Review Article

A Review on Efficacy of Biomedicinal Plants as Antidiabetic Therapeutic Agents

Faria Fatima and Pallavi Chaudhary

Department of Agriculture, IIAST, Integral University, Kursi Road Lucknow, Uttar Pradesh, India

Abstract

Diabetes, a non-communicable condition, is typically a state of poorly controlled sugar and fat metabolism homeostasis that has recently become one of the main health concerns. In most developed countries, it is the fourth leading cause of death and will also become an epidemic in many other developing countries if not controlled. About 70 percent of the world's population uses conventional medications derived from several horticultural plants. This analysis emphasizes on Indian herbal remedies used and provides a list of bio-medicinal herbs used as antidiabetics in Ayurveda as well as marketing preparations for Diabetes mellitus formulations, especially in India. Several of the herbal medicines with confirmed anti-diabetic and associated beneficial properties used in diabetes care are as follows *Brassica juncea, Eugenia jambolana, Coccina grandis, Catharanthus roseus, Alangium lamarckii, Albizia odoratissima, Axonopus compressus, Dioscoreaopposita, Gymnema sylvestre, Momordica charentia, Azadirachta indica, Asparagus racemosus, Bauhinia variegata, Cinnamon zeylaniucm, Zizyphus spina-christi, Euphorbia hirta L, Stevia rebaudiana, Pterocarpus marsupium.* Further studies are essential and more effort should be paid to examine the biological processes of hundreds of commonly used horticultural herbs, both *in vitro* and *in vivo*, to assess the reported activity to identify potent antidiabetic possibilities from the natural resources.

Keywords: Ayurveda, antidiabetic, herbal, traditional

***Correspondence**
Author: Faria Fatima
Email: fatimafaria45@gmail.com

Introduction

Numerous supplements and medicines were tested for various medications in the biomedical sector to treat diabetes, even though they do have beneficial benefits due to their persistent and other adverse reactions. Thus natural therapeutic bio-medicinal products having growth performance encouraging the potential and tonic to boost the immune response by increasing consumption, antimicrobial capacity, antistress characteristics.

Diabetes mellitus is a serious and conspicuous disease that influences each developing and developed nation folks. This disease is anticipated to impact 25 percent of the global population. Diabetes mellitus is caused by glucose metabolism disorders linked to low levels of insulin throughout the blood or insensitivity of targeted organs to insulin [1]. Given considerable accomplishment with oral low blood sugar agents in the diagnosis of diabetes, searching for new drugs remains because allopathic drugs used for the treatment have their limitations, side effect & adverse effect such as hypoglycemia, vomiting, nausea, flatulence, diarrhea or constipation, headache, obesity, lactic acidosis/ketosis, anemia, dyspepsia, dizziness, joint pain, etc. and target several essential organs (**Figure 1**) [2]. Thus, instead of using allopathic medicines, herbal medications are a perfect option that has no side effects and detrimental effects (**Figure 2, Table 1**) [3]. There are about 800 Indian horticultural plants have found that may have the antidiabetic potential [4]. Although Complementary & Alternative Medicine (CAM) therapies are common, still there is a necessity for scientific pieces of evidence that supports the applicability of these herbs in diabetes treatment [5]. Previous work on CAM diabetes has primarily focused on single modalities but more often recommended comprehensive, multi-nutritional therapy by CAM practitioners. However, ayurvedic interventions can benefit patients with a high HbA1c baseline value, however, still, additional analysis is required [6]. Several horticultural plants having antidiabetic therapeutic agents are delineated as below and mentioned within the **Table 2**.

Horticultural plants possessing Anti-diabetic efficacy

Brassica juncea

In Tamil Nadu, *B. Juncea* spice is widely used in various food products that belong to the Cruciferae family. *B. Juncea* aqueous seed extract has a strong hypoglycemic function that was researched in male albino rat diabetic induced with STZ. Different doses with hypoglycemic activity have been recorded between 250 mg/kg- 450 mg/kg respectively.

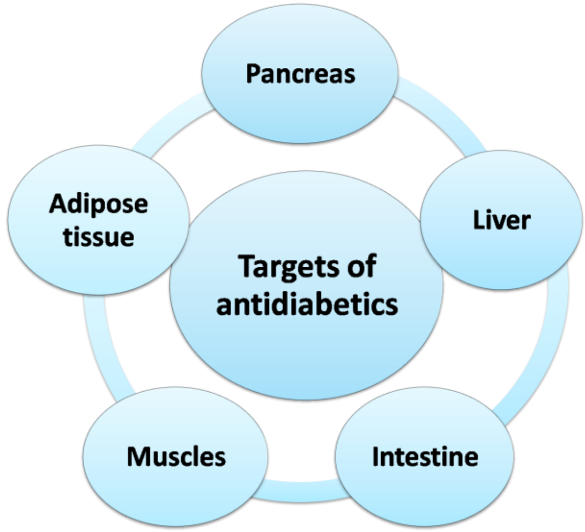

Figure 1 Targets of medicinal drugs in the body

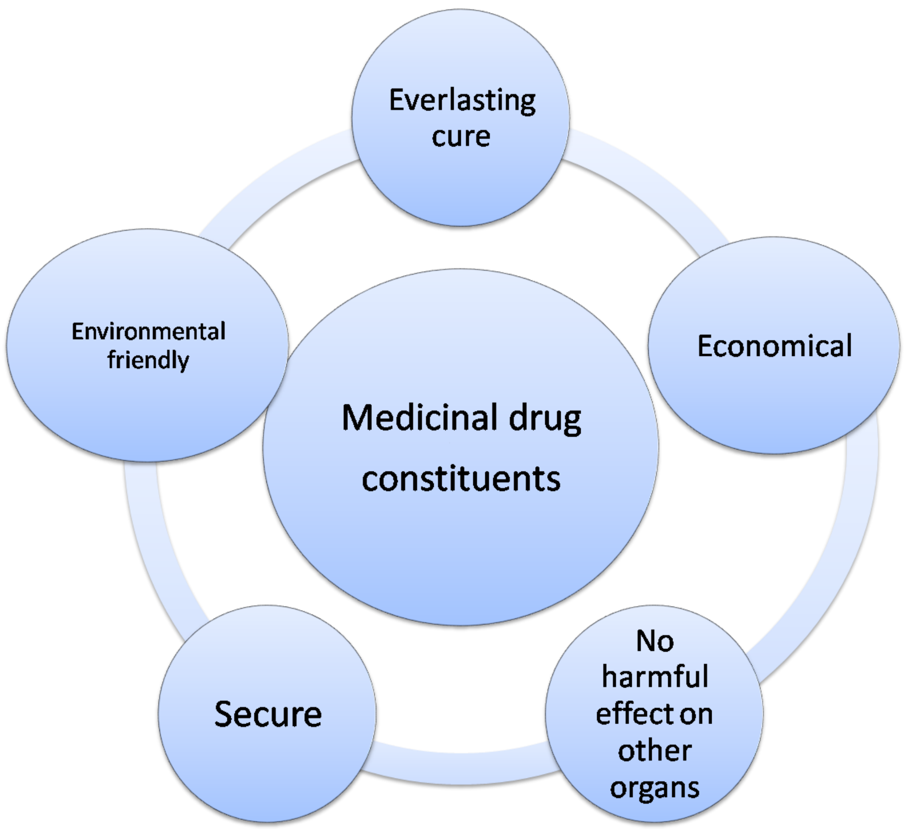

Figure 2 Advantages of using formulations from plant sources

Table 1 Advantage of Natural antidiabetic biomedicinal plants over synthetic antidiabetic medicines

S. No	Property	Synthetic antidiabetic medicines	Natural antidiabetic horticultural plants
1.	Benefits	Effective and quick action	Cheap, easily available, traditional use, less or no side effects
2.	Limitations	Side effects of insulin resistance, diarrhea, weight gain, flatulence, indigestion, lactic acidosis, fluid retention, interference by other diseases, costly, poor availability, prolonged use	Less explored, prolonged use, usually less effective, late effect

 ISSN 2278-6783

Table 2 Biomedicinal plants used in the treatment of Diabetes mellitus

Botanical name	**Common name**	**Family**	**Plant part used**	**chemical constituents**	**References**
Brassica juncea	Brown mustard/Chinese mustard/ Indian mustard/ leaf mustard/ Oriental mustard/ vegetable mustard	Cruciferae	Seed	Glucosinolates	[24]
Eugenia jambolana	*Jamun*	Myrtaceae	Seeds, foliage, bark and wood	2-O-cis-p-coumaroyl maslinic acid, Triterpenoid	[25]
Coccinagrandis	ivy gourd/ scarlet gourd/ tindora/ kowai fruit	Cucurbitacea	leaves and roots	Heptacosane, Cephalandrol, β -sitosterol, Alkaloids Cephalandrins A and B,	[26]
Catharanthus roseus	bright eyes/Cape periwinkle, graveyard plant/ Madagascar periwinkle/ Old maid/pink periwinkle/ rose periwinkle	Apocynaceae	Roots and leaves	bisindole alkaloids vinblastine and vincristine	[27]
Alangium lamarckii	Akola	Cornaceae	Leaves, Bark, seeds	deoxytubulosine, alangimarckine, dehydroprotoemetine etc. Three new phenolic glycosides, salviifoside, emetine, cephaeline, N-methylcephaeline, psychotrine, betuline, betulinaldehyde, lipeol, betulinic acid and ß-sitosterol. Stigmasta- 5, 22, 25- trien-3ß-ol, myristic acid, E-cis- fused neohopane derivetives, alangidiol and its isomer; N- benzoyl-L-Ph-alaninol, and 3 unidentified triterpenoids also isolated from the plant	[28]
Albizia odoratissima	Ceylon Rosewood, Kali Siris' or 'Black Siris	Fabaceae	stem, leaves, flowers	glycosides, quercitrin and isoquercitrin	[29]
Axonopus compressus	carpet-grass,/American carpet grass/ tropical carpet grass/ blanket grass/ lawn grass/ Louisiana grass	Poaceae	stem, leaves	Alkaloids Phenolics Flavonoids Saponins Tannins, Alloxan monohydrate	[30]
Dioscorea polystachya	Chinese yam	Dioscoreaceae	tuber, stem	triterpenoids, proteins, glycosides, saponins, flavonoids, fats and oils, tannins, and phenolic compounds	[31]

Gymnema sylvestre	Gurmar	Apocynaceae	stem, leaves	gymnemic acids, gymnemasaponins, and a polypeptide, gurmarin	[32]
Momordica charantia	Bitter melon	Cucurbitaceae	stem and fruit	triterpene, proteid, steroid, alkaloid, inorganic, lipid, and phenolic compounds	[33]
Azadirachta indica	Neem	Meliaceae	Leaves	Nimbidin, azadirachtin and the others are nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinate, gedunin, salannin, and quercetin, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7-benzoylazadiradione, 7-desacetyl-7-benzoylgedunin, 17-hydroxyazadiradione.	[34]
Asparagus racemosus	satavar	*Asparagaceae*	leaves and roots	2-Propanone, 1,3-dihydroxy 1), 2-Fruancarboxy aldehyde, 5-(hydroxymethyl) 2), Hexadecanoic acid 3), n-Hexadecanoic acid 4), Ethanol,2(Octyloxy)- 5), 1,9-Nonanediol 6).	[35]
Bauhinia variegata	orchid tree/ mountain ebon	Fabaceae	Leaves, stem	roseoside	[36]
Cinnamon zeylaniucm	daalchini	Lauraceae	Inner bark and oil distilled from bark and leave	volatile oil (up to 4% consisting of cinnamaldehyde, cinamyl acetate, cinnamyl alcohol, cuminaldehyde, eugenol, and methyleugenol), tannins, cinnzelanin, cinnzelanol, coumarin, methylhydroxychalcone polymers	[37]
Zizyphus spina-christi	Christ's thorn jujube	Rhamnaceae	leaves	Geranyl acetone, methyl hexadecanoate, methyl octadecanoate, farnesyl acetone C, hexadecanol and ethyl octadecanoate	[38]
Euphorbia hirta L,	Asthma-plant	Euphorbiaceae	flower	alkaloids, saponins, flavonoids, tannins phenolic acids and amino acids	[39]
Stevia rebaudiana	candyleaf, sweet leaf or sugarleaf.	Asteraceae	leaves	stevioside and rebaudiosides A, B, C, D, and E; dulcoside A; and steviolbioside	[40]
Pterocarpus marsupium	Malabar kino, Indian kino tree, vijayasar	Fabaceae	Fabaceae	pterostilbene 45%, alkaloids 0.4%, tannins 5%, protein, pentosan, pterosupin, pseudobaptigenin, liquiritigenin, isoliquiritigenin, garbanzol, 5deoxykaempferol, Phydroxybenzaldehyde, beudesmol, erythrodirol3 monoacetate, l-epicatechin, marsupol, carpusin, propterol, propterol B, marsupinol, irisolidone7 OALrhamnopyranoside	[41]

Eugenia jambolana

Eugenia jambolana (*E. jambolana*), popularly known as Jamun or Indian blackberry was reported in traditional ayurvedic treatment for diabetes. It belongs to family Myrtaceae. In keeping with its suspected anti-diabetic role in conventional medicine, *E. jambolana* results in low blood sugar, reported in both the experimental and clinical models [7]. The phytoconstituents present are ferulic acid, anthocyanin, malvidin- 3-laminaribiosidea, and delphinidin-3-gentiobioside. Diabetics are also advised to eat 1 tsp of this Jamun seed powder in an empty stomach regularly.

Coccia grandis

The hypoglycemic function of *Coccinia grandis (C. grandis)* leaves was tested by isolating its extract in alcohol. A 600 mg/kg by weight alcoholic extract was orally injected into the mice by oral mode of administration. In normal fasted rats, hypoglycemic effects were observed [8].

Catharanthus roseus

Hypoglycemic activity of *Catharanthus roseus (C. roseus)* methanolic leaf extract was examined in alloxan-induced diabetic rats. When compared with monitoring rodent, blood glucose levels gets substantially lowered and it was found that the effect of methanolic extraction lowering blood sugar levels was more prominent than allopathic drugs such as Glibenclamide and Metformin [9].

Alangium lamarckii

Alangium lamarckii (A. lamarckii) alcoholic extract has also possessed an antidiabetic effect which is proved when the alcoholic leaves extract having a concentration of 250 and 500 mg/kg bw were used and it was found that it has effective antidiabetic activity in diabetic rat [10].

Albizia odoratissima

Antidiabetic influence of *A. odoratissima* methanolic bark extract in alloxane-induced diabetic mice was investigated. When methanol extraction was fed to animals at 250 and 500 mg/kg bw, major physiological characteristics such as serum cholesterol levels, SGOT, SGPT, alkaline phosphatase, and total protein levels in alloxane-induced albino mice were also decreased [11].

Axonopus compressus

A. compressus methanolic leaf extract has been studied for anti-diabetic benefit. The injection of alloxan caused diabetes in rats which are treated by methanol leaf extract with the 250, 500, and 1000 mg/kg bw concentrations. Further, it was observed that *A. compressus* significantly reduced the blood glucose at all doses (250, 500 and 1000 mg/kg) (by 31.5 %, 19.8 %, and 24.5 %) when compared to the control groups the antidiabetic properties of *A. compressus* herb [12]

Dioscoreaopposita (Yam)

Yam is a general term in the genus Dioscoreae (family Dioscoreaceae) for certain species. The Chinese yam plant is significantly smaller than those of the African, with the branches approximately 3 meters (10 feet) thick. It is resistant to frost and can be developed much cooler than other yams. Yam products typically have a low glycemic index that proves that they can be a more sustainable source of energy, and have better protection from diabetes and heart diseases [13].

Gymnema sylvestre (Gurmar)

The drugs compose of crushed *Gymnema sylvestre* leaves that belong to the family- Asclepiadaceae. It usually grows in Central and Southern India's tropical rainforests and they could utilize it as a natural diabetes drug. Such drug components are useful for diabetes management and care as they include chemical phytoconstituents such as hentriacontane, inositol, gymnemic acid, and pentatriacontane. In India, it has been used as a horticultural drug for the treatment of diabetes for more than 2000 years[14].

Momordica charentia (Karela, bitter gourd)

Momordica charantia, a common medical drug used for the treatment of type 2 Mellitus diabetes. It is a part of the Cucurbitaceae family and the primary constituents are mimordicin and chiratin (steroidal saponin) present in it. However, it is not only used for diabetic diagnosis, but is also beneficial in the diagnosis of nausea, carminative, tonics, rheumatism, gout, spleen, and liver disorders [15].

***Azadirachta indica* (Neem)**

Azadirachta indica from family maliaceae is used as an active diabetes cure ingredient. After many studies and analyses by leading research institutes, it has been clinically proven that its sections have high effectiveness in the treatment of the disease. Natural neem tablets are developed and distributed across the world for the treatment of large numbers of patients as their extracts boost blood supply by dilating the capillaries and also help to minimize the need for hypoglycaemic medications [16].

Asparagus racemosus

The study was conducted to diagnose diabetes by digestive enzyme inhibitory activity using *the Asparagus racemosus* (Liliaceae). Specific alcoholic extracts such as aqueous, n-hexane, ethyl acetate, chloroform, and methanol have been used for the extraction phenomenon and their research on the inhibitory ability of digestive enzymes (α-amylase and α-glucosidase inhibitory) were studied and It was stated that α-amylase and α-glucosidase enzymes have a major inhibitory effect at a different dosage. Thus, it has revealed that this horticultural crop possesses antidiabetic ability [17]

Bauhinia variegata

To test the antidiabetic and antioxidant activities of *the Bauhinia variegata* flower, the ethanolic extract was administered intravenously to Streptozotocin-induced diabetic rats and the glucose levels were measured at alternate days [18]. The anti-oxidant activity was also assessed by performing 1,1-diphenylpicrylhydrazyl (DPPH) and hydrogen peroxide scavenging (H2O2) assays. The flower extract showed a decrease in blood glucose levels (90.00 mg / dL) at the maximum dose of 400 mg/kg compared to diabetic control rats (224.50 mg / dL) which proved it to be a possible antidiabetic herbal medicine.

Cinnamon zeylaniucm

A plant species from the Lauraceae family has been used to evaluate the anti-diabetic influence of ethanolic extract on Alloxan induced rats. The findings showed that the administration of *C. zeylanicum* alcoholic extract induced a dose-dependent decrease in blood glucose levels. The maximum dose (200mg / kg) of blood sugar was greatly decreased relative to the medium dose (50mg / kg) and median dose (100mg / kg) of the LSD study. This is compared with the effect of Glibenclamide, which suggests that chronic oral administration of a *C. zeylanicum* extract at a sufficient dose could be a reasonable alternative antidiabetic agent [19].

Zizyphus spina-christi

The purpose of this study was to assess the anti-diabetic activity of the leaf extract *Zizyphus spina-Christi* (200 mg/kg b.w.) in STZ-diabetic rats. Oral administration of *Z. spina-Christi* leaf extract decreased blood glucose levels for 28 days with substantial rises in serum insulin levels and C-peptides. Recorded marked elevation in total antioxidant ability with percentage normalization of glycated hemoglobin (HbA1C percent) was examined. *In vitro experiments in Zizyphus extract having a dose-dependent inhibitory activity against α-amylase enzyme (IC50) at 0.33 mg/ml. Such finding was followed in healthy rats by In vivo inhibition of starch digestion and absorption by the Zizyphus extract.* The current work confirmed that *Z spina-Christi* leaf extract, plain and formulated, increased the use of glucose in diabetic rats by boosting the insulin secretion due to the functionality of saponin and polyphenols and controlling high blood sugar by attenuating the absorption of meal-derived glucose that could be attributed to the total polyphenols [20]

Euphorbia hirta L

The antidiabetic activity of *E. hirta L* under In-vivo condition was developed to explain the plant's conventional use in the treatment of diabetes. The findings of this study indicated that the methanol extract of *E. hirta* has substantial *In-vivo* anti-diabetic activity, which indicates that plants can produce drugs in the battle against diabetes [21].

Stevia rebaudiana

Stevia rebaudiana is stated to have the antidiabetic. For the purpose, a test was conducted to evaluate the efficacy of *S. rebaudiana* anti-diabetic activity against independent doses against the disease control community and the standard Glibenclamide product. This work presents a detailed analysis mong the doses of *S. rebaudiana* in healthy albino rats administered by the STZ for their anti-diabetic activities. The *S. rebaudiana* administration demonstrates a substantial decrease when compared with the Glibenclamide induced dosage [22].

Pterocarpus marsupium

Pterocarpus marsupium Roxb., a deciduous tree that is widely grown in India and Sri Lanka, has been well known in Ayurveda due to its healing and sensitivity. P. marsupium heartwood extracts are stated to have various pharmacological agents and are used in diabetes care. Nevertheless, it was investigated that it has been shown that the flavonoid fraction from *P. marsupium* induces Beta-cells present in the pancreas to degranulate. Epicatechin, a defensive and restorative substance, has been isolated from its bark which is used to resist insulin and turn proinsulin into insulin. However, significant studies into antidiabetic activities and other therapeutic properties of *P. marsupium* combined with plant-isolated bioactive compounds will contribute to the development of new medicines to treat several diseases with limited side effects [23].

Phytochemicals with Antidiabetic Potential

The introduction of new natural antidiabetic drugs could be extremely promising as a result of the marginal effectiveness and safety concerns of existing antidiabetic drugs for the millions of people who are trying to seek stronger diabetes care. The analysis of bioactive compounds responsible for antidiabetic effects has progressed in this respect over the past few decades. A combination of bioactive compounds or a single component of plant extracts was attributed to the antidiabetic effect of plant materials. Natural products make a wide range of phytochemicals including tannin, saponins, glycosides, phenolic acids alkaloids, flavonoids, and polysaccharides, In **Table 3** are represented sources, structures, and targets of some potential antidiabetic phytochemicals. The positive influence of these phytochemicals may be through various mechanisms such as insulin release, NF-kB signaling pathway, glucose and fatty acid metabolism, and protective action of the reactive oxygen species (ROS), β cell stimulation and gluconeogenic enzyme inhibition.

Alkaloids

For potential antidiabetic efficacy the following alkaloids — berberine, boldine, lupanine, never, oxymatrine, piperine, and sanguinarine are studied. The antidiabetic effect of many alkaloids with specific reference to their molecular targets in *In vitro* and *In vivo* insulin signaling pathway-related cascades as they possess glucose-lowering potent antioxidant, anti-inflammatory, and lipid-lowering properties [42].

Flavonoids

Flavonoids are a broad class of plant secondary metabolites present in a broad variety of fruits, vegetables, and herbs. They can perform as natural antioxidants attributed to the prevalence of hydroxyl groups and aromatic rings of the flavonoid structures. Foods containing flavonoids should be used regularly in antidiabetic diets. Catechins, chrysin, baicalein, icariin, isoliquiritigenin fisetin, naringenin, quercetin, rutin, morin, silymarin kaempferol, genistein, and others were tested for their antidiabetic properties [49].

Terpenoids

Findings from certain plants regarding the chemistry and bioactivities of tetracyclic triterpenoids were studied. Multiple biological processes on glucose uptake and their absorption, insulin secretion, and retinopathy and nephropathy were improved [58].

Others phytoconstituents

Several other phytochemicals were also reported that improves health and survival rate, promotes glucose uptake through glucose transporter to the plasma membrane, and suppress blood glucose levels in T2DM model db/db mice [65].

Table 3 Sources, structures, and targets of some potential antidiabetic phytochemicals

Examples	Types	Source	Role	Ref
Phyto chemicals				
1. Alkaloids				
Berberine	Isoquinoline alkaloid	*Berberis* (Berberidaceae)	Inhibit α-glucosidase and decrease glucose transport through the intestinal epithelium	[42]
Lupanine	quinolizidine alkaloid	*Lupinus perennis Lupinus*	improves glucose homeostasis by influencing ATP-sensitive potassium (KATP) channels and insulin genes	[43]
Boldine	Benzyliso-quinoline class alkaloid	*Peumus boldus* Moliba (Chilean boldo tree, family Monimiaceae)	inhibition of angiotensin II-mediated BMP4 oxidative stress cascade, reduces overproduction of ROS	[44]
Neferine	bisbenzyl isoquinoline alkaloid	*Nelumbo nucifera* (Nelumbonaceae).	decreasing the expression of CCL5 and CCR5 mRNA	[45]
Oxymatrine	quinolizidine	*Sophora flavescens* (family Fabaceae)	decreases blood glucose, urinary protein and albumin excretion, serum creatinine, and blood urea nitrogen	[46]
Piperine		*Piper sp.*	showed bio-enhancing effects with metformin	[47]
Sanguinarine	benzophenanthridine alkaloid		excellent intercalator of DNA and RNA	[48]
Catechins		tea and cacao products	protective effects against oxidative damage and enhancing SOD, glutathione S-transferase (GST), and CAT activities of catechins	[49]
2. Flavonoids				
Fisetin		wide variety of plants	reduces blood glucose, improves glucose homeostasis through the inhibition of gluconeogenic enzymes, and increases the level and activity of glyoxalase	[50]
Kaempferol	natural flavonol	wide variety of plants	antioxidant by reducing oxidative stress. It promotes insulin sensitivity and preserves pancreatic β-cell mass	[51]
Luteolin	flavone	aromatic flowering plants	treating diabetic nephropathy	[52]
Naringenin	flavanone	grapefruit	anti-inflammatory and anti-fibrotic activities, decreased expression of interleukin	[53]
Quercetin	flavonol	wide variety of plants	decreased the cell percentages of G(0)/G(1) phase, Smad 2/3 expression, laminin, and type IV collagen and TGF-β (1) mRNA levels	[54]
Rutin	flavonoid	many types of fruits and vegetables	improves glucose homeo stasis by altering glycolytic and gluconeogenic enzymes.	[55]
Morin	flavonoid	*Morus alba*	activator and sensitizer of the insulin receptor stimulating the metabolic pathways.	[56]
Silymarin	complex of flavonoids	milk thistle plant	nephroprotective effects and cardiomyopathy treatment	[57]
3. Terpenoids				
Boswellic Acids	pentacyclic triterpene	*Boswellia* species	stimulating β cells to release more insulin	[58]
Celastrol	triterpene	*Tripterygium wilfordii*	improves insulin resistance, and attenuates renal injury, suppresses the obesity	[59]

Oleanolic Acid	triterpenoid	fruits, herbs, and vegetables	process via increasing antioxidant capacity reduces hyperglycemia	[60]
Ursolic Acid	pentacyclic triterpenoid	*Eriobotrya japonica*	inhibit PTP1B and improve insulin sensitivity	[61]
Triptolide	diterpenoid	*Tripterygium wilfordii.*	alleviated glomerular hypertrophy and podocyte injury	[62]
4. Polysaccharides				
Galactomannan		*Amorphophallus konjac*	delay the rate of glucose absorption	[63]
Inulin		*Helianthus tuberosus*	modulation of blood metabolites and liver enzymes	[64]
5. Others				
Resveratrol	Polyphenol	pea nuts, berries, red grapes	antioxidants, protecting the body against damage that can put you at higher risk for things like cancer and heart disease	[65]
Piceatannol	stilbenoid, a type of phenolic compound	red wine, grapes, passion fruit, white tea	enhanced glucose tolerance	[66]
Curcumin	polyphenol	*Curcuma longa*	effective in liver disorders, adipocyte dysfunction, neuropathy, nephropathy, vascular diseases, pancreatic disorders	[67]
Tocopherol	Vitamin	wide variety of plants	attenuates diabetic nephropathy by the involvement of the NF-*k*B signaling pathway	[68]
Ellagic Acid	phenol	fruits and vegetables	stimulates insulin secretion and decreases glucose intolerance	[69]
Gambogic Acid	pyranoxanthone	*Garcinia* plant species	ameliorates diabetes-induced proliferative retinopathy through inhibition of the HIF-1α/VEGF expression	[70]
Garcinol	polyisoprenylated benzophenone	*Garcinia indica*	decreases plasma insulin, homeostasis model assessment of β-cell function (HOMA-β-cell) functioning index, glycogen, high-density lipoprotein cholesterol, body weight, and antioxidant enzyme activities	[71]
Honokiol	polyphenol lignan	*Magnolia sp.*	increases phosphorylations and downstream insulin signaling factors	[72]

Conclusion

Natural resources are still perceived as strong candidates for research and development and play a crucial role in pharmaceutical research programs. Furthermore, many pharmaceutical herbs have a rich mine for bioactive compounds that are notably free of unwanted side effects and have effective pharmacological action. Information on the biological activities of several biomedicinal plants is now increasing immensely. However, it is not practical to specify the output of a multi-component mixture, because it is present in plant extracts containing a wide variety of phytochemical constituents. Secondary metabolites may serve as lead chemicals for the discovery of potentially active and safer antidiabetic agents of various new groups. The description of the usual modes of action of their components and the isolated pure compounds should be given further consideration. However, the field of assumptions and interpretation seems to be endless because of the constant molecular biological studies. Therefore, a great deal of effort should be made to refine a protocol for antidiabetic analysis of extracts from various plants as well as extracted biologically active compounds for the emergence of new potential herbal antidiabetic drugs.

Acknowledgement: The authors are highly thankful to the Chancellor, Integral University for their support and guidance.

References

[1] Maiti, R., Jana, D., Das, U.K., and Ghosh, D. 2004. The antidiabetic effect of aqueous extract of the seed of Tamarindus indicates streptozotocin-induced diabetic rats. Journal of ethnopharmacology, 92 (1):85-91.

[2] Wadkar, K.A., Magdum, C.S., Patil, S.S., and Naikwade, N.S. 2008. Antidiabetic potential and Indian horticultural plants. Journal of Herbal Medicine and Toxicology, 2(1): 45-50.

[3] Kokar, R., and Mantha, S.V. 1998. Increased oxidative stress in rat liver & pancreas during the progression of streptozotocin induced diabetes. Journal of Clinical science,19:623-632

[4] Gupta, A.K. 1986. Quality Standards of Indian Horticultural Plants, ICMR, New Delhi, I:168-173.

[5] Tripathi, K.D. 2007. Essential medical pharmacology, Sixth edition, 254-274.

[6] Grover, J.K., Yadav, S. and Vats, V. 2002. Horticultural plants in India with antidiabetic potential. Journal of ethnopharmacology, 81: 81-100.

[7] Ravi, K., Ramachandran, B. and Subramanian, S. 2004. Effect of Eugenia Jambolana seed kernel on antioxidant defense system in streptozotocin induced diabetes in rats. Life Sciences, 75: 2717-2731.

[8] Ajay, S.S. 2009. Hypoglycemic activity of Coccinia indica (Cucurbitaceae) leaves. International Journal of Pharm Tech Research,2009; 1: 892-893.

[9] Ohadoma, S.C. and Michael, H.U. 2011. Effects of co-administration of methanol leaf extract of Catharanthus roseuson the hypoglycemic activity of metformin and glibenclamide in rats. Asian Pacific Journal of Tropical Medicine, 4: 475-477.

[10] Kumar, R., Kumar, D., Pate, S. and Prasad, K., Kirshnamurthy, S. and Siva, H. 2011. Antidiabetic activity of alcoholic leaves extract of Alangium lamarckiiThwaites on streptozotocin-nicotinamide induced type 2 diabetic rats. Asian Pacific Journal of Tropical Medicine: 904-909.

[11] Kumar, D., Kumar, S., Kohli, S., Arya, R. and Gupta, J. 2011. Antidiabetic activity of methanolic bark extract of Albizia odoratissima Benth in alloxan induced diabetic albino mice.Asian Pacific Journal of Tropical Medicine: 900-903.

[12] Ansari, S.H. Essentials of Pharmacognosy. First edition. Birla Prakashan, Delhi – 32, 2005-2006. 588-590.

[13] Tiwari, P., Mishra, B. N., and Sangwan, N. S. 2014. Phytochemical and pharmacological properties of Gymnema sylvestre: An important horticultural plant. BioMed Research International, 830285. https://doi.org/10.1155/2014/830285.

[14] Joseph, B. and Jini, D. 2013. Antidiabetic effects of Momordica charantia (Bitter melon) and its horticultural potency. Asian Pacific Journal of Tropical Disease, 3, 93–102.

[15] Shinde, V.M., Dhalwal, K., Potdar, M. and Mahadik, K.R. 2009. Application of Quality Control Principles to Herbal Drugs. International Journal of Phytomedicine, 1:4- 8.

[16] Vadivelan, R., Gopala Krishnan, R. and Kannan, R. 2018. Antidiabetic potential of Asparagus racemosus Willd leaf extracts through inhibition of α-amylase and α-glucosidase. Journal of traditional and complementary medicine, 9, 1–4. https://doi.org/10.1016/j.jtcme.2017.10.004.

[17] Tripathi, A.K., Gupta, P.S. and Singh, S.K. 2019. Antidiabetic, anti-hyperlipidemia and antioxidant activities of *Bauhinia variegata* flower extract.Biocatalysis and Agricultural Biotechnology, 19:101142.

[18] Rajesh, P., Sonia, S.S., Reddy, Y.V. and Kumar, M.S. 2016. Anti-Diabetic Profile of *Cinnamon* Powder Extract in Experimental Diabetic Animals. *International Journal of Pharmaceutical* Sciences and *Research*, 7: 824-28.

[19] Michel, C.G., Nesseem, D.I. and Ismail, M.F. 2011. Anti-diabetic activity and stability study of the formulated leaf extract of *Zizyphus spina-christi* (L.) Willd with the influence of seasonal variation. Journal of Ethnopharmacology, 133:53-62.

[20] Devi, S. and Kumar, M. 2017. In-vivo Antidiabetic Activity of Methanolic Extract of Euphorbia hirta L. International Journal of Diabetes and Endocrinology, 2:36-39.

[21] Singh, R., Srivastava, R. K. and Srivastava, A. 2020. Pharmacological evaluation of anti-diabetic effects of combined doses of Momordica charantia and Stevia rebaudiana against STZ induced diabetes model. *International Journal of Pharmaceutical* Sciences and *Research*, 11:832-38.

[22] Dhayaney, V. and Sibi, G. 2019. Pterocarpus Marsupium for the Treatment of Diabetes and Other Disorders. Journal of Complementary Medicine & Alternative Healthcare, 9: 555754.

[23] Nawaz, H., Shad, M. A. and Muzaffar, S. 2018. Phytochemical Composition and Antioxidant Potential of Brassica, Brassica Germplasm - Characterization, Breeding and Utilization, Mohamed Ahmed El-Esawi, IntechOpen: 76120.

[24] Lia Y., Xub J., Yuan C., Liua T., Ma H., Liu T., Lui F., Seeram N P., Mu Y., Huang X., Li L. 2017. Chemical composition and anti-hyperglycaemic effects of triterpenoid enriched Eugenia jambolana Lam. berry extract.

Journal of Functional Foods, 28: 1-10.
[25] Mallick, C., Chatterjee, K., Biswas, M.G. and Ghosh, D. 2007. The antihyperglycemic effect of the separate and composite extract of root of Musa paradisiaca and leaf of Coccinia indica in streptozotocin induced diabetic male albino rats. African Journal of Traditional, Complementary and Alternative Medicine, 4 : 362 - 371.
[26] Al-Shaqha, W.M., Khan, M., Salam, N., Azzi, A., and Chaudhary, A. A. 2015. Anti-diabetic potential of Catharanthus roseus Linn and its effect on the glucose transport gene (GLUT-2 and GLUT-4) in streptozotocin induced diabetic wistar rats. BMC Complement Alternative Medicine, 15:379.
[27] Kumar, R., Pate, D.K., Prasad, S.K., Sairam, K. and Hemalatha, S. 2011. Antidiabetic activity of alcoholic leaves extract of Alangium lamarckii Thwaites on streptozotocin-nicotinamide induced type 2 diabetic rats. Asian Pacific Journal of Tropical Medicine, 4:904-909.
[28] Ahmed, D., Kumar, V., Verma, A., Gupta, P. S., Kumar, H., Dhingra, V., Mishra, V., and Sharma, M. 2014. Antidiabetic, renal/hepatic/pancreas/cardiac protective and antioxidant potential of methanol/dichloromethane extract of Albizzia LebbeckBenth. stem bark (ALEx) on streptozotocin induced diabetic rats. BMC Complementary and Alternative Medicine, 14: 243.
[29] Ibeh, B.O. and Ezeaja, M.I. 2011. Preliminary study of antidiabetic activity of the methanolic leaf extract of Axonopus compressus (P. Beauv) in alloxan-induced diabetic rats. Journal of Ethnopharmacology, 138:713-716.
[30] Maithili, V., Dhanabal, S. P., Mahendran, S., & Vadivelan, R. 2011. Antidiabetic activity of ethanolic extract of tubers of Dioscorea alata in alloxan induced diabetic rats. Indian journal of Pharmacology, 43:455–459.
[31] Khan, F., Sarker, M.M.R., Ming, L.C., Mohamed, I.N., Zhao, C., Sheikh, B.Y., Tsong, H.F. and Rashid, M.A. 2019. Comprehensive Review on Phytochemicals, Pharmacological and Clinical Potentials of Gymnema sylvestre. Frontiers in Pharmacology 10:1223.
[32] Joseph, B., and Jini, D. 2013. Antidiabetic effects of Momordica charantia (Bitter melon) and its horticultural potency. Asian Pacific Journal of Tropical Disease, 3: 93–102.
[33] Alzohairy, M. A. 2016. Therapeutics Role of Azadirachta indica (Neem) and their Active Constituents in Diseases Prevention and Treatment. Evidence-based Complementary and Alternative Medicine: eCAM, 7382506. https://doi.org/10.1155/2016/7382506
[34] Vadivelan, R., Gopala, K.R., and Kannan, R. 2018. Antidiabetic potential of Asparagus racemosus Willd leaf extracts through inhibition of α-amylase and α-glucosidase. Journal of Traditional and Complementary Medicine, 9:1–4.
[35] Kumar, P., Baraiya, S., Gaidhani, S. N., Gupta, M. D. and Wanjari, M. M. 2012. Antidiabetic activity of stem bark of Bauhinia variegata in alloxan-induced hyperglycemic rats. Journal of Pharmacology & Pharmacotherapeutics, 3, 64–66.
[36] Ranasinghe, P., Galappaththy, P., Constantine, G.R. 2017. Cinnamom umzeylanicum (Ceylon cinnamon) as a potential pharmaceutical agent for type-2 Diabetes mellitus: study protocol for a randomized controlled trial. Trials 18: 446.
[37] Abdel-Zaher, A.O., Salim, S.Y., Assaf, M.H. and Abdel-Hady, R.H. 2005. Antidiabetic activity and toxicity of Zizyphus spina-christi leaves. Journal of Ethnopharmacology, 101: 129-138.
[38] Kumar, S., Malhotra, R., and Kumar, D. 2010. Antidiabetic and Free Radicals Scavenging Potential of Euphorbia hirta Flower Extract. Indian Journal of Pharmaceutical Sciences, 72:533–537.
[39] Shivanna, N., Naika, M., Khanum, F. and Kaul, V.K. 2013. Antioxidant, anti-diabetic and renal protective properties of Stevia rebaudiana.Journal of Diabetes and Its Complications. 27(2):103-113.
[40] Bharti, S. K., Krishnan, S., Kumar, A., and Kumar, A. 2018. Antidiabetic phytoconstituents and their mode of action on metabolic pathways. Therapeutic Advances in Endocrinology and Metabolism, 81–100.
[41] Pan, G.Y., Huang, Z.J., Wang, G.J. 2003. The antihyperglycaemic activity of berberine arises from a decrease of glucose absorption. Planta Medica, 69 :632-636.
[42] Wiedemann, M., Gurrola-Diaz, C.M., Vargas-Guerrero, B., Wink, M., Garcia-Lopez, P.M. and Dufer, M. 2015. Lupanine Improves Glucose Homeostasis by Influencing KATP Channels and Insulin Gene Expression.Molecules, 20: 19085–19100.
[43] Lau, Y.S., Tian, X.Y., Mustafa, M.R.and Murugan, D. 2013. Boldine improves endothelial function in diabetic db/db mice through inhibition of angiotensin II-mediated BMP4oxidative stress cascade. *British Journal of Pharmacology*, 170:1190–1198.
[44] Li, G., Xu, H., Zhu, S., Xu, W., Qin, S., Liu, S., Tu, G., Peng, H., Qiu S., Yu, S., et al. 2013. Effects of neferine on CCL5 and CCR5 expression in SCG of type 2 diabetic rats. *Brain Research Bulletin*, 90:79–87.
[45] Oza, M.J. and Kulkarni, Y.A. 2016. Phytochemical and complication in type 2 Diabetes—An

update. International Journal of Pharmaceutical Sciences and Research, 7:14–24.

[46] Atal, S., Atal, S., Vyas, S. and Phadnis, P. 2016. Bio-enhancing effect of piperine with metformin on lowering blood glucose level in alloxan induced diabetic mice. *Pharmacognosy* Research. 8:56-60.

[47] Wang, Q., Zhao, Z., Shang, J. and Xia, W. 2014. Targets and candidate agents for type 2 diabetes treatment with computational bioinformatics approach. Journal of Diabetes Research. 763936.

[48] Mackenzie, T., Leary, L. and Brooks, W.B. 2007. The effect of an extract of green and black tea on glucose control in adults with type 2 Diabetes mellitus: double-blind randomized study.Metabolism, 56:1340-1344.

[49] Prasath, G.S., Pillai, S.I. and Subramanian, S.P. 2014. Fisetin improves glucose homeostasis through the inhibition of gluconeogenic enzymes in hepatic tissues of streptozotocin induced diabetic rats. *European* Journal of *Pharmacology*, 740:248–254.

[50] Alkhalidy, H., Moore, W., Zhang,Y., McMillan, R., Wang, A., Ali, M., Suh, K.S., Zhen, W., Cheng, Z. and Jia, Z. 2015. Small molecule kaempferol promotes insulin sensitivity and preserved pancreatic b-cell mass in middle-aged obese diabetic mice. Journal of Diabetes Research, 532984.

[51] Wang, G.G., Lu, X.H., Li, W., Zhao, X. and Zhang, C. 2011. Protective effects of luteolin on diabetic nephropathy in stz-induced diabetic rats. Evidence Based Complement. Alternative Medicine, 323171.

[52] Tsai, S.J., Huang, C.S., Mong, M.C., Kam, W.Y., Huang, H.Y. and Yin, M.C. 2012). Anti-inflammatory and antifibrotic effects of naringenin in diabetic mice. Journal of Agricultural and Food Chemistry, 60:514–521.

[53] Li, X.H., Xin, X., Wang, Y., Wu, J.Z., Jin, Z.D., Ma, L.N., Nie, C.J., Xiao, X., Hu, Y. and Jin, M.W. 2013. Pentamethylquercetin protects against diabetes-related cognitive deficits in diabetic goto-kakizaki rats.*Journal* of *Alzheimer's disease*, 34:755–767.

[54] Prince, P. and Kamalakkannan, N. 2006. Rutin improves glucose homeostasis in streptozotocin diabetic tissues by altering glycolytic and gluconeogenic enzymes. Journal of Biochemical and Molecular Toxicology, 20 :96–102.

[55] Paoli, P., Cirri, P., Caselli, A., Ranaldi, F., Bruschi, G., Santi, A. and Camici, G. The insulin-mimetic effect of Morin: A promising molecule in diabetes treatment. Biochimica et Biophysica Acta, 1830:3102-3111.

[56] Bijak, M. 2017. Silybin, a major bioactive component of milk thistle (*Silybum marianum* L.Gaernt.)-Chemistry, Bioavailability and Metabolism. Molecules, 22(11):1942.

[57] Madhuri, K. and Naik, P.R. 2017. Modulatory effect of garcinol in streptozotocin-induced diabetic wistar rats. Archives of *Physiology* and *Biochemistry*, 123:322–329.

[58] Jadhav, R. and Puchchakala, G. 2011. Hypoglycemic and antidiabetic activity of flavonoids: Boswellic acid, ellagic acid, quercetin, rutin on streptozotocin-nicotamide induced type 2 diabetic rats. International Journal of Pharmacy and Pharmaceutical Sciences, 4:251–256.

[59] Kim, J.E., Lee, M.H., Nam, D.H., Song, H.K., Kang, Y.S., Lee, J.E., et al. 2013. Celastrol, an nf-κB inhibitor, improves insulin resistance and attenuates renal injury in db/db mice. PLoS ONE, 8(4):e62068.

[60] Camer, D., Yu, Y., Szabo, A. and Huang X.F. 2014. The molecular mechanisms underpinning the therapeutic properties of oleanolic acid, its isomer and derivatives for type 2 diabetes and associated complications. Molecular Nutrition and Food Research, 58(8):1750-1759.

[61] Mancha-Ramirez, A.M. and Slaga, T.J. 2016. Ursolic Acid and Chronic Disease: An Overview of UA's Effects on Prevention and Treatment of Obesity and Cancer. Advances in Experimental Medicine and Biology, 928:75-96.

[62] Huang, S.H., Lin, G.J., Chu, C.H., Yu, J.C., Chen, T.W., Chen, Y.W., Chien, M.W., Chu, C.C. and Sytwu, H.K. 2013. Triptolide ameliorates autoimmune diabetes and prolongs islet graft survival in nonobese diabetic mice. Pancreas, 42:442–451.

[63] Doi, K., Matsuura, M., Kawara, A. and Baba, S. 1979. Treatment of diabetes with glucomannan (konjac mannan). Lancet, 1:987–988.

[64] Ma, X.Y., Zhang, L.H., Shao, H.B., Xu, G., Zhang, F., Ni, F.T. and Brestic, M. 2011. Jerusalem artichoke (*Helianthus tuberosus*), a medicinal salt-resistant plant has high adaptability and multiple-use values. Journal of *Medicinal Plants* Research, 5:1272–1279.

[65] Minakawa, M., Miura, Y. and Yagasaki, K. 2012. Piceatannol, a resveratrol derivative, promotes glucose uptake through glucose transporter 4 translocation to plasma membrane in l6 myocytes and suppresses blood glucose levels in type 2 diabetic model db/db mice. Biochemical and Biophysical Research Communications, 422:469-475.

[66] Oritani, Y., Okitsu, T., Nishimura, E., et al. 2016. Enhanced glucose tolerance by intravascularly administered piceatannol in freely moving healthy rats. Biochemical and Biophysical Research Communications, 470:753-758.

[67] Kunwar, A. and Priyadarsini, K.I. 2016. Curcumin and its Role in Chronic Diseases.Advances in Experimental

Medicine and Biology, 928:1-25.

[68] Haghighat, N., Vafa, M., Eghtesadi, S., Heidari, I., Hosseini, A. and Rostami, A. 2014. The effects of tocotrienols added to canola oil on microalbuminuria, inflammation, and nitrosative stress in patients with type 2 diabetes: A randomized, double-blind, placebo-controlled trial. International Journal of Preventive Medicine, 5:617–623.

[69] Fatima, N., Hafizur, R.M., Hameed, A., Ahmed, S., Nisar, M. and Kabir, N. 2017. Ellagic acid in *Emblica officinalis* exerts anti-diabetic activity through the action on β-cells of pancreas.*European Journal of Nutrition*, 56:591-601.

[70] Cui, J., Gong, R., Hu, S., Cai, L. and Chen, L. 2018. Gambogic acid ameliorates diabetes-induced proliferative retinopathy through inhibition of the hif-1α/vegf expression via targeting PI3K/AKT pathway. Life Sciences, 192:293-303.

[71] Li, C.G., Ni, C.L., Yang, M., Tang, Y.Z., Li, Z., Zhu, Y.J., Jiang, Z.H., Sun, B. and Li, C.J. 2018. Honokiol protects pancreatic β cell against high glucose and intermittent hypoxia-induced injury by activating Nrf2/ARE pathway in vitro and In vivo. Biomedicine and Pharmacotherapy, 97; 1229-1237.

[72] Poivre, M., and Duez, P. 2017. Biological activity and toxicity of the Chinese herb Magnolia officinalis Rehder & E. Wilson (Houpo) and its constituents. Journal of Zhejiang University. Science. B, 18:194–214.

Publication History

Received	29.07.2020
Revised	19.08.2020
Accepted	15.09.2020
Online	30.09.2020