of *Allium sativum* bulbs, which belong to the Liliaceae family (Figure 3).

Fig. 3 Garlic.

Chemical constituents: Garlic bulbs contain 29% carbohydrate, approximately 56% protein (albumin), 0.1% fat (mucilage), and 0.06-0.1 percent volatile oil. Phosphorus, iron, and copper are also present. The drug's main active ingredient is volatile oil, which contains allyl propyl disulphide, diallyl disulphide, and allicin. Alliin is transformed to allicin by the enzyme allinlyase. The colour of garlic oil is yellow [5].

Uses: Garlic cloves have a considerable effect on blood sugar levels. Following that, scientific research has shown that disulfides found in garlic, such as allyl propyl and diallyl sulphide, play a role in lowering blood glucose levels. They've been found to work similarly to Tolubutamide, a first-generation sulfonylurea medication. They work by stimulating the synthesis of insulin in the pancreas, which helps to keep blood sugar levels in check. Patients with type 2 diabetes stand to benefit the most from this.

Scientific work done:

- Garlic has been shown to have anti-diabetic and hypolipidaemic effects.

Dosage form: Juice extract of it is used.

Dose: Juice extract - 50 ml/daily.

2.4 Bael

Biological source: It is made up of unripe or half-ripe fruits from the *Aegle marmelos* plant, which belongs to the Rutaceae family (Figure 4).

Fig. 4 Bael.

Chemical constituents: Marmelosinn (0.5%), a furocoumarin, is the main component of the medication. Marmesin, psoralin, and umbelliferone

are examples of coumarins. Carbohydrate, protein, volatile oil, and tannins are also present in the medication. Vitamins A and C are also abundant in the pulp. Fruits contain two alkaloids: O-methyl halfordinol and isopentylhalfordinol [6].

Use: It is used as anti-diabetic drug.

Scientific work done:

- Aegle marmelos leaf and callus extract has been proven to have anti-diabetic properties.

Dosage forms: It is used as aqueous decoction & aqueous leaf extract.

Dose: Aqueous decoction - 1 ml/100 mg, aqueous leaf extract - 1 gm/kg.

2.5 Amla

Biological Source: It is obtained from the dried as well as fresh fruits of *Emblica officinalis,* belonging to the family Euphorbiaceae. It's made from the dried and fresh fruits of *Emblica officinalis*, which belongs to the Euphorbiaceae family (Figure 5).

Fig. 5 Amla.

Chemical Constituents: Vitamin C is abundant in amla, which is a natural source of the vitamin. It has 0.5% fat, phyllemblin, and 5% tannin in it. Phosphorus, iron, and calcium are also present. It contains pectin and has a moisture content of 75% [7].

Use: It is used as anti-diabetic.

Scientific work done:

- In animal models, *Emblica officinalis* has shown anti-diabetic efficacy.

Dosage form: It is used as amalaki capsules.

Dose: Capsule - 1 capsule/twice a day before meal.

2.6 Nayantara

Biological source: It's made from the dried whole plant of *Catharanthus roseus*, a member of the Apocynaceae family (Figure 6).

Fig. 6 Nayantara.

Chemical constituents: Alkaloids and tannins are the most active chemicals in this plant. Vincamine is the main alkaloid. Vinpocetin is a closely related semi-synthetic derivative of vincamine. Vindoline, vinblastine, vincristine, learocristine, vinine, ajmalicine, leurocine, vinomine, and over 130 other constituents have an indole or dihydroindole structure, including the main component vindoline, vinblastine, vincristine, learocristine, vinine, ajmalicine, leurocine, vinomine, and others [8].

Use: It is used as antihyperglycemic agent.

Scientific works done:

- The effect of a *Catharanthus roseus antidiabetic* extract has been observed.
- The juice of fresh *Catharanthus roseus* leaves has been demonstrated to lower blood glucose levels.

Dosage forms: It is used as tincture & infusion.

Dose: Tincture - 1-2 ml/3 times daily, Infusion - 2-3 cups daily.

2.7 Neem

Biological source: It's made from the leaves of *Azadirachta indica,* which belongs to the Meliaceae family (Figure 7).

Chemical constituents: It comprises saturated and unsaturated fatty acid glycerides. The most common fatty acids are oleic (50%) and stearic (20%) acids. Bitters, which are sulpher-containing chemicals, such as nimbidin, nimbin, nimbinin, and nimbidol, make up

2.0% of the oil. Nimbosterol is found in the unsaponifiable portion (0.03%). It contains azadirachtin as the major limonoid, as well as azadiradione, fraxinellone, nimbin, salannin, salannol, vepinin, and vilasinin [9].

Fig. 7 Amla.

Use: It is used in diabetes.

Scientific work done:

- The leaf extract of *Azadirachta indica* has been demonstrated to have antihyperglycemic and antidyslipidemic properties.

Dosage form: Capsules are used.

Dose: Capsule - 1-2 capsules/twice daily.

2.8 Cinnamon

Biological source: It is made up of the dried inner bark of coppiced *Cinnamomum zeylanicum* shoots, which belongs to the Lauraceae family (Figure 8).

Fig. 8 Cinnamon.

Chemical constituents: Volatile oil, tannins, mucilage, calcium oxalate, starch, and mannitol are all found in cinnamon bark. Cinnamaldehyde, as well as other terpenes such as phellandrene, pinene, cymene, and caryophyllene, are found in cinnamon oil [10].

Uses: Cinnamon is used in the treatment of type II diabetes mellitus & insulin resistance.

Scientific works done:

- *Cinnamomum zeylanicum* Leaves Alcoholic Extract has been found to have anti-diabetic properties.
- Cinnamon helps people's glucose and cholesterol levels.

Dosage form: It is mostly used as powdered form.

Dose: Powder- ½ teaspoon daily.

2.9 Bitter Melon

Biological source: It's made from the *Momordica charantia* plant's edible fruit, which belongs to the Momordica family (Figure 9).

Fig. 9 Bitter melon.

Chemical constituents: The plant contains several biologically active compounds

- Chiefly momordicin I & momordicin II, cucurbitacin B
- Glycosides (momordin, charantin, charantosides, goyaglycosides)
- Terpenoid compounds - momordicinin, momordicilin, momordol
- Cytotoxic (ribosome inactivating) proteins such as momorcharin & momordin [11].

Uses: Bitter melon is an anti-diabetic fruit. It contains lectin, which acts like insulin because of its non-protein specific binding to insulin receptors. By acting on peripheral tissues, this lectin reduces blood glucose levels. Lectin is a key player in the hypoglycemia effect.

Scientific work done:

- Bitter Melon triterpenoids have been found to have anti-diabetic properties.

Dosage form: It is used as fresh juice, tincture, juice extract & powered leaf.

Dose: Fresh juice - 57-113 gm daily, Tincture - 1.3 ml/twice/daily, Juice extract - 300-600 mg, Powered leaf - 1-2 gm.

2.10 Blackberry

Biological Source: It comes from the edible fruits of the *Rubus fruticosus* plant, which belongs to the Rosaceae family (Figure 10).

Fig. 10 Blackberry.

Chemical Constituents: Hydrolyzable tannins are the main components identified from red blackberry leaves. Simple molecules like 1,2,6-tri-O-galloyl-glucose74 and penta-O-galloyl glucose are oxidatively connected through galloyl groups to generate more complex compounds like casuarictin, pedunculagin, sanguin H-6, and lambertianin A, which have up to 15 galloyl groups coupled to three glucose units.

The leaves have also been used to isolate common flavonoids. Rutin, kaempferol, quercitin, quijaverin, and kaempferol 3-O-β-D-glucuronopyranoside were all isolated. The monoterpenes geraniol and linalool, as well as 1-octane-3-ol and decanal, were among the major leaf volatiles investigated by GC-MS. The Rosaceae family's phenolic acids have also been discovered [12].

Use: It is used as anti-diabetic.

Dosage form: It is used as fruit powder.

Dose: Dried fruit powder - 20 mg/day.

2.11 Blueberry

Biological source: It's made from the leaves of *Vaccinium myrtillus,* which belongs to the Ericaceae family (Figure 11).

Chemical constituents: The most important chemical components are: flavonoids (hyperoside, isoquercitrin, quercitrin, astragaline), anthocyanosides (myrtillin, malvidin, cyanidin, delphinidin and others), catechin tannins (2-10%), others (carbohydrates including invertose, organic acids, pectins, alkaloids) [13].

Fig. 11 Blueberry.

Uses: When blood sugar levels are somewhat raised, blueberry is a natural herb for managing or reducing them. It contains myrtillin, an anthocyanoside that acts as an active ingredient. It is less powerful and harmful than insulin.

Scientific works done:

- *Vaccinium myrtillus* has been proven to have anti-diabetic properties.
- *Vaccinium myrtillus* has been demonstrated to have hypoglycemic properties.

Dosage form: Leaf extracts are used.

Dose: Leaf extract - 3 cups/day

3. Herbal Home Remedies for Diabetes [14]

Ayurveda calls diabetes 'Madhumeh'. This disease is caused by an imbalance of the hormone insulin (which regulates blood sugar levels) which must be taken externally by diabetic patients on a regular basis. Many Indian medicines and general practices are recommended by Ayurvedic therapy to enhance insulin secretion naturally. The following are some of the Ayurvedic home and herbal cures.

- Include turmeric and cinnamon in your diets. You

can even take one teaspoon of cinnamon powder daily.

- Soak one teaspoon of fenugreek seeds in 1 cup of water overnight. Drink this water in the morning on an empty stomach and eat the seeds.
- Take a bitter gourd, remove the seeds and saturate in a cup of water. Drain this preparation and drink every morning.
- Boil around fifteen mango leaves in one cup of water. Keep it over night and filter in the morning. Drink every morning on an empty stomach.
- Avoid oily, fried and starchy foodstuffs.
- Avoid coffee, sugar, refined flour and alcohol.
- Eat smaller meals (low fat diet) five to six times a day instead of having three large meals.
- Increase intake of vegetables like spinach, cucumber, tomatoes, onion, sprouts, beans, garlic etc.
- Refrain from taking stress.
- Do regular exercise. Walk for at least 40 minutes a day.
- Avoid red meat and excessive salt in your meals. Fish and soy can be taken due to their good protein value.
- Bitter herbs like *Azadirachta Indica* (Neem), bitter gourd and fenugreek are like miracle drugs for diabetics. Take them in any form you can.
- Avoid white bread, rice, potatoes, sweet and sugary foods.
- Chew 8-10 curry leaves (Meetha Neem) on an empty stomach. It is very effective for bringing the urine and blood sugar to their normal levels, even in hereditary diabetic patients.
- *Emblica officinalis* or Indian gooseberry (Amla) is very beneficial for diabetic patients. Prepare a fine powder of dry amala and put this powder in water. Allow it to stand for some time. Then filter the solution and mix some lemon juice in it. Take this early in the morning. You can even use extract of amla easily available in the market.
- *Syzygium cumini* or Indian plum (Jamun) is considered a panacea for diabetes. Eating this fruit is very beneficial for patients of diabetes. In fact, more than fruit, the seeds of jamun fruit is beneficial when taken in powdered form mixed with some water.
- The holy fruit of India- the bel fruit or the *Aegle marmelos* has anti-diabetic properties. The herbal extract of its leaves should be taken preferably with a pinch of black pepper.
- Garlic contains allicin that helps in reducing sugar level in blood.
- The leaves of *Butea monosperma* (Palas) tree are very useful in diabetes. They reduce blood sugar and are useful in glycosuria- the presence of large amount of glucose inurine.
- Tenner's cassia (Tarwar) is an effective remedy for diabetes. A decoction of the whole plant or bubs is used to treat diabetes. The powder of the herb, mixed with honey, is very effective. Seeds can also be used in the similar manner as flowers.

4. Some Marketed Antidiabetic Polyherbal Formulations (Table 2) [15]

Because chromium works as a cofactor in all insulin-regulating actions, experimental and epidemiological evidence now suggests that chromium levels are a primary determinant of insulin sensitivity. Chromium aids insulin binding and subsequent glucose uptake by the cell. Supplemental chromium has been proven in normal, geriatric, and type 2 diabetic people to lower fasting glucose levels, improve glucose tolerance, lower insulin levels, lower total cholesterol and triglycerides, and increase HDL cholesterol while decreasing total cholesterol and triglycerides. The action of insulin is hindered without chromium, and glucose levels rise.

Trivalent chromium (Cr^{3+}) in the form of chromium picolinate is one of the forms of chromium that has biological action. The benefit of chromium picolinate for type 2 diabetic patients has been documented in a

comprehensive clinical research involving 180 diabetic individuals. Patients were randomly assigned to one of three groups in the study: placebo, 100 micrograms of chromium picolinate (twice daily), or 500 micrograms of chromium picolinate (twice daily). Glycosylated haemoglobin, fasting glucose, two-hour postprandial glucose levels, fasting and two-hour postprandial insulin values, and total cholesterol all showed significant dose- and time-dependent reductions, notably in the 500 mcg twice daily group. However, not all chromium research has had beneficial outcomes. Lee and Reasner reported a decrease in triglycerides but no statistical difference between control and chromium-treated subjects on measured glycemic control parameters in a controlled six-month research to investigate the effect of 200 mcg/day chromium picolinate on individuals with type 2 diabetes. This dosage is far lower than that proven to be successful at lowering glucose in previous trials, which could explain the discrepancies in results.

Although no recommended daily allowance (RDA) for chromium has been published, it appears that above 200 mcg/day is required for optimal blood sugar control. Supplemental chromium, in addition to dietary sources, ensures a sufficient amount of chromium. Brewer's yeast and barley flour are good sources of chromium, but refined carbohydrates, white wheat products and lack of activity can reduce chromium levels. For a long time, trivalent chromium has been thought to be a safe nutritional supplement. Although the hexavalent form of chromium is a proven human respiratory tract carcinogen when inhaled in high-exposure industrial settings, the trivalent form of chromium present in chromium supplements has not been linked to cancer in humans. It's possible that more research on the safety and efficacy of trivalent chromium in the treatment of diabetes is needed.

Table 2 Some marketed antidiabetic polyherbal formulations.

Name	Company	Ingredients
Diabecon	Himalaya	*Gymnema sylvestre, Pterocarpus marsupium, Glycyrrhiza glabra, Casearia esculenta, Syzygium cumini, Asparagus racemosus, Boerhavia diffusa, Sphaeranthus indicus, Tinospora cordifolia, Swertia chirata, Tribulus terrestris, Phyllanthus amarus, Gmelina arborea, Gossypium herbaceum, Berberis aristata, Aloe vera,* Triphala, *Commiphora wightii, shilajeet, Momordica charantia, Piper nigrum, Ocimum sanctum, Abutilon indicum, Curcuma longa, Rumex maritimus*
Diasulin	Tobbest Busindo	*Cassia auriculata, Coccinia indica, Curcuma longa, Emblica officinalis, Gymnema sylvestre, Momordica charantia, Scoparia dulcis, Syzygium cumini, Tinospora cordifolia, Trigonella foenum-graecum*
Bitter gourd Powder	Garry and Sun natural remedies	*Momordica charantia.*
Dia-care	Admark Herbals Limited	Sanjeevan Mool; Himej, Jambu beej, Kadu, Namejav, Neem chal
Diabetes-Daily Care	Nature's Health Supply	Alpha Lipoic Acid, Cinnamon 4% Extract, Chromax, Vanadium, Fenugreek 50% extract, *Gymnema sylvestre* 25% extract, *Momordica charantia* 7% extract, Licorice Root 20% extract
Gurmar powder	Garry and Sun natural Remedies	*Gymnema sylvestre*
Epinsulin	Swastik Formulations	*Pterocarpus marsupium*
Diabecure	Nature beaute sante	*Juglans regia*, *Berberis vulgaris*, *Erytherea centaurium*, Millefolium, Taraxacum
Diabeta	Ayurvedic cure Ayurvedic Herbal Health Products	*Gymnema sylvestre, Vinca rosea, Curcuma longa, Azadirachta indica, Pterocarpus marsupium, Momordica charantia, Syzygium cumini, Acacia arabica, Tinospora cordifolia, Zingiber officinale*
Syndrex	Plethico Laboretaries	Germinated Fenugreek seed extract

Vanadium: Vanadium was used to manage blood sugar before the discovery of insulin in 1922. The usefulness of vanadyl sulphate at a dose of 100 mg/day in enhancing insulin sensitivity has been proven in two small studies (one with six type 2 diabetes patients and the other with seven type 2 diabetic patients) [16, 17].

Magnesium: Magnesium shortage is much more common in type 2 diabetics than it is in the general

population. Magnesium insufficiency has been linked to diabetic problems, including retinopathy. Patients with the most severe retinopathy had the lowest magnesium levels, according to one study [18].

5. Physical Interventions: Acupuncture and Hydrotherapy

In the United States, acupuncture is primarily known as a pain-relieving treatment. However, throughout the last several decades, it has been utilized to treat diabetes and its consequences. Although there are many Chinese publications on the use of acupuncture for diabetes, only those published in English will be referenced.

Acupuncture may be useful in not just treating diabetes, but also in preventing and managing its consequences. Acupuncture's benefits on diabetes have been studied both experimentally and clinically. Acupuncture has been found in animal studies to activate glucose-6-phosphatase (a key enzyme in carbohydrate metabolism) and influence the hypothalamus. Acupuncture works on the pancreas to stimulate insulin manufacturing, increase the number of receptors on target cells, and speed up glucose utilization, reducing blood sugar levels. Acupuncture has been proven in other trials to have a favorable anti-obesity impact, which is the most modifiable risk factor for type 2 diabetes. Acupuncture's therapeutic effect on diabetes appears to be the result of its activity on numerous systems rather than a single organ.

Four commonly used points are:

1) Zusanli point, located three inches below the lateral knee depression, one finger width from the lateral side of the anterior crest of the tibia;
2) Sanyinjiao point, located three inches above the tip of the inner ankle, on the posterior margin of the metatarsal bone;
3) Feishu point, located 1.5 inches lateral and inferior to the spinous process of the third thoracic vertebra in a prone position;
4) Shenshu point, located 1.5 inches lateral to the posterior midline, lateral and inferior to the spinous process of the second lumbar vertebra in a prone position.

Traditional Chinese medical theory guided the selection of these acupuncture locations. Other points can be added to the treatment depending on the symptoms and indicators. Other approaches, such as point injections with normal saline, tiny dose insulin, and Chinese herbal medicine extracts, have also been used. Treatment is usually given once a day or every other day over the period of 14-21 days. It is thought that the more time spent on treatment, the more noticeable the result will be. Acupuncture has been shown to be useful in treating diabetes complications, with significant improvements in clinical symptoms. Patients with dietary control have better therapeutic outcomes than those who do not. Physical activity, breathing exercises, and massage can all contribute to a better therapeutic effect.

Although acupuncture has been shown to be successful in the treatment of diabetes, the processes by which it works are yet unknown. Hot-tub therapy has been advised for people with type 2 diabetes who are unable to exercise because it can enhance blood flow to skeletal muscles. Eight patients were encouraged to sit in a hot tub for 30 minutes every day for three weeks, according to a research. Patients' weight, mean plasma glucose level, and mean glycosylated haemoglobin all decreased during the study period.

The water should not be overly hot, as the patient's neuropathy may prevent them from noticing they are burning themselves. Furthermore, when the feet become hot, poor circulation might result in increased metabolic demands that the diabetes patient cannot meet. When recommending hot-tub therapy for diabetic patients, proper water sanitation and suitable counseling should be taken into account [19].

6. Medicinal Plants with Antidiabetic and Their Reported Effect on Experimental Models (Table 3)

Table 3 Medicinal plants with antidiabetic and their reported effect on experimental models.

Botanical Name	Family	Antidiabetic and other beneficial effects	Reference
Achiliea santolina L.	Asteraceae	Hypoglycemic, antioxidant	20
Artemisia patterns	Asteraceae	Hypoglycemic, increases peripheral glucose utilization	21
Areca catechu L.	Arecaceae	Hypoglycemic	22
Beta vulgaris L.	Chenopodiaceae	Increases glucose tolerance in OGTT	23
Boerhaavia diffusa L.	Nyctaginaceae	Decreases blood glucose level and increases plasma insulin levels, antioxidant	24
Bombax ceiba L.	Malvaceae	Hypoglycemic	25
Butea monosperma (Lam)	Caesalpinaceae	Anti-hyperglycemic	26
Carum carvi L.	Apiaceae	Potent anti-hyperglycemic	27
Cogniauxia podoleana Baillon	Cucurbitaceae	Hypoglycemic and anti-hyperglycemic	28
Commelina communis L.	Commelinaceae	Anti-hyperglycemic, management of non-insulin-dependent diabetes	29
Croton cajucara Benth.	Euphorbiaceae	Anti-hyperglycemic	30, 31
Curcuma longa L.	Zingiberaceae	Hypoglycemic, plays a role in PPAR-gamma activation	32
Cynodon dactylon Pers	Poaceae	Anti-hyperglycemic	33
Enicostemma littorale Blume	Gentianaceae	Decreases plasma glucose level, glycosylated haemoglobin and glucose-6-phosphatase activity in liver	34
Eriobotrya japonica Lindl.	Rosaceae	Hypoglycemic	35
Gentiana olivieri L.	Gentianaceae	Hypoglycemic, anti-hyperlipidemic	36
Ginkgo biloba L.	Ginkgoaceae	Hypoglycemic, increases pancreatic beta-cell in NIDDM	37, 38
Globularia alypum L.	Globulariaceae	Hypoglycemic, increases plasma insulin levels	39
Glycyrrhiza uralensis Fish.	Papilionaceae	PPAR-gamma ligand-binding activity, decreases the blood glucose levels	40
Gymnema nwntanum Hook	Asclepiadaceae	Anti-peroxidative, antioxidant, may prevent the cholinergic neural and retinal complications of hyperglycemia in diabetes	41
Gymnema sylvestre R. Br.	Asclepiadaceae	Hypoglycemic. Hypolipidemic	42
Hintonia standleyana	Rubiaceae	Anti-hyperglycemic	43
Ibervillea sonorae (S. Watson)	Cucurbitaceae	Acute and chronic hypoglycemic	44
Ipomoea aquatic Forsk.	Convolvulaceae	Decreases serum glucose concentration by 29.4% in Type II diabetic patients. hypoglycemic	45
Kalopanax pictus (Thunb.)	Araliaceae	Anti-diabetic activity, hypocholesterolemic and hypolipidemic	46
Lagerstroemia speciosa L.	Lythraceae	Insulin-like actions, glucose uptake, anti-adipogenesis	47, 48
Medicago sativa L.	Fabaceae	Anti-hyperglycemic, insulin-releasing and insulin-like activity	49
Morus alba L.	Moraceae	Protects pancreatic beta cells from degeneration and diminishes lipid peroxidation	50

7. Traditional Phytotherapies [51]

7.1 Antidiabetic Extracts

Adhatoda vasica Nees: A water-based extract made from the plant's fresh leaves. To treat sugar, 10 cc of extract is used three times a day.

Aloe vera Mill + *Fagonia indica* L. + *Tylophora hirsuta* L.: Fresh aerial parts of *Fagonia indica*, fresh leaves and stems of Aloe vera, and fresh branches of *Tylophora hirsuta* L. were used to make an equal amount of extract. The three extracts are then combined and taken three times a day as a tiny

teaspoon. According to the area's rural residents, this mixture has been around for hundreds of years and can reduce diabetics' blood glucose levels by 100%.

Ficus benghalensis L.: The latex is extracted from the plant's aerial parts (leaves and young branches) and combined with honey before being taken orally to manage excessive blood glucose levels.

Psidium guajava L.: Diabetics can use a hot water extract produced from the dried leaves of the plant to lower their blood glucose levels. This hot tea was particularly popular among the area's residents.

Momordica charantia L.: One tiny cup of fresh fruit juice is consumed every day. This juice has anti-diabetic properties.

Cajanus cajan and *Vigna mungo* (Burm. f.) Walp: Diabetics should consume the cooked pulse derived from the seeds of these plants.

Allium cepa L.: One tea spoon of the subterranean bulb's juice is consumed 3 times a day. This is given to diabetics to help them control their blood sugar and high blood pressure.

Caralluma edulis (L.) Benth. ex Hook. f.: Locals prepare the aerial parts as veggies to treat diabetic mellitus.

7.2 Antidiabetic Leaves

Ziziphus jujuba Mill: To reduce blood glucose levels, 4-5 fresh leaves are chewed every day.

Dodonaea viscosa (L.) Jacq: Masticating 2-3 fresh plant leaves twice a day with a glass of water is recommended.

7.3 Antidiabetic Powder (Safoof)

Ocimum sanctum L. + Oc*imum album* L.: Leaves of these plant species are dried under shade, then ground to make powder (*Safoof*). 1 gm power is given with water twice a day for prophylactic and the treatment of diabetes.

Momordica charantia L.: The fruits of the plant are dried under shade, then ground to obtain powder. One table spoon is administered twice a day to lower blood glucose level.

Syzygium cumini Skeels: Seeds of the plant are dried under shade, then ground to make powder About 25 gm powder is used thrice a day with water. This decreases blood glucose level very significantly.

Kickxia ramosissima (Wall.) Janchen: The whole plant is dried under shade and is ground to make powder. This powder is prescribed for treatment of diabetes by the inhabitants of the study area.

Cichorium intybus L.: The roots are dried under shade and then ground to obtain powder. About 15 gm of this powder is taken with glass of water twice a day before meal to lower blood glucose level.

Melia azedarach L.: The dried fruits of the plant are ground to make powder. About half small teaspoon is given with glass of water before breakfast daily for a month. It is claimed by the inhabitants that it is an effective therapy for the treatment of diabetes.

Hordeum vulgare L. + *Cicer arietinum* L. + *Elettaria cardamomum* Maton: Seeds of *Hordeum vulgare* 125 gram are roasted and mixed with each of 50 gm of *Cicer arietinum* and *Elettaria cardamomum* and used a half teaspoon with water thrice a day to control blood glucose level.

7.4 Antidiabetic Bread

Equal quantity of *Cicer arietinum* (Seeds), *Daucus carota* (Dried form), *Hordeum vulgare* (Seeds), *Oryza sativa* (Seeds), *Triticum aestivum* (Seeds) and *Zea mays* (yellow variety) are ground and made into powder. The bread is cooked from this mixed flour and taken as breakfast with fresh butter of cow for 2-month. This remedy is used as dietary supplement to control diabetes.

7.5 Antidiabetic Seeds

Trigonella foenum-graecum L.: Twenty five gm seeds are given daily for 21 days with water. The inhabitants claimed that it is one of the effective treatments to reduce blood glucose in diabetic patients.

Withania coagulens (L.) Dunal. Fifteen gm seeds of the plant are soaked in water for the whole night. This is given early morning before breakfast to diabetic patients.

7.6 Antidiabetic Potherbs/Vegetables

Solanum nigrum L.: Fresh aerial parts of the plant are cooked as vegetable and are recommended to control diabetes.

Taraxicum officinale Weber: Fresh leaves are cooked as vegetable (locally-called Saag).

Cajanus cajan & Vigna mungo (Burm. F.) Walp.: Diabetic patients should eat pulses made from the seeds of these plants, which are cooked.

Allium sativum L.: Cooked or uncooked subterranean bulbs are used to treat diabetes and hypertension in diabetics.

Caralluma edulis (L.) Bth. ex Hk. F.: Locals cook the aerial sections like vegetables to treat diabetic mellitus.

7.7 Antidiabetic Fruits

Vigna sinensis (L.) Savi ex Hassk: The plant's immature pods are used to lower blood glucose levels.

Syzygium cuminii Skeels: Diabetes is treated with fresh fruits.

Olea ferruginea Royle: In the summer, fresh fruit is harvested, dried, and suggested to diabetics for lowering blood glucose levels in the winter.

7.8 Antidiabetic Herbal Mixtures

Syzygium cumini, *Momordica charantia*, 12 gm *Cyperus rotundus*, and Rosa alba seeds are ground into powder. Residents of a certain area are fed this chemical with efficacy in decreasing blood glucose levels.

Tylophlra hirsuta (leaves), *Trigonella foenum-graecum* (seeds), and aerial parts of *Fumaria indica* are all mashed and powdered in equal amounts. This mixture is said to be an effective medication for diabetic individuals who want to lower their blood sugar levels.

8. Conclusions

Diabetes mellitus is the most common endocrine disease, affecting about 300 million individuals globally. As a result, therapies based on the principles of western medicine (allopathic) are generally ineffective, carry the danger of side effects, and are prohibitively expensive, especially in developing countries. As a result, treating diabetes mellitus with plant-derived chemicals that are readily available and do not require time-consuming pharmaceutical production appears to be very appealing. All of the herbal medicines addressed in this review have clinical and pharmacological efficacy.

Herbal anti-diabetic medications offer a higher potency and fewer negative effects than synthetic anti-diabetic drugs. The isolation and identification of active ingredients from these plants, as well as the production of a standardized dose and dosage regimen, can all help improve hypoglycemic efficacy. This review article focuses on hypoglycemic activity of plants and other natural treatments methods of acupuncture, home remedies which may be valuable to health professionals, scientists, and academics working in the field of pharmacology and therapeutics that are developing evidence-based alternative medicine to treat various types of diabetes in humans and animals. Due to risk of adverse effect of allopathic medicine treatment the world is searching alternative treatment therapy. So this paper helps to study the all the other methods of treatment for diabetic disorder.

References

[1] Zheng, Y., Ley, S. H., and Hu, F. B. 2018. "Global Aetiology and Epidemiology of Type 2 Diabetes Mellitus and Its Complications." *Nat Rev Endocrinol* 14 (2): 88-98.

[2] Kokate, C. K., Purohit, A. P., Gokhale, S. B. Turmeric "Text book of Pharmacognosy", 'Nirali Prakashan' New

Delhi, 2nd edition Page No: 414.

[3] Kokate, C. K., Purohit, A. P., Gokhale, S. B. Turmeric "Text book of Pharmacognosy", 'Nirali Prakashan' New Delhi, 2nd edition Page No: 267.

[4] Kokate, C. K., Purohit, A. P., Gokhale, S. B. Turmeric "Text book of Pharmacognosy", 'Nirali Prakashan' New Delhi, 2nd edition Page No: 360.

[5] Kokate, C. K., Purohit, A. P., Gokhale, S. B. Turmeric "Text book of Pharmacognosy", 'Nirali Prakashan' New Delhi, 2nd edition Page No: 152.

[6] Kokate, C. K., Purohit, A. P., Gokhale, S. B. Turmeric " Text book of Pharmacognosy", 'Nirali Prakashan' New Delhi, 2nd edition Page No: 264.

[7] Kokate, C. K., Purohit, A. P., Gokhale, S. B. Turmeric " Text book of Pharmacognosy", 'Nirali Prakashan' New Delhi, 2nd edition Page No: 486.

[8] Kokate, C. K., Purohit, A. P., Gokhale, S. B. Turmeric "Text book of Pharmacognosy", 'Nirali Prakashan' New Delhi, 2nd edition Page No: 296.

[9] Kokate, C. K., Purohit, A. P., Gokhale, S. B. Turmeric "Text book of Pharmacognosy", 'Nirali Prakashan' New Delhi, 2nd edition Page No: 35.

[10] Kokate, C. K., Purohit, A. P., Gokhale, S. B. Turmeric "Text book of Pharmacognosy", 'Nirali Prakashan' New Delhi, 2nd edition Page No: 218.

[11] Krzaczek, T. 1984. "Phenolic Acids in Some Tannin Drugs from the Rosaceae Family." *Farm Pol* 40 (8): 475-477.

[12] Skrede, G., Wrolstad, R. E., and Durst, R. W. 2000. "Changes in Anthocyanins and Polyphenolics during Juice Processing of Highbush Blueberries (*Vaccinium myrtillus* L.)." *Journal of Food Science* 65 (2): 357-364.

[13] Sridharan, K., Mohan, R., Ramaratnam, S., and Panneerselvam, D. 2011. "Ayurvedic Treatments for Diabetes Mellitus." *Cochrane Database Syst Rev* doi: 10.1002/14651858.CD008288.pub2.

[14] Khan, C. R., and Shechter, Y. "Insulin: Oral Hypoglycemic Agents and the Pharmacology of Endocrine Pancreas." in Goodman and Gillman's: The Pharmacological Basis of Therapeutics. 8th ed. New York: Pergaman Press; 1991. p. 1463.

[15] Halberstam, M., Cohen, N., Shlimovich, P., et al. 1996. "Oral Vanadyl Sulfate Improves Insulin Sensitivity in NIDDM But Not in Obese Nondiabetic Subjects." *Diabetes* 45 (5): 659-66.

[16] Sjogren, A., Floren, C. H., and Nilsson, A. 1988. "Magnesium, Potassium and Zinc Deficiency in Subjects with Type II Diabetes Mellitus." *Acta Med Scand* 224 (5): 461-6.

[17] McNair, P., Christiansen, C., Madsbad, S., et al. 1978. "Hypomagnesemia, a Risk Factor in Diabetic Retinopathy." *Diabetes* 27 (11): 1075-7.

[18] Hooper, P. L. 2000. "Hot-tub Therapy for Type 2 Diabetes Mellitus." *N Engl J Med* 342 (12): 924-5.

[19] Yazdanparast, R., Ardestani, A., and Jamshidi, S. 2007. "Experimental Diabetes Treated with *Achillea santolina*: Effect on Pancreatic Oxidative Parameters." *J Ethnopharmacol* 112 (1): 13-8.

[20] Subramoniam, A., Pushpangadan, P., Rajasekharan, S., et al. 1996. "Effects of *Artemisia pollens* Wall. On blood Glucose Levels in Normal Andalloxan-induced Diabetic Rats." *J Ethnopharmacol* 50 (1): 13-7.

[21] Chempakam, B. 1993. "Hypogiycemic Activity of Arecoline in Betel Nut *Areca catechu* L." *Ind J Exp Biol* 31 (5): 474-5.

[22] Yoshikawa, M., Murakami, T., Kadoya, M., et al. 1996. "Medicinal foodstuff. III. Sugar beet. (1): Hypoglycemic oleanolic acid oligoglycosides, betavulgarosides I, II, III, and IV, from the Root of Beta vulgaris L. (Chenopodiaceae)." *Chem Pharm Bull (Tokyo)* 44 (6): 1212-7.

[23] Pari, L., and Amarnath Satheesh, M. 2004. "Anlidiabetic Activity of *Boerhaavia diffusa* L. Effect on Hepatic Key Enzymes in Experimental Diabetes." *J Ethnopharmacol* 91 (1): 109-13.

[24] Saleem, R., Ahmad, M., Hussain, S. A., et al. 1999. "Hypotensive, Hypoglycemic and Toxicological Studies on the Flavonol C-glycoside shamimin from *Bombax ceiba*." *Planta Med* 65 (4): 331-4.

[25] Somani, R., Kasture, S., and Singhai, A. K. 2006. "Antidiabetic Potential of *Butea monospenna* in Rats." *Fitoterapia* 77 (2): 86-90.

[26] Eddouks, M., Lemhadri, A., and Michel, J-B. 2004. "Caraway and Caper: Potential Anti-hyperglycaemic Plants in Diabetic Rats." *J Ethnopharmacol* 94 (1): 143-8.

[27] Diatewa, M., Samba, C. B., Assah, T. C. H., and Abena, A. A. 2004. "Hypoglycemic and Antihyperglycemic Effects of Diethyl Ether Fraction Isolated from the Aqueous Extract of the Leaves of *Cogniauxia podoleana* Baillon in Normal and Alloxan-induced Diabetic Rats." *J Ethnopharmacol* 92 (2-3): 229-32.

[28] Youn, J-Y., Park, H-Y., and Cho, K-H. 2004. "Anti-hyperglycemic Activity of *Commelina communis* L.: Inhibition of Alpha-glucosidase." *Diabetes Res Clin Pract* 66 Suppl 1: S149-55.

[29] Farias, R. A., Rao, V. S., Viana, G. S., et al. 1997. "Hypoglycemic Effect of Trans-dehydrocrotonin, A Nor-clerodanc Diterpene from *Croton cajucara*." *Planta Med* 63 (6): 558-60.

[30] Rodrigues, G., Marcolin, E., Bona, S., et al. 2010. "Hepatics Alterations and Genotoxic Effects of *Croton cajucara* Benth (SACACA) Indiabetic Rats." *Arq Gastroenterol* 47 (3): 301-5.

[31] Kuroda, M., Mimaki, Y., Nishiyama, T., et al. 2005. "Hypoglycemic Effects of Turmeric (*Curcuma longa* L. rhizomes) on genetically diabetic KK-Ay Mice." *Biol Pharm Bull* 28 (5): 937-9.

[32] Jarald, E. E., Joshi, S. B., and Jain, D. C. 2008. "Antidiabetic Activity of Aqueous Extract and Non-polysaccharide Fraction of Cynodon dactylon Pers." *Indian J Exp Biol* 46 (9): 660-7.

[33] Vijayvargia, R., Kumar, M., and Gupta, S. 2000. "Hypoglycemic Effect of Aqueous Extract of *Enicostemma littorale* Blume (chhotachirayata) on Alfoxan Induced Diabetes Mellitus in Rats." *Indian J Exp Bioi* 38 (8): 781-4.

[34] Tanaka, K., Nishizono, S., Makino, N., et al. 2008. "Hypoglycemic Activity of *Eriobotrya japonica* Seeds in Type 2 Diabetic Rats and Mice." *Biosci Biotechnol Biochem* 72 (3): 686-93.

[35] Sezik, E., Aslan, M., Yesilada, E., and Ito, S. 2005. "Hypoglycaemic Activity of *Gentiana olivieri* and Isolation of the Active Constituent through Bioassay-directed Fractionation Techniques." *Life Sci* 76 (11): 1223-38.

[36] Sugiyama, T., Kubota, Y., Shinozuka, K., et al. 2004. "*Ginkgo biloba* Extract Modifies Hypoglycemic Action of Tolbutainide via Hepatic Cytochrome P450 Mediated Mechanism in Aged Rats." *Life Sci* 75 (9): 1113-22.

[37] Kudolo, G. B. 2001. "The Effect of 3-month Ingestion of *Ginkgo biloba* Extract (EGb 761) on Pancreatic Beta-cell Functionin Response to Glucose Loading in Individuals with Non-insulin-dependent Diabetes Mellitus." *J Clin Pharmacol* 41 (6): 600-11.

[38] Skim, F., Lazrek, H. B., Kaaya, A., et al. 1999. "Pharmacological Studies of Two Antidiabetic Plants: *Globularia alypum* and *Zygophyllum gaetulum*." *Therapie* 54 (6): 711-5.

[39] Kuroda, M., Mimaki, Y., Sashida, Y., et al. 2003. "Phenolics with PPAR-gamma Ligand-binding Activity Obtained from Licorice (*Glycyrrhiza uralensis* Roots) and Ameliorative Effects of Glycyrin on genetically Diabetic KK-A(y) Mice." *Bioorg Med Chem Lett* 13 (24): 4267-72.

[40] Ramkumar, K. M., Latha, M., Ashokkumar, N., et al. 2005. "Modulation of Impaired Cholinesterase Activity in Experimental Diabetes: Effect of *Gymnema montanum* Leaf Extract." *J Basic Clin Physiol Pharmacol* 16 (1): 17-35.

[41] Daisy, P., Eliza, J., and Mohamed Farook, K. A. M. 2009. "A Novel Dihydroxy Gymnemic Triacetate Isolated from *Gymnema sylvestre* Possessing Normoglycemic and Hypolipidemic Activity on STZ-induced Diabetic Rats." *J Ethnopharmacol* 126 (2): 339-44.

[42] Guerrero-Analco, J. A., Hersch-Martínez, P., Pedraza-Chaverri, J., et al. 2005. "Antihyperglycemic effect-of constituents from *Hintonia standleyana* in streptozotocin-induced diabetic rats." *Planta Med* 71 (12): 1099-105.

[43] Alarcon-Aguilar, F. J., Calzada-Bermejo, F., Hernandez-Galicia, E., et al. 2005. "Acute and Chronic Hypoglycemic Effect of *Ibervillea sonorae* Root Extracts-II." *J Ethnopharmacol* 97 (3): 447-52.

[44] Malalavidhane, T. S., Wickramasinghe, S. M. D. N., Perera, M. S. A., and Jansz, E. R. 2003. "Oral Hypoglycaemic Activity of *Ipomoea aquatica* in Streptozotocin-induced, Diabetic Wistar Rats and Type II Diabetics." *Phytother Res* 17 (9): 1098-100.

[45] Park HJ, Kim DH, Choi JW, Park JH, Han YN. A potent anti-diabetic agent from *Kalopan axpictus*.Arch Pharm Res 1998, 21, 24-29.

[46] Hattori, K., Sukenobu, N., Sasaki, T., et al. 2003. "Activation of Insulin Receptors by Lagerstroemin." *J Pharmacol Sci* 93 (1): 69-73.

[47] Klein G, Kim J, Himmeldirk K, Cao Y, Chen X. Antidiabetes and Antiobesity Activity of *Lagerstroemia speciosa*. Evid Based Complement Alternat Med 2007, 4, 401-407.

[48] Gray, A. M., and Flatt, P. R. 1997. "Pancreatic and Extra-pancreatic Effects of the Traditional Anti-diabetic Plant, *Medicago saliva* (lucerne)." *Br J Nutr* 78 (2): 325-34.

[49] Singab, A. N. B., El-Beshbishy, H. A., Yonekawa, M., et al. 2005. "Hypoglycemic Effect of Egyptian *Moms alba* Root Bark Extract: Effect on Diabetes and Lipid Peroxidation of Streptozotocin-induced Diabetic Rats." *J Etnnopharmacol* 100 (3): 333-8.

[50] Goldman, P. 2001. "Herbal Medicines Today and the Roots of Modern Pharmacology." *Ann Intern Med* 135 (8 Pt 1): 594-600.

[51] *National Diabetes Fact Sheet: National Estimates and General Information on Diabetes in the United States*. Rev. ed. Atlanta, Ga: Centers for Disease Control and Prevention; 1998.