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Review Article

A SYSTEMATIC REVIEW ON INDIAN FLORAL BIODIVERSITY AS EMINENT RESERVES FOR ALTERNATIVE TREATMENT STRATEGY OF DIABETES MELLITUS

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ABSTRACT

Among the most common chronic diseases in the world, Diabetes mellitus (DM) is an extremely studied and widely manifested multi-factorial disease which deliberately requires multi-modal therapeutic strategies [1]. It has an age-old history of being recognized and even symptomised in various cultures of the world majorly as glycosuria (sweet urine). Hence, the treatment strategies for DM have been in the process of development and documentation since a long time in traditional medicine systems. Back then the nature of drug used to be mostly unorganized and crude. The major difference now in the modern era is that the treatment strategies basically concentrate on identifying, isolating, modifying or searching alternatives of the lead compounds and exact active principles which attribute to the desired therapeutic nature of the plant. The aim of this paper is to acknowledge the various treatment methods available for Diabetes mellitus and to review the Traditional Indian herbs and plants which are most efficiently, safely and widely accepted medicament for DM and source of future lead compounds and family-wise segregation of these plants. This review is in total compliance with the strong and effective traditional medicinal systems of India.

Keywords: Traditional medicinal herbs, Diabetes treatment, Alternative Anti-diabetics, Herbal Drugs

INTRODUCTION

Diabetes mellitus (DM), or commonly known as 'diabetes' is a very common metabolic disorder of human endocrine system having a significant impact on the health, quality of life and life expectancy of the patient and health care systems and is becoming alarmingly common worldwide. The estimated cases of the disease around the globe are around 6.4%, and more than 280 million people in the world suffer from diabetes. The majority affected, live in the developing world [2]. The World Health Organization (WHO) has estimated that there are 33 million diabetes cases in India, and that number will reach 80 million by 2030 [3].

This primary defect in fuel metabolism of the body has been acknowledged since ages in several early civilizations as Indian, Egyptian, Greek, Chinese, Iranian, Arabians and Spanish histories. In India, the disease was known as 'Asrava' during the Vedic era (600 BC) and a detailed description of it is available in Brahatta, viz. Charak Samhita, Sushruta Samhita, and Vagbhatta. Asthanga Haridaya (600 AD) is the first medical treatise in which we get a clear definition of 'Madhumeha' by mentioning glycosuria (madhviv mehati-honey like urine) [4]. The word diabetes was coined by the Greek physician Aeretaeus in the first century A. D. in the 17th century.

It is an important chronic ailment characterized by profound disturbances in glucose, fat and protein metabolism which in turn results in widespread, multi-organ secondary complications that ultimately encompass virtually every system of the body and indulges every specialty of medicine [5, 6]. The disease is caused due to the failure of a number of metabolic activities in which a person shows high blood sugar, either because the body is not able to move out sugar from the bloodstream into tissues rapidly or efficiently after a meal, or because the body cells behave unresponsive to the insulin that is produced.

Etiologically two main categories of diabetes recognized are Primary diabetes and Secondary Diabetes. Primary diabetes is of two types- Insulin dependent diabetes mellitus (IDDM) in which there is a profound decrease in the number of 'b cells' in the islet of Langerhans, because of which there is absolute deficiency of insulin (Type 1) and Non-insulin-dependent diabetes mellitus (NIDDM) which is caused due to insulin resistances as well as loss of insulin secretion. The person with type 1 diabetes needs daily insulin treatment for his sustenance while a person with type 2 may get rid of this disease by taking oral hypoglycemic drugs or through natural diet. The symptoms of Secondary Diabetes results from factors like pancreatic dysfunction, hormonal imbalance, drugs or chemical induced reactions.

Various symptoms associated with the disease are hyperglycemia (fasting plasma glucose level>126 mg/dl, or glycosylated hemoglobin A1c (HbA1c)>6.9%) [7] resulting in 'polyuria' (frequent urination), 'polydipsia' (increased thirst) and 'polyphagia' (increased hunger), glycosuria (release of glucose in urine), loss of weight, ketosis (accumulation of ketone bodies in blood), ketonuria (elimination of ketone bodies in urine), acidosis (lowering of pH of blood due to circulating keto acids), dehydration and lipemia (increased levels of lipid, fatty acids and cholesterol in blood) etc. [8].

Diagnostic criteria for diabetes

The blood glucose levels of a healthy man are 80 mg/dl on fasting and up to 160 mg/dl in the postprandial state. Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating one of the following:

fasting plasma glucose level at or above 126 mg/dl or 7.0 mmol/l, plasma glucose at or above 200 mg/dl or 11.1 mmol/l two hours after a 75 g oral glucose load in a glucose tolerance test, random plasma glucose at or above 200 mg/dl or 11.1 mmol/l.

Two fasting glucose measurements above 126 mg/dl or 7.0 mmol/l or random blood sugar level>200 mg/dl on two different occasions is considered diagnostic for diabetes mellitus. Patients with fasting sugars between 6.1 and 7.0 mmol/l (110 and 125 mg/dl) are considered to have impaired fasting glucose and patients with plasma glucose at or above 140 mg/dl or 7.8 mmol/l two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance [9]

Various treatments strategies available for diabetes

Different methods to ameliorate or control diabetic symptoms, prescribed and practiced with varying degrees of success, are Drugs which lower the blood sugar and can treat the symptoms of DM known as hypoglycemic drugs. These drugs could be categorized as insulin, and insulin preparation, which is employed only

parenterally and oral hypoglycemic drugs are administered orally [9], Antibodies (monoclonal antibodies) [10], Organ Transplantation [11], Islet transplantation [12], mineral supplementation [13, 14,15] and Physical interventions as Acupuncture [16] and hydrotherapy [17] but lifestyle management like exercise, weight control, and medical nutrition therapy is at the most accepted of therapy options.

The richness of Indian floral biodiversity and the medicinal potentials of their extracts more precisely phytochemicals and secondary metabolites have been used since ages and documented in various ancient scriptures for medicament against various ailments. Till date, rural India depends solely on herbal remedies as the non-prescription cure of several minor and severe ailments. Moreover, modern inclinations of researchers and medical practitioners towards Herbal remedies and Naturopathy, and technical advancements with biotechnology have generated new horizons for the better and complete exploitation/utilisation of the available floral resources with lots of efficacy and potency and in most instances over and above the existing conventional and chemotherapeutic treatments for various diseases including Diabetes mellitus [18].

Conventional diabetic drugs

Since in the development of diabetic symptoms insulin related imbalances play a most important role, pathological impact involves three key organs, i.e., pancreatic islets, liver, and skeletal muscle. Almost all anti-diabetic drug formulations aim at these organs. Absence, under-production or in sensitization of insulin can lead to severe biochemical imbalances in the metabolic control of the body fuel, glucose causing diabetes.

Western treatments thereby treat DM by supplementing insulin or administering medicaments for improving cellular sensitivity for insulin, improving insulin secretion from the pancreatic cells, preventing gluconeogenesis in the liver or some target gastric emptying regulations to maintain euglycemic condition (72–126 mg/dl) [19].

Insulin and insulin preparations

Human insulin is a peptide hormone synthesized in the pancreas as an inactive single chain precursor preproinsulin having a signal sequence responsible for its targeting to secretory vesicles and which undergoes proteolytic cleavage to form proinsulin. This proinsulin is now stored in pancreatic b cells and in elevated levels of glucose gets secreted and cleaved by specific proteases to yield active insulin consisting of two amino acid chains A and B, which are linked by two disulphide (–S–S–) linkages. The chain A contains 21 amino acids and chain B contains 30 amino acids. The disulphide bridges are essential for its biological activity. This active insulin now starts the chemical cascade for conversion of the excess blood glucose to two storage forms-glycogen (in liver and muscle cells) and triacyl glycerols (in adipose tissue)[20].

Human insulin is an amphoteric protein, forms salts with weak acids and alkalis. Its properties such as water solubility and combining potency with proteins such as protamine and with zinc do not bring any change in its biological activity. The solubility of insulin depends on three factors, its physical state (that is, amorphous or crystalline), on the concentration of zinc and on the nature of buffer in which it is being suspended. It is not suitable for oral administration because it is inactivated by digestive enzymes. The normal human pancreas contains about 8-10 mg of insulin. In normal individuals, pancreas contains about 8-10 mg of insulin, and its secretion is low between meals and increase with each meal. The amount of insulin secreted per day in a normal human is about 40 units (286 mmol). All tissues have the ability to metabolize insulin, but 80% of exerted insulin is normally degraded in the liver and kidneys. Diabetic patients, in whom the defect seems from a paucity or apoptosis of pancreatic b cells, completely rely on external insulin injections which could be either intravenous or subcutaneous. The dose of insulin required to control diabetes varies from patient to patient and from time to time in the same patient [4].

Table 1: Various western drugs and their side effects in diabetes [21]

Drug group	Representative drug/s		Mode of action	Major clinical effect/s	Side effects reported
Sulfonylureas	1st generation Tolbutamide Chlorpropamide Acetohexamide Tolazamide	2nd Generation Glibenclamide Glipizide Gliclazide	Activate receptors on the â islet cells of the pancreas to release more stored insulin in response to glucose.	Reduced blood glucose	Hypoglycemia, weight gain
Biguanides	Fenformin Metformin		Impaired hepatic gluconeogenesis, Decreased production of very-low-density lipoprotein	Decrease fasting glucose levels, thereby reducing hemoglobin A1c (A1C).	Gastrointestinal upset, including nausea, vomiting, anorexia, and diarrhea.
Thiazolidinediones	Rosiglitazone Pioglitazone Troglitazone		Binds to peroxisome proliferator–activated receptors (PPARs) in cells forming drug-PPAR complex stimulate the production of proteins that increase insulin sensitivity, such as adiponectin. It also acts by blocking transcription of other proteins responsible for insulin resistance or inflammation.	glucose-lowering effects and lower triglyceride levels	Hepatotoxicity
α-glucosidase inhibitors	Miglitol Acarbose		Inhibits the intestinal enzyme that cleaves polysaccharides into monosaccharides.	slowdowns the absorption of carbohydrates after a meal limiting postprandial hyperglycemia an A1C reduction of 0.5–0.8% is typical	flatulence and other gastrointestinal symptoms
Meglitinides	Repaglinide		Augments insulin secretion	Glycemia control	weight gain, gastrointestinal disturbances, and hypoglycemia
DPP-4 inhibitors			Inhibits the enzymatic degradation of glucagon-like peptide 1 (GLP-1) which acts to delay gastric emptying, suppress glucagon release, and increase glucose-stimulated insulin release.	Limit postprandial hyperglycemia, A1C reduction of 0.5–1% in patients with type 2 diabetes.	Hypoglycemia

Oral hypoglycemic and antidiabetic drugs

Any drug which has the power and potency to treat diabetic complications upon oral administration is termed as oral hypoglycemic drug. Since insulin is ineffective orally and also is not required always (viz. NIDDM), oral agents which target or effect some or the other phenomenon which directly or indirectly affects the control of glucose metabolism may be of great help. But anyway these drugs can never show an effect if any reluctance is taken on controlled diet regime and other lifestyle management steps.

The various classes of glucose-lowering drugs include sulfonylureas, biguanides, alpha-glucosidase inhibitors, thiazolidinediones, and meglitinides [21]. These drugs may be categorized on the basis of their major action mechanism as insulin secretagogues (sulfonylureas, meglitinides), insulin sensitizers (biguanides, thiazolidinediones), α glucosidase inhibitors (miglitol, acarbose). Serum GLP-1 concentration enhancers and gastric emptying down-regulators (exenatide, liraglutide, and DPP-4 inhibitors) [19]. Though these drugs have been proved for their efficacy in controlling diabetic symptoms most of them have been reported to pose one or other physiological complication or side effects on use [table 1].

Traditional Indian herbal anti-diabetics

It is now internationally accepted and acknowledged that traditional medicines systems of India and other ancient origins report, advocate and justify the significance of floral biodiversity as an effective and reliable treatment strategy of hyperglycemia and related malfunctions.

Several disadvantages associated with insulin and synthetic drugs and their failure to divert the course of diabetic complications have opened up tremendous horizons for searching possibilities in complementary and alternative medicine (CAM) for diabetes as well as many other chronic diseases. Plants, herbs and their derivatives owing to their wide spectrum of active principles representing numerous chemical compounds hold promising potentials for their consistent usages in the treatment of Diabetes [4]. According to WHO, 21,000 plants around the globe have been reported for medicinal uses. India is posted to have an enormous medicinal flora of some 25,000 species, out of these 150 species are commercially exploited for medicinal extractions or drug formulation [22]. There are about 800 plants species reported having the probability of possessing antidiabetic potentials in the ethnobotanical surveys [23]. The antidiabetic effects of the plants are attributed to the wide range of chemicals and secondary metabolites. Reports have essayed approximately 200 pure compounds from plant sources to show blood glucose lowering effect. These compounds range vividly in chemical nature like alkaloids, carbohydrates, glycosides, flavonoids, steroids, terpenoid, triterpenoid, peptides and amino acids, lipids, phenolics, glycopeptides, and iridoids. Here we review traditional Indian herbs which are most efficiently, safely and widely accepted as a medicament for DM and source of future lead compounds for the disease with family-wise segregation of these plants [table 2].

Table 2: Family wise segression of the most scientifically validated antidiabetic plants

Family	Plants	Indian vernacular name	Reference
Acanthaceae	*Asteracantha longifolia*	Kokilaksha, Talmakhana	[24]
	Andrographis paniculata	Kalmegh	[25]
	Barleria prionitis	kuranta, Vjradanti	[26]
	Barleria lupulina	Vishalyakarani	[27]
Amaranthaceae	*Achyranthes aspera*	Aghata, Khara-manjari	[28]
	Aerva lanata	Astmabayda	[29]
	Amaranthus spinosus	Tanduliuyah, Kanta chaulai	[30]
Anacardiaceae	*Mangifera indica*	Aam	[31]
	Anacardium occidentale	Kajutak, Agnikrit	[32]
Annonaceae	*Annona squamosa*	Sharifa	[33]
Apiaceae	*Daucus carota*	Garjara	[34]
	Coriandrum sativum	Dhaniya	[35]
	Cuminum cyminum	Karavi, Krishna jeeraka	[36]
	Cuminum nigrum	Kala jeera	[37]
	Carum Carvi	Karavi, Krishna jeeraka	[38]
	Ferula assafoetida	Hing	[39]
Apocynaceae	*Catharanthus roseus*	Sadabahaar	[40]
	Carissa carandas	Karamarda, Karonda	[41]
Arecaceae	*Cocos nucifera*	Nariyal	[42]
Asclepiadaceae	*Gymnema sylvestre*	Vrikshamla, Gur-mar	[43]
	Calotropis gigantea	Madar	[44]
Asteraceae	*Tridax procumbens*	Khal muriya, Ghamra	[45]
Basellaceae	*Basella rubra*	Poi, Safed Bachla	[46]
Bignoniaceae	*Tecoma stans*	Piliya	[47]
Bombacaceae	*Bombax ceiba*	Semal	[48]
Brassicaceae	*Eruka sativa*	Safed Sarson	[49]
	Brassica juncea	Rai	[50]
Burseraceae	*Commiphora mukul*	Guggul	[51]
Capparidaceae	*Capparis deciduas*	Kurira, Karira	[52]
Compositae	*Artemisia pallens*	Davana	[53]
Chenopodiaceae	*Beta vulgaris*	Chukandar	[54]
Combretaceae	*Terminalia arjuna*	Arjuna	[55]
	Terminalia chebula	Harad, Haritaki, Harra	[56]
Convolvulaceae	*Ipomoea batatas*	Shakrkand	[57]
	Cressa cretica	Rudravanti	[58]
Crassulaceae	*Bryophyllum pinnatum*	Pashanbhed, patharchatta	[59]
Cucurbitaceae	*Citrullus colocynthis*	Indravaruni, Mahendravaruni	[60]
	Coccina indica	Bimba	[61]
	Cucurbita ficifolia	Chappan kaddu	[62]
	Momordica charantia	Karela	[63]
	Momordica cymbalaria	Athalkkai, Karchikai	[64]
	Momordica dioica	Kakori	[65]
	Cucumis sativus	Khera	[66]

	Luffa acutangula	Torai	[67]
	Luffa cylindrica	Ghiya torai	[68]
Cupressaceae	*Juniperus communis*	Dal chini	[69]
Euphorbiaceae,	*Phyllanthus amarus*	Bhumiamalaki, Jangli amla	[70]
Fabaceae	*Cajanus cajan*	Adhaki, Tur	[71]
(Leguminosea/Papilionaceae)			
	Mucuna pruriens	Kapikachhu	[72]
	Pterocarpus marsupium Roxb.	Vijaysar	[73]
	Caesalpinia bonducella	Kantkarej, Kantikaranja	[74]
	Erythrina variegate	Pangara, Paribhadra	[75]
	Acacia arabica	Babula	[76]
	Trigonella foenum greacum	Methika	[77]
	Medicago sativa	Ashvabala	[78]
	Pongamia pinnata	Karanja	[79]
	Phaseolus vulgaris	Balka, Rajma	[80]
	Saraca Asoca	Asokah, Tamra Pallav	[81]
	Butea monosperma	Palash	[82]
	Clitoria ternatea	Aparajit	[83]
	Tephrosia villosa	Sarampukha	[84]
	Prosopis cineraria	Shami	[85]
Flacourtiaceae	*Casearia esculenta*	Kirmar	[86]
Gramineae	*Hordeum Vulgare*	Yava	[87]
	Bambusa vulgaris	Bakal	[88]
	Cynondon dactylon	Doab, arugampul	[89]
Gentianaceae	*Swertia chirayita*	Kirata-tikta	[90]
	Enicostemma littorale	Nahi, Maja-makka booti	[91]
Guttifarae	*Garcinia indica*	kokum, punar puli	[92]
Hippocastanaceae	*Aesculus hippocastanum*	Kanor, Bankhor	[93]
Hippocrateaceae	*Salacia macrosperma*	Saptrangi	[94]
	Salacia reticulata	Saptachakra	[95]
	Salacia oblonga	Vairi, pitika	[96]
Juglandaceae	*Juglans regia*	Akschota	[97]
Labiatae	*Prunella vulgaris*	Dharu	[98]
Lamiaceae	*Ocimum sanctum*	Tulsi	[99]
	Teucrium polium	Amberved	[100]
	Vitex negundo	Nirgundi, Sephali	[101]
	Clerodendrum phlomidis	Agnimantha, Jaya	[102]
	Clerodendrum serratum	Bharangi	[103]
	Clerodendron infortunatum	Titabhamt	[104]
Liliaceae	*Allium sativum*	Lahsun	[105]
	Allium cepa	Pyaj	[106]
	Aloe barbadensis/Aloe vera	Kumari	[107]
	Asparagus officinalis	Shatavari	[108]
Logoniaceae	*Strychnos nux-vomica*	Kuchila, Bailewa	[109]
Lythraceae	*Lagerstroemia speciosa*	Arjuna	[110]
Malvaceae	*Hibiscus rosa-sinesis*	Gurhal	[111]
	Sida cordifolia	Bala, Khareti	[112]
	Thespesia populnea Soland. ex Correa	Parisha	[113]
	Abelmoschus esculentus (L.) Moench	Bhinda	[114]
Melastomaceae	*Memecylon umbellatum* Burm.	Anjan	[115]
	Osbeckia octandra	Heen bowitiya	[116]
Meliaceae	*Azadirachta indica*	Neem	[117]
Menispermaceae	*Tinospora cordifolia*	Guduchi, Amrita.	[118]
	Tinospora crispa	Akar patawali	[119]
Mimosaceae	*Acacia arabica*	Babul	[120]
	Acacia catechu	Khadira	[121]
Moraceae	*Ficus carica*	Anjeera	[122]
	Ficus bengalensis L.	Vata	[123]
	Ficus exasperata	Karapatra	[124]
	Ficus religiosa	Pippala	[125]
	Artocarpus heterophyllus	Panasa, katahal	[126]
	Morus alba	Tuta	[127]
Myrsinaceae	*Embelia ribes*	Bidanga, Vidanga	[128]
Myrtaceae	*Eucalyptus globulus* Labill	Tailapatra, Sugandhapatra	[129]
	Eugenia jambolana	Jambu, jamun	[130]
	psidium guajava	Amruta-phalam	[131]
Musaceae	*Musa sapientum*	Kela	[132]
Nyctaginaceae	*Boerhavia diffusa*	Punarnava	[133]
Nymphaeaceae	*Nelumbo nucifera*	Kamal, Sarsija	[134]
	Nymphaea pubescens	Kumuda	[135]
Oleaceae	*Olea europea*	Jaitun	[136]
	Schrebera swietenioides	Banpalas	[137]
Oxalidaceae	*Averrhoa bilimbi*	Karamaranga	[138]

	Biophytum sensitivum	Jallapushpa, Lajjalu	[139]
	Oxalis corniculata	Changeri, Amlapatrika	[140]
Pandanaceae	*Pandanus amaryllifolius*	Rampe	[141]
Piperaceae	*Piper longum*	Pippali	[142]
	Piper betel	Tambuli	[143]
	Piper nigrum	Kalimirch	[144]
Plantaginaceae	*Plantago psyllium*	Isaphgula.	[145]
	Plantago ovata	Isabgolam, Snigdhbijam	[146]
	Picrorrhiza kurroa	Katuka katurohini	[147]
	Bacopa monnieri	Brahmi	[148]
Polypodiaceae	*Adianthum capillus veneris*	Hansraj	[149]
Primulaceae	*Primula denticulata*	drumstick primula	[150]
Punicaceae	*Punica granatum*	Dalima, Anaar	[151]
Ranunculaceae	*Nigella sativa*	Upakuncika, Kalonji	[152]
Rhamnaceae	*Zizyphus mauritiana*	Ber, Badri	[153]
	Zizyphus nummularia	Jhar Beri	[154]
Rhizophoraceae	*Rhizophora mucronata*	Kullalaji, Kala Lakri	[155]
Rosaceae	*Eriobotrya japonica*	Lokat	[156]
	Prunus amygdalus	Vatadha, Badam	[157]
Rubiaceae	*Morinda citrifolia*	Ayushka, Achuka	[158]
Rutaceae	*Aegle marmelose*	Bengal quince, Bel	[159]
	Murraya koenigii	Kadipatta	[160]
Sapotaceae	*Madhuca longifolia*	Mahua, Mahwa	[161]
Scrophulariaceae	*Scoparia dulcis*	Mithi patti	[162]
Simarubiacea	*Ailanthus excelsa*	Aaralu,aldua bhootjhad	[163]
Smilacaceae	*Smilax glabra*	Copchini, dvipantarvaca	[164]
Solanaceae	*Solanum torvum*	Bhurat, Bhankatiya	[165]
	Withania somnifera	Ashvagandha	[166]
	Solanum nigrum	Kakamachi, Kakahva	[167]
	Lycium barbarum.	Kad Mool	[168]
Sterculiaceae	*Abroma augusta*	Ulatkambal	[169]
	Helicteres isora L.	Maror phali	[170]
Theaceae	*Camellia sinensis*	Chai	[171]
Verbenaceae	*Lantana camara*	Raimuniya	[172]
	Gmelina arborea	Gambhar, bhadraparni	[173]
Zingiberaceae	*Costus speciosus*	Keukand, Keu	[174]
	Curcuma longa	Haridra, Haldi	[175]
Zygophyllaceae	*Tribulus terrestris*	Gokshura	[176]
	Balanites aegyptiaca	Hingn, hingot	[177]

Concerns and complications of herbal treatments

Herbal medicines are very often used as therapeutic remedies in combination with allopathic drugs [178]. The potency of herbal drugs has been proved to be significant, and they have negligible side effects than the synthetic anti-diabetic drugs [179]. Although phytotherapy for Diabetes continues to be used in several countries till date but there are some facts which should not be ignored in the context of their regular use. First, only a few plants have undergone scientific or medical scrutiny. Secondly, a large number of medicinal plants possess some degree of toxicity. For example, it was reported that about one-third of medicinal plants used in the treatment of diabetes are considered to be toxic [180]. Thirdly, the test results of hypoglycemic plants are subject to several factors. Like, each herb contains thousands of components, only a few of which may be therapeutically effective [181]. Different parts of a herb have different ingredient profiles. Moreover, different extraction methods may yield different active ingredients [182]. Also herbal formulae containing multiple herbs may have synergistic effects [183] and [184]. The multiple constituent natures of botanical products have made standardization a challenging task. Advocates of herbal remedies have also suggested that in standardizing one plant constituent, resulting extracts may lose a proportion of benefit as compared with the whole plant [185]. Also precise considerations of purity, chemical composition, and potency of derivatives may be grossly influenced by the age of the plant (especially of roots), the source location, the season of harvest, the method of drying and crude preparation, etc. [186].

DISCUSSION

Diabetes mellitus is the most common multifactorial chronic disease. High levels of free radicals and malfunction in antioxidant defence mechanism formed as a result of glucose oxidation and non-enzymatic glycation of proteins generates a condition of high oxidative stress in the patient which in turn produces stress-induced damage of cellular organelles, enzymes, increased lipid peroxidation and insulin resistances [187]. DM has been a target for study and multiple therapy options since ages, and several effective therapies have been documented for its treatment and control. Recently because of much growing mass awareness about prominent side-effects of western treatments, attentions are concentrating on plant based treatments including whole drug and poly herbal formulations.

Plant-based medicinal products have been known to man since ancient times [188]. Plants have been the primary source of drugs and lead compounds, and many of the currently available drugs have been directly or indirectly derivatized from them. The families of plants with the most potent and also widely studied hypoglycemic effects include Leguminosae, Lamiaceae, Liliaceae, Cucurbitaceae, Asteraceae, Moraceae, Rosaceae, Euphorbiaceae, and Araliaceae. The plant kingdom is owing to a wide spectrum of its phytol antioxidants resulting in vast medicinal potency exhibit tremendous opportunity to reduce the oxidative stress induced symptoms of diabetes mellitus.

Scientific findings on the action mechanisms of the plant compounds have proposed many means in which they act to provide the anti-hyperglycemic and anti-hyperlipidemic effects. Some of them relate to their effects on the activity of pancreatic ß cells (synthesis, release, cell regeneration/revitalization) or the increase in the protective/inhibitory effect against insulinase and the increase of the insulin sensitivity or the insulin-like activity of the plant extracts. Other mechanisms involve improved glucose homeostasis including an increase of peripheral utilization of glucose, an increase of synthesis of hepatic glycogen and/or decrease of glycogenolysis acting on enzymes, inhibition of intestinal glucose absorption, reduction of glycogenic index of carbohydrates, reduction of the effect of glutathione [189].

CONCLUSION

Plants with acknowledgments in common folklore and traditional Indian medicinal systems (IMS) are very significant and medically potent in the treatment of various human ailments including Diabetes mellitus. Alternative therapies with anti-hyperglycemic effects are becoming increasingly popular among patients and are certainly significant because of the inability of conventional treatments to relieve one from the complications without having threats of additional ill-effects. Moreover, the constants like high cost and inaccessibility mostly to the rural population add up to the reasons for general inclinations towards alternative therapies. So, Consuming plants with potent anti-diabetic activity for the treatment of diabetes is now becoming very popular macrobiotics treatment regime for diabetes all over the world, as most of the times, it promises no additional pains in the form of side effects. This also proves a famous saying in India;

"Any disease is half way treated if the fear for its cure is gone,"

But major hindrance in the amalgamation of traditional knowledge with modern medical practices is a lack of sufficient scientific and clinical trials, especially on human subjects. It is unfortunate that even though plant based drugs have tremendous medicinal priority over synthetic drugs, but the significant trials are not adequately available in order to advocate their scientific merit and supremacy over the existing drugs. Nonetheless, it should never be ignored that there are always probabilities of any adverse herb-drug interaction in the case of patients also receiving conventional anti-diabetic medications [21]. This review has presented a comprehensive list of a few scientifically validated anti-diabetic plants. There are absolute possibilities for developing novel and useful drugs, formulations and lead compounds from these plants. Also, some specific genetic markers which can account for the phylogenetic relationship between the different plants and families owing to the anti-diabetic character could be developed in near future which would narrow up and limit the studies and searches for herbal drug development. The scope of utilizing chemoinformatics and bioinformatics to test the harnessable and adverse synergistic behavior of various herbs and their components would also help to define the clear-cut outline of drug designing and clinical research.

CONFLICT OF INTERESTS

Declared none

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