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# A review on Strength of Medicinal Plants against Diabetes Mellitus

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**Abstract**
Diabetes mellitus is an acute metabolic disarray and in traditional medicine many plants were used in abundance for treating diabetes. Because they have no harmful impacts and mostly available drugs are obtained through these medicinal plants. Purpose of the review is to select and highlight the importance of medicinal plants traditionally used against diabetics. Also checking physical properties and counting ADMIT compounds. Studies on plants with diabetic resistance mainly due to the existence of a secondary metabolite. .Medicinal plants are not only productive in treating diabetes, but in lot of cases have wide range of impacts on more ill conditions, together with DM discrepancies. Those plants could be suitable alternative or supplement as convenient anti-diabetic drugs. Therefore, the data presented in this review will help researchers to develop alternative approaches to the cure diabetes rather than oral hypoglycemic agents and insulin, thereby reducing diabetes and related disorder.

**Keywords**: diabetes, medicinal plants, herbal, symptom, treatment.

**Introduction**:

Diabetes mellitus are the most common atrocious disease resulting to a group of metabolic disorders depicted by hyperglycemia, evolving in secretion of insulin, activity of insulin, or couple. It is said to be fifth major reason of illness and death in 21st century (Mukesh.,

2013). As stated by enumeration, 2.8% population of the world suffers with this disease and it is estimated that it will extend by more than 5.4% to 20% (Kazi, 2014).

**Diabetes Epidemiology**

The term diabetes comes out of Greek designation "diab"(refers the heavy cycle thirst and frequent urination); and a Latin word 'Mellitus' means "Sweeter than honey" (indicates the existence of sugar in Urine). Greeks had idea of disease from polyuria and waste of body, whereas Cappadocia Aretaeus allude to sickness of dehydration. As stated by former Hindu, 'diabetes (medical practitioner Madhumeha)' is a disorder in which effected individual discharge sweet urine also reveal sweetness all over the body.

**Prevalence**

Diabetes mellitus causes noteable opperssion and deaths due to microvascular discrepancies such as retinopathy, heart attack, stroke and peripheral vascular diseases (F.Thévenod., 2008) . Worldwide, it is one of the most important public health issue. Diabetes-related incidence and outcome are more common in countries such as India (31.7% and the United States (17.7%)) (AK Balaraman., 2010). It is estimated that by 2030 the amount of people affecting from diabetes will be the highest in the United States India and China (TS Fröde 2008).

**Types & Causes of diabetes mellitus**

There are 3 sorts of Diabetes specifically Insulin Dependent Diabetes Mellitus, Non- Insulin Dependent Diabetes Mellitus and Gestational (Hui H.et.al 2009). NIDDM (Type II Diabetes) is also known as adult onset Diabetes mellitus, the more widespread form affecting 90-95% of population with diabetic. Depending on cause is the type of diabetes, type 1 is mostly occurs due to beta-cell devestation, umpired by the immunity system and mostly occurs in children, while the other type 2 diabetes is mainly cause due to resistance of insulin and occurs in the elder people with respective insulin insufficiency. It is related with genetics and lifestyle (Craig. 2009). The main indicative basis for diabetes are blood sugar levels and the absence or presence of indications such as blurred vision and loss of weight, along with polyarthritis, polydipsia and fatigue, glycosuria and ketonuria (Warjeet, 2011).

**Available Treatment for diabetes**

Treatment of diabetes contemplate as a major worldwide issue and a victorious treatment has not yet been found. Although the frontline medication for diabetes now a days is insulin therapy and oral hypoglycemic agents but have few negative impacts and fail to be effective against diabetic complications( SVenkatesh. 2010).

**Therapeutic uses**

In ethno medicinal practices and Ayurvedic medicine system for the treatment of diabetes, huge amount of medicinal plants and their parts are utilize (H Pareek, .2009). From the ethnobatanical data, anti-diabetic potential has been found in approximately 800 plants. (DK Patel. 2011). Despite the blossoming of various synthetic medicines for the treatment of diabetes yet there are minimum amount of drugs available (S Dewanjee. ,2009)To reduce oxidative stress many restorative plants having antioxidant possessions are beneficial for diabetes and its damages (A .Baradaran,.2018) and these days, mostly accessible drugs are plant derived(DS .Fabricant ,.2001) . In addition to multiple hypoglycemic activities, research has

shown that anti-diabetic plants have many worthwhile features like antisupersensitive, preservation of neuronal integrity and retinoprotective enterprises that are utilized in opposition to common problems of diabetes. Therefore, the utilization of plants could be turn into advantage for control of diabetes and related problems (E .Aghadavoud, 2017).

**Ethno pharmacological data**

Approximately 200 natural molecules extracted through plants have been considered to have blood sugar decreasing effects. Ingredients may include carbohydrates, alkaloids, flavonoids, steroids, glycosides, amino acids, and terpenoids, phenolics, glycopptides, peptides, lipids, and iridoids. Herbal originated anti-diabetic products are now mostly available in the market. Above 1,200 plants species have been recorded for activities based on ethnobotanical applications (S. Warjeet, 2011). Anti-hyperglycemic effects caused by medication through plants are frequent due to their capacity to enhance pancreatic tissue function, either by rising insulin secretion or by diminishing glucose absorption from intestine.

**Biological activity of natural plant components**:

There are multiple bioactive compounds found in medicinal plants that improve level of glucose in blood and also boost the hyperlipidemia, enhance secretion of insulin, enforce the effects of antioxidant, ameliorate the function of kidney, and also tend to neuropathy and diabetic retinopathy.

The secondary metabolites of plants includes : alkaloids, flavonoids, polysaccharides and terpenoids that in medicinal plants are accomplish ubiquitous and mostly reported due to anti-diabetic potential (Chen,.2015). Additionally Flavonoids appeared as supportive impacts in case of diabetic inconveniences such as hypertension, heart disease, retinopathy, and neuropathy. likewise, the terpenoidsoleanolic acid, corosolic acid, glycyrrhetinic acid, gymnemic acid andbetulinic acid, trigonelline, catharanthine, the alkaloids, cryptolepine, vindoline,berberine and polysaccharides derived from pumpkin, ginseng, mulberry, tea, guava, and peach-gum have demonstrated an assorted scope of hostile to diabetic impacts in vitro and in vivo. (Gaikwad,. 2014).

A few terpenes, sesquiterpenes, diterpenes and triterpenes, proceed to revive the delivery of insulin and decline accumulation of reactive oxygen species (Afolayan,.2011), hence bringing about the standardization of blood glucose levels. As they likewise show hypolipidemic action (Eliza.2009), in the control and treatment of diabetes these substances may be valuable. Coumarins are the member of a category of plant constituents having diverse biological processes, such as, prevention of diseases ,antioxidant effects and progress of growth; differentiation and regulation of cell growth (Thome, 2012).

Alkaloids are nitrogen containing heterocyclic rings with cyclic amines. By stimulating secretion of insulin and increasing uptake of blood glucose in peripheral tissues antidiabetic effects exerted by them, and might have the option to prevent diabetic complexities, for example, neuronal and renal damage (H.Yankuzo,.2011). . Phenolic plant parts assume a significant job for the avoidance of diabetes difficulties through diminishing the arrangement of ROS, and ensuring kidney function (Suman, 2010).

For the effect of anti-diabetic the biochemical processes of medicinal plants specified such as, inhibition of intestinal glucose digestion, and absorption, stimulating release of insulin through B-cells of pancreas also modulation of enzymes like, glucose-6-phosphatase aldosereductase, lactate dehydrogenase and lipoprotein lipase.

**Evidences from literature**

In literature different articles found at medicinal plants which are implicit for the diabetic treatment. There is broad conventional utilization of medicinal plants in many traditions for ebullience to medicate diabetes (J Grover, 2002).

In Persian medicinal system most of the drugs are natural agents. Pharmaceutical science and practices play a significant role in Persian medicine (Larijani, 2006).

In Chinese medicine, the conviction is to utilize not to just pivot on the cure of hyperglycemia even so related to discrepancies of diabetes. Li et al [2004] reported, 82 natural plants with diabetic effect utilized in orthodox medicine for handling diabetes through *Radix ginseng, Alliisativi bulbus , Rhizoma anemarrhenae, Radix paeoniae alba, Morus alba, Radix paeoniae, , Radix puerariae*, and *Gymnema sylvestre* (Zheng.,2004).

Bedouin ethnic medication contains plants with 22 species of semi- desert and desert as anti-diabetic in which, *Teucrium polium, Larrea tridentate, Artemisia herba-alba Ziziphusspina-christi,* and *Balanites aegyptica* are mentioned ( Harlev et al,. 2013).

A review by Moradi et al. [2018] in his review enlist different medicinal plants which are effective against diabetes found worldwide such as, in Afghanistan and Iran *Ferula assafoetida* use, in India *Trigonella foenum-graecum, Liriope spicata* in China and East Asia *Combretum micranthum* in Africa, *Bauhinia forficate* in Brazil, Argentina and Peru, in Mexico *Symplocos coccinea,* furthermore *Allium sativum, Aloe vera.*Burm, and *Coccinia indica* that are circulated around the world. For type 2 diabetic patients Aniseed ,cumin, bay leaves, cardamom, dill, ginger, hops, saffron, rosemary, sage and turmeric are recommended as effective (Pereira,.2019).

In Bangladesh Traditional medicinal plants are mostly utilize to treat diabetes. Through ethnobotanical survey of selected rural and urban areas ,belonging to 25 families total 37 medicinal plants were recorded as effective for the treating diabetes. The most frequently mentioned plants were *Coccinia indica, Azadirachta indica, Trigonella foenum-graecum, Syzygium cumini, Terminalia chebula, Ficus racemosa, Swietenia mahagoni,Momordica charantia*.(Ocvirk, .2013)

Kooti et al, [2016] reported plants having anti diabetic potential are*; Aloe barbadensis Miller, Artemisia herba,Achyranthesaspera, Aeglem armelose, Andrographis paniculata,Allium sativum (garlic), Acosmium panamense, Averrhova bilimbi , Annona squamosa, Acacia Arabica, Argyreia nervosa,Azadirachta indica, Bryonia alba, Biophytum sensitivum,Brassica nigra, Barleria prionitis, Cajanus cajan, Caesalpinia bonducella, Carum carvi, Casearia esculenta, Cichorium intybus, Citrulus colocynthis, Chamaemelum nobile, Coriandrum sativum, Dorema aucheri, Eclipta alba, Fraxinu sexcersior, Helicteres isora, Hypoxis hemerocallidea, Lepidium sativum, Mangifera indica, Myrciabella, Nigella sativa, Ocimum sanctum, Origanium vulgare, Phyllanthus amarus, Prangos ferulacea (L.) lindl., Securinegra virosa*.

Nazarian et al, [2018] Studies related to antidiabetic action of restorative plants have shown nearly all of them produce hypoglycemic mechanisms by revitalizing secretion of insulin (*Trigonella foenum graecum*), augmenting peroxisome proliferator-activated receptors (*Momordica charantia* L.), inhibiting α-glucosidase or α-amylase (*Azadirachta indica*), glucagon-like peptide-1 release (*Citrus aurantium*), advanced glycation end product formation (*Rehmannia glutinosa*), antioxidant activity plus free radical scavenging against reactive oxygen or nitrogen species RNS /ROS (*T. foenum graecum*), assessing or up-regulating translocation of glucose transporter 4 type GLUT-4 *(A. cepa*) and halting development of insulin resistance(*Galega officinalis, Ocimum sanctum*).

Patel DK [2012] suggest that etiological and pathophysiological characteristics of diabetes coupled with experimentally screening model escorted by related process and treatment mostly used these days. The plant families with dynamic effects of hypoglycaemic include Liliaceae, Lamiaceae, Leguminoseae, Asteraceae, Cucurbitaceae, Euphorbiaceae,s Moraceae, Araliaceae, and Rosaceae.For evaluating anti diabetic activity of a particular drug streptozotocin and alloxan are excessively used .Here is the list of plants that are pharmacologically evaluated in the alloxan urged diabetic rat's model system. *Achyranthes rubrofusca, Argyriea cuneata, Andrographis paniculata, Acacia Arabica, Barleria prionitis, Cassia grandis, Ceriops decandra, Capparis deciduas, Colocasia esculenta, Costusigneus, Eucalyptus citriodora, Ficus bengalensis, Heinsia crinata, Helicteres ssisora, Juglans regia, Ipomoea reniformis, Limonia acidissima, Lantana aculeate, Luffa aegyptiaca, Momordic charantia, Mukiamader aspatana, Ocimum gratissimum, Nymphaea pubescens, Paspalum scrobiculatum, Phyllanthus niruri, Phyllanthus simplex, Phoenix dactylifera, Pongamia pinnata, Solanum nigrum, Sphenostylis stenocarpa, Tephrosia villosa, Trigonella foenum-graecum, Triumfettar homboidea, Vaccinium arctostaphylos, Vernonia amygdalina, Zaleya decandra, Zizyphus mauritiana.*

Gushiken [2015] reported an outline based on medicinal plants extracts, concerning the mode of activity proceed, the basic rules of antidiabetic mechanism and show the recently investigated hypoglycemically favourable medicinal plants. The main characteristic feature of diabetes is hyperglycemia, which reflects the deterioration in the use of glucose due to a faulty or poor response to insulin secretion. When assessing pharmacologically, most of the plants appointed as antidiabetic compounds have been shown to display antihyperglycemic and hypoglycemic activities, and to hold chemical constituents that may be used as new antidiabetic agents.

Odeyemi [2018] probe a plan to empower accessible restorative plants utilize for the control of diabetes by evaluating the medicinal description in the Eastern Cape, of South Africa. Moreover studies for the recognition of the active compounds of medicinal plants so far need to be accomplish; this may escort advance particles in discovery and progress of drugs.

## Conclusion

Diabetes mellitus is a complaint accompanying high sugar level in blood, a condition in which metabolism of glucose is not effectively regulated by the body.

Plants have been used for centuries as main source of wide variety of curative matter for sustaining human health and also improved the quality of human life through disease prevention and treatment. Scientists are exploring countries within traditional medicine to find future antidiabetic agents.

The people suffering from diabetes is increasing at terrible rate worldwide .In developing countries controlling of glucose levels in blood with fewer negative impacts medicinal plants are frequently utilize as possible approaches to treat diabetes and some chronic complication of diabetes such as blindness, heart disease, and kidney failure.

The most common bioactive compounds of medicinal plants are phenolics, flavonoids, tannins, and alkaloids and the importance of the anti-diabetic plants are due to the existence of these compounds. The mechanisms of actions for hypoglycemic plants include: increasing of glucoses absorption by muscle and fat tissues, increasing insulin secretion and prevention of absorption of glucose from the liver cell and intestine.

Most of the anti-diabetic plants belonging to certain families, are identified as Liliaceae, Leguminoseae, Araliaceae, Cucurbitaceae, Lamiaceae, Asteraceae, Rosaceae, Moraceae, and Euphorbiaceae.

The plants with anti-diabetic potentiality are appraised in experiments or clinical practices. In this study it is worth noting that, rats are the mostly used animal model for the investigation of anti-diabetic activity from plant extracts. For screening methods of anti-diabetic drugs alloxan and streptozotocin induced diabetes model are used.

Some ingredients obtained from medicinal plants may have curative potential, while others may generate hypoglycemia as consequences and may even be virulent, specifically in relation with hepatocytes. Before in vivo studies it is necessary to explore the anti-diabetic activities and toxicity of plants in vitro to verify the process for the reason that many hypoglycemic activities of plants cause side effect due to their toxicity. Therefore, as the prevalence of diabetes and the conventional management increase simultaneously, the purification and segregation of bioactive compounds should be activated, determining the comparison and action of their activity against already available traditional medicine.

**References**

Afolayan AJ, Sunmonu TO. Artemisia afraJacq.amelio-rates oxidative stress in the pancreas of streptozotocin-induced diabetic Wistar rats. BiosciBiotechnolBiochem 2011. 75(11):2083-2086.

Aghadavoud E, Nasri H, Amiri M. Molecular signaling pathways of diabetic kidney disease; new concepts. J Prev Epidemiol.ss2017;2(2):e03.

Ahmad A, Balakrishnan BR, Akhtar R, Pimprikar R. Antidiabetic activity of leaves of Tephrosiavillosa Pers. in alloxan induced diabetic rats. J Pharm Res 2009; 2: 528-531.

Al Jamal, A. Effect of rosemary (Rosmarinusofficinalis) on lipid profiles and blood glucose in human diabetic patients (type-2). African J. Biochem. Res. 2014, 8, 147–150.

Aljamal, A. Effect bay leaves on the patients with diabetes mellitus. Res. J. Med. Plants2011, 5, 471–476.s

Andallu, B.; Ramya, V. Antihyperglycemic, cholesterol-lowering and HDL-raising effects of cumin (Cuminumcyminum) seeds in type-2 diabetes. J. Nat. Remed. 2007, 7, 142–149.

Arjun P, Shivesh J, Sahu AN. Antidiabetic activity of aqueous extract of Eucalyptus citriodora Hook. inalloxan induced diabetic rats. PharmacognMag 2009; 5: 51-54.

Asai M, Iwata N, Yoshikawa A, Aizaki Y, Ishiura S, Saido TC, Maruyama K. Berberine alters the processingof Alzheimer's amyloid precursor protein to decrease Abeta secretion. BiochemBiophys Res Commun 2007. 352(2):498-502.

Azimi, P.; Ghiasvand, R.; Feizi, A.; Hariri, M.; Abbasi, B. Effects of cinnamon, cardamom, saffron, and ginger consumption on markers of glycemic control, lipid profile, oxidative stress, and inflammation in type 2 diabetes patients. Rev. Diabetic Studies RDS 2014, 11, 258–266.

Balaraman AK, Singh J, Dash S, Maity TK. Antihyperglycemic and hypolipidemic effects of Melothriamaderaspatana and Cocciniaindica in Streptozotocin induced diabetes in rats. Saudi Pharm J 2010; 18: 173-178.

Baradaran A. The role of biomarkers to detect progression of diseases.J Negat Results Clin Exp Stud. 2018;1(1):e05.

Behradmanesh, S.; Derees, F.; Rafieian-kopaei, M. Effect of Salvia officinalis on diabetic patients. J. Renal Injury Prevention 2013, 2, 51–54.

Bihari CG, Manaswini B, Keshari PS, Kumar TS.Phytochemical investigation & evaluation for antidiabetic activity of leafy extracts of various Ocimum (Tulsi) species by alloxan induced diabetic model. J Pharm Res 2011; 4: 28-29.

Biradar SM, Rangani AT, Kulkarni VH, Joshi H, Habbu PV, Smita DM. Prevention of onset of hyperglycemia by extracts of Argyrieacuneata on alloxan-induced diabetic rats. J Pharm Res 2010; 3: 2186-2187.

Broca C, Manteghetti M, Gross R, Baissac Y, Jacob M, Petit P, et al. 4-Hydroxyisoleucine: Effects of synthetic and natural analogues on insulin secretion. Eur. J. Pharmacol. 2000;390:339–45

Chattopadhyay RR. Hypoglycemic effect of Ocimum sanctum leaf extract in normal and streptozotocin diabetic rats. Indian J. Exp. Biol. 1993;31:891–3

Chaturvedi N, Sharma S. Antidiabetic and antihyperlipidemic activity of water soluble solid extract of Ficusbengalensis Linn. bark in rats. Biochem Cell Arch 2010; 10: 65-69.

Choi H-J, Jang H-J, Chung T-W, Jeong S-I, Cha J, Choi J-Y, et al. Catalpol suppresses advanced glycation end-products-induced inflammatory responses through inhibition of reactive oxygen species in human monocytic THP-1 cells. Fitoterapia. 2013;86:19–28.

Chuang C-Y, Hsu C, Chao C-Y, Wein Y-S, Kuo Y-H, Huang C. Fractionation and identification of 9c, 11t, 13t-conjugated linolenic acid as an activator of PPARalpha in bitter gourd (Momordicacharantia L.). J Biomed Sci. 2006;13:763–72.

Chuengsamarn, S.; Rattanamongkolgul, S.; Luechapudiporn, R.; Phisalaphong, C.; Jirawatnotai, S. C Chen, J.; Mangelinckx, S.; Adams, A.; Wang, Z.-t.; Li, W.-l.; De Kimpe, N. Natural flavonoids as potential herbal medication for the treatment of diabetes mellitus and its complications. Nat. Prod. Commun.2015, 10,187–200.

Craig ME, Hattersley A, Donaghue KC. Definition, epidemiology and classification of diabetes in children and adolescents. Pediatr Diabetes 2009; 10: 3-12.

Dewanjee S, Das AK, Sahu R, Gangopadhyay M. Antidiabetic activity of Diospyrosperegrina fruit: effect on hyperglycemia, hyperlipidemia and augmented oxidative stress in experimental type 2 diabetes. Food ChemToxicol 2009; 47: 2679-2685.

Dheer R, Bhatnagar P. A study of the antidiabetic activity of Barleriaprionitis Linn. Indian J Pharmacol 2010; 42: 70-73

Duganath N, Krishna DR, Reddy GD, Sudheera B, Mallikarjun M, Beesetty P. Evaluation of anti-diabetic activity of Triumfettarhomboidea in alloxan induced Wistar rats. Res J PharmBiolChemSci 2011; 2: 721-726.

Ezuruike, U.F.; Prieto, J.M. The use of plants in the traditional management of diabetes in Nigeria: Pharmacological and toxicological considerations. J. Ethnopharmacol. 2014, 155, 857–924.

Eliza J, Daisy P, Ignacimuthu S, Duraipandiyan V. Normoglycemic and hypolipidemic effect of costunolideiso-lated from Costusspeciosus (Koen ex. Retz.) Sm. in streptozotocin-induced diabetic rats.ChemBiol Interact 2009. 179(2-3):329-334.

F röde TS, Medeiros YS. Animal models to test drugs with potential antidiabetic activity. J Ethnopharmacol 2008; 115: 173-18 , 3.

Fabricant DS, Farnsworth NR. The value of plants used in traditional medicine for drug discovery. Environ Health Perspect.2001;109(1):69–75.

Feshani AM, Kouhsari SM, Mohammadi S. Vacciniumarctostaphylos, a common herbal medicine in Iran: molecular and biochemical study of its antidiabetic effects on alloxan-diabetic Wistar rats. J Ethnopharmacol 2011; 133: 67-74

Gaikwad, S.; Krishna Mohan, G.; SandhyaRani, M. Phytochemicals for diabetes management. Pharm. Crops 2014, 5, 11–28.

Geetha G, KalavalarasarielGopinathapillai P, Sankar V. Anti diabetic effect of Achyranthesrubrofusca leaf extracts on alloxan induced diabetic rats. Pak J PharmSci 2011; 24: 193-199.

Grover, J.; Yadav, S.; Vats, V. Medicinal plants of India with anti-diabetic potential. J. Ethnopharmacol.2002,81, 81–100.

Gushiken, L. F., Beserra, F. P., Rozza, A. L., Bérgamo, P. L., Bérgamo, D. A., &Pellizzon, C. H. (2016). Chemical and biological aspects of extracts from medicinal plants with antidiabetic effects. *The review of diabetic studies: RDS*, *13*(2-3), 96.

Hajian S. Positive effect of antioxidants on immune system ImmunopatholPersa. 2015;1(1):e02.

Harlev, E.; Nevo, E.; Mirsky, N.; Ofir, R. Antidiabetic attributes of desert and steppic plants: A review.Planta Med. 2013, 79, 425–436.

Ilango K, Chitra V. Antidiabetic and antioxidant activity of Limoniaacidissima Linn. inalloxan induced rats. Der Pharmacia Lettre 2009; 1: 117-125.

Jafari, S.; Sattari, R.; Ghavamzadeh, S.i. Evaluation the effect of 50 and 100 mg doses of Cuminumcyminum essential oil on glycemic indices, insulin resistance and serum inflammatory factors on patients with diabetes type II: A double-blind randomized placebo-controlled clinical trial. J. Trad. Complemen.Med.2017, 7,332–338.

Jain S, Bhatia G, Barik R, Kumar P, Jain A, Dixit VK. Antidiabetic activity of Paspalumscrobiculatum Linn.inalloxan induced diabetic rats. J Ethnopharmacol 2010; 127: 325-328.

Jarald EE, Joshi SB, Jain DC. Antidiabetic activity of extracts and fraction of Zizyphusmauritiana.PharmBiol 2009; 47: 328-334.

Kazi S. Use of traditional plants in diabetes mellitus.Int J Pharm. 2014; 4(4):283-9.

Kianbakht, S.; Dabaghian, F.H. Improved glycemic control and lipid profile in hyperlipidemic type 2 diabetic patients consuming Salvia officinalis L. leaf extract: A randomized placebo. Controlled clinical trial.Complement. Therapies Med. 2013, 21, 441–446.

Kim KS, Jang HJ. Medicinal plants qua glucagon-like peptide-1 secretagogue via intestinal nutrient sensors. Evid Based Complement Alternat Med. 2015;2015:171742. https://doi.org/ 10.1155/2015/171742

Kooti, W., Farokhipour, M., Asadzadeh, Z., Ashtary-Larky, D., &Asadi-Samani, M. (2016). The role of medicinal plants in the treatment of diabetes: a systematic review. *Electronic physician*, *8*(1), 1832.

Kumar DB, Mitra A, Manjunatha M. Azadirachtolide. PharmacognCommun. 2011;1:78–84.

Kumar KV, Sharief SD, Rajkumar R, Ilango B, Sukumar E. Antidiabetic potential of Lantana aculeata root extract in alloxan-induced diabetic rats.Int J Phytomed 2010; 2: 299-303.

Kumawat NS, Chaudhari SP, Wani NS, Deshmukh TA, Patil VR.Antidiabetic activity of ethanol extract of Colocasiaesculenta leaves in alloxan induced diabetic rats. Int J Pharm Tech Res 2010; 2: 1246-1249. 420 Patel DK et al./Asian Pac J Trop Biomed 2012; 2(5): 411-420

Lanjhiyana S, Garabadu D, Ahirwar D, Bigoniya P, Rana AC, Patra KC, et al. Hypoglycemic activity studies on aerial leaves of Pongamiapinnata (L.) in alloxan-induced diabetic rats. Der Pharmacia Lettre 2011; 3: 55-70.

Larijani B, Zahedi F. An introductory on medical ethics history in different era in Iran.Daru J Pharm Sci. 2006;14:10-16

Li, W.; Zheng, H.; Bukuru, J.; De Kimpe, N. Natural medicines used in the traditional Chinese medical system for therapy of diabetes mellitus. J. Ethnopharmacol. 2004, 92, 1–2.

Liu C, Zhang M, Hu M-Y, Guo H-F, Li J, Yu Y-L, et al. Increased glucagon-like peptide-1 secretion may be involved in antidiabetic effects of ginsenosides. J Endocrinol. 2013;217:185–96.

Lodha SR, Joshi SV, Vyas BA, Upadhye MC, Kirve MS, Salunke SS, et al. Assessment of the antidiabetic potential of Cassia grandis using an in vivo model. J Adv PharmTechnol Res 2010; 1: 330-333.

Mard SA, Jalalvand K, Jafarinejad M, Balochi H, Naseri MKG. Evaluation of the antidiabetic and antilipaemic activities of the hydroalcoholic extract of Phoenix dactylifera palm leaves and its fractions in alloxan-induced diabetic rats. Malaysian J Med Sci 2010; 17: 4-13.

Medagama, A.B. The glycaemic outcomes of Cinnamon, a review of the experimental evidence and clinical trials.Nutri. J. 2015, 14, 108.

Meenakshi P, Bhuvaneshwari R, Rathi MA, Thirumoorthi L, Guravaiah DC, Jiji MJ, et al. Antidiabetic activity of ethanolic extract of Zaleyadecandra in alloxan-induced diabetic rats. ApplBiochemBiotechnol 2010; 162: 1153-1159.

Michael UA, David BU, Theophine CO, Philip FU, OgochukwuAM, Benson VA. Antidiabetic effects of combined aqueous leaf extract of Vernoniaamygdalina and metformin in rats. J Basic ClinPharm 2010; 1: 197-202.

Milajerdi, A.; Jazayeri, S.; Hashemzadeh, N.; Shirzadi, E.; Derakhshan, Z.; Djazayeri, A.; Akhondzadeh, S. The effect of saffron (Crocus sativus L.) hydroalcoholic extract on metabolic control in type 2 diabetes mellitus:A triple-blinded randomized clinical trial. J. Res. Med. Sci. 2018, 23, 1–6.

Mobasseri, M.; Payahoo, L.; Ostadrahimi, A.; Bishak, Y.K.; Jafarabadi, M.A.; Mahluji, S. Anethumgraveolenssupplementation improves insulin sensitivity and lipid abnormality in type 2 diabetic patients. Pharm.Sci.2014, 20, 40.

Moradi, B.; Abbaszadeh, S.; Shahsavari, S.; Alizadeh, M.; Beyranvand, F.The most useful medicinal herbs to treat diabetes.Biomed. Res. Therapy 2018, 5, 2538–2551.

Mowla A, Alauddin M, Rahman MA, Ahmed K. Antihyperglycemic effect of Trigonellafoenum-graecum (fenugreek) seed extract in alloxan-induced diabetic rats and its use in diabetes mellitus: A brief qualitative phytochemical and acute toxicity test on the extract. Afr J Tradit Complement Altern Med 2009; 6: 255-261.

Mukesh R, Namita P. Medicinal Plants with Antidiabetic Potential-A Review. American-Eurasian J AgricEnviron Sci. 2013; 13(1): 81-94.

Nabeel MA, Kathiresan K, Manivannan S. Antidiabetic activity of the mangrove species Ceriopsdecandra in alloxan-induced diabetic rats. J Diabetes 2010; 2: 97-103.

Nazarian-Samani, Z., Sewell, R. D., Lorigooini, Z., &Rafieian-Kopaei, M. (2018). Medicinal plants with multiple effects on diabetes mellitus and its complications: A Systematic review. *Current diabetes reports*, *18*(10), 72.

Ocvirk, S., Kistler, M., Khan, S., Talukder, S. H., &Hauner, H. (2013). Traditional medicinal plants used for the treatment of diabetes in rural and urban areas of Dhaka, Bangladesh–an ethnobotanical survey. *Journal of ethnobiology and ethnomedicine*, *9*(1), 43.

Okokon JE, Umoh EE, Etim EI, Jackson CL. Antiplasmodial and antidiabetic activities of ethanolic leaf extract of Heinsiacrinata. J Med Food 2009; 12: 131-136.

Okoli CO, Ibiam AF, Ezike AC, Akah PA, Okoye TC. Evaluation of antidiabetic potentials of Phyllanthusniruri in alloxan diabetic.Afr J Biotechnol 2010; 9: 248-259.

Odeyemi, S., & Bradley, G. (2018). Medicinal plants used for the traditional management of diabetes in the Eastern Cape, South Africa: Pharmacology and toxicology. *Molecules*, *23*(11), 2759.

PakkirMaideen NM, Balasubramaniam R. Pharmacologically relevant drug interactions of sulfonylurea antidiabetics with common herbs. J HerbmedPharmacol. 2018;7(3):200–10. https://doi.org/ 10.15171/jhp.2018.32. This article presents a list of herbal drugs having interacting potentials with sulfonylurea antidiabetics. This subject has high level of clinical and investigational implications

Pareek H, Sharma S, Khajja BS, Jain K, Jain GC. Evaluation of hypoglycemic and anti hyperglycemic potential of Tridaxprocumbens (Linn.).BMC Complement Altern Med 2009; 9: 48.

Patel DK, Kumar R, Laloo D, Hemalatha S. Evaluation of phytochemical and antioxidant activities of the different fractions of Hybanthusenneaspermus (Linn.) F. Muell. (Violaceae). Asian Pac J Trop Med 2011; 4: 391-396.

Patel, D. K., Kumar, R., Laloo, D., &Hemalatha, S. (2012). Diabetes mellitus: an overview on its pharmacological aspects and reported medicinal plants having antidiabetic activity. *Asian Pacific Journal of Tropical Biomedicine*, *2*(5), 411-420.

Patil RN, Patil RY, Ahirwar A, Ahirwar D. Evaluation of antidiabetic and related actions of some Indian medicinal plants in diabetic rats. Asian Pac J Trop Med 2011; 4: 20-23.

Pereira, A. S., Banegas-Luna, A. J., Peña-García, J., Pérez-Sánchez, H., &Apostolides, Z. (2019). Evaluation of the anti-diabetic activity of some common herbs and spices: providing new insights with inverse virtual screening. *Molecules*, *24*(22), 4030.

Poongothai K, Ahmed KSZ, Ponmurugan P, Jayanthi M. Assessment of antidiabetic and antihyperlipidemic potential of Solanumnigrum and Musa paradisiaca in alloxan induced diabetic rats. J Pharm Res 2010; 3: 2203-2205.

Putta, S.; SastryYarla, N.; Kumar Kilari, E.; Surekha, C.; Aliev, G.; BasavarajuDivakara, M.; Sridhar Santosh, M.; Ramu, R.; Zameer, F.; Prasad, M. Therapeutic potentials of triterpenes in diabetes and its associated complications. Curr. Topics Med. Chem. 2016, 16, 2532–2542.

Rathee S, Mogla OP, Sardana S, Vats M, Rathee P. Antidiabetic activity of CapparisdeciduaForskEdgew. J Pharm Res 2010; 3: 231-234.

Ravikumar P, Anuradha CV. Effect of fenugreek seeds on blood lipid peroxidation and antioxidants in diabetic rats. Phytother Res. 1999;13:197–201

Ravikumar R, Krishnamoorthy P, Kalidoss A. Antidiabetic and antioxidant efficacy of Andrographispaniculata in alloxanized albino rats. Int J PharmTechnol 2010; 2: 1016-1027.

Sangameswaran B, Ilango K, Chaurey M, Bhaskar VH. Antihyperglycemic and antihyperlipidaemic effects of extracts of Ipomoea reniformisChois on alloxan induced diabetic rats. Ann Biol Res 2010; 1: 157-163.

Saxena SCRC, Chaurasia ID, Shrivastav R. Antidiabetic activity of Luffaaegyptiaca (Mill) in alloxan induced diabetic rats. J ChemPharm Res 2011; 3: 522-525.

Shabeer J, Srivastava RS, Singh SK. Antidiabetic and antioxidant effect of various fractions of Phyllanthus simplex in alloxan diabetic rats. J Ethnopharmacol 2009; 124: 34-38.

Shobha, R.I.; Andallu, B. Antioxidant, Anti-Diabetic and Hypolipidemic Effects of Aniseeds (Pimpinellaanisum L.): In vitro and in vivo Studies. J. Complement Med. Alt. Healthcare 2018, 5, 1–12.

Soman S, Rauf AA, Indira M, Rajamanickam C. An-tioxidant and antiglycative potential of ethyl acetate fraction of Psidiumguajava leaf extract in streptozotocin-induced diabetic rats. Plant Foods Hum Nutr 2010. 65(4):386-391.

Sreenathkumar S, Arcot S. Andiabetic activity of NymphaeapubescensWilld - a plant drug of aquatic flora. J Pharm Res 2010; 3: 3067-3069.

Teimoori M, Kouhsari MS, Ghafarzadegan R, Hajiaghaee R. Antidiabetic effects of Juglansregia leave's methanolic extract on alloxan-induced male Wistar rats. J Med Plants 2010; 9: 143-149.

Thévenod F. Pathophysiology of diabetes mellitus type 2: Roles of obesity, insulin resistance and 毬-cell dysfunction. Front Diabetes Basel Karger 2008; 19: 1-18.

Thome RG, Santos HB, Santos FV, Oliveira RJ, Camargos LF, Pereira MN, Longatti TR, Souto CM, Franco CS, Schüffner RO, et al. Evaluation of healing wound and genotoxicity potentials from extracts hydroalcoholic of Plantago major and Siparunaguianensis. Exp Biol Med (Maywood) 2012. 237(12):1379-1386.

Tripathi UN, Chandra D. Anti-hyperglycemic and anti-oxidative effect of aqueous extract of Momordicacharantia pulp and Trigonellafoenumgraecum seed in alloxan-induced diabetic rats. Indian J BiochemBiophys 2010; 47: 227-233.

Ubaka CM, Ukwe CV. Antidiabetic effect of the methanolic seed extract of Sphenostylisstenocarpa (Hoechst ex. A. Rich. Harms) in rats. J Pharm Res 2010; 3: 2192-2194.

Venkatesh S, Madhava Reddy B, Dayanand Reddy G, Mullangi R, Lakshman M. Antihyperglycemic and hypolipidemic effects of Helicteresisora roots in alloxan-induced diabetic rats: A possible mechanism of action. J Nat Med 2010; 64: 295-304.

Vishnu B, Naveen A, Akshay K, Sikarwar MS, Patil MB.Antidiabetic activity of insulin plant (Costusigneus) leaf extract in diabetic rats. J Pharm Res 2010; 3: 608-611.

Wani VK, Dubey RD, Verma S, Sengottuvelu S, Sivakumar T. Antidiabetic activity of methanolic root extract of Mukiamaderaspatana in Alloxan induced diabetic rats. Int J PharmTechnol Res 2011; 3: 214-220.

Warjeet Singh L. Traditional medicinal plants of Manipur as antidiabetics. J Med Plants Res 2011; 5: 677-687.

World Health Organisation.Definition and diagnosis of diabetesmellitus and intermediate hyperglycaemia [Internet]. 2006.Available from:http://www.who.int/diabetes/publications/diagnosis_diabetes2006/en/.

Yajima, H.; Ikeshima, E.; Shiraki, M.; Kanaya, T.; Fujiwara, D.; Odai, H.; Tsuboyama-Kasaoka, N.;Ezaki, O.; Oikawa, S.; Kondo, K. Isohumulones, bitter acids derived from hops, activate both peroxisomeproliferator-activated receptorαandγand reduce insulin resistance. J. Bio. Chem.2004, 279, 3345633462.

Yankuzo H, Ahmed QU, Santosa RI, Akter SF, Talib NA. Beneficial effect of the leaves of Murrayakoenigii (Linn.)Spreng (Rutaceae) on diabetes-induced renal damage in vivo. J Ethnopharmacol 2011. 135(1):88-94non-sulfonylurea hypoglycemic agents: pharmacological properties and tissue selectivity. Diabetes Res ClinPract 2004. 66(1):75-78.

Zheng, Y.; Bai, L.; Zhou, Y.; Tong, R.; Zeng, M.; Shi, J.; Lib, X. Polysaccharides from Chinese herbal medicine for anti-diabetes recent advances. Int. J. Biol. Macromol. 2019, 121, 1240–1253. urcumin extract for prevention of type 2 diabetes. Diabetes Care 2012, 35, 2121–2127.

Zhou J, Chan L, Zhou S. Trigonelline: a plant alkaloid with therapeutic potential for diabetes and central nervous system disease. Curr Med Chem. 2012;19:3523–31.