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ANTIDIABETIC PLANTS AND THEIR ACTIVE INGREDIENTS: A REVIEW

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ABSTRACT

Diabetes mellitus is a lifestyle disorder that is rapidly becoming a major threat to populations all over the globe. Over the past 30 years, the status of diabetes has changed from being considered as a mild lifestyle disorder of the elderly to one of the major causes of morbidity and mortality, affecting people of all ages. India is slated to be the diabetic capital of the world, with 50.8 million diabetics. There seems to be a renewed interest in herbal medicines across the world today and plants are a powerhouse of sources for antidiabetic principles. Hence, a review on the antidiabetic plants has been done and the plants with antidiabetic principles isolated have been tabulated. Electronic searches were conducted in numerous databases and relevant journals. Sources also included various books and newspaper articles. Hand searches were also carried out in additional journals and secondary references. Researchers in the field of Ayurveda, Siddha, Unani and Homeopathy were consulted for access to ongoing research and various references. Molecular docking studies were performed on three selected plants to authenticate their affinity and therapeutic efficacy.

INTRODUCTION: Diabetes mellitus, being a multifactorial disease, demands multiple therapeutic approaches. Global studies on diabetes mellitus have reiterated that primary prevention is necessary and drastic steps must be taken to diagnose the disease early on, provide effective management and also take steps to prevent the onset of disease in high-risk subjects. According to WHO, plant-based traditional system of medicine is still the mainstay of about 75–80% of the world population, mainly in the developing countries, for primary healthcare because of better cultural acceptability, better compatibility with the human body and lesser side effects [1]. According to the fifth edition of the World Diabetes Atlas released by the International Diabetes Federation (IDF), as of 2011, the total adult population in the age group of 20-79 years stands at 4.3 billion, out of which 366 million live with diabetes, which is set to increase to 552 million by 2030 [2]. Recent molecular investigations all over the world highlight the power of herbs. There is a need to transform “traditional anecdotes” to “evidence-based medicine”. The transformation of digitalis from a folk medicine, foxglove, to a modern drug, digoxin, illustrates principles of modern pharmacology that allow development of safe and effective drugs from nature [3].

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Historical Account: Fossil records date human use of plants as medicines at least to the Middle Paleolithic age some 60,000 years ago [4]. A study of Ayurvedic literatures, written as early as 4th to 5th century B.C., indicate that diabetes, known as "Madhumeha (honey urine)", was fairly well known and well conceived in ancient India. The earliest recorded evidence of their use in classical Indian texts such as Rigveda and Atherveda, Chinese, Egyptian, Greek, Roman and Syrian texts dates back to about 5000 years [5-6]. The most authentic medical treatise, Sushruta Samhita, describes 760 species of antidiabetic plants, while Charaka Samhita describes 500 species. They also describe about glycosuria, polyphagia, and polyuria.

Historical references to diabetes mellitus occur in an ancient Egyptian medicine document, Ebers Papyrus, from the 3rd Dynasty in 1500 B.C. In China, Ben Jing, written in 104 B.C., describes about 252 species of antidiabetic plants. In Unani system of medicine, which originated in Greece and evolved within the Muslim world, there are various references to diabetes and antidiabetic herbs. South America and Africa, which have less documentation, also describe about various treatments for diabetes using medicinal plants. A comprehensive review on antidiabetic medicinal plants has been compiled by Atta-ur-Rahman and Zaman, providing information regarding nearly 343 antidiabetic plants [7-9].

The earliest recorded attempt to treat diabetes mellitus dates back more than 3,500 years and the treatment used was of plant origin [10]. Hence, there are various evidences of treatments with antidiabetic medicinal plant in Native American, Traditional Chinese Medicine, Kampo, Ayurvedic, Siddha, Unani, Homeopathy, Tribal, and Folk from time immemorial. According to the folklore of North Carolina, collected by Dr. Frank C. Brown during the years 1912 to 1943, a strange sounding suggestion to cure diabetes is to allow a poisonous snake to bite the sufferer.[11].

Alternative Therapy - Plants as Source of Antidiabetic Drugs: Diabetes mellitus is a chronic disease with serious long-term debilitating complications and no known cure. Nowadays, insulin and other oral blood glucose lowering agents are used in the clinical management of diabetes mellitus. Unfortunately, the prevalence of this disease continues to rise worldwide and little can be done to prevent the delay of its secondary complications. Thus, search for new antidiabetic drugs with novel mechanisms of action should still be pursued. Man has used plants heavily to treat diabetes mellitus, so much so, there are 700 recipes containing more than 400 plants reputed for their antidiabetic activity. The last few years have seen a major surge in the use of herbal medicines the world over. India is sitting on a gold mine of well-recorded and well-practiced knowledge of traditional herbal medicine, and hence must capitalize on this herbal wealth by promoting its use worldwide [12].

In the field of bioinformatics, molecular docking studies are widely used to predict suitable drug candidates in the pharmaceutical drug designing industry. Binding orientation of these small molecules or active ingredients to their protein targets reveals their affinity and activity as possible drug candidates [13].

MATERIALS AND METHOD: For this review, electronic searches were conducted in various databases and online journals. Sources also included books and newspaper articles. Hand searches were also carried out in additional journals and secondary references. Researchers in the field of Ayurveda, Siddha, Unani and Homeopathy were consulted for access to references and ongoing research. To authenticate the promising effect of the antidiabetic phytochemicals, molecular docking studies were performed on three chosen antidiabetic plants - *Pterocarpus marsupium* (**Figure 1-3, Table 1**), *Glyzyrrhiza glabra* (**Figure 4-6, Table 2**), *Syzygium cumini* (**Figure 7-9, Table 3**), using a web-based software application for protein and ligand molecular docking.

RESULTS:

Docking Studies:

Pterocarpus marsupium:

(Phytochemical - Pterostilbene)

IUPAC Name: 4-[(E)-2-(3,5-dimethoxyphenyl) ethenyl] phenol

Molecular Weight: 256.296440 g/mol

Molecular Formula: $C_{16}H_{16}O_3$

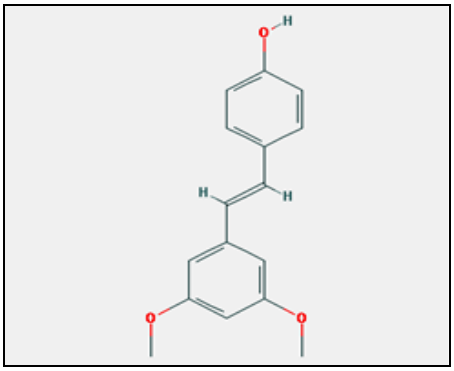

FIG. 1: 2D STRUCTURE

FIG. 2: 3D Structure

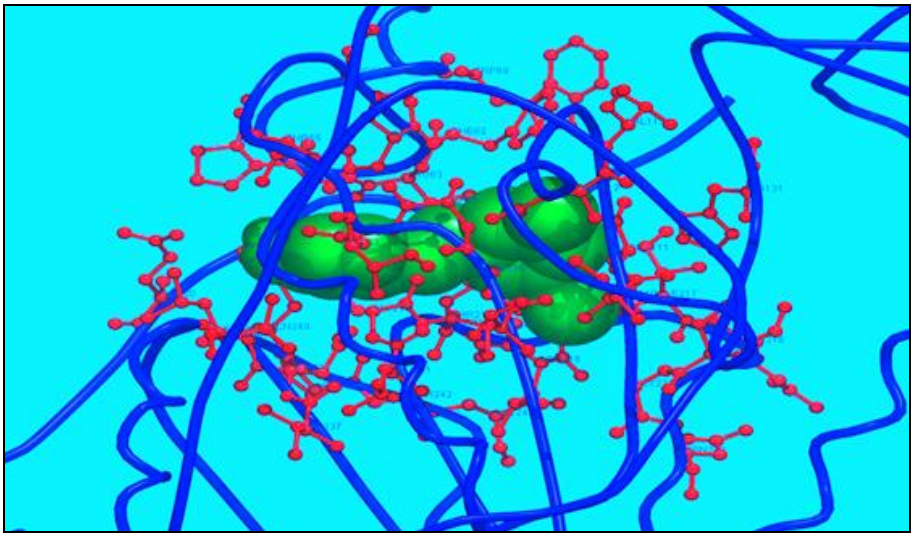

FIG. 3: DOCKING OF 4-[(E)-2-(3,5-DIMETHOXYPHENYL) ETHENYL] PHENOL WITH PROTEIN (SIRTUIN 6) WITH ANALYSIS DONE ON DOCKING SERVER SHOWING RECEPTOR (BLUE), LIGAND (RED) AND ACTIVE SITE (GREEN)

TABLE 1: DOCKING STUDIES SHOWING ENERGY VALUES OF *PTEROCARPUS MARSUPIUM* (PHYTOCHEMICAL - PTEROSTILBENE)

Rank	Est. Free Energy of Binding	Est. Inhibition Constant Ki	vdW + Hbond + desolv Energy	Electrostatic Energy	Total intermolec. Energy	Frequency	Interact. Surface
1	-6.56 kcal/mol	16.66 uM	-7.85 kcal/mol	-0.15 kcal/mol	-8.00 kcal/mol	50%	706.58

Glycyrrhiza glabra:

(Phytochemical - Glycyrrhiza - Flavonol A)

IUPAC Name: 3, 5, 7-trihydroxy-2-(3-hydroxy-2, 2-dimethyl-3, 4-dihydrochromen-4-one
Molecular Weight: 370.35272 g/mol
Molecular Formula: $C_{20}H_{18}O_7$

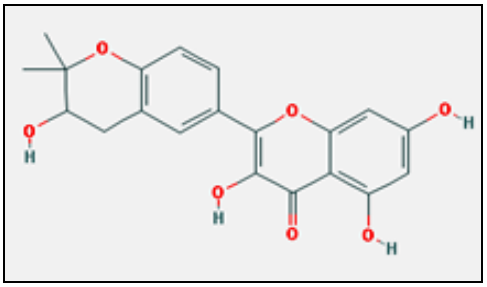

FIG. 4: 2D STRUCTURE

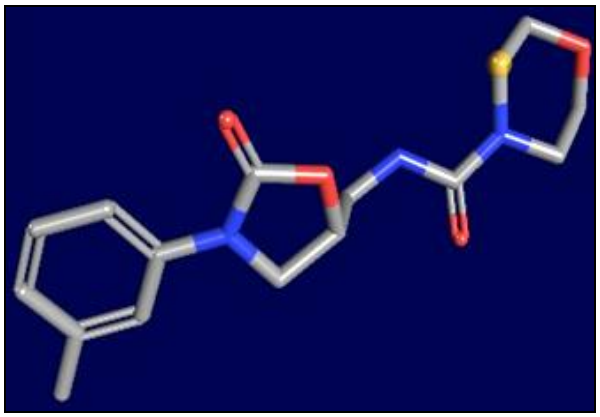

FIG. 5: 3D STRUCTURE

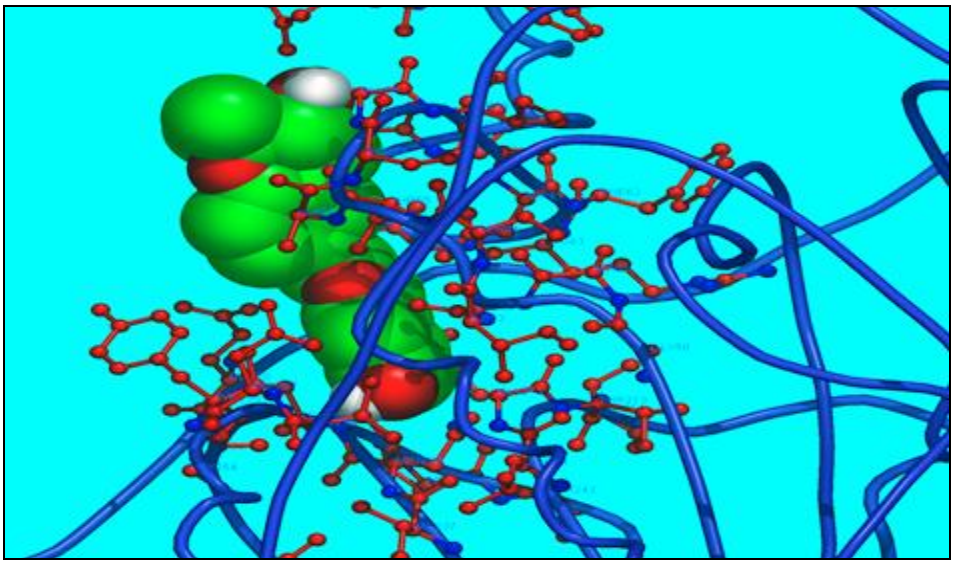

FIG. 6: DOCKING OF 3,5,7-TRIHYDROXY-2-(3-HYDROXY-2,2-DIMETHYL-3,4-DIHYDROCHROMEN-4-ONE WITH PROTEIN (SIRTUIN 6) WITH ANALYSIS DONE ON DOCKING SERVER SHOWING RECEPTOR (BLUE), LIGAND (RED) AND ACTIVE SITE (GREEN)

TABLE 2: DOCKING STUDIES SHOWING ENERGY VALUES OF *GLYCYRRHIZA GLABRA* (PHYTOCHEMICAL - GLYCYRRHIZA - FLAVONOL A)

Rank	Est. Free Energy of Binding	Est. Inhibition Constant Ki	vdW + Hbond + desolv Energy	Electrostatic Energy	Total intermolec. Energy	Frequency	Interact. Surface
1	-5.48 kcal/mol	95.87 uM	-5.69 kcal/mol	-0.33 kcal/mol	-6.02 kcal/mol	50%	761.887

Syzygium cumini:

(Phytochemical - Cuminyl alcohol)

IUPAC Name: (4-propan-2-ylphenyl)methanol

Molecular Weight: 150.217560 g/mol

Molecular Formula: $C_{10}H_{14}O$

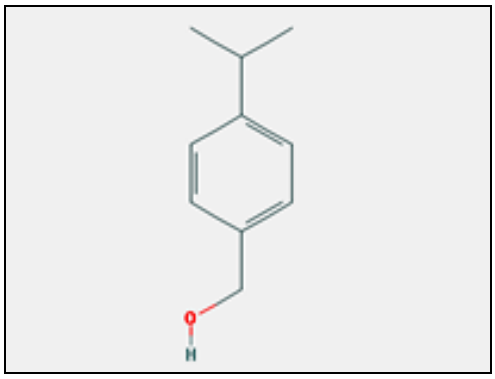

FIG. 7: 2D STRUCTURE

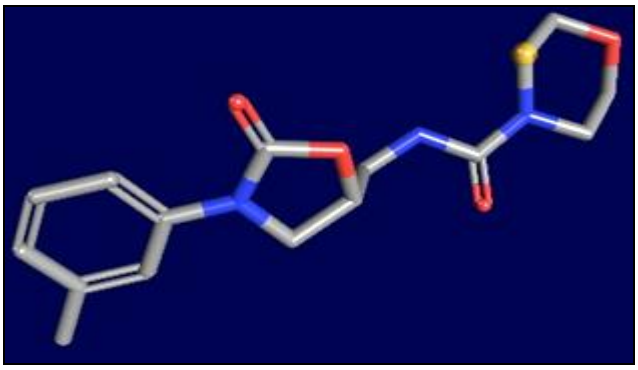

FIG. 8: 3D STRUCTURE

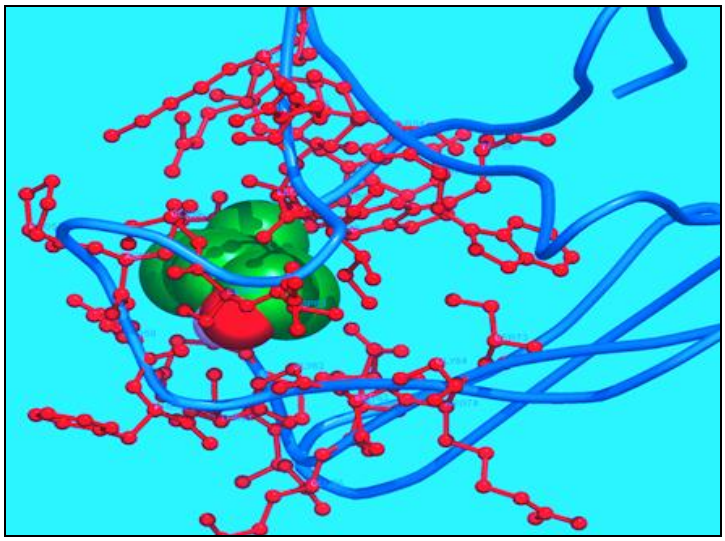

FIG. 9: DOCKING OF (4-PROPAN-2-YLPHENYL)METHANOL WITH PROTEIN (SIRTUIN 6) WITH ANALYSIS DONE ON DOCKING SERVER SHOWING RECEPTOR (BLUE), LIGAND (RED) AND ACTIVE SITE (GREEN)

TABLE 3: DOCKING STUDIES SHOWING ENERGY VALUES OF *SYZYGIUM CUMINI* (PHYTOCHEMICAL - CUMINYL ALCOHOL)

Rank	Est. Free Energy of Binding	Est. Inhibition Constant Ki	vdW + Hbond + desolv Energy	Electrostatic Energy	Total intermolec. Energy	Frequency	Interact. Surface
1	-5.01 kcal/mol	213.71 uM	-5.91 kcal/mol	-0.01 kcal/mol	-5.92 kcal/mol	50%	469.309

DISCUSSION: Before the advent of insulin injections and oral hypoglycemic drugs, healers relied heavily upon the use of herbs to treat diabetes. Various active ingredients were isolated from the medicinal herbs and animal experimentations were carried out to study their mode of action. In recent times, due to the surge in interest in herbal medicines, various antidiabetic plants are being studied to identify a wide array of chemically derived plant compounds for their possible treatment of diabetes. Often extracts from natural sources provide excellent pharmacological actions and negligible or no adverse effects. Hence, this review will throw light on the various explored and unexplored antidiabetic plants, which could enable efficacious and cost-effective antidiabetic therapy.

Most antidiabetic plants belong to the family Leguminoseae, Curubitaceae, Liliaceae, Laminaceae, Asteraceae, Rosaceae, Euphorbiaceae, Moraceae, and Araliaceae.

Although a number of plants have some degree of antidiabetic activity, a significant amount of research as well as traditional usage is confined only to a few useful plants, some of which are the following:

1. *Gymnema sylvestre* - gurmar
2. *Trigonella foenum-graecum* - fenugreek
3. *Momordica charantia* - bitter gourd
4. *Opuntia streptacantha* - nopal or prickly pear cactus
5. *Pterocarpus marsupium* - Indian kino
6. *Polygala senega* - Seneca snake-root
7. *Allium cepa* - onion
8. *Allium sativum* - garlic
9. *Panax quinquefolius* - ginseng
10. *Aloe vera* - aloe
11. *Lagerstroemia speciosa* - banaba
12. *Tinospora cordifolia* - Guduchi
13. *Syzygium cumini* - Jamun or jambul
14. *Azadirachta indica* - neem
15. *Murraya koenigii* - curry leaf
16. *Embilica officinalis* - Indian gooseberry or amla
17. Phyllanthus amarus - keezhkai nelli
18. *Cyamopsis tetragonaloba* - guar gum
19. *Withania sominifera* - winter cherry
20. *Hordeum vulgare* - barley
21. *Ginko biloba* - ginko
22. *Bauhinia forficate* - pata de vaca
23. *Ocimum sanctum* - holy basil
24. *Coccinia indica* - Ivy gourd
25. *Vaccinium myrtillus* - bilberry
26. *Glycyrrhiza glabra* - licorice

Some plants, *Pterocarpus marsupium* [14] and *Bauhinia forficata* [15], even promote regeneration of the damaged beta cells in the Islet of Langerhans in pancreas. Most of the plants have blood glucose lowering activity and some in addition have antioxidant, as well as hypocholesterolemic activities. Not all the antidiabetic plants have their active ingredients identified and are yet to be isolated. Most of the experimentation takes place using plants in aqueous or hydroalcoholic extracts. The effect of these antidiabetic plants have been tested in vivo and in vitro on rats, mice, rabbits and dogs. Very few have been tested on humans for their efficacy.

Alloxan or streptozotocin has been used to induce diabetes in the animal studies, as well as pancreatectomy in a few. Mechanism of action is described in a few plants, in comparison with the oral hypoglycemic drugs. The active ingredients play a role

in enhancing glucose utilization, lowering plasma glucose, and improving insulin sensitivity in diabetic animals. Different extracts of numerous plants were studied and found to show hypoglycemic effects. The aqueous extracts show maximum effect. They were compared to glibenclamide, tolbutamide, and metformin as standard [16-22].

Abies pindrow (silver fir) and its active ingredient D-pinitol, exert an insulin-like effect to improve glycemic control in hypoinsulinemic STZ-diabetic mice. D-pinitol may act via a post-receptor pathway of insulin action affecting glucose uptake. Hypoglycemic activity due to increase in the peripheral metabolism of glucose was seen in some plants and these experiments were carried out on rabbits with experimentally induced diabetes [23]. The leaves of *Bauhinia purpurea* (orchid tree) were found to possess, in addition to antidiabetic activity, antioxidant and antihyperlipidemic activities [24].

The saponins of root bark of *Berberis vulgaris* aqueous extract exhibited significant antihyperglycemic activity. The results suggest that the hypoglycemic effect was due to the stimulating effect of the remnant beta cells [25]. Root of *Beta vulgaris* is known to reduce blood glucose levels by regeneration of beta cells. The leaf of the bitter plant, *Biophytum sensitivum*, exhibited hypoglycemic activity, which may be mediated through stimulating the synthesis/release of insulin from the beta cells of Langerhans [26-29]. Ethanolic extracts of the roots and leaves of Boerhaavia diffusa (red spiderling) was found to have potent antidiabetic activity that reduces blood sugar level in streptozotocin-induced diabetic rats [30].

The study on the leaves of Bougainvillea spectabilis suggests that aqueous and methanolic extracts have good glucose tolerance and significantly reduced intestinal glucosidase activity, with regeneration of insulin-producing cells and increase in plasma insulin. These results suggest a potential for development of new nutraceutical treatment for diabetes [31].

Buddleja officinalis was found to have a hypoglycemic effect, which was due to the inhibition of DPP-IV. DPP-IV inhibitors have been proved to prevent GLP-1 degradation, and thus, effectively decrease blood glucose. It also possesses antioxidant activity. Pancreatic α-amylase inhibitors offer an effective strategy to lower the levels of post-prandial hyperglycemia via the control of starch breakdown [32]. *Caesalpinia sappan* shows moderate porcine pancreatic α-amylase inhibitory (PPA) activity [33]. Root of *Dioscorea oppositifolia* is used in Chinese herbalism to treat diabetes. This root is a key ingredient in "the herb of eight ingredients" used in Traditional Chinese Medicine to treat hyperthyroidism, nephritis, and diabetes [34].

Leaves of *Eucalyptus globulus* is found to ameliorate the diabetic state by partial restoration of pancreatic beta cells and repair of STZ-induced damage in rats. Eucalyptus alcoholic extract can serve as a good adjuvant in the present armamentarium of antidiabetic drugs.[37]

According to Urmila Thatte, many studies have been made on leaves, fruits, or flowers of antidiabetic plants, which is better than using the whole plant or the root of the plant, as the continued availability of raw material will be a challenge. Sustainability and environmental conservation should be taken into account as well. It was also found that combinations of herbal extracts showed better efficacy as compared to individual herbal plant extracts used. This was seen in *Abroma augusta* and *Curcuma longa*, which showed efficient antidiabetic activity and also reduced oxidative stress in diabetic animals [35-37].

Coccinia indica, a member of the Cucurbitaceae family, had the same ability to lower glucose levels as tolbutamide. Inhibition of adipocyte differentiation and peroxisome proliferator-mediated receptor-α or (PPARα)-mediated mechanisms might be relevant pathways for the antidiabetic activity of the *Fraxinus excelsior* extract. *Majorana hortensis*, a native of Cyprus and Turkey, has alpha-glucosidase inhibition activity, which indicates that inclusion of herbs from Lamiaceae family could potentially help manage hyperglycemia linked to type 2 diabetes [38-42].

It is important to study the efficacy of the antidiabetic herb, shelf-life, and stability as well. Studies show that animal studies are poor predictors of effects in humans. Though many plants have shown promising results as antidiabetic agents, their efficacy varies from patient to patient. As a result, clinical studies must be

carried out in large populations before any plant-based product can be introduced into clinical practice. Studies should be designed to identify and determine any undesirable side effects that result from their consumption [12].

Gossypium herbaceum, a potential antidiabetic plant, is a part of Diabecon (D-400), which is an antidiabetic herbomineral preparation, which reduces hyperlipidemia and may possibly delay the lipid-mediated secondary complications of arteriosclerosis [32]. The seeds of *Irvingia gabonensis* significantly reduce body weight and improve metabolic parameters in overweight humans in a randomized double-blind placebo controlled investigation. Leaf decoction of *Jatropha curcas* was found to stimulate insulin release. Furthermore, depending upon the cultivation conditions, the amount of secondary metabolites will vary, which may possess additional pharmacological activity, leading to variability in bioactivity. Hence, the geographic distribution of the plants and their place of origin has to be traced as well [43-46].

The bitter seeds of *Holarrhena pubescens* have potent immuno-stimulant property, antihyperlipidemic activity without any toxicity induction. The methanolic and ethanolic extracts have favorable effects on blood glucose levels, liver glycogen, serum lipids and body weight. *Ilex paraguayensis*, a native plant of Brazil, inhibits the formation of advanced glycation-end products (AGEs), with an effect comparable to that of two pharmaceutical AGE-inhibitor drugs. The formation of AGEs play a part in the development of diabetic complications. The bioactive compounds might be capable of interfering in glucose absorption, by decreasing SGLT1 expression [47-50].

Evaluation and identification of some new natural molecules with antidiabetic property have become one of the major preludes of present day diabetic research. Although few marine natural products are currently in the market or in the clinical trials, marine organisms still remain the greatest unexploited source of potential pharmaceuticals. Because of the unusual diversity of chemical structures isolated from marine organisms, there is intense interest in screening marine natural products for their biomedical potential. One such marine flora is *Cynometra ramiflora* L., belonging to the family Leguminoseae, which declined the hyperglycemia of the normal rats [51-52].

Shilajit, which is considered one of the wonder medicines of Ayurveda, neither a plant nor animal substance, but a mineral pitch that oozes from the rocks of the Himalayas, as they become warm in the summer months, is said to be used extensively for a variety of diseases including diabetes. Shilajit is among the best herbs for the long-term management of diabetes mellitus where it should be combined with gurmar [56]. *Hericium erinaceus* (Lion's mane), a fungi, native to China, Japan, North America and Asia, is found to be antidiabetic. Non-starch polysaccharides of the fruiting body are found to reduce blood glucose levels [58]. *Ramulus mori* or *Sang Zhi*, dried twig of mulberry tree, which is a traditional Chinese medicinal herb that appears to have properties similar to those of alpha-glucosidase inhibitors [59]. Alpha-glucosidase inhibitors are oral antidiabetic drugs. Triphala, which is a combination of 3 myrobalans - *Embelica officinalis*, *Terminalia chebula*, *Terminalia bellirica*, is a well-known hypoglycemic agent.

Gossypin, a pentahydroxy flavone glucoside found rich in the flowers of *Hibiscus vitifolius*, possess many biological properties including antidiabetic, anti-oxidant, anti-inflammatory and anticancer. Oral administration of gossypin to diabetic rats normalized the levels of plasma protein and blood urea. The obtained data were comparable with gliclazide, a standard reference drug for diabetes. Hence, it was concluded that gossypin has potent antidiabetic activity in streptozotocin-induced experimental diabetes in rats. Petroleum ether and ethyl acetate fractions of the leaves of *Coccinia cordifolia* have potential antidiabetic activity [60-61]. Most of the active compounds isolated from the antidiabetic plants are secondary metabolites. These hypoglycemic constituents include alkaloids, flavonoids, triterpenoids, polysaccharides, glycopeptides, aminobutyric acid derivatives, steroids, iridoids, phenolics, peptides, alkyldisulfides and inorganic ions [62].

Natural products provide important clues for identifying and developing synergistic drugs that research has largely neglected. We have a rich historical record from ancient physicians, which might provide important clues for developing new drugs. The

popularity of natural products will continue simply because they are a matchless source of novel drug leads and inspiration for the synthesis of non-natural molecules [63].

The antidiabetic principles isolated from numerous antidiabetic plants [64-100] are listed (**Table 4**). There are many antidiabetic plants which are yet to have their active ingredients isolated.

TABLE 4: ANTIDIABETIC PRINCIPLES ISOLATED FROM ANTIDIABETIC PLANTS

Medicinal Plant	Part Used	Active ingredient
Abroma augustum	Root	Abromine, its hydrochloride and a phytosterol
Abies pindrow	Root, leaf	D-pinitol (3-O-methyl-chiroinositol)
Abelmoschus moschatus	Aerial part of plant	Myricetin (3,5,7-trihydroxy-2-(3,4,5-trihydroxyphenyl)chromen-4-one)
Bumelia sartorum	Root bark	Unsaturated triterpene acid - bassic acid
Bryonia alba	Root	Trihydroxyoctadecadienoic acids
Bougainvillea spectabilis	Leaf paste, leaf juice	D-pinitol (3-O-methyl-chiroinositol)
Boswellia serrata	Gum resin	Oleo-gum resin
Bombax ceiba	Fruit, heartwood, leaf	C-flavonol glucoside - Shamimin
Blighia sapida	Fruit	Hypoglycin A and B
Bidens pilosa	Whole plant, leaf	Cytopiloyne
Bergenia ciliata	Root, leaf	(−)-3-O-galloylepicatechin, (−)-3-O-galloylcatechin
Berberis vulgaris	Root bark	Saponins
Berberis aristata	Stem, root	Berberine
Bauhinia variegata	Bark, leaves	Flavonoids
Bauhinia purpurea	Leaf	Flavonoid-containing fractions
Bauhinia candicans	Leaf	Trigonelline, kaempferol dirhamnoside
Balanites aegyptiaca	Mespcarp of fruit	Pure saponin, steroidal saponins
Bacopa monnieri	Aerial parts, leaf	Hersaponin, bacoside A
Camellia sinensis	Leaf	Epigallocatechin 3-gallate
Cajanus cajan	Leaves, seed, fruit	Arginine, ascorbic acid
Caesalpinia ferrea	Fruit	Ellagic acid (EA), 2-(2,3,6-trihydroxy-4-carboxyphenyl)ellagic acid (TEA)
Caesalpinia digyna	Root	Bergenin
Caesalpinia bonducella	Seeds	Caesalpin F
Caesalpinia bonduc	Seed kernel	Caesalpinianone
Dioscorea dumetorum	Tuber	Alkaloid - Dioscoretine, dihydrodioscorine
Eugenia uniflora	Leaf	Uniflorin A, uniflorin B, (+)-(3a, 4a, 5ß)-1-methylpiperidine-3, 4, 5-triol
Eriobotrya japonica	Leaf	corosolic acid, 3-epicorosolic acid methyl ester, 2-α hydroxy-3-oxo urs-12-en-28-oic acid, tormentic acid methyl ester, ursolic acid
Erigeron breviscapus	Plant extract	Scutellarin
Equisetum myriochaetum	Aerial parts	kaempferol glucosides, caffeoyl glucoside, kaempferol-3-Osophoroside-4'-O-beta-D-glucoside
Ephedra distachya	Whole plant	Ephedran C
Enicostema littorale	Whole plant	Swertiamarin, ophelic acid, tannins, alkaloid (gentianine)
Emblica officinalis	Fruit, seed, leaf	Polyphenols: flavonoids, kaempferol, ellagic acid, gallic acid
Eleusine coracana	Seed coat	Polyphenols
Eichhornia crassipes	Shoot, rhizome	Terpenoids, glycoside, flavonoid, tannin, alkaloid
Exostema mexicanum	Stem bark	4-phenylcoumarins glycosides, chlorogenic acid, ursolic acid
Exostema caribaeum	Stem bark	4-phenylcoumarins glycosides, chlorogenic acid, ursolic acid
Eclipta alba	Whole plant, leaf	Coumestans like wedelolactone, desmethylwedelolactone, furanocoumarins, oleanane, taraxastane glycosides
Ficus religiosa	Bark	β-sitosteryl-d-glucoside
Ficus racemosa	Stem bark	Beta-sitosterol
Ficus glomerata	Leaves, stem bark, fruit	Flavonoids, tannins
Ficus bengalensis	Bark, aerial roots, fruits	Leucopelargonin
Fumaria parviflora	Whole plant	Sanguinarine
Fraxinus excelsior	Seed, plant extract	Iridoids - secoiridoid glucosides, excelsides A and B
Gymnema sylvestre	Leaf	Gymnemic acids, gymnemagenin, gymnestrogenin

Medicinal Plant	Part Used	Active ingredient
Ginkgo biloba	Leaf	Ginkgo-flavone glycosides fraction - quercetin, kaempferol, isorhamnetin
Glycyrrhiza uralensis	Root	Glycyrrhizin
Glycyrrhiza glabra	Root	Glycyrrhizin
Gentiana olivieri	Plant extract	Isoorientin
Galega officinalis	Leaf, flowering tops	Alkaloid - galegine
Garcinia kola	Seed	alkaloid and biflavonoid extracts of seeds
Hygrophila auriculata	Aerial parts	Betulin, lupeol
Hovenia dulcis	Entire plant	Flavonoids
Hydrastis canadensis	Root	Berberine and hydrastine
Holostemma ada-kodien	Root	Flavonoids
Hintonia standleyana	Leaf	Phenylcoumarins
Hintonia latiflora	Leaf, root	Neoflavonoid coutareagenin
Hydnocarpus wightiana	Seed hulls	Acetyllbetulinic acid, betulinic acid, ursolic acid, acetylursolic acid
Hypoxis hemerocallidea	Root, tuber	Hypoxoside
Hemidesmus indicus	Root	Isovanillic acid - 3-Hydroxy-4-methoxy-benzoic acid
Harpagophytum procumbens	Root	harpagoside, beta-sitosterol
Ipomoea batatas	Root, leaf	An acidic glycoprotein
Juniperus communis	Dried berries	Isocrupressic acid
Juglans regia	Roots, leaves, unripe fruits	4-hydroxy-α-tetralone-4-O-β-D-[6′-O-(3″,4″,5″-trihydroxybenzoyl) glucopyranoside and 4-hydroxy-α-tetralone
Kalopanax pictus	Stem bark	kalopanaxsaponin A
Kalanchoe pinnata	Leaf	Bryophyllin A
Larrea tridentata	Leaf	Masoprocal (nordihydroguaiaretic acid)
Lagerstroemia speciosa	Leaf	Gallotannin - Penta-O-galloyl-glucopyranose (PGG)
Murraya koenigii	Leaf, fruit juice	Quercetin, murrayacine, carbazole
Momordica charantia	Fruit, seed	Charantin
Melia azadirachta	Pericarp of fruit, leaf, seed	Nimbin, nimbidin, nimbinin; azadirachtin
Marrubium vulgare	Leaf, roots	Marrubiin, marrubiol
Mangifera indica	Stem bark, leaf	Mangiferin – protocatechic acid, catechin,
Nigella sativa	Seeds, oilseed	Thymoquinone
Oryza sativa	Roots, external seed coat, seed	Glycans - oryzarans A, B, C, D
Otholobium pubescens	Plant extract	Bakuchiol - [4-(3-Ethenyl-3,7-dimethyl-1,6-octadienyl)phenol]
Origanum vulgare	Leaf	4'-O-beta-D-glucopyranosyl-3',4'-dihydroxybenzyl protocatechuate, 4'-O-beta-D-glucopyranosyl-3',4'-dihydroxybenzyl 4-O-methylprotocatechuate
Opuntia dillenii	Fruit	Polysaccharides
Ophiopogon japonicus	Roots	Polysaccharides
Olea europaea	Leaf	oleuropein, hydroxytyrosol
Ocimum sanctum	Leaf	Eugenol
Pterocarpus marsupium	Gum resin, bark, heartwood	Pterocarpol, pterostilbene
Phyllanthus amarus	Leaf	Bitters, lignans - phyllanthin, hypophyllanthin, bioflavanoids
Quercus infectoria	Leaf	Quercetin
Quercus rubra	Seed	Vanadium, manganese, magnesium, copper, chromium
Quercus alba	Bark	Quercetin
Rhizophora apiculata	Roots	Inositol, pinitol
Sesamum indicum	Seeds	Lignan - sesamin, phenolic derivative - sesamol, sesamolin
Semecarpus anacardium	Fruit, nut	Flavonoids and phenolic compounds

Medicinal Plant	Part Used	Active ingredient
Scrophularia ningpoensis	Root	Harpagoside
Scrophularia deserti	Aerial part of plant	Scropolioside-D, harpagoside-B
Schisandra chinensis	Fruit	Schizandrin B
Salacia chinensis	Root	mangiferin, salacinol, kotalanol
Salacia reticulata	Root, stem, leaves	polyphenol constituents - catechins, mangiferin, salacinol and kotalanol
Salacia oblonga	Root	Mangiferin, salacinol, kotalanol, kotalagenin 16-acetate
Saccharum officinarum	Stalk	Glycans A, B, C, D, E, F from the non-sucrose portion, saccharin
Tinospora cordifolia	Root	Tinosporin, berberine, tinosporinone
Vinca rosea	Whole plant; leaves, roots	Catharanthine, lochnerine, vindoline, leurosine, vindoline, vindolinine
Vernonia amygdalina	Leaves	Vernonioiside B and myricetin (flavonol)
Withania somnifera	Leaf, root	Chlorogenic acid, withaferin A, choline
Wedelia paludosa	Stems, root	Hypoglycemic diterpene - kaurenoic Acid (Ent-16-kauren-19-oic acid)
Xanthium strumarium	Seed, fruit	carboxyatractyloside (CAT)
Zea mays	Plant, seed, root, fruit, silk stigma style, cob, leaf, oil	Alpha-tocopherol, quercetin
Zingiber officinale	Juice of ginger, fresh and dried rhizome	[6]-gingerols, tannins, polyphenolic compounds (e.g. coumarins), flavonoids, triterpenoids
Zizyphus spina-christi	Leaves	Principal saponin glycoside - christinin-A
Zygophyllum gaetulum	Aerial parts, leaves	Triterpenene acid bisdesmosides with different sugar residues at C3 and C8 of the aglycones

In the light of docking analysis made, it is apparently evident that the plants have promising antidiabetic phytochemicals, able to complement the target and seem to possess therapeutic attributes, as authenticated by the energy value of them, especially in the case of *Syzygium cumini*. Since promising antidiabetic plants along with the active ingredients isolated have been tabulated, docking studies can be performed on all of them, which would throw more light on the antidiabetic efficacy of medicinal plants.

CONCLUSION: Many medicines in use today have their origin in plants. Herbal medicines are increasingly becoming popular and hence, it is prudent to search for options from medicinal plant extracts for new antidiabetic hypoglycemic substances. There is an urgent need to document traditional knowledge, as the current pace of urbanization may lead to the permanent loss of this precious knowledge. There are concerns regarding their safety, efficacy, and quality, but with greater efforts towards isolation, identification, and purification of active ingredients from the medicinal plant extracts and with meticulous study of the proper antidiabetic mechanisms, which will improve their understanding and pave the way for quality in traditional medicines. The herbal medicine market must be properly regulated. Plant products can be used as adjuvants or even may replace the synthetic drugs in the antidiabetic treatment, as they have no proven side effects and they can help reduce the costs associated with the treatment of diabetes mellitus.

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