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A review: Antihyperglycemic plant medicines in management of diabetes

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ABSTRACT

Diabetes is a serious metabolic disorder prevailing among people with ageing and sedentary lifestyle associated with rapidly growing urbanization and industrialization. Medicinal plants prescribed in the-saurus of Ayurveda and used by folklore have been a source of relief in controlling different types of diabetes all over the world. At the present time, the use of these herbal drugs is growing at high pace because of its cost effectiveness and free from the side effects over pharmaceutical hypoglycemic agents. The current review presents the profiles of approximately 35 plants having anti-diabetic activity and potential to reduce the oxidative stress, reported in the literature from 2005 to 2015. This review has been presented in such a fascinating manner which includes the plant along with its family, part used, phyto-constituents responsible for particular action in a tabulated form. Present study might provide a momentum to find newer antidiabetic entities.

Contents

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1. Introduction

Diabetes is recognized as the wide-reaching chronic disorder affecting almost people of every age group. Along with cancer, cardiovascular and cerebrovascular diseases, diabetes is becoming the third killer of the health of mankind [1]. The occurrence of this disease was seen to be high in India, China and USA. It is classified under genetically disorder and dietary disorder [2].

Recent estimations suggested that up to the year 2030, approximately 438 million people (7.8%) of the adult population, is expected to have diabetes [3]. Diabetes mellitus is a group of metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both [4]. Diabetes mellitus is caused by the abnormality of carbohydrate metabolism which is related to low blood insulin level or insensitivity of target organs to insulin [5]. Some effects of diabetes are found to be mediated through oxidative stress associated with increased Reactive oxygen species (ROS) production which adversely affects the antioxidative machinery of our body. Disturbance of antioxidative machinery in diabetes is due to alteration in antioxidative enzymes, impaired glutathione metabolism and decreased ascorbic acid levels [6] [7].

Herbal plants have been traditionally used for the treatment of diabetes throughout the world. Plant drugs are frequently considered to be less toxic and free from side effects than synthetic ones [8]. Besides chemotherapeutic agents, the present century is switching towards naturopathy especially in developing countries where resources are in scanty and the cost of conventional medicines is a burden to the population [9]. The phyto-constituents present in herbal plants have been reported to retain pancreatic beta cells regenerative capacity, insulin secretion and fight against the problem of insulin resistance [10]. Concurrently, phyto-constituents identified from traditional medicinal plants can be used for developing new types of therapeutics.

The purpose of present review is to enlighten about some medicinal plants with their valuable phyto-constituents along with their possible molecular mechanism in the management of diabetes.

2. Material and method

The information of plants having antidiabetic activity was collected from different articles published in various journals and books available. This review contains 33 plants of 25 families along with 9 major phyto-constituents with their possible mechanism of action against diabetes. These plants are selected on the basis of their traditional usage and also reported several times in the literature since 2005–2015. Table 1 contains list of plants having antidiabetic activity, parts used for extraction, taxonomical status, basic biological activities with their phyto-constituents, and solvent used for extraction; whereas phyto-constituents with their possible mechanism of action against diabetes has been described in Table 2. To understand the mechanism of action Fig. 1 is showing major phyto-constituents of plants and Fig. 2 showing mechanism of action to control glucose metabolism [11], have been provided in this review.

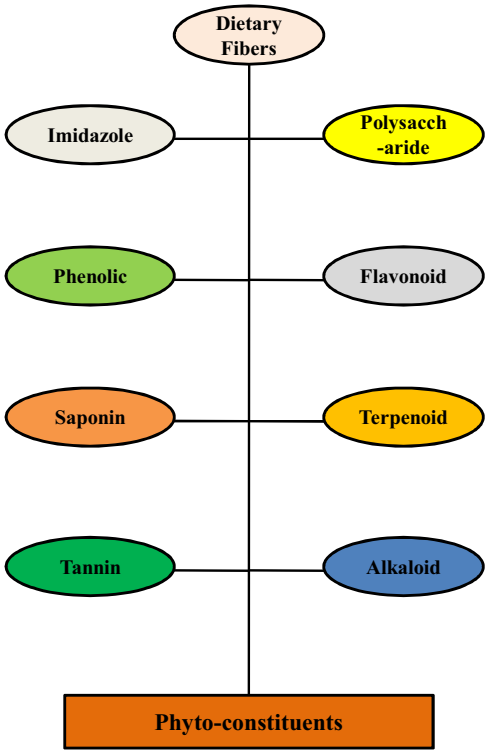

Fig. 1. Phyto-constituents present in herbal plants.

3. Mechanism of action of phyto-constituents against diabetes

Plants contain different types of phyto-constituents of different chemical classes (Fig. 1). Phyto-constituents show various biological activities like Hypoglycemic, Hypolipidemic, Anti-

Table 1
Summary of some medicinal plant exhibiting Antidiabetic activity.

S. No.	Plant name	Family	Part used	Solvent Used	Active components	Biological activity	References
1.	*Aframomum melegueta* (K.Schum.)	Zingiberaceae	Leaves	Aqueous	Saponins, Tannins, Flavonoids, Terpenoids	Hypoglycemic, Prophylatic, Antimicrobial, Antiulcer activity	[13]
2.	*Alangium lamarckii* (Thw.)	Cornaceae	Leaves	Alcoholic	Terpenoids, Alkaloids, Flavonoids, Steroids, Tannins, Phenol	Hypoglycemic, Antioxidative, Anti-inflammatory, Antibacterial activity	[14]
3.	*Aloe vera* (L.)	Asphodelaceae	Leaves	Aqueous	Aloin glycoside, Sitosterol, Lupeol, Aspirin, Saponins.	Hypoglycaemic, Antioxidative, Antiulcer, Antiseptic activity	[15]
4.	*Boerhaavia diffusa* (L.)	Nyctaginaceae	–	Crude	β-Sitosterol, alpha-2-Sitosterol	Hypoglycemic, Antioxidative, Hepatoprotective, Antistress activity	[16]
5.	*Brassica juncea* (L.)	Brassicaceae	Seeds	Aqueous	Glucosinolates, Isothiocyanates, Phenolic, Kaempferol, glycosides, Flavonoid	Hypoglycemic, Antioxidative activity	[17]
6.	*Bridelia retusa* (L.)	Phyllanthaceae	Bark	Methanolic, Pet ether, *n*-butanol	Terpenoids, Tannins	Hypoglycemic, Antioxidative, Anti-inflammatory, Antinociceptive, Antibacterial activity	[18]
7.	*Calotropis procera* (Ait.)	Asclepiadaceae	Roots	Pet ether, Aqueous, Methanolic	Triterpenoids, Cardenolides, Anthocyanins, β-sitosterol, Flavonoids	Hypoglycemic, Antioxidative, Anthelmintic activity	[19]
8.	*Carica papaya* (L.)	Caricaceae	Leaves	Aqueous	Quinones, Alkaloids, Steroids, Flavonoids, Tannins	Hypoglycemic, Antihyperlipidemic, Antifungal, Antibacterial, Anticarcinogenic activity	[20]
9.	*Carthamus tinctorius* (L.)	Asteraceae	Flowers	Ethanolic	Caryophyllene, P-allyltoluene, 1-Acetoxytetralin, Heneicosane, Carthamin	Hypoglycemic, Antioxidative, anti-inflammatory, Analgesic activity	[21]
10.	*Catharanthus roseus* (L.)	Apocynaceae	Leaves	Aqueous	Alkaloids, Glycosides, Flavonoids, Tannins, Saponins	Hypoglycemic, Antioxidative, activity	[22]
11.	*Cynanchum acutum* (L.)	Apocynaceae	Aerial	Methanolic, *n*-butanol	Kaempferol, Flavonoids, Quercetin	Increase insulin level, Antimicrobial, Antitumour, Antifebrile, Diuretic, Antitussive, Anti-oxidative, Antiulcer activity	[23]
12.	*Dioscorea bulbifera* (L.)	Dioscoreaceae	Tuber	Ethanolic	Alkaloids, Flavonoids, Saponins	Hypoglycemic, Antioxidative, Analgesic, Antiinflammatory activity	[24]
13.	*Eugenia jambolana* (Lam.)	Myrataceae	Seeds	Pet ether, Ethanolic	Gallic acid, Ellagic acid, Corilagin, Ellagitannins	Hypoglycemic, Antioxidative, Diuretic, Hypolipidemic, activity	[25]

Table 1 (*Continued*)

S. No.	Plant name	Family	Part used	Solvent Used	Active components	Biological activity	References
14.	*Gentiana olivieri* (Griseb.)	Gentianaceae	Aerial	Aqueous, Methanolic, Chloroform, *n*-butanol	Alkaloids, Gymnemic acid, Saponins, Tannins	Hypoglycemic, Antioxidative, Hepatoprotective, Antihypertensive avtivity	[26]
15.	*Helianthus annuus* (L.)	Asteraceae	Seeds	Ethanolic	Alkaloids, Saponins, Polysaccharides, Flavonoids, Polyphenols	Antidiabetic, Antimicrobial, Antioxidative activity	[27]
16.	*Leonotis leonurus* (L.)	*Lamiaceae*	Leaves	Aqueous	Diterpenoids, Tannins, Flavonoids, Alkaloids	Hypoglycemic, Antibacterial, Antihelmintic, Antioxidative activity	[28]
17.	*Mallotus philippinensis* (Muell.Arg.)	Marsileaceae	Bark	Ethanolic	Flavonoids, Phenolic, Saponins, Steroids, Tannins, Terpenoids	Hypoglycemic, Antibacterial, Antioxidative, Antifungal activity	[29]
18.	*Marsilea minuta* (L.)	Marsileaceae	Leaves	Ethanolic	Flavonoids, Glucosides, Alkaloids, Tannins	Hypoglycemic, Antidepressant, Antioxidative activity	[30]
19.	*Mollugo nudicaulis* (Lam.)	Molluginaceae	Whole plant	Ethanolic	Tannins, Flavonoids, Carbohydrate, Phenolic compound	Hypoglycemic, Antioxidative activity	[31]
20.	*Moringa Oleifera* (Lam.)	*Moringaceae*	Pods	Methanolic	Tannins, Steroids, Triterpenoids, Flavonoids, Saponins, Anthraquinones, Alkaloids	Hypoglycemic, Antioxidative, Antiulcer, Antiinflammatory, Hypocholesterolemic activity	[32]
21.	*Morus alba* (L.)	Moraceae	Roots Bark	Aqueous	Lupeol, β- Sitosterol, Rutin, Moracetin, Quercetin-3-triglucoside, Isoquercitrin, Coumarins, Volatile oil, Alkaloids, Apigenin	Antidiabetic, Antioxidative, Antimicrobial, Antibacterial activity	[33]
22.	*Ocimum sanctum* (L.)	*Lamiaceae*	Leaves	Aqueous	Vallinin, Vicenin, Vitexin, Vllinin acid, Orientin, Circineol, Gallic Acid, vitamin A, vitamin C, Eugenol, Cardinene, Cubenol, Borneol, Linoleic acid, Linolenic acid, Oleic acid, Palmitric acid, Steric acid	Hypoglycemic, Antioxidative, Antiulcer, Antibacterial, activity	[34]
23.	*Opuntia joconostle*	Cactaceae	Mesocarpium Cladode	Aqueous	Phenolic compound, Terpenoids, Saponins	Antidiabetic, Antioxidative, Antimicrobial, Hypolipidemic activity	[35]
24.	*Orthosiphon stamineus* (Benth.)	*Lamiaceae*	Whole Plant	Chloroform	Triterpenoids, Saponins, Flavonoids	Hypoglycemic, Antioxidative, Hepatoprotective, Antiapoptotic activity	[36]
25.	*Panax ginseng* (L.)	Araliaceae	Roots	Aqueous	Roseoside, Strictinin, Isostrictinin, Pedunculagin, Epicatechin, Christinin	Antihyperglycemic, Antiinflammatory, Anti-hyperlipidemic, Antioxidative activity	[37]
26.	*Phoenix dactylifera* (L.)	Arecoceae	Fruits	Fruit powder	Alkaloids, Steroids, Flavonoids, Vitamins, Tannins	Antidiabetic, Antioxidative Antifungal, Antihyperlipidemic, Hepatoprotective activity	[38]

27.	*Physalis pubescens* (L.)	Solanaceae	Fruits	Juice	Flavonoids, Glucosides, Alkaloids, Tannins	Antiangiogenesis, Hypoglycemic, Antihypertension activity	[39]
28.	*Pseudarthria viscid* (L.)	Fabaceae	Whole Plant	Ethanolic	Alkaloids, Saponins, Tannins, Flavonoids, Anthraquinones, Sterols	Hypoglycemic, Antioxidative, Antimirobial, Antibacterial activity	[40]
29.	*Syzygium cumini* (L.)	*Myrtaceae*	Seeds	Chloroform, Methanolic, Aqueous, Pet ether, Acetone	Alkaloid, Jambosine, Glycoside, Jambolin	Antidiabetic, Antimicrobial, Antibacterial, Antioxidative, Antifungal activity	[41]
30.	*Trichosanthes dioica* (Roxb.)	*Cucurbitaceae*	Leaves	Aqueous	Vitamin A, Vitamin C, Tannins, Saponins, Alkaloids, Triterpenes	Hypoglycemic, Wound healing, Hypocholesterolemic, Antitumour, Antiinflammatory activity	[42]
31.	*Tridax procumbens* (L.)	Asteraceae	Whole Plant	Ethanolic	Alkaloids, Flavonoids, Carotenoids, β-sitosterol, *n*-hexane, Fumaric acid, Luteolin, Quercitin, Oxoester, Lauric acid, Myristic, Palmitic, Arachidic, Linoleic acid, Tannins	Hypoglycemic, Hypolipidemic, Immunomodulatory, Wound healing activity	[43]
32.	*Vinca rosea* (L.)	*Apocynaceae*	Whole Plant	Alcoholic	Reserpine, Vincamine, Alstonine, Leurocristine, Ajmalicine, Vinine, Vinomine, Vinoxine, Vintsine, Leurosine	Antihyperglycemic, Antioxidative, Pro-healing action, Anticarcinogenic activity	[44]
33.	*Wedelia chinensis* (Osbeck.)	Asteraceae	Leaves	Alcoholic	Saponins, Tannins, Steroids, Flavonoids, Alkaloids, Glycosides	Antidiabetic, Hepatoprotective, Wound healing, Antistress, Antiinflammatory, Antibacterial, Anticonvulsant activity	[45]

These plants are selected on the basis of their traditional usage and also reported several times in the literature since 2005–2015.

Table 2
Phyto-constituents with their possible mechanism of action against Diabetes.

Phyto-constituents	Mechanism of action
Alkaloids	Induce high glucose uptake in pancreatic β-TC6 or myoblast C2C12 cells [46] Inhibit α-glucosidase activity to depress the glucose level in blood [47]
Flavonoids	Stimulate β-cells to release more insulin and inhibit glucose transport [48]
Saponins	Stimulate insulin secretion, inhibit the glucose formation in blood stream and suppress the transport of glucose [11]
Phenolics	Inhibit α-amylase and α-glucosidase and inhibit starch digestion [49].
Terpenoids	Reduce blood glucose level, increase glycogenesis and decrease glycogenolysis [50]. Inhibit aldose reductase [51]
Ursolic acid	Preserve pancreatic β-cells, increase insulin secretion [52].
Imidazoline	Increase insulin level [53]
Polysaccharides	Induce insulin secretion, decrease the level of glucose and recover glucose homeostasis [54]
Dietary fibers	Inhibit carbohydrate digestion and absorption, Increase antioxidative activity [55] Inhibit the activity of alpha-amylase and retard glucose diffusion [56]

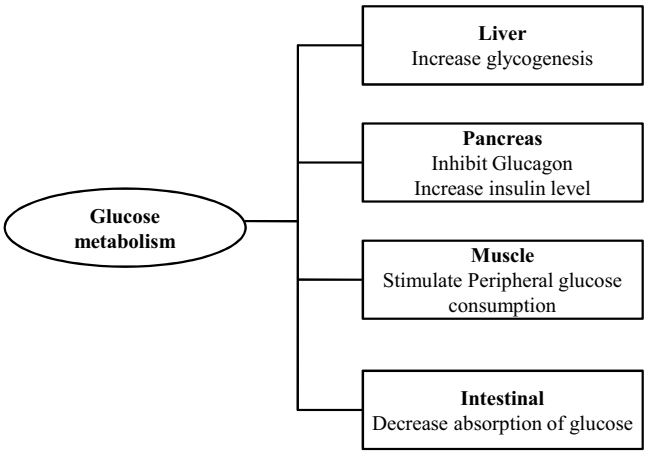

Fig. 2. Mechanisms of action of phyto-constituents to control glucose metabolism.

bacterial, Anti-microbial, Anti-inflammatory, Anti-fertility etc. These phyto-constituents like Alkaloids, Flavonoids, Tannins, Saponins, Terpenoids, Phenolics, Ursolic acid and Imidazoline and other contents such as Polysaccharides and Dietary fibers also play an important role in managing diabetes via interfering in carbohydrate metabolism (Table 2). Phyto-constituents control glucose metabolism in a regulatory manner in blood and organs such as liver, muscle, pancrease and intestine. Phyto-constituents such as alkaloids decrease glucose transport through intestinal epithelium. Flavonoids stimulate insulin secretion in blood and saponins inhibit glucagon activity (Fig. 2) [11]. In addition to phyto-constituents possess an antioxidant activity. Antioxidants decrease the oxidative stress in cells and so valuable in the management of diabetes [6,7].

4. Summary of some medicinal plants with brief description

India has an officially recorded list of 45,000 plant species among which approximately 7500 species are of medicinal importance [12]. India has a rich history of using various potent herbs and herbal components for managing diabetes. Many Indian plants have been investigated for their beneficial use in different types of diabetes and reported in numerous scientific journals. Some medicinal plants are described below which play a key role in managing diabetes:-

4.1. Aframomum melegueta

The aqueous leaves extract of *Aframomum melegueta* was given to alloxanized (250 mg/kg/b.wt.) male rats at the dose of 20, 50, 100 and 200 mg/kg, significantly reduced blood sugar level. Final weight gain and organ restoration were seen in both diabetic and non-diabetic rats after treatment when compared with their controls. This study revealed that the extract has hypoglycaemic and prophylactic effects [13].

4.2. Alangium lamarckii

Alcoholic leaves extract of *Alangium lamarckii* was given to streptozotocin-nicotinamide induced type 2 diabetic rats at the dose of 250 and 500 mg/kg. The results showed a significant reduction in the blood plasma glucose level and restoration of liver glycogen, antioxidant activity and improvement in glucose tolerance in diabetic rats [14].

4.3. Aloe vera

The aqueous leaves extract of *Aloe vera* (*AVL*) (0.5 ml/100 gm b.wt.) was given to alloxan (65 mg/100 gm b.wt.) induced diabetic rats for 30 days. The results showed a significant reduction in serum glucose level in *AVL* extract feeded rats. Reduction in glucose level may be due to stimulation of β-cells of pancreas for increased secretion of insulin. Thus, the present studies reveal that *Aloe vera* has a significant anti-diabetic potential [15].

4.4. Boerhaavia diffusa

The crude extract of *B. diffusa* was given to streptozotocin induced diabetic rats at the dose of 100 and 200 mg/kg. Both high and low doses showed a significant reduction in blood glucose levels. Hence, the study revealed that *B. diffusa* possesses anti-hyperglycaemic activity [16].

4.5. Brassica juncea

The aqueous seed extract of *Brassica juncea* was given to streptozotocin induced diabetic male albino rats at the dose of 250, 350 and 450 mg/kg. The result showed a significant reduction in blood glucose level. A significant dosage dependant augmenting effect of the seed extract on the serum insulin was observed in both short term as well as long term groups. The study revealed that the aqueous extract of *Brassica juncea* (seeds) has potent hypoglycaemic activity [17].

4.6. Bridelia retusa

The hypoglycaemic potential of *B. retusa* bark was studied in alloxanized diabetic rats. Albino rats were divided into 6 groups received different treatments consisting of control, methanolic, pet-ether and *n*-butanol extracts (at a dose of 200 and 400 mg/kg) and compared with a standard drug glibenclamide (5 mg/kg).

Results indicated that *B. retusa* extracts does not affect blood glucose level on normal rats but in alloxan induced diabetic rats *n*-butanol extract showed significant reduction in blood sugar level [18].

4.7. Calotropis procera

Diabetes was induced by administration of single dose of streptozotocin (50 mg/kg, I.P). Pet ether, methanol and aqueous extracts of *C. procera* (roots) at dose of 250 mg/kg were oral administered as single dose per day to diabetes-induced rats for the period of 15 days. After extract treatment, the blood glucose, cholesterol and triglycerides level were seen to be decreased in diabetic rats. The activities were also compared to that effect produced by a standard anti-diabetic agent, glibenclamide 500 μg/kg. Results concluded that it is an anti-diabetic and anti-hyperlipidaemic agent [19].

4.8. Carica papaya

Daily oral administration of *C. papaya* aqueous leaves extract in streptozotocin induced diabetic rats was examined for 24 weeks by assessing fasting blood sugar and serum lipid profile. Treatment of STZ-diabetic rats with *C. papaya* leaves extract produced significant reductions in glucose and cholesterol level. The high AI (atherogenic index) and CRI (coronary risk index) caused by STZ diabetes was significantly reduced in the *C. papaya* treated diabetic rats. The study suggests that the aqueous leaf extract of C. papaya possess long term anti-diabetic and anti-hyperlipidaemic, as well as anti-atherogenic effects [20].

4.9. Carthamus tinctorius

The extract of *Carthamus tinctorius* was given to rabbits orally for 30 days and the values of blood glucose levels were observed after 15th and 30th day of treatment. Results revealed that *Carthamus tinctorius* has significant hypoglycaemic effect at 200 mg/kg and 300 mg/kg doses. Insulin levels were significantly increased in Glibenclamide treated as well as *Carthamus tinctorius* treated groups as compared to diabetic control [21].

4.10. Catharanthus roseus

Oral administration of aqueous extract of *Catharanthus roseus* flowers at the doses of 250 mg, 350 mg, and 450 mg/kg/b.wt. for 30 days in alloxan induced diabetic rats, resulted a significant reduction in blood glucose, reduction in lipid profile and also prevented a decrease in body weight. Histological observation demonstrated significant fatty acid changes and inflammatory cell infiltrates in pancreas in diabetic rats [22].

4.11. Cynanchum acutum

Oral administration of the butanol fraction (100 mg kg D1 body wt.) and isolated compounds 1D3 (50 mg kg D1 b.wt.) for 8 weeks were given to alloxanized rats. The butanol fraction was initially tested for its acute anti-diabetic activity at a dose of 100 mg/kg/b.wt. Results showed its significant hypoglycaemic activity that encouraged further investigation of its major isolates for their chronic anti-diabetic activity through measuring glucose and insulin levels [23].

4.12. Dioscorea bulbifera

Ethanolic tuber extract of *Dioscorea bulbifera* was administered in diabetic rats at the dose of 380, 760 and 1140 mg/kg, significantly reduced blood glucose level. The extract of *Dioscorea bulbifera* showed the presence of alkaloids, carbohydrate, protein, glycosides and these compounds indicates the antioxidant activity of this plant. Hence, the study revealed that ethanolic extract of *Dioscorea bulbifera* possesses anti-hyperglycaemic activity [24].

4.13. Eugenia jambolana

The ethanolic extract of seed of *Eugenia jambolana* (*EJs*) was given to STZ-induced diabetic rats at the dose of 100 mg/kg for 30 days. Daily oral administration of *EJs*-kernel increased the activity of antioxidant enzymes and may help to avoid the free radicals generated during diabetes. From the obtained result, it was found that *Eugenia jambolana* have anti-diabetic and anti-oxidative potential [25].

4.14. Gentiana olivieri

The methanolic and aqueous extracts of aerial part of *Gentiana olivieri* was given to normoglycaemic and hyperglycaemic rats at dose of 5 ml/kg/b.wt. An active component isoorientin was isolated from the plant through in vivo bioassay-guided fractionation which restored plasma level of insulin, decreased glucose level and possesses an antioxidative activity. Therefore, the study revealed that *Gentiana olivieri* and its active component has a potential antidiabetic activity [26].

4.15. Helianthus annuus

Ethanolic extract of sunflower seeds and its fractions were given to albino rats at dose level 250 mg/kg and 500 mg/kg. The phytochemical screening showed that ethanolic extract of sunflower seeds contain tannins, steroid, terpenoids, saponins, flavonoids, and alkaloid, cause a reduction in diabetes and its complications. Results concluded that the ethanolic extract of sunflower seeds have potential antidiabetic activity [27].

4.16. Leonotis leonurus

The aqueous leaves extract of *Leonotis leonurus* to streptozotocin (45 mg/kg I.P) induced diabetic rats orally at the doses of 125, 250 and 500 mg/kg for 15 days, significantly reduced blood glucose level, high density

lipoprotein (HDL) and increased the level of low density lipoprotein (LDL). The phytochemical screening showed presence of phenolic, flavonoid and proanthocyanidins in extract [28].

4.17. Mallotus philippinensis

The ethanolic bark extract of *Mallotus phillipinensis* was given to streptozotocin induced diabetic rats at the dose level 200 and 400 mg/kg for 30 days. The result showed significant increase in the levels of insulin and decrease in blood glucose, glycosylated hemoglobin. The study concluded that the presence of phytoconstituents such as phenolic compound in the bark extract of plant, associate with its anti-diabetic activity [29].

4.18. Marsilea minuta *linn*

The ethanolic extract of *Marsilea minuta* (EEMM) leaves was given to alloxan-induced diabetic albino at the dose level 250 and 500 mg/kg body wt rats for three weeks. The level of blood glucose, cholesterol and serum triglyceride were found to be significantly reduced in EEMM treated rats and the extract also showed the potent elevation in the level of serum HDL. From the obtained

data, it may be concluded that EEMM leaves has significant anti-hyperglycaemic property [30].

4.19. Mollugo nudicaulis

The ethanolic extract of *Mollugo nudicaulis* to alloxanized (120 mg/kg b.wt.) diabetic rats at the dose level 200 mg/kg for 21 days, resulted a significant reduction in blood glucose, cholesterol, triglycerides, LDL, lipid Peroxidation (LPO), liver glycogen, serum creatinine, urea, uric acid and liver marker enzymes such as aspartate aminotransferase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP). Glibenclamide was used as a reference standard drug. It also significantly increased the HDL, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione-*S*-Transferase (GST), Reduced glutathione (GSH) and vitamin C. From the data obtained, the study concluded that plant extract possess antihyperglycaemic and antioxidative property [31].

4.20. Moringa oleifera

Daily oral treatment of methanol extracts of *M. oleifera* pods (*MOMtE*) (150 or 300 mg/kg) to STZ-induced diabetic rats for 21 days resulted a significant reduction in serum glucose and nitric oxide, with increases in serum insulin and protein levels. Two phyto-constituents, quercetin and kaempferol, were isolated from the *MOMtE*. The study concluded that the methanolic extract of pods from *M. oleifera* protects β-cells against ROS-mediated damage by enhancing cellular antioxidant defenses and minimizing hyperglycemia in STZ-induced diabetes [32].

4.21. Morus alba

The leaves and root bark extract of *Morus alba*, have various types of constituents such as imino sugars, flavonoids and other phenolic compounds, glycopeptides and ecdysteroids, which have been suggested to be responsible for the anti-diabetic activity The volatile-oil like fraction of the hot water extract of *M.alba* leaves, containing several phenyl-propane derivatives, can increase the glucose consumption of adipocytes. Significant amounts of the aglycons of both compounds were liberated, suggesting that these compounds can be metabolized in the large intestines and absorbed without the sugar moiety after the consumption of a traditional mulberry tea. The study suggested that both the glycosides and their aglycons have a potential contribution to the beneficial effects of mulberry leaves in type-2 diabetes [33].

4.22. Ocimum sanctum

The effects of aqueous suspension of *Allium sativum* and *Ocimum sanctum* on cultured pancreatic β-cells were observed in normal rats. The cultured pancreatic β cells treated with aqueous suspension of *Allium sativum* and *Ocimum sanctum* shows the increased level of insulin and islet viability. Aqueous suspension of *Allium sativum* and *Ocimum sanctum* signified its insulin secretagouguge activity and regeneration of pancreatic β islet cells functions. Thus, concluded that it may be a potential antidiabetic agent. [34].

4.23. Opuntia joconostle

The aqueous extract of mesocarpium and cladode of *Opuntia joconostle* was given to streptozotocin-induced diabetes (40 mg/kg/b.wt) rats at the dose of 100 mg/kg for 12 weeks. The result showed reduction in glucose levels and triglycerides. The result revealed that *O. joconostle* possesses a glucose and lipid lowering effect in both healthy and diabetes-induced rats [35].

4.24. Orthosiphon stamineus

Daily administration of chloroform extract of *O. stamineus* at a dose of 1 gm/kg/b.wt twice was given to streptozotocin induced diabetic rats. Result showed that the chloroform extract of *O. stamineus* causes a significant reduction in the final blood glucose level compared to pre-treatment level. Hence, concluded that the chloroform extract of *O. stamineus* may possess extra pancreatic mechanisms indicative of its hypoglycaemic activity [36].

4.25. Panax ginseng

Extract of *Panax ginseng* was given to albino diabetic rats. The mean values of blood glucose, cholesterol, triglycerides, LDL and VLDL- cholesterol showed significant decrease in treated diabetic group as compared to their values in diabetic group. Serum IL − 6, TNF − α levels and Liver antioxidants were significantly increased after treatment with ginseng in diabetic rats [37].

4.26. Phoenix dactylifera

The powdered form of *Phoenix dactylifera* dried dates (*Karchure chooranam*) was given to alloxan induced diabetic rats at the dose of at 500 mg/kg. Result showed a significant reduction in blood glucose level. Glibenclamide (10 mg/kg) used as reference standard. The study revealed that *Karchure chooranam* possesses an antidiabetic activity [38].

4.27. Physalis pubescens

Physalis was given to alloxan monohydrate (150 mg/kg/b.wt) induced diabetic albino rats at a single 1 ml dose per day for 21 days. The result showed a significant reduction in blood glucose, troponin, TNF-alpha and IL6, dopamine, serotonin and serum insulin were significantly increased. Study suggested that *Physalis* have anti-diabetic and anti-oxidative potential [39].

4.28. Pseudarthria viscid

Anti-diabetic and hypolipidaemic activity of *P. viscida* in streptozotocin-nicotinamide induced type-II diabetes in rats was examined. The ethanolic extract of *P. viscida* at a dose of 100 mg/kg, 200 mg/kg was given to Streptozotocin treated rats and result suggested that this ethanolic extract significantly reduced blood glucose levels, SGOT, SGPT and lipid profiles, indicating the antihyperglycaemic potential of *P. viscida* [40].

4.29. Syzygium cumini

The petroleum ether, chloroform, acetone, methanol and water extract of *Syzygium cumini* in diabetic rats at 100 mg/kg, p.o. for 21 days treatment, significantly decreased the fasting blood glucose level. Moreover, among all the extracts, methanol extract was found to be most active. The study concluded that *Syzygium cumini* have a potential anti-hyperglycaemic activity [41].

4.30. Trichosanthes dioica

The anti-hyperglycaemic activity of leaves extract of *Trichosanthes dioica* was studied in streptozotocin induced (45 mg/kg) diabetic rats. Daily administration of leaves extract (800 mg/kg and 1600 mg/kg) reduced blood glucose significantly when compared to control but it was not as effective as glibenclamide. The study

revealed that the aqueous extract of *Trichosanthes dioica* have anti-hyperglycaemic activity [42].

4.31. Tridax procumbens

The ethanolic extract of whole plant of *Tridax procumbens* was given to streptozotocin induced diabetic rats at the dose of 250 and 500 mg/kg/b.wt for 21 days. The phytochemical screening of extract showed the presence of phyto-constituents such as sterol, alkaloids, tannins, flavonoids, saponins and phenolic compounds which is responsible for the significant reduction in the level of lipid, glucose and inhibits weight loss in diabetic rats [43].

4.32. Vinca rosea

The methanolic whole plant extract at high dose (500 mg/kg) exhibited significant anti-hyperglycaemic activity in diabetic rats. The methanolic extracts also showed improvement in parameters like body weight and lipid profile as well as regeneration of β-cells of pancreas in diabetic rats. Histopathological studies reinforce the healing of pancreas, by methanolic *Vinca rosea* extracts, as a possible mechanism of their anti-diabetic activity [44].

4.33. Wedelia chinensis

Ethanol extract (*WcEe*) of *Wedelia chinensis* (2 mg/kg/b.wt) was given to alloxan (Alloxan monohydrate 150 mg/kg/b.wt) induced diabetic rats for 30 days. The results showed reduction in the level of cholesterol, LPO, and blood glucose. From the data obtained it may be concluded that *Wedelia chinensis* have an insulinogenic and antioxidative activity [45].

5. Discussion

Diabetes is a serious debilitating, life challenging disease, arising as a major issue of concern all over the globe. To prevent this alarming health issue there is a need to switch on better alternatives in the form of herbal hypoglycemic agents. Current review depicts the plants along with their phyto-constituents evaluated and their mode of reduction in blood glucose via different mechanisms. Besides using rat animal models the hypoglycemic activity of these herbal plants have also been carried out on other animal models such as rabbit, guinea pig etc.

But still toxicological investigation of all plants should be carried out to avoid the risk of side effect related to phyto-medicines. On the basis of positive confirmatory test further research should be done in the direction of clinical trials which may prove beneficial for human welfare.

6. Conclusion

Folklore remedies are used for managing diabetes due to its nontoxic nature, cost effectiveness, easy availability and long lasting effects over their synthetic counterparts. The current review depicted a systematically arranged description of medicinal plants possessing hypoglycaemic activity as well as their active phyto-constituents which may help researchers for easy access to active constituents for making newer effective drugs which possess almost equal or more potency as seen in the case of synthetic drugs.

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